



SUFFERING SOULS SUFFERING SOCIETY

A study of Empathy Processing and
Oxytocin Effects on Socio-Emotional
Behavior in Psychopathy

Ronald J.P. Rijnders

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Lijdende Zielen Lijdende Maatschappij

Studie naar empathieverwerking en effecten van oxytocine
op sociaal-emotioneel gedrag in psychopathie
(met een samenvatting in het Nederlands)

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Ronald J.P. Rijnders

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Dedicated to the psychopathic
patients studied

Chapter 1
General introduction
and outline

I am not I: thou art not he or she:
they are not they

— Evelyn Waugh

1 General introduction

1.1 *The story of Lennart*

“My real mother always supported me and never let me down. She is a wonderful woman. Thanks to her I have become a strong and loving person.” Speaking is Lennart, an athletically dressed man in his early 30s, who has been admitted by court order to the forensic observation clinic Pieter Baan Centrum (PBC) for a seven-week psychological and psychiatric examination of his mental capacity, and by extension, the assessment of his criminal responsibility (in Dutch: toerekeningsvatbaarheid) at the time of the crimes charged. The above words conclude a minute-long eulogy to his biological mother. Then Lennart turns to me even more emphatically: “Do you love your mother and take good care of her? You should call her regularly. Do you?” I find myself nodding affirmatively and at the same time resolving to call more often.

The crimes Lennart is charged with are attempted manslaughter, rape of a 19-year-old woman (committed multiple times), human trafficking, stalking, and possession of hard drugs. Lennart is considered a denying defendant. According to him, the sexual intercourse was consensual and there could be no question of human trafficking, for the woman was in prostitution voluntarily, and stalking cannot be spoken of either, for it was she who regularly contacted him herself. The charge of attempted manslaughter was grossly exaggerated by the prosecutor, Lennart said. According to him, there was indeed a brawl that started after the woman attacked him with a knife, so he had to defend himself by taking the knife away and in that process he did stab her, but purely in self-defense. The possession of hard drugs must also be put into perspective, Lennart further explained, the 278 grams of cocaine was not his, he kept it for an addicted friend who had been admitted to a rehab clinic.

From the first contact with Lennart, the psychiatric examination interviews went very smoothly. Despite his vehement denial of the allegations, he says he is happy to cooperate with the psychologist and me. He accepts the research of the forensic environmental investigator, who will conduct as many interviews as possible with people and agencies who know Lennart, but points out that this is likely to yield inaccurate information, after all, many people do not understand him well or are jealous of him. The first weeks of the examination period fly by. Lennart is an engaging narrator, elaborates on his past with all kinds of traumatic experiences, can put situations in perspective and also names his problems in interpersonal relationships, while emphasizing

that his intentions are always good. He grew up loving and has a big heart for family, acquaintances, friends, and also strangers, Lennart says. In particular, he praises his biological mother; to this day their relationship is important and gives him great strength. Indeed, there were contacts with the police and probation services, but compared to people in the neighborhood where he grew up, it was not much. By this he means to say that, given the context of that neighborhood, he is actually a very normal person.

Lennart makes an intelligent impression, which is also amply confirmed in the intelligence test taken at the PBC. From the conversations, I notice that he is able to distinguish right from wrong and to assess the consequences of his actions. He only stole from rich people or big chain stores, he indicates, not from poor people because they should be spared. Lennart casually discusses his weekly caring duties for his indigent grandmother until his arrest. He also seems able to take another person's position and imagine what the other person is experiencing emotionally; an important behavioral characteristic that indicates well-developed cognitive empathic abilities. When talking about his sexual development and sexual identity, Lennart does not seem shy about answering my questions on sensitive subjects. He indicates that consensual sex is always central to him.

In the first few weeks of the examination period in the PBC, the emphasis is on biography and diagnostics, where, based on the anamnesis and my own observations, I find no evidence of the presence of psychosis, mood or anxiety disorders, trauma disorders, paraphilia and/or other psychiatric disorders. He reports drinking alcohol with some regularity, using cannabis twice a week and snorting cocaine at most once every three months, "never a lot, never for a long time," according to Lennart, who goes on to say that substance use has never gotten him into trouble. I also focus on the result of blood tests that show a hormonal imbalance possibly coinciding with a disease of the pituitary gland. Therefore, I refer him to an endocrinologist at a nearby university hospital. At the end of the investigation period, it becomes clear that no pituitary disease or other major physical problems are present. The PBC examination also uses collateral information gathered by the forensic environmental investigator and observations by the PBC group leaders of Lennart's daily behavior in the living group. However, the requested collateral information is not yet available in the first weeks of Lennart's stay at the PBC, nor is the extensive criminal file complete. Therefore, during these first weeks I depend on my own interviews and observations. I discuss these with the group leaders and the co-reporting psychologist, a young woman who, like me, still has little reporting experience. They tell me that conversations and interviews with Lennart are difficult and that

he is often disparaging about their perceived lack of experience and knowledge. He gives them little insight into his psychological processes. They also notice that Lennart is very domineering toward women. I partially take these comments for granted and indicate that the tide may turn as he becomes accustomed to them and their contact with him intensifies. After all, with me the conversations are going very well. As for Lennart's personality traits, I notice that he is lively, witty and quick-thinking. Sometimes he is a bit impulsive in his reactions and behavior, but he knows how to behave. He compliments me regularly, which he does in an exaggerated way and a bit theatrically. I notice that sometimes he tells a story that was slightly different a few days earlier. He also frequently gives various apologetic explanations for failures in his school and work career and for the fact that his love affairs never lasted long. According to Lennart, the real story is different: it was all because his good intentions were never appreciated, and there was also frequent discrimination because of the disadvantaged neighborhood in which he was born and raised.

Due to an unforeseen interim absence of more than a week and a half, I cannot begin to discuss the charges with Lennart. In such an interview, Lennart's story of what according to him had happened is combined with collateral information such as the criminal file to create a so-called crime scenario and ultimately a crime analysis. These crime scenarios and analyses are important in determining Lennart's criminal responsibility during the crimes charged. It refers to a potentially diminished accountability resulting from the pathological influence of any mental disorders on the offender's free will during the criminal act charged. I return to the PBC on the day of an important diagnostic meeting, two weeks before the end of the examination period. In this meeting, group leaders, forensic environmental investigator, psychologist and I discuss the interim status of the examination, especially with regard to the diagnosis. We do this together with both a psychiatrist supervising the investigation team and the team's jurist. The task of the latter two is to provide an organized rebuttal of both the diagnosis and the assessment of the criminal responsibility during the criminal acts charged (if later proven in court). Then the forensic environmental investigator reveals an overwhelming amount of information that completely tilts my view of Lennart's personality.

From birth, Lennart seems to have been neglected and severely traumatized. He never knew his biological father, his single mother was an alcoholic and drug addict and gave him hardly any attention and absolutely no love. Only after nine months did government agencies intervene and Lennart was placed out of the home and taken into foster care, but only after he had been treated in the hospital for six weeks due to severe malnutrition and numerous

infections. Over the years, he saw his mother on average once every four months; often she did not show up for appointments. He always expressed hope that he could return to her. For the past 12 years there has been no contact with her or his indigent grandmother. Early in his childhood, Lennart showed developmental problems. He listened poorly and was insensitive to correction or punishment while looking at the educators expressionless. He regularly bullied peers and seemed to enjoy hurting the cat and rabbit. Once they found under his bed the dismembered remains of the neighbor's parrot. Lennart was 8 years old at the time. His school career was disastrous, Lennart was repeatedly suspended and attended a total of three elementary schools. The high school period was marked by conflicts with teachers and the justice system. He regularly served time at the police station for arson, thefts, assaults and driving under the influence of drugs and alcohol. He spent time in three forensic juvenile institutions and ultimately failed to complete his degree. Descriptions of his behavior show that he had no respect for authorities, denigrated women and lacked affective empathy for people and animals. He took no responsibility for his mistakes and externalized to a high degree when something failed. His love relationships usually lasted short and were characterized by quarrels and physical and sexual abuse. He frequently visited prostitutes and abused them regularly as well. His criminal record contains fifteen pages of numerous convictions for drug trafficking, burglaries, thefts, scams, stalking, insulting officials and about six sexual assaults on various women. Added together, Lennart has spent more than eight years in prison since he was 16.

During this meeting, it becomes clear to me that Lennart had given me a totally different representation of the person he really is. He had been able to put up a façade of health in the environment of the PBC where everything is orderly and structured and the use of alcohol and drugs is not allowed. Lennart had cunningly deceived me and almost drawn me into his imaginative lies and excuses. He had come far in his attempt to succeed, until the moment when objective collateral information became known. Without it, the chances of me falling into his trap would have been high.

In the remaining two weeks of the examination period in the PBC, I confront Lennart with all the additional information and contradictions and finally manage to pull him out of his comfort zone. Then I see a person who contrasts enormously with the person with whom I seemed to have genuine contact in the first weeks. He is indifferent, sometimes surly and no longer makes attempts to charm me, nor does he sympathize with me when I burn myself on a water cooker with boiling water; on the contrary, I even see a smile appear around his lips.

In late 2008, five months after Lennart's departure from the PBC, the court determines that our diagnosis of "personality disorder with antisocial, borderline and narcissistic features" is adopted and that a very high degree of psychopathy is present in Lennart. The judges especially denounce both Lennart's ruthless actions and his demonstrated lack of affective empathy for the victim. He is found guilty while a diminished criminal responsibility by reason of a mental disorder (i.e., his personality disorder including psychopathy) is established. Lennart is sentenced to prison combined with state-imposed mandatory treatment under the Entrustment Act (in Dutch: *Beginnelenwet verpleging terbeschikkinggestelden*). In mid-2011, he is transferred from prison to a forensic psychiatric clinic (in Dutch: *tbs-kliniek*).

1.2 *Lessons learned*

To avoid recognition of Lennart, I changed some essential life events and characteristics in the above description, but in the end I do describe Lennart as the person he really was. Due to circumstances, I was absent for a while and did not have access to independent and collateral information in the first weeks of the examination period. So I had to rely largely on my own impressions. It is fascinating that psychopathic individuals are apparently able to paint a false positive picture of themselves in their free communication, putting the other party at great risk of being led astray. Ostensibly, psychopathic individuals are positive-minded individuals who can be charming and charismatic and can make you believe they are special and have good intentions. However, the danger of wrong perception also lies largely within yourself. This applies not only to the possible assessment that the other person is very special, but - if you look closely in the mirror - also to your own willingness to go along with their exciting stories and presentation. Essentially, it's about your own, personal narcissistic trap. It almost happened to me as a psychiatrist with only two years of forensic experience. In hindsight, could I have been warned earlier? Yes, I do think so. There were already some cracks in Lennart's way of interacting with me, for example, his excessive complimenting, telling different stories, repeatedly externalizing problems and constantly insisting on his good intentions while not being heard or understood by others. In other words: Lennart displayed a façade of health, aptly described earlier by Hervey Cleckley (1941) as "the mask of sanity" (see below). Also, the signals from the group leaders and the co-reporting psychologist (almost all relatively young women) can be interpreted

in retrospect as that Lennart was very selective in terms of age and gender. This experience has taught me that when you are simultaneously observer and thermometer (i.e., an active conversation participant and diagnostician), you cannot always oversee the big diagnostic picture alone. For that, you need the observations and critical rebuttals of others. Without these, you are lost in diagnostics. Therefore, examination in the PBC is designed so that others continually provide critical rebuttals while the substantiation of both diagnostic conclusions and criminal responsibility undergoes an intensive process of both verification and refutation.

Not only Lennart's case fascinated me. Other alleged perpetrators with psychopathy observed in the PBC also caught my attention. The difference with Lennart was that none of these others had Lennart's high intelligence and thus lacked the cognitive ability to sustain their mask of sanity for long. In other words, the other psychopathic individuals fell through much faster, so to speak. I became convinced that the combination of psychopathy and high intelligence is a potentially explosive mixture that can lead to much damage in interpersonal relationships, in the social sphere and ultimately in society. At the time I was making research plans for my PhD research, I was already interested in empathy and empathy deficits. Partly because of Lennart with his good skills in cognitive empathy but poorly developed affective empathic components, I decided that empathy deficits in psychopathy should be an important part of my dissertation.

1.3 *Psychopathy and the general public*

Regardless of time and culture, lay people have a remarkably strong fascination with law-breaking psychopathic individuals. News, books and movies about them and their sometimes staggering crimes are eagerly consumed. The question is why. It is said that the Greek philosopher Socrates' favorite motto was "know thyself" (γνωθι σεαυτόν, gnōthi seauton). This ancient Greek maxim stems from the sixth century B.C. and was inscribed above the entrance to the temple of Apollo in Delphi, Greece. By using one's own intellect combined with the Socratic dialogue, people could gain insight and bring the truth to light. The constant pursuit of truth about oneself or about the world undoubtedly requires continuous effort and sacrifice in life. This may be true and fruitful for philosophers, but for the average person, awareness and understanding of the self and the world will be a dynamic process that is not unambiguous and can produce versatile results within that person over time. Nothing as painful as

revealing one's own embarrassing negative personality traits. Therefore, in order to conceal these painful self-perceptions of one's own negative aspects, one may take refuge in psychological processes that mask the stressful discrepancy between one's positive self-image and the way one actually behaves in daily life. For example, attempts at self-inspection may be preemptively aborted or remain superficial, or the ambivalence can be reduced by fantasizing about one's own greatness while denying one's real-life actions. In addition, if a shameful confrontation with reality cannot be avoided, one can always fall back on the self-serving bias (Heider, 1958), in which one's own failure is attributed to the decisive role of negative external circumstances or to the detrimental actions of others. Through this external attribution, which should be seen as a narcissistic defense, one might try to maintain an internal psychological homeostasis.

In contrast, when we consider the faults of others, we tend to do the opposite of what we mobilize in the self-serving bias, which is to apply the fundamental attribution error (Ross, 1977). We then attribute these faults to the other person's negative personality traits, and we underestimate the influence of external circumstances that led to their failure. I suppose the intriguingly contradictory words above from Evelyn Waugh hint to these processes that are so connected to humanity. Are we who we really are? Or are we the ones who we believe we are? And they, are they really who they are? Or are they who they imply they are? By seeing ourselves as positive while evaluating the other as negative, we introduce good versus bad, which is in concordance with Melanie Klein's (1952) object relations theory. There is nothing like occupying extremes in our perceptions and understandings, and that is what we humans do, vigorously excusing ourselves for our flaws but as argued above also tending to discern and blame the prototypical bad other. We may even become fascinated by it. This fascination applies pre-eminently to what we consider the extreme form of evil as personified by the psychopathic other. Partly for this reason, the psychopathic offender appears abundantly in lurid books and horror films, and his serious criminal acts guarantee extensive media coverage.

Although laypersons' assumptions about what constitutes prototypical psychopathic behavior rarely match reality, psychopathic individuals are highly associated with criminal behavior (Bergstrøm and Farrington, 2022). However, this relationship is not automatically reciprocal, that is, extremely serious criminal acts can also be committed by non-psychopathic individuals. Moreover, psychopathic personality traits can be quite fruitful for society in special or extreme circumstances. Boldness, for example, a phenotypic component of the triarchic model of psychopathy (which further includes the phenotypic dispositions disinhibition and meanness; Patrick et al., 2009) can

be beneficial in managing the consequences of major bankruptcies, currency collapses, pandemics and political or natural disasters, and even war situations. In such circumstances, boldness characteristics can make a huge difference in outcomes and, as a result, be of significant evolutionary value. As with any personality trait, characteristics we attribute to psychopathy should be considered primarily as continuous rather than discrete variables. Society can deal well with continuous variables such as boldness in the above emergencies, but it may become a problem for society if a person with such characteristics responds the same to all interpersonal situations, or worse if a simultaneous combination of the three previously mentioned phenotypic dispositions (i.e., boldness, disinhibition and meanness) is invariably present. Particularly in the latter circumstance, there is a high probability that societal rules will be violated and that, for example, financial crimes or (sexual) violence will be committed to all degrees, up to and including atrocities. The fact that the psychopathic perpetrator of heinous crimes may then not be automatically identified as a socially disabled, obviously psychiatric patient, but, on the contrary, may initially come across as an ordinary human being, can cause great confusion and fear among the lay public and, in its slipstream, fuel their fascination for this topic even further. Perhaps this partly explains the avid consumption of news, books and movies about psychopathic individuals and their staggering crimes.

In this dissertation, I address both the construct of empathy and empathy processing in psychopathy and describe a study with several social-emotional behavioral tasks in forensic psychopathic patients involuntarily admitted for treatment in five Dutch forensic psychiatric clinics by order of the criminal court. In this introduction, I will first briefly discuss the topic of psychopathy. Next, I will also focus briefly on the neuropeptide oxytocin, which, based on research among volunteers and patients, may be a candidate for treating some behavioral aspects of psychopathy.

1.4 Psychopathy

Etymologically, the term psychopathy comes from the conjunction of the classical Greek words ψυχή and πάθος (psyche and pathos, respectively) and stands for “suffering soul”. Psychopathy as a lifetime personality disorder is not a unitary concept, but rather characterized by varying intensities and diversity of symptoms in the interpersonal, emotional, and behavioral domains, resulting in heterogeneous clinical expression (Brinkley et al., 2004; Hare, 1996, 2003).

At the interpersonal level, their presentation is glib and superficial, larded with statements about their own grandiose qualities. Their actions, meanwhile, often consist of lying and conning to gain benefits purely for themselves, while neglecting and disrespecting their counterpart's interests. Observant others quickly sense the pressure and manipulation imposed, while naive others risk, due to the psychopath's glib presentation, not seeing through their manipulation in time. At the emotional level, their lack of empathy particularly is striking (Soderstrom, 2003; Verschuere et al., 2017; Verschuere & te Kaat, 2020), although in psychopathy the cognitive aspects of empathy are more intact than the affective empathy aspects (see, for example, Rijnders et al., 2021a, this dissertation). Partly because of deficient affective empathy aspects, their affect in emotionally tense situations usually appears shallow, and when it comes to situations involving their own mistakes or guilt, psychopathic individuals experience a lack of remorse or guilt. Finally, at a behavioral level, psychopathic individuals frequently portray egocentric, parasitic, and impulsive actions toward others. Their inhibitory control is weak, so they quickly become involved in dangerous or aggressive situations or break their agreements with others or legal supervisors. Mainly because of these behavioral problems, they are overrepresented in the criminal justice system (Hare, 1996; Coid and colleagues, 2009; Kiehl & Sinnott-Armstrong, 2013) and are at a two to five times higher risk of reoffending (Hemphill et al., 1998). This pattern exists even before they reach adulthood (Kahn et al., 2013). Their interpersonal, emotional and behavioral problems also occur in partner relationships. Psychopathic individuals therefore often have loose, impersonal sexual relationships and are not good at maintaining lasting love relationships.

The exact prevalence of psychopathy in the general population worldwide is not precisely known, but estimates range from 0.5% to 1.2% (Hare, 1996; Neumann & Hare, 2008; Sanz-García et al., 2021), with a higher proportion of males to females (Thompson et al., 2014), although this could be partly due to different psychometric properties of the diagnostic test for psychopathy (i.e., PCL-R; see below) across gender (Klein Haneveld et al., 2021). Psychopathy is a mental disorder that, according to a study by Anderson (1999), entails astronomical costs for society. Kiehl & Hoffman (2011) calculated that approximately 460 billion US dollars in criminal social costs are incurred annually in the United States alone (US dollars in 2009). Extrapolated to 2024, these annual costs would now be about 680 billion US dollars (www.in2013dollars.com). This overwhelming figure does not include the costs of psychiatric treatment of psychopathic individuals themselves, nor other indirect costs, such as, for example, the treatment of victims or their non-quantifiable emotional suffering.

Psychopathy is of all times and all cultures. Throughout history, psychopathic individuals have continually used their self-centered personality traits to serve their own interests. In retrospect, it is not actually possible to diagnose psychopathy in a person one has not examined oneself. Based on abundant oral history and historical writings, it is nevertheless indisputably true that individuals with what we today consider to be psychopathic traits already left a large mark on people and society in ancient times (see also Cleckley's chapter "The psychopath in history", 1941/1976). On the one hand, they can boldly make changes that are fruitful for society, but on the other hand, they can also cause untold human and social suffering. Descriptions of extreme determination, manipulation, egocentrism, suspicion, supposed absence of empathy and forgiveness, unreliability on a personal level and in alliances, low moral standards, the careless sacrifice of countless human lives without taking responsibility, relentless cruelty, alongside lecherous drinking and perverse sexuality, to name a few descriptions that reach us from lore that point to psychopathic traits. From distant history, one could think of the first Tsar of Russia, Ivan IV (1530-1684), also known as Ivan the Terrible. Consider infamous names such as those of the Roman emperor Nero (37-68), the Mongolian ruler Dzhengis Khan ("Ruler of the World") (1155/1162 - 1227), and Qin Shi Huangdi (259-210 B.C.), the first emperor of China, founder of the Qin dynasty. Countless others come to mind, predominantly men. Names of rulers from the recent past and the present also loom large, but as mentioned, a retrospective diagnosis of psychopathy is not possible if the person in question has not been examined by a certified diagnostician according to the present diagnostic rules.

Only quite recently have the personality characteristics of the psychopathic individual been studied methodologically. In 1941, both Karpman and Cleckley published their studies on psychopathy. Karpman distinguished symptomatic psychopathy, that is, psychopathic-like behavior behind which a dynamic psychogenesis was identifiable, versus idiopathic psychopathy, in which this psychogenesis is not traceable. In his seminal work, Cleckley (1941/1976) wrote 15 vignettes of individuals who fulfilled psychopathy. He showed that this diagnosis was not unitary but multifaceted in its presentation. In addition to the few interpersonally aggressive psychopathic individuals in his study, he also described socially successful psychopathic persons. Concluding his observations, he gave 16 characteristics of psychopathy (see Table 1). His results caused the study of psychopathy to take a significant leap forward (Patrick, 2006). It was Hare (1980) who, based on these Cleckley criteria, further developed the contemporary concept of psychopathy with his clinical psychopathy assessments, particularly in criminal individuals (see Table 2).

He eventually included them in the diagnostic criteria of what later became known as the Psychopathy Checklist - Revised (PCL-R; Table 3). Unlike Cleckley, he focused primarily on the negative characteristics of psychopathy (Patrick, 2006), leaving the positive characteristics of Cleckley's concept of psychopathy weakly represented (Patrick et al., 2009).

1	Superficial charm and good "intelligence"
2	Absence of delusions and other signs of irrational thinking
3	Absence of 'nervousness' or psychoneurotic manifestations
4	Unreliability
5	Untruthfulness and insincerity
6	Lack of remorse or shame
7	Inadequately motivated antisocial behavior
8	Poor judgement and failure to learn by experience
9	Pathologic egocentricity and incapacity for love
10	General poverty in major affective reactions
11	Specific loss of insight
12	Unresponsiveness in general interpersonal relations
13	Fantastic and uninviting behavior with drink and sometimes without
14	Suicide rarely carried out
15	Sex life impersonal, trivial, and poorly integrated
16	Failure to follow any life plan

▲ Table 1. List of 16 characteristics of psychopathy (Cleckley, 1941/1976)

Lykken (1957) found a distinction in anxiety responses in people who could be considered psychopathic individuals according to Cleckley's criteria. He identified "primary sociopathy" versus "neurotic sociopathy", with the latter category reflecting a tendency in which more anxiety is processed and expressed compared to the former. The term sociopathy was originally coined by Karl Birnbaum in 1909, who claimed "that antisocial behavior only rarely stems from inherent immoral traits of character; rather, it reflects most often the operation of societal forces that make the more acceptable forms of behavior and adaptation difficult to acquire" (Millon et al., 2003, pp. 11-12).

The terms primary vs. secondary psychopathy are kept for a dichotomization in the psychopathy spectrum, although a clear distinction between the two is rarely possible. The etiology of these distinct phenotypes is likely the result of a complex gene-environment interaction (Hare, 1999) in which neither nature nor nurture alone can cause both types. Primary psychopathic individuals are thought to have innate deficiencies in emotional processing that prevent them from experiencing negative emotions such as severe anxiety, panic or depression. Partly because of this deficiency, they have no problem being dominant and superior. In contrast, secondary psychopathic individuals are thought to have disturbances in emotional processing because of a stressful or traumatic early socialization process that can lead to aberrant emotional states such as anxiety, depressive emotions and hostility (Thompson et al., 2014). Consistent with Birnbaum's assertions, Lykken's neurotic sociopathy shows diagnostic overlap with secondary psychopathy.

As stated above, Hare based his criteria of psychopathy on the Cleckley criteria. In 1980 he formulated his clinical judgments of psychopathy (see Table 2). Few years later, he published the Psychopathy Checklist (PCL; Hare, 1986). His advocacy for this diagnostic list and the subsequent revisions of the PCL in what eventually came to be known as the Psychopathy Checklist - Revised (PCL-R; Hare, 1991; Hare, 2003) can unquestionably be considered his greatest contribution to forensic behavioral science. Based on the research of Harpur and colleagues (1988; 1989) the PCL and PCL-R originally consisted of two factors, but adjustments were made in the latest version (Hare, 2003) by introducing four facets (see Table 3). This four-facet model holds 1) an interpersonal facet, 2) an affective facet, 3) a behavioral lifestyle facet, and 4) an antisocial facet, leaving two PCL-R items (namely "promiscuous sexual behavior", and "many short-term marital relationships") separately as they do not load on any of the four facets. The four-facet model builds on the original two-factor model. Facet 1 and facet 2 of the four-facet model are derived from the original factor 1, while factor 2 is subdivided into facet 3 and facet 4. Facet 4 also contains the PCL-R item "criminal versatility" that did not load on either factor 1 or factor 2 in the two-factor model (see Table 3).

Assessment of the 20 PCL-R items is done according to a three-point scale (0 = clearly not present; 1 = possibly present; 2 = clearly present), such that a maximum score of 40 points represents maximum psychopathy. A PCL-R score of less than 20 does not correspond to psychopathic tendencies. Although comparisons between North America and Europe did not reveal cross-cultural structural biases in PCL-R ratings, cross-cultural biases in ratings of individual psychopathic symptoms are indeed statistically significant and meaningful

1	Glibness/superficial charm
2	Previous diagnosis as psychopath (or similar)
3	Egocentricity/grandiose sense of self-worth
4	Proneness to boredom/low frustration tolerance
5	Pathological lying and deception
6	Conning/lack of sincerity
7	Lack of remorse or guilt
8	Lack of affect and emotional depth
9	Callous/lack of empathy
10	Parasitic lifestyle
11	Short-tempered/poor behavioral controls
12	Promiscuous sexual relations
13	Early behavior problems
14	Lack of realistic, long-term plans
15	Impulsivity
16	Irresponsible behavior as parent
17	Frequent marital relationships
18	Juvenile delinquency
19	Poor probation or parole risk
20	Failure to accept responsibility for own actions
21	Many types of offense
22	Drug or alcohol abuse not direct cause of antisocial behavior

▲ Table 2. Hare's (1980) original clinical judgments of psychopathy as derived from the 16 Cleckley criteria

(Cooke et al., 2005). As a result, compared to a diagnostic cut-off score of 30 in North America (Bolt et al., 2007), lower cut-off scores may be used in several European countries for the diagnosis of psychopathy (even as low as 25; e.g., Cooke et al., 2005). Until recently, the cut-off score for the PCL-R in the Netherlands was 26, but partly due to concerns among professionals about the impact this diagnosis has within the legal system and for treatment providers, the cut-off score was increased to 30.

Recent attempts to unravel the psychopathic construct include the triarchic conceptualization of psychopathy (Patrick et al., 2009). In their model, the authors propose three distinct phenotypic constructs, i.e., boldness, meanness

PCL-R factor domains	PCL-R factor	PCL-R items	PCL-R facets	PCL-R facet domains
<i>Interpersonal/ Affective factor</i>	1	glib/superficial grandiose self-worth pathological lying conning/manipulative	<i>Facet 1</i>	<i>Interpersonal facet</i>
	1			
	1			
	1			
	1	lack of remorse or guilt shallow affect callousness or lack of empathy failure to accept responsibility	<i>Facet 2</i>	<i>Affective facet</i>
	1			
	1			
	1			
<i>Impulsive lifestyle/ Antisocial factor</i>	2	stimulation seeking impulsivity irresponsibility parasitic orientation lack of realistic goals	<i>Facet 3</i>	<i>Lifestyle facet</i>
	2			
	2			
	2			
	2	poor behavior controls early behavior problems juvenile delinquency revocation of conditional release criminal versatility	<i>Facet 4</i>	<i>Antisocial facet</i>
	2			
	2			
	2			
	#			
	#			
	#	promiscuous sexual behavior many short-term marital relationships	<i>Two items that do not load on any of the four facets</i>	

▲ **Table 3. The two-factor and four-facet model of the PCL-R (Hare, 1991, 2003).** Note that the three items in the two-factor model marked with # do not load on these two factors, while in the four-facet model this is the case for two items. In our study, we refer to these two items as the Category “Other”.

and disinhibition. Boldness can be described as “the capacity to remain calm and focused in situations involving pressure or threat, an ability to recover quickly from stressful events, high self-assurance and social efficacy, and a tolerance for unfamiliarity and danger” (Patrick et al., 2009, p. 926). Disinhibition encompasses “a general phenotypic propensity toward impulse control

problems entailing a lack of planfulness and foresight, impaired regulation of affect and urges, insistence on immediate gratification, and deficient behavioral restraint” (p. 925). Meanness, which the authors define as aggressive resource seeking without regard for others, is described by them as “a constellation of phenotypic attributes including deficient empathy, disdain for and lack of close attachments with others, rebelliousness, excitement seeking, exploitativeness, and empowerment through cruelty” (p. 927). The meanness and disinhibition components of psychopathy reflect mainly factor 1 and factor 2 of the PCL-R, respectively. In contrast, boldness items of the triarchic model are barely represented in the PCL-R. Perhaps this is because the PCL-R focuses primarily on the negative features of psychopathic individuals rather than the positive adjustments of psychopathy, partially missing the “successful psychopaths”, since boldness can be considered as the combination of venturesomeness, social dominance and emotional resiliency (Patrick et al., 2009; p. 921). According to the authors, these three phenotypic constructs are a better lens through which to view psychopathy in its broadest manifestations, i.e., criminal and non-criminal, primary and secondary, stable and aggressive, unsuccessful and successful. Although promising, I will not use the triarchic model in this dissertation. This is largely because the selected psychopathic patients who participated in our study were all examined, identified and categorized using the PCL-R.

1.5 Oxytocin

Oxytocin (OT) is a neuropeptide whose name is etymologically rooted in the classical Greek word ὠκυτόκος (ōkutókos), meaning “swift delivery”. The discovery, identification and synthesis of this neuropeptide occurred in several steps. In 1906, Dale noted that an extract from the posterior pituitary gland had oxytonergic properties, i.e., it could stimulate uterine contraction. It was not until 1928 that Kamm succeeded in isolating and concentrating two active components of this extract, which he named vasopressin and oxytocin, respectively (Leng & Sabatier, 2016). In 1955, Du Vigneaud was awarded the Nobel Prize in chemistry for identifying the amino acid sequence and synthesizing OT (Hope & Holleberg, 1968; www.nobelprize.com). With its nine amino acids, OT is a so-called nonapeptide, consisting of a ring of six amino acids (namely cysteine-tyrosine-isoleucine-glutamine-asparagine-cysteine) with sulfur bridges at the two cysteine sites and a tail of three amino acids

(namely proline-leucine-glycine-(NH₂)). OT is primarily synthesized in the brain by neurons of the paraventricular nucleus and the supraoptic nucleus of the hypothalamus (Knobloch & Grinevich, 2014).

The regulatory role of OT on social behavior is diverse and complicated; it is involved in intimate attachment relationships, altruism and competition, reward, aggression, as well as pain management, appetite, fear and anxiety (Jin et al., 2023; Camerino, 2023). In current human behavioral research, an intranasal dose of 24 international units (IU) of the synthetic version of OT is most often used (Yang et al., 2021). According to the rules of the 4th International Standard for Oxytocin (NIBSC, 2013), 24 IU corresponds to approximately 40 µg OT, which is close to the total content of OT in the human pituitary gland (Leng et al., 2022). In plasma, the half-life of exogenously administered OT is about 3-6 min and in cerebrospinal fluid approximately 20 min (Jurek and Neumann, 2018). It is assumed that intranasally admitted OT enters the brain directly via an extracellular route. This route involves the trigeminal and olfactory nerves and perineural clefts in the nasal epithelium, thus bypassing the blood-brain barrier (Yao et al., 2023). Pharmacokinetic studies show highly contradictory results of OT distribution in plasma, extravascular fluid, cerebrospinal fluid and the central nervous system in terms of peak concentrations and the corresponding wash-in and wash-out time periods (Churchland & Winkielman, 2012; Leng & Ludwig, 2016). Only 1-2% of peripherally synthesized and released OT (including secretion from the posterior pituitary into venous blood outside the brain) crosses the blood-brain barrier (Reichel, 2021). Until date, there is ongoing debate whether indirect routes (i.e., intravenous, subcutaneous and intraperitoneal) are also having similar effects on brain activity although they do not permit direct entry into the brain (Yao et al., 2023), while there are indications that stimulation of the peripheral vagus nerve mediates the central effects of peripheral OT (Reichel, 2021).

The effects of OT administration were investigated in various mental disorders like autism spectrum disorder (ASD), personality disorder, schizophrenia, anxiety disorders and post-traumatic stress disorder. Interestingly, daily nasal administration of 24 IU OT for 4 weeks in adult men with ASD resulted in a significant and long-term decrease in the intrinsic functional connectivity of the amygdala to various regions of the social-emotional circuitry, particularly with respect to the orbitofrontal cortex and superior temporal sulcus. These effects, including reduced ASD-related behaviors, persisted up to one year after treatment (Alaerts et al., 2020). Since the social salience hypothesis of OT predicts that OT is associated with attentional modulation depending on salience of external social cues (Shamay-Tsoory & Abu-Akel, 2016), it can be understood that OT is of great importance in interpersonal relationships. In

both animal and human studies, it has been established that OT encourages social approach, increases eye contact, emotion recognition, trust, influences amygdala function, and enhances submissive behavior in social groups (Caldwell, 2017; Domes et al., 2007; Guastella et al., 2008; Hellmann et al., 2015; Landgraf and Neumann, 2004; Liu et al., 2012; Meyer-Lindenberg et al., 2011; Schiller et al., 2023; Tillman et al., 2019; Timmer et al., 2011; Veening and Olivier, 2013). OT is also positively associated to empathy (Barchi-Ferreira & Osório, 2021; Hurlemann et al., 2010), ingroup social bonding and caring behavior (Bos et al., 2012), and is involved in discriminating between outgroup and ingroup members (de Dreu & Kret, 2016). However, a caveat should be added. Recently, there have been worrisome reports that quite a few promising studies of OT interventions are not reproducible (Lang et al., 2022). Perhaps this is due to underpowered studies (Walum et al., 2016).

Despite studies in the mental conditions above, most OT studies have been conducted in (healthy) men, leaving (healthy) women underrepresented (Quintana et al., 2020). Furthermore, it appears that OT-related studies in psychopathy are scarce. High psychopathic traits in children and adolescents are positively related to OT receptor gene methylation (Aghajani et al., 2018; Dadds et al., 2014a) and OT receptor polymorphisms (Dadds et al., 2014b) as well as lower OT concentrations in saliva and blood plasma (Dadds et al., 2014b). Conversely, Verona and colleagues (2018) showed that lower psychopathic traits in adults were negatively correlated with OT-related single-nucleotide polymorphisms (SNPs), including an SNP on the OT receptor. Interestingly, in male adolescents with high psychopathic traits, salivary OT concentrations were lower in those with low levels of emotional neglect (indicative of primary psychopathy) compared with those with high emotional neglect, which could reflect secondary psychopathy (Fragkaki et al., 2019). I am not aware of any OT administration studies in psychopathy, except for a recent functional-MRI study in which nasal application of 40 IU OT abolished differences in the processing of fearful facial expressions in violent male offenders with both antisocial personality disorder and psychopathy (Paloyelis et al., 2023). Thus, more research is needed. The design of this dissertation attempts to fill this gap and describes a study with various computer tasks after intranasal administration of OT in PCL-R-confirmed psychopathic patients involuntarily admitted to a forensic psychiatric hospital under the aforementioned Entrustment Act.

2 Outline of this dissertation

In this dissertation, I focus on parts of the psychopathy construct as it occurs in forensic psychopathic patients. The central question here is whether OT can influence psychopathic symptoms in this patient group, and if so, in what direction. First, we describe the empathy construct and, by extension, impaired empathy processing in psychopathy, which is said to be the hallmark of psychopathy (Soderstrom, 2003). Due to limitations in the temporal resolution of neural dynamics in empathy processing, it is impossible to directly measure OT-induced empathy changes. Therefore, we chose to examine OT-induced changes in some proxies of the empathy construct, starting with mimicry of emotional facial expressions, which is believed to be a precursor of the empathy process (Hatfield et al., 1994, 2009; Rijnders et al., 2021a, this dissertation). Although not proven, both reactive dominance and morality may also be proxies of the empathy construct, albeit more remotely than mimicry. The effect of OT on reactive dominance is not precisely known. Perhaps it works indirectly via lowering plasma testosterone levels (Procyshyn et al., 2020). Testosterone is associated with status-seeking behavior, e.g., dominant behavior and aggression, possibly due to context-dependent rapid changes in local neural sensitivity to this steroid in the forebrain (Bos et al., 2012; Terburg et al., 2009; van Honk et al., 2011).

There is also not much evidence for a direct link between morality and empathy. If one considers both morality and empathy as evolutionarily rooted functions with the goal of thriving and surviving, Decety's conclusions that there is a complex and ambiguous relationship between morality and empathy are somewhat comprehensible (Decety, 2014, 2021; Decety and Cowell, 2014). Although the effect of OT on morality has not been established, we hypothesize that some aspects of morality can be changed (see below).

This dissertation is divided into four parts, consisting of (I) this Introduction, (II) several articles on empathy and the OT intervention study in psychopathic patients, (III) the General discussion, the follow-up story of Lennart, and future directions (IV) the references, a Dutch summary, acknowledgments, and my resume. In Chapter 2, we start by describing and unraveling the empathy construct and impaired empathy processing in psychopathy by discussing current theories of the empathy construct. We then present a new model of empathy processing that encompasses the dynamically interacting cognitive and emotional components of the empathy construct. This Zipping Model of Empathy describes the interaction of the various components of both

cognitive and affective empathy, including mimicry and emotional contagion as precursors of the empathy construct. Important drivers of this zipper process include both personal and contextual factors. Using our Zipper Model of Empathy with respect to psychopathic individuals, we attempt to shed light on their impaired empathy processing. We also discuss facial emotion processing in psychopathy that precedes the precursors mimicry and emotional contagion, hypothesizing dysfunctional facial emotion processing in the basolateral and central subregions of the amygdala. Then, in Chapter 3, we propose a neuropsychological battery to assess empathy processing in psychopathy. We attempted to empirically identify physiological and behavioral measures required for testing the various components of the empathy construct as described by the Zipper Model of Empathy. Special attention is paid to impaired empathy processing in psychopathic personalities.

Another part of this dissertation consists of an OT intervention study with three different tasks in a group of male psychopathic patients involuntarily admitted by court order to several high-security forensic psychiatric hospitals in the Netherlands. Moreover, we studied salivary concentrations of the steroid hormones testosterone and cortisol before and after the testing procedure. Psychopathic patients were selected if their PCL-R total score was 26 or higher. As this study also focused on empathy processing in psychopathy, the maximum score (i.e., 2) of PCL-R item "callousness / lack of empathy" (Hare, 2003) was required. The OT intervention study followed a within-subject, double-blind, counterbalanced, placebo-controlled, crossover design. Patients were therefore tested on two days. We also tested a control group of male guards and nurses who did not fulfill the criteria of psychopathy according to the Psychopathic Personality Inventory-Revised (Lilienfeld & Widows, 2005). Due to practical reasons, they did not undergo any OT or placebo intervention so they were tested on one day only. We therefore decided to use this group as a reference population.

The first OT intervention study is described in Chapter 4. We tested mimicry responses of two facial muscles to morphed emotional facial expressions of happiness and anger. Mimicry is part of a highly dynamic interpersonal communication process, and hampered empathy processing in psychopathic individuals is thought to be caused in part by impairments in mimicking others' expressed emotions. Therefore, studies of mimicry in psychopathy are needed. Mimicry responses were measured with facial electromyography. The two facial muscles examined were the corrugator supercilii and the zygomaticus major, respectively. The first muscle can be activated when watching a negative emotional facial expression, while looking at a positive emotional facial expression

can simultaneously elicit activation of the zygomaticus and relaxation of the corrugator. Because differences in mimicry can appear at very short latencies of 100 or 200 ms after stimulus onset, we examined the 600-ms early rise time of dynamic expressions after stimulus onset. We expected that compared with normal controls, psychopathic patients would exhibit weaker early onset corrugator activation to angry facial expressions and less corrugator inhibition to happy facial expressions. Furthermore, we expected that the increase in activity of the zygomaticus during the early rise time of happy facial expressions would be smaller in psychopathic patients compared with normal controls. Only the group of psychopathic patients was administered OT and placebo. We expected that happy facial expressions in the OT condition, compared with placebo, would elicit stronger activation of the zygomaticus and stronger inhibition of the corrugator. When looking at angry faces, a stronger corrugator response was also expected in the OT condition, compared with placebo.

In Chapter 5, we used a gaze aversion task, i.e., a reaction time task that reflects reactive dominance to masked facial stimuli. We tested the hypotheses that psychopathic patients are more dominant than normal controls and that dominance outcomes on the gaze aversion task would positively correlate with psychopathy measures in both groups of participants. For the group of psychopathic patients, we hypothesized that OT would causally reduce their reactive dominance.

Chapter 6 focuses on moral choices. Moral reasoning is basically thinking about right and wrong and involves intuitive and emotional processes, while also considering calculative and social consequences. Measuring moral reasoning is often done through moral dilemmas, i.e., specific vignettes in which the morality of an action is not clear. According to the dual-process theory of moral judgment (Greene et al., 2001), controlled cognitive and automatic emotional processes can be identified that are usually mutually exclusive. On the one hand, cognitive processes can result in utilitarian decisions in which the calculated outcome of harming others determines whether that action can be seen as right or wrong. On the other hand, an automatic aversive emotional response may result in deontological decisions in which the nature of the action itself determines whether that action is considered right or wrong. Psychopathic individuals are generally thought to prefer utilitarian choices over deontological decisions, which was also hypothesized in our study. We examined the influence of OT on moral choices and hypothesized that OT would reduce psychopathic patients' preference for utilitarian choices in favor of deontological choices. Moreover, we expected that the percentage of utilitarian choices would be positively related to psychopathy severity.

In Chapter 7 we examined the relationship between the severity of psychopathy and salivary concentrations of the steroid hormones testosterone and cortisol. Moreover, we examined the effect of oxytocin on both cortisol and testosterone salivary levels. Perhaps OT has an indirect lowering effect on plasma testosterone levels (Procyshyn et al., 2020). Only psychopathic patients participated in this study. The rationale for studying these steroid hormones is that psychopathy is associated to a higher incidence of aggressive acts and therefore psychopathic individuals are overrepresented in the forensic system. Testosterone is related to status-relevant behaviors, such as dominance and aggression, especially when status is challenged. It further facilitates approach and reward seeking, while cortisol is associated with withdrawal and anxiety (Montoya et al., 2012). Both hormones exhibit a reciprocal suppressive interaction. High cortisol levels block testosterone-related dominant behavior, while this is not the case in subjects with low cortisol levels. In the triple balance theory of emotions (van Honk & Schutter, 2006) describe a crosstalk between cortical and subcortical circuits that reciprocally influence either inhibitory or excitatory functioning of both these circuits. This crosstalk relies heavily on the intracerebral concentrations of cortisol and testosterone. Under a high level of testosterone, it is assumed that a cortical balance shift occurs in favor of reward sensitivity and to the detriment of punishment sensitivity. Cortisol, on the other hand, has an opposite effect on the cortical level: unlike testosterone, a high intracerebral cortisol concentration tends to shift the balance between reward sensitivity and punishment sensitivity towards the latter. In sum, in the case of combined high testosterone and low cortisol levels, the propensity for reward seeking and concomitant punishment insensitivity will prevail. We measured the steroid levels at the beginning of the above testing procedure and their changes over time. In addition to measuring both testosterone and cortisol levels, we also determined the testosterone-cortisol ratio because the latter is thought to be positively related to impulsivity and antisociality, aspects included in the PCL-R factor 2. We hypothesized that the testosterone-cortisol ratio would indeed show a positive association with the PCL-R factor 2. Moreover, since strong associations have been described between dominant behavior and PCL-R factor 1, we hypothesized that testosterone levels would have a positive association with PCL-R facet 1, but not or to a lesser extent with PCL-R facet 2, since the latter facet does not seem to affect dominance.

Chapter 2
Unzipping empathy
in psychopathy –
Empathy and facial affect
processing in psychopaths

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Abstract

Psychopathy is a neurodevelopmental disorder that has a highly deleterious effect upon both individuals and society at large. Psychopaths grossly neglect and disrespect the interests of others. Their antisocial behavior is thought to originate from a lack of empathy. However, empathy is multidimensional in nature, as evidenced by the considerable heterogeneity in extant theorizing on the subject. Here, we present the “Zipper model of empathy” that reconsiders how both its affective and cognitive components converge in mature empathic behavior. Furthermore, the Zipper model of empathy is expedient for explaining the empathy deficits in psychopathy, insofar as it brings together current theories on the dysfunctional affective components of empathy, violence inhibition, and automatic versus goal-directed attention. According to the literature, the neurobiological underpinnings of these theories are amygdala-centered; however, this article traces this specifically to the basolateral and central amygdala subregions. When viewed together, the cognitive and affective components of empathy are zipped together in a natural fashion in healthy empathic behavior, whereas psychopaths leave the zipper substantially unzipped in pursuit of their purely self-centered goals.

1 Introduction

Psychopathy is a personality disorder characterized by disturbances in the emotional, interpersonal, and behavioral domains. Psychopaths grossly take advantage of other people by both neglecting and disrespecting their interests. They behave like predators insofar as they do not care about the pain they inflict upon the persons they consider as prey. The estimated lifetime prevalence of psychopathy worldwide in the general population ranges from 0.5% to 1%, whereas psychopaths are overrepresented in the North-American correctional populations with prevalence figures as high as 15-25% (Hare, 1996). Coid and colleagues (2009) found in a representative national sample of English and Welsh prisoners that the psychopathy prevalence figures were 7.7% (95% CI 5.2–10.9) in men and 1.9% (95% CI 0.2–6.9) in women. There are strong indications that psychopathic traits in males are associated with psychopathic traits in their male and female offspring (Auty et al., 2015). This warrants serious attention considering the significant annual healthcare costs for children with antisocial behavior (Romeo et al., 2006). Reducing the disruptive actions of psychopaths in society might be cost-effective, insofar as psychopathy is a risk factor for perpetration of violence (odds ratio = 5-10, in relation to other offenders and psychiatric patients; Hart & Storey, 2013). Based on a study by Anderson (1999), Kiehl & Hoffman (2011) calculated that psychopaths were responsible for around \$460 billion of criminal social costs each year in the United States alone (US dollars in 2009). This figure did not include the costs of psychiatric treatment for psychopaths themselves, nor did it account for various indirect costs, such as, for example, treatment for victims and their non-quantifiable emotional suffering. These astronomical costs led Kiehl and Sinnott-Armstrong to conclude that “psychopathy is likely the most expensive mental health disorder known to man” (2013, p. 1).

The lay public’s assumptions about what constitutes prototypical psychopathic behavior rarely corresponds to the clinical reality. Due to both the diversity and varying intensities of the symptoms in the emotional, interpersonal, and behavioral domains that determine the diagnosis of psychopathy (Hare, 1996, 2003; Brinkley et al., 2004), heterogeneity is the rule in the clinical expression of psychopathy. Notwithstanding this heterogeneity, some core characteristics are invariably present (Martens, 1997), most notably, severe empathy deficits that are considered to be pivotal to the construct of psychopathy (Cleckley, 1976; Blair, 2007; Patrick et al., 2009; Verschuere et al., 2017; Verschuere & te Kaat, 2020). Indeed, Soderstrom (2003) has even argued that psychopathy should in fact be classified as an empathy disorder, based on the fact that psychopathic

predators' high involvement in violent criminality reflects either a lack of or ineffective empathic functioning on their behalf. Although we certainly believe that empathy deficits do play a central role in the construct of psychopathy, we will not argue that empathy deficits are identical to the entire clinical presentation of psychopathy. As described in § 2, psychopathy is characterized by behavioral, cognitive, and affective problems (Brinkley et al., 2004; Hare, 1996) that go beyond empathy deficits alone. However, in this contribution, we will focus primarily on empathy deficits in the construct of psychopathy.

Basically, empathic processes can be understood as the social glue in society (Chakrabarti & Baron-Cohen, 2011) that binds human beings. The capacity to communicate expressed emotions is essential for the establishment of social understanding and social relationships (Kraaijenvanger et al., 2017), and is primarily based on both the transmission and decoding of facial emotional expressions (Smith, et al., 2005). Contextual appraisal of emotional states and group variables allied with attentional and motivational factors are all important underpinnings of the empathy construct. Therefore, one can assume that healthy functioning people will display dynamic alterations in their empathic processing in a variety of different circumstances. The question as to what precise mechanism accounts for the empathic malfunctioning observed in psychopathy remains unanswered, yet. It is not known whether it should be considered as either a defective trait, and thus by definition difficult to change or perhaps even resistant to therapeutic interventions, or as a state-dependent, dynamic process, which might be altered by psychotherapy or pharmacotherapy. If the latter is the case, then one could assume that therapeutic interventions, for example those focused on attentional and motivational processes, could contribute toward improving the psychopath's disturbed empathic functioning. Indirect support for this assumption comes from a study that demonstrated how psychosocial interventions and high-quality foster care positively influenced both the development and impact of callous-unemotional traits in boys with a history of severe early deprivation (Humphreys et al., 2015).

The present article focuses on empathy processing in psychopathy as well as its relationship to the difficulties psychopaths have with facial emotional information processing. After giving a brief introduction to the Psychopathy Checklist, that is, the gold standard for psychopathy diagnosis, the multidimensional construct of empathy with its cognitive and affective components is discussed, followed by a proposal for an integrative model (the Zipper model of empathy). Within the Zipper model, cognitive and affective processes conjointly interact to build up ("zipping up") to mature empathic behavior, whereas the "unzipping" of these processes results in either hindered

empathic behavior or its disappearance entirely. Psychopaths are known to have little or no empathy-related affective responses, while, simultaneously, they are not necessarily being disturbed in their cognitive processing (Richell et al., 2003; Blair, 2007). Their poor empathic behavior might be due, in part, to deficits in facial emotional information processing, although there are debates over whether these deficits stem from either innate deficient amygdala processing (Blair, 2005) or the failure to allocate attention to stimuli that are considered of secondary importance (response modulation theory of psychopathy; see: Newman & Lorenz, 2003; Baskin-Sommers et al., 2009).

2 Psychopathy Checklist

Psychopathy is assumed to be a personality disorder that persists throughout life (Hare, 1996), and is operationally defined by the Psychopathy Checklist-Revised (PCL-R; Hare, 1991, 2003). This 20-item checklist with scores of 0, 1 or 2 for each item has a maximum score of 40, which represents the extreme end of the psychopathy scale. As it seems that various etiological pathways might produce high scores on the PCL-R, psychopathy should thus be considered as an etiologically heterogeneous entity (Brinkley et al., 2004). Numerous studies have tried to identify PCL-R sub-scores in the search for these heterogeneous components. Harpur and colleagues (1988), for instance, demonstrated that the PCL-R consists of two major factors: interpersonal/affective and impulsive/antisocial lifestyle items. Using confirmatory factor analysis of North American and Scottish PCL-R data, Cooke and Michie (2001) presented a three-factor hierarchical model of psychopathy, comprising 1) an arrogant and deceitful interpersonal style, 2) a deficient affective experience, and 3) an impulsive and irresponsible behavioral style. In their model, antisocial criminality was hardly emphasized, as the authors did not consider this to be a constitutive feature of psychopathy, although they did acknowledge that it was certainly a correlate (see also Cooke et al., 2004; Skeem & Cooke, 2010). Hare (2003) then proposed a four-factor model (also referred to as a four-facet model), comprising 1) an interpersonal factor (with PCL-R items: glib/superficial, grandiose self-worth, pathological lying, conning/manipulative), 2) an affective factor (lack of remorse or guilt, shallow affect, callousness or lack of empathy, failure to accept responsibility), 3) a behavioral lifestyle factor (stimulation seeking,

impulsivity, irresponsibility, parasitic orientation, lack of realistic goals), and 4) an antisocial factor (poor behavioral controls, early behavioral problems, juvenile delinquency, revocation of conditional release, criminal versatility). Two PCL-R items (promiscuous sexual behavior, and many short-term marital relationships) are left separately as they do not load under these four factors (facets).

Cooke et al. (2005) examined the generalizability of the PCL-R from North America to continental Europe, concluding that psychopathy appears to have a syndromic structure that is stable across cultures. Although no evidence of cross-cultural structural bias in PCL-R ratings was found, cross-cultural metric bias in ratings of psychopathic symptoms were found to be statistically significant and clinically meaningful. According to these authors, this should prompt the implementation of a lower diagnostic cut-off score in Europe. Although Bolt et al. (2007) stated that a PCL-R cut-off score of 30 provided the best global clinical assessment of psychopathy, Cooke et al. (2005) suggested that in Europe a PCL-R cut-off score of 28 points was equivalent to the North American cut-off score of 30 points, based on the fact that lower cut-off scores (even 25 and higher) were used in research and treatment programs in different European countries (Grann et al., 1998; Cooke, 1998; Rasmussen et al., 1999; Cooke & Michie, 1999; Mokros et al., 2013).

In all these three aforementioned models, factor analysis resulted in a distinct factor, namely disturbed affective processing (e.g., empathy dysfunction), being an important underpinning of psychopathy. Therefore, we will first discuss the concept of empathy and its mutually interacting affective and cognitive components.

3 Empathy construct

The literature galore on the construct of empathy provides a wide variety of definitions and nuanced interpretations from a broad range of academic fields, such as, for example, neurology, developmental psychology, neuro-economics, psychiatry, social psychology and primatology (Batson, 2009; see Hanson (2003) for a brief historical overview of the development of the concept of empathy, who also cited a model of eight different types of sympathy developed by Scheler in the 1920s). Indeed, the complicated and elusive character of empathy leads one to conclude that it is an “essentially contested concept” (Gallie, 1956).

Empathy is a multidimensional construct that results from conjointly operating cognitive and affective processes. Before unpacking empathy further, it is first important to emphasize that while the construct of empathy comprises cognitive and affective components, these components themselves are not synonymous with the end result, that is, empathic behavior. Considering this, and despite the frequent usage of these terms in extant literature and daily life, “cognitive empathy” and “affective empathy” should thus be considered as underlying factors that contribute to the expression of empathic behavior. Therefore, we recommend using terms such as “components” or “parts” when describing the cognitive or affective aspects of the empathy construct.

Empathy is thought to emerge during early developmental stages (Decety, 2015) and can serve as a powerful resource in personal adjustment during stressful circumstances (Feshbach, 1997). There is considerable evidence that empathy has deep evolutionary, neuroendocrine, and neurophysiological underpinnings (Decety et al., 2012). As such, empathy plays a pivotal role in social understanding and social relationships. Cohen and Strayer (1996) defined empathy as the ability to understand and share in another person's emotional state. Klimecki and Singer (2013) added to this definition by stating that there should be no confusion with one's own emotional state. This is in line with Hoffman's (2008) point that mature empathy is metacognitive, that is, one is cognizant of the fact that the emotion felt is a response to the emotional state of another person. According to Feshbach (1997), in her integrative cognitive-affective model of empathy, “the affective empathy reaction is postulated to be a function of three component factors: (a) the cognitive ability to discriminate affective cues in others; (b) the more mature cognitive skill involved in assuming the perspective and role of another person; and (c) emotional responsiveness, that is, the affective ability to experience emotions” (p. 36). She stressed that in both her own and other models of empathy, the ability to differentiate oneself from another is a critical requirement. It is instructive to note here that this integrative cognitive-affective model implies that the emergence of mature empathy (i.e., empathic behavior) is dependent on the interaction between both the affective and cognitive components.

Both Walter (2012) and Adriaense and colleagues (2020) provided an overview of the various components of the broader construct of empathy, including affective behavior, affective experience, affective isomorphism, perspective taking, self-other distinction, orientation toward the other, and prosocial motivation. When reflecting on empathy, one might easily overlook the fact that rather than consisting of a unidirectional operation in which someone perceives and processes the emotional signals of another person, empathy in fact results from a mutually driven process between persons. That is to say, the

self and the other are simultaneously both the “sender” and “receiver” (see also Main et al., 2017). In this reciprocal interplay, empathy processing takes place via ongoing adjustments in the transmission of one’s own emotional signals and the perception of those of the other person.

A phenomenon called mimicry precedes empathic processing. Mimicry is an automatically elicited motor muscle response that mirrors another person’s emotional expression, including his or her emotional postures, gestures, or facial expressions (Chartrand & van Baaren, 2009; Lipps, 1903). Although direct contact with others is of great importance in the empathy-inducing process, it is theoretically possible that empathy for non-present others is generated through semantic processing and the construction of visual or auditory images of others (of them suffering, for example), which, in turn, may induce mimicry processing and, consequently, empathic responses (Hoffman, 2008). Mimicking facially expressed emotions forms part of a highly dynamic interpersonal process (Chartrand et al., 2005) that eventually can elicit the corresponding emotional state in the perceiver (Söderkvist et al., 2018; Olszanowski et al., 2019). Bird and Viding (2014) posited that this can induce a process called emotional contagion, that is, an affectively resonant and similar (isomorphic) reaction in the self (perceiver) when observing another person’s emotion. They argued in their self to other model of empathy (SOME) that emotional contagion is at the root of the empathy construct. The basic premise of SOME is that the perceiver’s own emotional state might be activated and shaped by the sender’s expression of their emotional state. This isomorphic reaction is strictly self-oriented. Mimicry is also referred to as motor empathy (Blair, 2005). However, this term is perhaps confusing, since mimicry and emotional contagion are preceding components of the emerging empathy construct and, as such, should be regarded as precursors of empathy (Klimecky & Singer, 2013). Ultimately, mimicking induced emotional contagion can facilitate the processing of affective forms of empathy (Baird et al., 2011; Hermans et al., 2006; Hoffman, 2000; de Wied et al., 2006; Sonnby-Borgström, 2002). In emotional contagion, the self-other distinction is not present, while in the evolving process toward empathic behavior the cognitive notion arises that the emotion one is resonating with is the emotion of the other (Singer & Klimecki, 2014; Bird & Viding, 2014). Consequently, one should conclude that the boundaries of the perceiver’s capacity to experience his or her own emotions restrict both the kind and degree of empathy that can be felt. In their perception-action model of empathy, de Waal and Preston (2017) stated that motor mimicry and emotional contagion are the most basic expressions of their model in which the emotional states of the other are processed and synchronized through one’s own embodied representations. This provides the

opportunity for empathic behavior to emerge, albeit in the light of and depending on one’s own history with the associated personal and contextual factors.

Another component of the broader empathy construct is personal distress (Batson, 1991), which is adjacent to the concept of emotional contagion. Personal distress is “a self-focused, aversive, affective reaction to the apprehension of another’s emotion (e.g., discomfort or anxiety), such as the distress of a person feeling anxious when viewing someone who is sad” (Eisenberg, 2000, p. 762). In contrast to emotional contagion, in personal distress, the self-other distinction will be present. Moreover, with emotional contagion, the observer experiences the same (“isomorphic”) emotions as the sender, while this is not necessarily the case with personal distress.

Finally, the most mature form of empathy is arguably empathic concern, that is, an other-oriented response that is congruent with the perceived welfare of someone in need (Decety et al., 2012). Empathic concern is also known as sympathy or compassion and thus should be understood as primarily unselfish in nature. Eisenberg (2000) defined sympathy as “an emotional response stemming from the apprehension or comprehension of another’s emotional state or condition, which is not the same as what the other person is feeling (or is expected to feel) but consists of feelings of sorrow or concern for the other” (p. 671-672).

According to de Wied et al. (2010), empathic processing starts with a matching of emotions between the self and the other (‘feeling with the other’), before then proceeding to turn via further cognitive processing into either sympathy (‘feeling for the other’) or personal distress (‘feeling by the other’). These reactions are not dichotomous: some combination of sympathy and personal distress may well occur. Eisenberg (2000) noted in her overview of markers of empathy and prosocial behavior that in normal children and adults, observing another person’s distress is associated with the incitement of prosocial behavior, either via sympathy induced altruism or, in contrast, personal distress-related attempts to reduce one’s own aversive emotional state (such as, for example, in a situation in which one is unable to escape having to deal with the person causing one’s distress).

Joliffe and Farrington (2004) stated that numerous studies support the view that empathy facilitates prosocial behavior, which includes altruistic behavior, and, moreover, that a lack of empathy encourages antisocial or aggressive behavior, insofar as such actions may reflect an inability to appreciate the feelings of others. However, the cognitive components of the empathy construct should not be seen as prerequisites of prosocial or altruistic behavior, as can be inferred from animal-based research. Although humans show greater variation in prosocial or altruistic behavior than other animals, there is compelling empirical evidence

for unselfishly motivated prosocial behavior in non-human primates and other mammals (Yamamoto & Takimoto, 2012; de Waal & Suchak, 2010). Moreover, with respect to psychopaths, we will argue that their deficiency in the affective aspects of empathy does not derive from disturbed cognitive functioning per se (see, for example, Blair, 2008). This will be discussed in detail below.

4 Contextual factors in empathy

A key question in extant literature concerns whether the capacity to experience one's own emotions while perceiving another's is basically context- or state-dependent, that is, whether it is static in nature or, conversely, dynamic and situationally induced? Moreover, are personal characteristics of importance for enhancing both the kind and degree of empathy? Decety (2015), in response to Batson's earlier work, implied that this was indeed the case. Ultimately, he distinguished three dissociable facets of the empathy construct, based on the fact that a motivational facet is dissociable from affective sharing on the one hand and perspective taking on the other, with the latter being regarded as a cognitive component of empathy. This motivational facet is also accepted, at least to some extent, by Fischer and Hess (2017). Despite the aforementioned automatism of mimicking the emotional expression of others, they assumed that there is at least a minimal potential for affiliation between the sender ("expresser") and observer ("mimicker") that is dependent on the shared emotional meaning of the situation. Consequently, this implies that there is an inclination to focus on the other if that is appropriate and preferred in the situation. This tendency is likely to be stronger when an in-group member is involved. However, this does not imply that there is an unrestricted channel involved in processing the components of the empathy construct, as assessments, filters, and inhibitions can all serve to block the expression of empathy if it were maladaptive (de Waal & Preston, 2017). The authors pointed to observations consistent with evolutionary theory that "empathic response is increased by similarity, familiarity, and social closeness" (2017, p. 503). Regarding this theme, we will further use the terms in-groups versus out-groups. To cite an example of in-group versus out-group differences in empathy: contagious yawning that is thought to be related to precursors of the empathy construct is more common in chimpanzees who look at yawning in-group members than when they observe yawning individuals who are unknown

to them (Campbell & de Waal, 2011). So-called in-group preferences include the tendency to exhibit more (facial) mimicry toward an in-group member than toward a person from the out-group (Bourgeois & Hess, 2008; van der Schalk et al., 2011). This might prove beneficial from an evolutionary perspective, insofar as belonging to a social group and being accepted by group members have proven to be fundamental to human life (Kraaijenvanger et al., 2017). In their transcranial magnetic stimulation study, Avenanti et al. (2010) showed that Italian-Caucasian and black-African participants (living in Italy) who watched clips in which pain was being evoked upon the hands of either black or white models exhibited decreased sensorimotor resonance (i.e., a lack of empathic brain response) when the pain was being inflicted upon a model from the other race, compared to when pain was being inflicted upon their own racial group or when violet-colored models were used. The authors concluded that although empathic responses to pain in non-stereotypical strangers can be triggered, this is not the case when observing pain in either members of other races than one's own or in stereotypical out-group members. While racial in-group bias in empathy toward pain was also found by Han (2018), this research showed that despite being mediated by distinct neurological systems, empathic brain activity for same-race or other-race pain appeared to also be related to sociocultural and physical environment factors.

In the field of social conflict management, between-group empathy is paramount, insofar as its impediment or absence is strongly related to indifference toward out-group suffering, diminished helping responses, or even out-group "Schadenfreude" (a German term for taking pleasure in the failure or misfortune of others), which, ultimately, could result in a risk of intergroup aggression (Cikara et al., 2011). From an evolutionary point of view, individuals living in social groups in harsh environments who are experiencing insecure food supplies will develop a flexible empathic neural circuit related to sharing and responding to the suffering of in-group and even out-group members, which is likely to be based more on culturally acquired prejudices than on strictly racial grounds (Chiao & Mathur, 2010). Vanman (2016) pointed toward the reverse relationship between out-group empathy and strong prejudice. That is to say, effective out-group empathic changes can be achieved if participants are trained to adopt a multicultural perspective (i.e., recognizing group differences) as well as when in-group norms regarding out-group empathy become salient. In addition, intergroup communication centered on the expression of empathy, anger, or, for instance, victim-centered apologies can induce and/or improve out-group empathy, and therefore reduce prejudice. Inducing empathy in children (aged 8-13 years), irrespective of how advanced their social perspective skills

were, resulted in equally helpful behavior being shown toward both in-group and out-group members, while in-group preferences prevailed when empathy was not induced (Sierksma et al., 2015). Although there is a relative dearth of knowledge about gender differences in empathy processing, there are some indications that compared to women, men who participated in research in which an economic game was played, showed less empathy toward unfair opponents receiving pain stimuli (Singer et al., 2006).

Given that empathic processing appears to be dynamic in nature, the emergence of both the cognitive and affective components of empathy thus significantly depend on psychological factors (such as, for example, attention and motivation) as well as contextual appraisal of state-, group- and context-variables. This notion was endorsed by Singer and Lamm (2009), who stated in their review that flexible interpersonal and contextual factors are important pillars underlying the dynamics of empathic processing. As explained above, these factors and appraisals are by definition not static in and of themselves, which is to say that dynamic fluctuations in empathic functioning are part of everyday life. In some instances, this is also due to biological conditions, as is the case, for example, with motivation-driven empathic processing, which is temporarily reduced by fatigue or results from the consequences of sleep deprivation or obstructive sleep apnea syndrome (Nelson et al., 2003; Guadagni et al., 2014; Guadagni et al., 2018; Tempesta et al., 2018; Kheirandish-Gozal et al., 2014). Similarly, external, or environmental stressors, such as cold temperatures, can also mediate empathic responses (Luo et al., 2018). Therefore, the dynamically interacting cognitive and affective components of the empathy construct will be described below against the backdrop of these psychological and context variables.

5 Zipping of empathy components: the Zipper model of empathy

Based on our review of extant literature on empathy, we propose the Zipper model of empathy. The purpose of this heuristic model is to shed light on the dynamic and temporal interactive process that drives empathic behavior. Ultimately, it can provide guidance into clinical and scientific practice.

Mature empathy can be regarded as a balanced state resulting from conjointly operating cognitive and affective processes. Since this equilibrium appears to be dynamic, a mature empathic state can thus be said to be

sustained temporarily depending on various influencing forces. Both contextual factors and diverse psychological states (such as, for example, motivation and attention) act as “zipping” forces that direct the bidirectional alterations of the empathy construct. This process is presented in Figure 1.

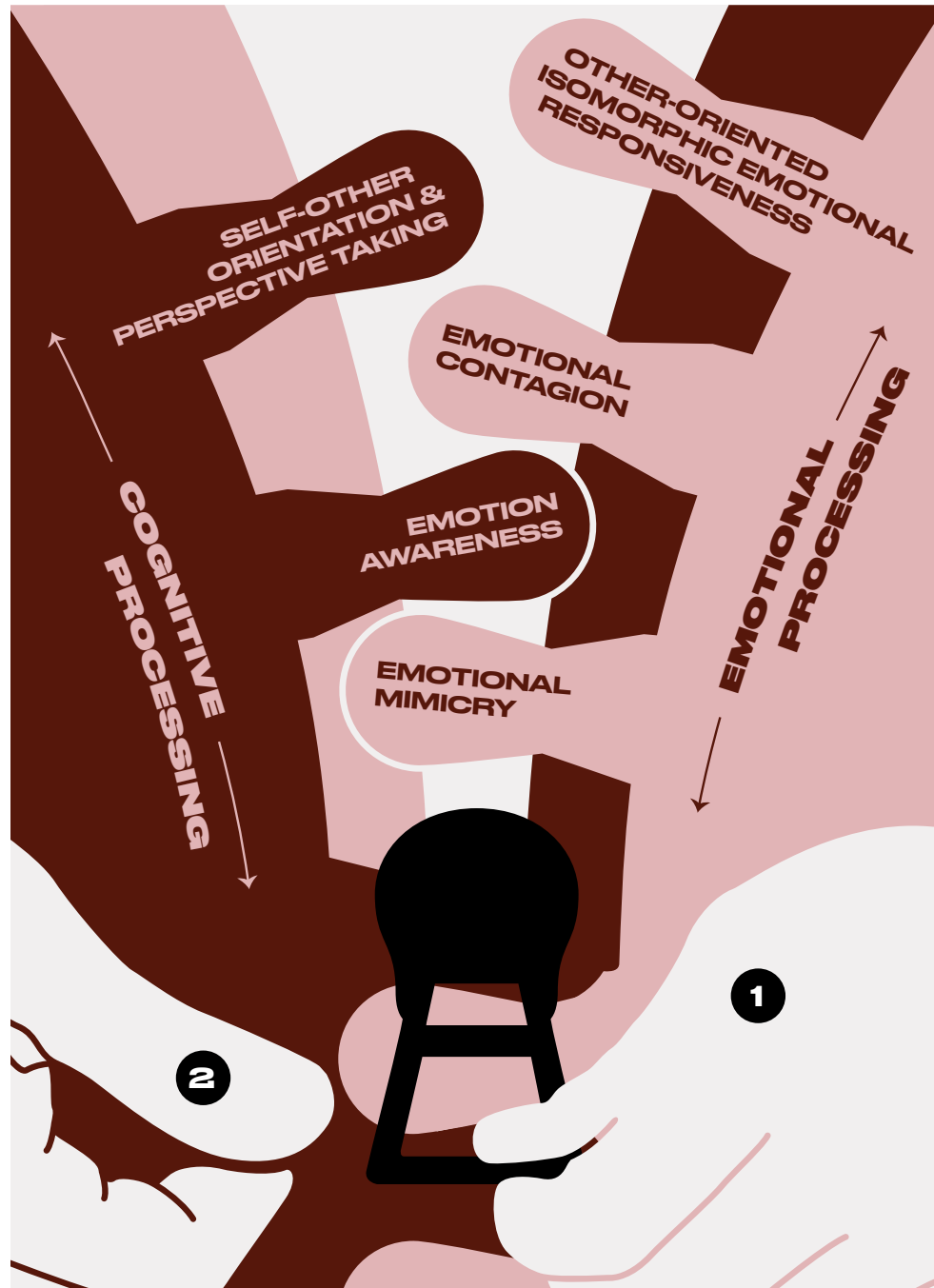
Facial emotional processing (see below) precedes the precursors of cognitive and affective components, such as the aforementioned mimicry and emotional contagion. Note that “zipping up” stands for approaching mature empathy and the expression of empathic behavior, while unzipping entails a looser collaboration between cognitive and affective processes and, as such, symbolizes either a reduction in empathy or its loss altogether.

This zipping process of the empathy components is dependent on the sound development of the neurological apparatus, not to mention personal features and the appraisal of contextual factors. For instance, fatigue or stress-inducing circumstances that alter mood states or cause demoralization might reverse both the direction and strength of the zipping forces, ultimately inducing a significant reduction (by unzipping) in the way that one empathizes with the other. Conversely, one can assume that high intrinsic motivation regarding the other easily paves the way by zipping up toward a mature empathic state. This might be even more the case for in-group members than it is for out-group members, insofar as the latter encounter more barriers to overcome in this zipping empathy process. With respect to psychopaths, we argue below that the zipper teeth that symbolize cognitive processing are present and relatively intact (see also Blair, 2008), whereas psychopaths are known to fall short when it comes to zipping up to mature empathy.

6 Empathy, aggression, and psychopathy

6.1 Aggression and psychopathy

In normal circumstances, aggression is context-dependent wherein species-specific communicative aspects between the aggressor and the opponent play a key role (Haller & Kruk, 2006). On the one hand, aggression can be conceptualized as a hostile reaction to a perceived threat or dangerous situation (Berkowitz, 1983), thus suggesting that it is an impulsive, reactive form of aggression that is relatively unplanned. On the other hand, aggression might



◀ **Figure 1. Zipper model of empathy** Conjointly interacting cognitive and affective components in bidirectional dynamic empathic processing, including mimicry and emotional contagion as precursors of the empathy process. The term emotional responsiveness stems from the work of Feshbach (1997). Fully “zipping up” leads to mature empathic behavior while “unzipping” results in either the hampering of empathic behavior or its disappearance altogether. Both the direction and strength of the zipper forces are dependent on both psychological states (hand 1) and contextual factors (hand 2). From Rijnders et al. (2021a) *Neuroscience and Biobehavioral Reviews*, 131, 1116-1126. Figure used with permission.

also include intentional, goal-directed, premeditated, purposeful, instrumental behavior (Cornell et al., 1996), which is why this latter form of aggression is also referred to as instrumental or proactive aggression. However, both impulsive/reactive and instrumental aggressive elements are not mutually exclusive, as demonstrated by Barratt and colleagues (1999) who found that only 20-25% of aggressive acts could be accounted for by either impulsive/reactive or instrumental aggression alone. Psychopathy is strongly related to engagement in both the impulsive-reactive and instrumental forms of aggression, whereas violent non-psychopaths are unlikely to engage in instrumental violence (Porter & Woodworth, 2006). Moreover, it appears that psychopaths' involvement in instrumental violence and aggression decreases very little with age (Hare, 1999).

There is a vast body of literature pinpointing the links between psychopathic traits and aggressive behavior, such as violent crimes (see Porter & Woodworth, 2006). However, the question of why psychopaths are more likely to engage in instrumental violence is hitherto unresolved. Blair (2001) argued that psychopaths fail to interpret cues of emotional distress in their victims, which could indicate an abnormal cognitive processing. Marsh and colleagues (2013) concluded that adolescents with disruptive behavior disorders and psychopathic (callous-unemotional (CU)) traits experience dysfunction in responding to other's pain, which, in turn, may contribute to their behavioral deficits as observing the pain of others should normally trigger empathic distress in the observer and, consequently, dampen aggression. Similar results were found in children with conduct problems who showed reduced fMRI responses to other people's pain. Those with high CU traits exhibited anterior insula and anterior cingulate cortex responses, which potentially reflects a neurobiological marker for empathy deficits (Lockwood et al., 2013). These results are of paramount importance, insofar as CU traits in adolescence predispose someone to psychopathy in adulthood (Lynam et al., 2007).

6.2 *Are empathy components necessary intermediaries between aggression and psychopathy?*

Notwithstanding the defective affective processing in psychopaths, little is known about their processing of precursors of the empathy construct (i.e., mimicry and emotional contagion). Testimonies of victims describing perpetrators as displaying a cold gaze and unemotional facial expressions during the course of committing their criminal acts are indicative of absent

emotional mimicry and hampered emotional contagion, which, consequently (see Bird & Viding, 2014), may lead to a failure of empathic processing to mature empathy, as also presented in our aforementioned Zipper model (see Figure 1).

Mullins-Nelson and colleagues (2006) found a negative relationship between the affective components of empathy and psychopathy in their community sample, whereas the perspective-taking ability (that is, a cognitive part of empathy) was found to be no different in either psychopaths or non-psychopaths. In contrast with these findings, Fonagy (2003) postulated in adults who lacked the ability to inhibit violent behavior due to either a disturbed or absent mentalization, that is, the capacity to both recognize and attribute mental states to others in different situations by using contextual information that may have evolved from a brain system representing actions that lead to successful social adaptation (Frith & Frith, 1999; Achim et al., 2011). Although mentalizing includes cognitive parts of empathy, it could not be established that psychopathic individuals present a generalized impairment in the cognitive components of empathy (Richell et al., 2003). Several other studies of this kind led Blair (2007) to conclude that there is no evidence-base to suggest that psychopathic individuals are impaired in their Theory of Mind, that is, the cognitive ability to conceive of the mental states of others (Baron Cohen et al., 1985). These mental states include inferences related to “purpose or intention, as well as knowledge, belief, thinking, doubt, guessing, pretending, liking, and so forth” (Premack & Woodruff, 1978, p.515).

According to Dawel and colleagues (2012), impaired empathic functioning in psychopaths stems from pervasive emotion recognition deficits, while Blair (2008) and Blair and colleagues (2001, 2004) highlighted psychopaths' inability to process specific (i.e., negative) emotions. In their fMRI study of psychopaths, Meffert and colleagues (2013) suggested that reduced empathy in psychopaths results from impaired stimulus driven, bottom-up attention to the emotions of others. This biased bottom-up attention could thus be a cofactor in the maldevelopment of moral functioning and social learning seen in psychopaths, as victims' distress will not be automatically detected, thus preventing the incitation of negative emotions that are normally associated with observing distress in others (as is the case in emotional contagion and personal distress; see also §4). This does not necessarily imply a hard-wired neurological defect, but may reflect hypostimulation or the non-stimulation altogether of the zipping forces that lead to empathic behavior (see Figure 1). These forces are significantly dependent on both psychological states and contextual factors. Simply put, in the absence of either interest or motivation to interact with others, psychopaths have a heightened threshold to sufficiently

process other people's emotional stimuli to generate empathic processing toward that person. On the other hand, if psychopaths are genuinely interested in and highly motivated to interact with another person (we assume that this would most likely be a close family member or another in-group member), then the likelihood of building up to empathic behavior increases. This begins with detecting and processing emotional stimuli from the other, which, in turn, will eventually activate the aforementioned precursors of empathy. As demonstrated by our Zipper model of empathy, psychological and contextual factors are paramount to the induction of empathic processing. Notwithstanding this, one should not be blind to the possibility that through exhibiting false interest and antisocial motivations, psychopaths may exclude the affective parts and instead only use the cognitive parts of the empathy process, such as, for example, by displaying emotional awareness, to attain what they want. Obviously, in these instances, mature empathy can never be achieved. Ordinarily, simulating the mental states of others within our own mental mechanisms brings about an intuitive understanding of that other person's mind. According to Blair (2007), in normal circumstances this association is critical for preventing instrumental aggression from evolving, which is in line with his violence inhibition mechanism model (VIM; Blair, 1995). Hence, activating these circuits in a different way might explain, at least in part, the lack of empathy in psychopaths.

Although several studies point to a link between aggression and empathy, it is important to note that what this exact link is remains vague, not least because the aspects of empathy that are studied are not always clearly defined. However, along with impulse control and either prosocial or antisocial tendencies, the cognitive aspects of empathy appear to be a cofactor in behavioral control and, hence, in controlling aggression. While one can also hypothesize that the affective components of empathy play a protective role, its relationship with aggression induction also remains unclear. Furthermore, it is not known whether, and if so to what extent, empathic functions potentially influence either the inhibition or induction of aggressive behavior toward both in-group and out-group members, respectively. According to Blair (2008), the recognition of emotional facial expression is critically important, if not in fact a precondition, for the development of affective components in the empathy construct. This seems to especially be true for psychopaths who “fail to recognize cues that would otherwise lead them to inhibit aggressive behavior by activating the neural networks involved in empathic processing” (Brook et al., 2013, p. 980). In the Zipper model of empathy, this recognition underlies the precursors of empathy, namely mimicry and emotional contagion. Under normal circumstances of genuine interest and motivation and adequate contextual

factors, detecting and processing cues from other people's emotional states will induce these root processes of empathy and, in turn, initiate the processing of cognitive and affective aspects. Given that psychopaths' failure to “build up” mature empathy may derive from either the lack of or incorrect detection of emotional stress signals in their victims, the processing of emotional facial information in psychopaths will thus be discussed in the next two sections.

6.3 *Facial affect information processing in psychopaths*

Patterson and Newman (1993) argued that during their instrumental actions, psychopaths have severe difficulties in switching their attention to initially less salient aversive contingencies as they manifest. These observations formed the basis of the response modulation theory of psychopathy (Newman & Lorenz, 2003). In addition, Baskin-Sommers et al. (2009) found that the PCL-R factor 1 was associated with superior attentional control, that is, a tendency to focus superiorly on primary goals with less attention being paid to secondary stimuli. They concluded that their findings advocated for the response modulation theory of psychopathy, which they eloquently summarized by underlining “that the inhibitory and affective deficits associated with psychopathy reflect a failure to allocate attention to such information rather than a core inhibitory or affective deficit. According to the response modulation model, psychopathic offenders are less likely to suspend an established focus of attention to process peripheral information. Consequently, they are less responsive to affective, inhibitory, and even motivationally-neutral information unless it is an integral aspect of their pre-potent focus of attention. Though this insensitivity to peripheral information is associated with inhibitory deficits, paradoxically a deficit in response modulation may be associated with superior attention control because it entails less responsiveness to peripheral information once a person is engaged in goal-directed behavior” (2009, p. 628). Similarly, Zeier and Newman (2013) found that incarcerated psychopathic men showed selective attention abnormalities when carrying out a modified flanker task, which was in line with the response modulation theory. Hence, psychopaths' actions lack inhibition causing deficient self-regulation in their social interplay with others and society at large.

Given that difficulties in switching attention appear to be important for psychopaths' goal-directed behavior, this raises the question of whether attention deficits form the basis of facial recognition deficits in psychopathy,

and if so, to what extent. As stated by Blair (2001), several studies with psychopaths have shown selective deficits in interpreting emotional stress signals from their victims, thus meaning that they are impaired in processing fearful, sad and, possibly even, disgusted facial expressions. No impairment in the processing of angry, happy, or surprised expressions was reported. Blair and colleagues (2004) found a lower overall affect recognition in highly psychopathic prisoners compared to those with lower levels of psychopathy, but, most notably, significant group differences in recognizing fearful expressions. Harris and Picchioni (2013) agreed that Blair's findings do indeed lend some support to the aforementioned VIM model (Blair, 1995), wherein a disturbance in recognizing distress cues fear and sadness is associated with disruptive social cognition and reduced violence inhibition. In accordance with Blair's previous findings, Marsh and Blair (2008) found in their meta-analysis robust impairments in recognizing fearful, sad, and surprised expressions, but not in terms of recognizing happiness, anger, or disgust. In his integrated emotion systems model, Blair (2005) postulated that these significant recognition deficits arise from amygdala dysfunction. The latter prevents psychopaths from associative learning in the conditioning process of conditioned stimuli interacting with unconditioned stimuli like fearful and sad expressions. This results in empathy deficiencies and socially inappropriate behavior toward the other (we discuss amygdala dysfunction further in the next section). The meta-analysis by Dawel and colleagues (2012), however, partially contradicted Blair's conclusion regarding selective deficits of psychopaths in emotion signaling, as they described pervasive emotion recognition deficiencies related to all six basic emotional expressions (fear, anger, happiness, sadness, disgust, and surprise). Further evidence for a possible relation between psychopathic traits and emotional recognition deficits came from both Habel and colleagues (2002) and Cigna and colleagues (2017), who found that impaired facial emotion discrimination was related to PCL-R factor 2, whereas PCL-R factor 1 was positively correlated with increased performance in facial emotion discrimination. According to both groups of authors, this positive correlation could be explained in terms of heightened desire and the ability of psychopaths to manipulate those around them by correctly interpreting the emotional expressions in their faces. The Zipper model of empathy explains that although psychopaths may correctly interpret emotional expressions of other people and, as such, have the cognitive zipper teeth available, the problem is that the affective zipper teeth do not (fully) interact, as no emotional contagion is processed. As described above, it is also imperative that empathy-building forces such as motivation are present (see the dissociable motivational facet as

described by Decety, 2015 and the minimal potential of connection and shared emotional meaning mentioned by Fischer & Hess, 2017). In other words, the Zipper model's cognitive teeth do not falter, but the affective teeth do, and, moreover, the psychological state is too weak as a driving force to eventually build up to mature empathetic behavior.

All the abovementioned studies showed evidence for a relation between (either general or specific) emotion recognition deficits and psychopathic traits. However, not all of the results from these studies are wholly convincing. Harris and Picchioni (2013) mentioned in their review three studies that showed impaired facial emotion recognition in psychopathic patients (Munro et al., 2007; Hastings et al., 2008; Blair et al., 2004). On the contrary, in three other studies that they reviewed (Richell et al., 2003; Dolan & Fullam, 2004; Glass & Newman, 2006), no differences in emotion recognition accuracy could be established between high and low psychopathy ratings. Harris and Picchioni (2013) also noted that some of the methodological inconsistencies between the studies cited also prompted cautious interpretation of the findings. Pham and Philippot (2010) found that criminal non-psychopaths showed greater accuracy in terms of decoding happiness, anger, and disgust in comparison to criminal psychopaths, while no group differences were established for sadness and fear. According to these authors, these results were in contradistinction to Blair's hypothesis regarding amygdala dysfunction (Blair et al., 2001). Rather, they suggested that distinct research findings related to decoding facial expressions of sadness and fear in psychopathy could be explained by the different populations that were studied.

Brook and colleagues (2013) reviewed eleven facial recognition studies in psychopathy and concluded that there was no consistent evidence for either the general emotional processing deficit perspective or the specific emotional processing perspective. The general emotional processing deficit implies an overall reduced capacity to process emotional expressions across the emotional spectrum, which in fact parallels the above conclusions of Dawel and colleagues (2012). In contrast, the specific emotional processing deficit only involves a reduced capacity for specific types of emotions. The latter perspective is consistent with the aforementioned VIM model that describes recognition deficits for sadness and fear (Blair, 1995). Moreover, Brook and colleagues (2013) noted that most of the studies addressing emotion processing ignored anxiety as a co-factor. They supported Newman's argument that research on cognitive deficits in psychopathy should include a measure of trait anxiety, because low-anxiety vs. high-anxiety traits may well be important in disentangling mechanisms of emotional deficits in psychopaths.

As aforementioned, extant literature on facial recognition in psychopathy presents rather contradictory results, not least due to the multitude of methodological issues in the various study designs. For example, Koenigs and colleagues (2011) emphasized the heterogeneity of the research data of the different populations studied, which often consisted of difficult-to-compare groups of psychopathic patients, psychopathic non-patients, and persons with psychopathic characteristics who do not fully meet the criteria for a psychopathy diagnosis. Furthermore, significant discrepancies in diagnostic procedures between the study groups might also lead to diagnostic bias in the level of estimated psychopathy. The authors also warned that because of such variations in the research data, the brain regions associated with these characteristics could be easily misidentified as dysfunctional brain regions thought to be involved in psychopathy. Moreover, research data on emotional deficits cannot be automatically generalized outside of Caucasian psychopathic male offender samples to, for example, African American psychopathic offenders, or even to female samples (Brook et al., 2013). Both level of intelligence and duration of educational training also often remain underexplored in different studies, despite research showing that they are clearly associated with emotion recognition results (Pham & Philippot, 2010; Igoumenou et al., 2017). It should also be noted that the picture complexity of the presented stimuli is another complicating factor (Sadeh & Verona, 2012) that might lead to difficulties in comparing the different studies. Using difficult-to-compare stimuli (be it facial expressions or non-facial expressions) in the different studies can also serve as a methodological barrier, while the emotional intensity of the triggers portrayed also differs across the studies. For example, artificially morphed expressions of different facial emotions can result in fake emotional expressions of the faces displayed (Krumhuber et al., 2013). Calvo and colleagues (2018) advocated for the use of dynamic facial expressions rather than static expressions, as the former have more of an impact upon those brain regions believed to be related to the processing of social-relevant and emotion-relevant information. Furthermore, the use of colored facial expressions instead of non-colored expressions influences emotion recognition, while there are also different detection thresholds for different emotions (Calvo et al., 2016). Moreover, Brook and colleagues (2013) suggested that psychometric artefacts of tests with diverse discriminating power might yield different results when assessing positive and negative facial emotions; for example, good performances in identifying facial happiness may be related to lower test sensitivity rather than a normal capacity in identifying positive emotions.

6.4 *Amygdala functioning and facial affect information processing in psychopaths*

According to Dadds and colleagues (2011), amygdala dysfunction is associated with psychopaths' impaired ability to detect and attend to the human eye region. However, despite various neuropsychological and neuroimaging studies (see, for example, Blair's overview, 2005 and 2008), extant literature on psychopaths' amygdala anatomy and dysfunctionality remains inconclusive. The general idea is that a psychopath's amygdala is less reactive to emotional events, in turn, leading to emotionally callous behavior, and thus blocking the "building up" to mature empathic behavior. From this perspective, the amygdala directs attention automatically toward emotional stimuli, like facial expressions, especially in the eye region, thereby providing emotionality to one's behavior. However, this perspective fails to explain why the blunted emotional reactivity of psychopaths (Baskin-Sommers et al., 2011; Newman et al., 2010) and their blunted empathy (Meffert et al., 2013) can be resolved when the emotional stimuli lines up with their own self-interest. In accordance with our Zipper model of empathy, this suggests that a motivational component might be at work here. Indeed, a lack of automatic attention due to motivational factors may very well result in a "downstream" face recognition deficit. The response modulation theory of psychopathy (Newman & Lorenz, 2003) predicts that even when psychopaths are remotely aware of peripheral information, they nevertheless tend to ignore this information that is of secondary interest to them, while, simultaneously, being overwhelmingly attracted to achieving their primary goal. This tendency to ignore contextual information might thus reflect that emotional processing deficits are preceded by a motivational impairment (Baskin-Sommers et al., 2009). Interestingly, recent theories of amygdala functioning are beginning to emphasize its role in motivation as well as in psychopathy (Moul et al., 2012).

Importantly, the amygdala is not a single brain structure, but rather a heterogeneous collection of nuclei, with animal models showing that an interplay of the basolateral (BLA) and central (CeA) subregions of the amygdala not only determines the level of emotional reactivity (Terburg et al., 2018), but also influences goal-directed motivation at the level of the striatum and prefrontal cortex (Balleine & Killcross, 2006). Simply put, while the CeA promotes automatic emotional reactivity and general motivation, these tendencies can be modulated by the BLA in favor of more instrumental goal-directed motivation and behavior. In other words, when the current goal does not align with the automatic emotion reactivity, then the BLA can reduce the latter to promote instrumental action.

Although research in humans has only recently started to investigate this mechanism, studies confirm that the integrity of the BLA is necessary to control emotional reactivity in favor of goal-directed escape (Terburg et al., 2018). Furthermore, the BLA is necessary for both learning and expressing calculative actions to yield maximum rewards at the expense of others (Rosenberger et al., 2019; van Honk et al., 2013). In line with this, psychopaths' BLA shares increased functional connectivity with frontolimbic structures like the striatum, anterior cingulate cortex, and prefrontal cortices, while the psychopaths' functional connection between the CeA and such frontolimbic structures is reduced (Aghajani et al., 2017; Yoder et al., 2015). When viewed together, this suggests that the goal-directed behavior of psychopaths is relatively more strongly driven by instrumental motivation from the BLA and less affected by the automatic affective processing from the CeA. When the goal and emotion align, however, psychopaths might be perfectly capable of utilizing the CeA's emotionality. This motivational interpretation of amygdala functioning in psychopathy can therefore explain why psychopaths have blunted emotional reactivity and empathy in general, but not when these emotions are in alignment with their own self-interest. This is consistent with the findings of Meffert and colleagues (2013) that showed that there is no hardware problem in this respect, but rather that the problem is largely motivational, and, as such, can be manipulated by instruction or rewarding circumstances. It is also in line with the response modulation theory of psychopathy (Newman & Lorenz, 2003), which explains why psychopaths with their superior attentional control are less responsive to affective facial information unless it is an integral aspect of their pre-potent focus of attention. In terms of our Zipper model of empathy, then, if it helps psychopaths to achieve their goals, they can "zip up" parts of the empathy concept and thus come across as charming and empathic toward others. However, due to their assumed lack of experience of regularly "building up" mature empathic behavior, they will likely do this in a clumsy and not entirely credible way, as the "use it or lose it" paradigm implies.

7 Conclusions

Empathy is a multidimensional construct with cognitive, affective, and behavioral characteristics and can be symbolically interpreted as the social glue in society that binds human beings. Empathic processing is primarily shaped and maintained by constant mutual communication between the perceiver and the outside world and is based on the combination of appraisal of contextual variables and intrapsychic aspects, such as attentional and motivational factors. We propose a Zipper model of empathy in which mature empathic behavior can be regarded as a dynamically balanced state resulting from conjointly operating cognitive and affective processes that "zip up" toward empathic behavior. Against the background of neurodevelopmental underpinnings, both zipper direction and zipper strength depend on intrapsychic conditions and contextual factors (see Figure 1). This balance, by definition, persists only temporarily and can be reversed by "unzipping," resulting in reduced expression of empathic behavior.

The purpose of this article was to shed light on the empathy components in psychopathy and, subsequently, how facial affect processing substantiates empathy deficits in psychopathy. Although not exclusive, one of the main channels of communication between conspecifics involves the processing of facial affect information. In this respect, extant literature on facial recognition in psychopathy shows rather contradictory results, namely because the research of different groups is difficult to compare due to manifold methodological issues in the various study designs. Despite these methodological problems and often conflicting results (see also Chapman et al., 2018), there are nevertheless strong indications that facial emotion recognition deficits in psychopaths exist. Whether these consist of general deficits or specific deficits is not yet proven, but we argue that psychopaths' drive to reach their own goals comes at the cost of the automatic emotional processing needed for efficient facial affect processing. This concept furthermore touches upon the idea of psychopaths' preferential unwillingness to engage with or attach to other people, especially when they are out-group members. In such a state of basic disinterest and lacking motivation, psychopaths tend to ignore people and thereby fail to explore people's emotional facial expressions, as can be deduced from the study by Boll and Gamer (2016), who found reduced face exploration and reduced gaze bias for the eye region in participants with high psychopathic traits, while the accuracy of emotion classification was not linked to psychopathic features. Consequently, psychopaths will also fall short in inducing the precursors of the empathy construct (mimicry and emotional contagion) and, therefore, in "zipping up" parts of the empathy

concept as they do not automatically share an understanding or emotional meaning with other people whom they deem to be of secondary interest. Indeed, psychopaths' primary interest lies in pursuing their own goals, thus effectively reducing their automatic emotional reactivity in favor of goal-directed motivation, a process that is heavily supported by BLA preponderance over the CeA subregion of the amygdala. In contrast, variables related to in-group members or other important contextual information can motivate psychopaths to deliberately focus on certain people, which, in turn, increases the attention paid by psychopaths to the emotional expressions of others. This might increase the likelihood of mimicry and emotional contagion occurring, which are known to be precursors of the cognitive and affective empathy components that “zip up” in the direction of empathic behavior. In this sense, we believe no substantiated arguments exist as to why amygdala dysfunction and superior attentional control (as predicted by the response modulation theory of psychopathy; Newman & Lorenz, 2003) should mutually exclude each other.

As argued above, according to the Zipper model of empathy, the zipper teeth that symbolize cognitive processing are present and relatively intact, whereas psychopaths are known to fail in “zipping up” to mature empathic behavior. This should come as no surprise, as affective components (symbolized by affective zipper teeth) are equally important in achieving mature empathic behavior, and thus it is very likely that this is where psychopaths' empathy deficits mainly lie, even when they pursue it: namely, a downregulated or even absent affective capacity.

Based on the abovementioned methodological, diagnostic, and procedural limitations of emotion recognition research, we believe that future research into psychopathy should include well-defined groups of PCL-R confirmed psychopaths. Clear descriptions of their ethnic and educational background, assessments of their intellectual functioning and state measures of stress (anxiety and mood), alongside clarification over either their non-forensic or forensic status (e.g., type of offenses, patient versus non-patient detainee) should be provided. Preferably, PCL-R assessed psychopathic women would also be included in future research. Test procedures should at the very least also include dynamic expressions of emotional expressions from protagonists from different ethnicities and genders. In particular, we welcome emotion recognition research in psychopaths that using stimuli from both in-group and out-group protagonists. As we argued in sections 4 and 5 regarding the Zipper model of empathy, intrapsychic factors such as attention and motivation are of great importance in the zipping process that builds up to mature empathy. The same considerations also apply to emotional stimuli that are related to psychopaths' current and prior living environments, as the Zipper model also defines contextual factors as being of significance.

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Chapter 3
Designing a neuroclinical
assessment of empathy deficits
in psychopathy based on the
Zipper Model of Empathy

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Abstract

The heterogeneity of the literature on empathy highlights its multidimensional and dynamic nature and affects unclear descriptions of empathy in the context of psychopathology. The Zipper Model of Empathy integrates current theories of empathy and proposes that empathy maturity is dependent on whether contextual and personal factors push affective and cognitive processes together or apart. This concept paper therefore proposes a comprehensive battery of physiological and behavioral measures to empirically assess empathy processing according to this model with an application for psychopathic personality. We propose using the following measures to assess each component of this model: (1) facial electromyography; (2) the Emotion Recognition Task; (3) the Empathy Accuracy task and physiological measures (e.g. heart rate); (4) a selection of Theory of Mind tasks and an adapted Dot Perspective Task, and; (5) an adjusted Charity Task. Ultimately, we hope this paper serves as a starting point for discussion and debate on defining and assessing empathy processing, to encourage research to falsify and update this model to improve our understanding of empathy.

1 Introduction

The ability to empathize is a highly valued characteristic, which has initiated a wide range of research for conditions in which it is reduced, like psychopathy (e.g., Viding et al., 2014), callous-unemotional traits present in conduct disorder (e.g., Blair et al., 2014), autism (Song et al., 2019) or alexithymia (e.g., Krystal, 1979; Williams & Wood, 2010). Despite this, clear and consistent definitions have not yet been derived, resulting in problems of ‘same words: different concepts’ and ‘different words: same concept’. For instance, Cuff and colleagues (2016) provide a list of forty-three discrete definitions and conceptualizations of empathy, whereas terms such as “emotional recognition” and “emotional awareness” are poorly, if at all, distinguished. This leads to problems in both research, such as comparing studies that use the same concepts yet defined differently, and clinical practice, with therapeutic difficulties arising when concepts are understood differently (Cuff et al., 2016). To this end, we propose a neuroclinical assessment battery based on the Zipper Model of Empathy (Rijnders et al., 2021), using a multi-method psychoneurometric approach where neurophysiological variables are incorporated with psychological assessments (Iacono, 1991; Patrick et al., 2019). We hope that this approach may elucidate in which way empathy deficits may be seen in various conditions and disorders. The model may also provide an additional framework for interpreting the burgeoning neuroimaging literature on empathy.

1.1 *Affective and cognitive processes of empathy*

Empathy is often defined as a multidimensional construct that results from conjointly operating cognitive and affective processes, such as Feshbach’s (1997) Integrative Cognitive-Affective Model of Empathy (Adriaense et al., 2020; Cuff et al., 2016; Walter, 2012). These can be likened to “cognitive empathy” and “affective empathy” respectively. More specifically, these processes are underlying factors that contribute to empathic behavior, rather than being synonymous with the end result, i.e. empathic behavior. Indeed, on the one hand, empathic behavior requires the ability to understand another person’s feelings (Walter, 2012), which employs cognitive processes bearing similarities to Theory of Mind (Baron-Cohen et al., 1985) and mentalizing (Bateman & Fonagy, 2010). On the other hand, empathic behavior also requires the experience of

emotion (Cuff et al., 2016; Walter, 2012), which employs affective processes. Furthermore, research on personality and developmental disorders concur with this suggestion. For instance, adults with autism spectrum disorder often show cognitive empathy deficits and average affective empathy (Baron-Cohen & Wheelwright, 2004; Song et al., 2019), whereas adults with psychopathy show the opposite pattern (Blair, 2005). Although these affective and cognitive processes are distinct, total separation has not been supported due to their extensive interaction (Cuff et al., 2016). Indeed, mature empathy, that is appropriate empathic behavior, emerges from the interaction of the cognitive and affective processes (e.g., Feshbach, 1997).

1.2 Contextual and personal factors

Empathy maturity depends on different internal and external contextual factors. An example of an internal factor is motivation. Mature manifestations of empathy (i.e., more complex than automatic mimicry) may be dependent on positive motivation (Decety, 2015; Fischer & Hess, 2017), such as whether the goals of the person align with the present activity. Indeed, the Response Modulation Hypothesis proposes that highly psychopathic individuals behaviorally demonstrate a deficit in Theory of Mind (ToM) when the goals of that individual do not align with that of the activity, but demonstrate intact ToM when these goals align (Patrick, 2022). Here, such highly psychopathic individuals behaviorally demonstrate less mature empathy because of a lack of motivation, as well as attention (e.g., Newman & Lorenz, 2003; Patterson & Newman, 1993). Alternatively, in-group versus out-group membership serves as an example of an external contextual factor. Indeed, empathic responses are more prominently elicited when observing in-group members than out-group members (e.g., Avenanti et al., 2010; Han, 2018), such as the tendency to show more (facial) mimicry towards in-group members compared to out-group people (Bourgeois & Hess, 2008; van der Schalk et al., 2011); though efforts to increase empathy processing reduces this external contextual factor (Sierksma et al., 2015). Given the impact of these personal and external factors for empathy maturity, there is an evident need to find ways to include these factors when clinically assessing empathy.

1.3 The Zipper Model of Empathy

Based on a review of the literature on empathy, namely highlighting these aforementioned facets of empathy, Rijnders and colleagues (2021) proposed the Zipper Model of Empathy (Figure 1). They described mature empathy as a balanced state achieved only from conjointly operating cognitive and affective processes, as well as both internal and external factors. As indicated by the name of the model, these internal/external factors act as “zipping forces”; zipping together (“zipping up”) the cognitive and affective processes to achieve mature empathy, or zipping apart (“zipping down”) these processes, hampering empathic behavior.

The Zipper Model of Empathy consists of a number of states, or levels, of empathic maturity. At the bottom of the model is facial Emotional Mimicry, the simplest manifestation of empathy – an automatic motor muscle response mirroring emotions facially displayed by another person, and can be seen as a precursor to empathy. Zipping up, the next level is Emotional Awareness – the mostly preconscious awareness of what another is emotionally feeling. Zipping up further reaches Emotional Contagion – the elicitation of an emotional reaction in oneself that is of similar intensity and quality to that expressed by another person. Beyond this is Self-other Orientation and Perspective Taking, the ability to understand and focus on another individuals’ point of view - much like ToM (Baron-Cohen et al., 1985) and mentalizing (Bateman & Fonagy, 2010). Finally, empathic maturity is reached with Other-oriented Isomorphic Emotional Responsiveness, the emotional state allowing for the expression of mature empathic behavior directed towards others and at the same time congruent with the perceived welfare of that other person.

To illustrate the different states of this model, take the following fictional situation. Mary, a lawyer, and John, her first-year undergraduate intern, have been defending Peter, their client, for the past five months. Today, while testifying, Peter started to cry. Seeing this, as an initial, spontaneous, and non-conscious reaction, Mary and John scrunch up their faces in a similar way to Peter (emotional mimicry). Furthermore, both immediately noticed how sad and pained Peter looked, identifying his emotion as that of sadness and pain (emotional awareness). As Peter continues his testimony while crying, John the inexperienced intern feels a pang of pain and deep sadness, and starts to cry quietly (emotional contagion), whereas Mary, the seasoned attorney who has seen so many such cases that she has become habituated to such behaviors, does not emotionally react as intensely as John. John, who whole-heartedly believes Peter’s story, understands that his emotional reaction comes from a place of desperation, by automatically

putting herself into Peter's shoes. Mary, on the other hand, is concerned with the facts and the law, and thus does not automatically put herself into Peter's shoes (self-other orientation and perspective taking). Finally, when Peter broke down sobbing furiously, John, who went through all the previous states of emotional empathy, stands up with the intent to rush to Peter's side to comfort him with a hug (self-other isomorphic emotional responsiveness). However, he is prevented from doing so by Mary, who does not go to comfort his client for a number of reasons. First, she did not reach the state of self-other and perspective taking, which the Zipper Model of Empathy proposes to be necessary to reach the state of self-other isomorphic emotional responsiveness. Furthermore, she knows that, given the current situation and his professional role, it would be highly inappropriate to act in such a way now, even if the act would be emotionally congruent to Peter's emotional status. Finally, given her reputation as a disciplined and stoic attorney, it does not serve Mary's professional image to immediately emotionally comfort his clients when they cry in court.

1.4 Testing the Zipper Model in the clinical context

In this paper, we propose a battery of measures selected to assess each element of the Zipper Model of Empathy for two reasons. First, we hope to inspire attempts to test the proposed Zipper Model and discussion about the problems of defining and assessing the empathy construct. We do not aim to propose final answers to these problems, but rather want to provide starting points for discussion and development of strategies of assessment. Therefore, using this model built entirely on the literature of empathy, we propose a neuroclinical assessment to assess a model based entirely on existing literature designed to be thoroughly tested, falsified, and updated based on future scientific research.

Second, given the importance of empathy in many mental health conditions observed in clinical and forensic practice, the proposed battery of measures provides a method to assess both the cognitive and affective processes of empathy at different states of empathic maturity. The results could help better inform decisions made in clinical settings (e.g., selecting treatment programs). Note however that though we propose some methods to compensate for differences between individuals in personal and external factors, not all of these can realistically be controlled for, which means that the suggested battery of measures does not entirely examine the contextual and personal factors of empathy, which are also necessary for the zipping process.



▲ **Figure 1. Zipper model of empathy** Schematic representation of the Zipper Model of Empathy, where cognitive and affective components interact together to allow for bidirectional dynamic empathic processing, including empathic states such as emotional mimicry and emotional contagion. Psychological states (hand 1) and contextual factors (hand 2) act (both in strength and direction) as zipper forces, where fully “zipping up” leads to mature empathic behavior, while “zipping down” hampers, if not outright eliminates empathic behavior. From Rijnders et al. (2021a) *Neuroscience and Biobehavioral Reviews*, 131, 1116-1126. Figure used with permission.

2 Methodological proposal

2.1 Tools for the individual components

The tasks discussed in this review were identified through a non-systematic literature search with the objective of identifying existing methodologies that assess and target empathy at the different levels of the Zipper Model of Empathy.

2.1.1 Emotional mimicry

Facial Emotional Mimicry is an automatic motor muscle response that mirrors the emotions facially displayed (non-verbally) by another person (Hess & Fischer, 2014). In other words, this is the emotion-specific dimension of facial mimicry, which is restricted to just automatic facial muscle responses. It is currently understood that, during emotional mimicry, the valence of the displayed emotion is mirrored (Eisenbarth et al., 2011; Neumann et al., 2005), while the arousal of the displayed emotion can increase mimicry motor intensity (Fujimura et al., 2010). In the example above, Mary and John scrunching up their faces similar to Peter.

To measure motor muscle responses as the physiological manifestation of emotional facial mimicry (specifically valence), we propose using facial Electromyography (EMG). Described as “the current psychophysiological gold standard of measuring emotional valence” (Höfling et al., 2020, p. 1), facial EMG can measure the activation of facial muscles, such as, the corrugator supercilii or zygomaticus major muscles using electrodes, from which emotion processing is inferred: corrugator activity increases with unpleasantness (e.g., sadness and anger) and decreases with pleasantness (Hess & Blairy, 2001; Rymarczyk et al., 2011; Wolf et al., 2005), while the zygomaticus is selectively activated in pleasant states (Baur et al., 2015; Sato et al., 2008) and tends to decrease in unpleasant states.

We also considered using Automatic Facial Coding tools developed by various companies (e.g., Affectiva - Humanizing Technology, n.d.; iMotions, n.d.), as they present a few important advantages, namely that these automatic tools are simpler to install and use in daily practice: they do not require electrodes, only a laptop camera, and require less expertise to process the data. However, this type of software presents a number of limitations compared to facial

EMG. For instance, these tools performed poorer for negative valence and inhibited facial expressions (Höfling et al., 2020, 2021). Furthermore, although it achieves acceptable reliability with standardized prototypical images of facial expressions (e.g., Lewinski, 2015), as well as simulated facial expressions (e.g., Kulke et al., 2020), iMotions software performs worse with naturally expressed facial emotions, notably fearful faces (Stöckli et al., 2018). Given the above, we argue that these validity limitations of Artificial Intelligence based software outweigh the practical limitations of EMG for measuring emotional mimicry.

To measure facial emotional mimicry using EMG, we propose the following methodological procedure. Once set up with the EMG electrodes, participants are presented a collection of short video clips, where a protagonist portrays a neutral facial expression, before expressing one of different emotional expressions (e.g., van Boxtel et al., 2022). During each trial, the participant’s facial muscle activity is recorded by the EMG. Participants could also complete a secondary distractor task, such as recalling the identities of the protagonist. Note that this distractor task should not relate to higher levels of empathy, as the activation of higher level processes could interact with the spontaneous reactivity.

It should be noted that certain populations tend to show lower responses to such emotional mimicry tasks, though different studies use different and incompatible research strategies and methodologies. For instance, Deming and colleagues (2022) failed to elicit emotional facial mimicry across individuals from an incarcerated sample independent of psychopathic traits. Furthermore, van Boxtel and colleagues (2022) found reduced emotional mimicry using EMG specifically in conduct disordered youth with callous-unemotional traits (CU traits), which is thought to be a precursor for psychopathy in adulthood (see Frick & Morris, 2004). However, Künecke and colleagues (2018) found facial mimicry responses in their samples, but specific deficits in highly psychopathic offenders compared to non-offenders. We are proposing to investigate this further in large and forensic samples with a consistent methodology.

Another notable example of individuals that may show different responses in this task are those with autism spectrum disorders (ASD). Indeed, in comparison to healthy participants, ASD participants do not show spontaneous mimicry when watching pictures of happy and angry expressions (McIntosh et al., 2006) or show delayed responses (Oberman et al., 2009). However, these differences between ASD and non-ASD participants disappeared during voluntary mimicry activity, and tasks that encourage spontaneous mimicry (e.g., by adding sound) further diminished spontaneous mimicry differences between ASD and non-ASD participants (Magnée et al., 2007). Therefore, it might be of interest to manipulate spontaneous versus voluntary emotional mimicry with specific instructions.

In sum, we propose to measure spontaneous emotional mimicry using facial EMG. Despite the required expertise, other tools to date do not grant the accuracy this measure provides. As certain populations encountered in the forensic setting may present limited spontaneous emotional mimicry, tools with low margins of error are most desirable. Furthermore, as a part of a larger battery of measures to test the Zipper Model of Empathy, more data on spontaneous mimicry could be gathered, at least to replicate previous studies. Finally, as certain populations demonstrate low, or even negligible, facial mimicry, it would be of interest to examine whether these populations can “zip up” by aligning their goals with that of the study (i.e., identify the emotion expressed), or misaligning the goal (e.g., by remembering the identities of the actors).

2.1.2 *Emotion Awareness*

Emotional Awareness is defined as the mostly preconscious awareness of what another person is emotionally feeling. In the example above it is represented in Mary and John noticing Peter’s sadness and pain. To measure Emotional Awareness, we suggest measuring how accurately the individual can name what emotion another person is feeling or expressing. To do so, we considered two assessment methods. First, the Emotion Recognition Task paradigm (Montagne et al., 2007), and second, the Levels of Emotional Awareness Scale with Ecological Momentary Assessments (Versluis et al., 2021).

In the Emotion Recognition Task (ERT), participants are presented with videos of emotionally expressive faces, and are tasked with identifying the expressed emotion from a selection of six expressions: happy, angry, disgusted, sad, surprised, and fearful (Kessels et al., 2014; Montagne et al., 2007). Note that, instead of static facial picture stimuli, dynamic facial stimuli are preferable, as facial emotions are more often expressed in a dynamic way (Calvo et al., 2016, 2018; Kamachi et al., 2013), and the use of dynamic facial stimuli is further associated with a superior categorization rate of emotions compared to static stimuli (Fiorentini & Viviani, 2011; Wehrle et al., 2000). In Kessels’ and Montagne’s studies, a computer software was used to create an animation of the protagonist’s face morphing from a neutral expression to a fully expressive emotional expression. Thus, the authors could vary the final intensity of the expressed emotion by ending the morphing animation at a ‘state’ between 0% and 100% - the closer to 100%, the more intense the emotional expression. Note that while the original version (Montagne et al., 2007) presented the face

stimuli in morph states between 20% and 100% at 10% increments (resulting in nine different stimuli per emotional expression per face), the short form of this task (Kessels et al., 2014) used the morph states 0%, 40%, 60%, 80%, and 100%. While this approach offers the advantage of examining the relationship between expression intensity and expression identification, morphed expressions make a somewhat unnatural impression that is picked up by viewers (Bernstein & Yovel, 2015; Calvo et al., 2016; Krumhuber et al., 2013). Therefore, short dynamic film clips with naturalistic emotional expressions could be used instead, such as those used by Calvo and colleagues (2016) or de Wied and colleagues (2012).

The Levels of Emotional Awareness Scale (LEAS; Lane et al., 1990) is frequently used to measure Emotional Awareness (Versluis et al., 2021). The LEAS presents 20 hypothetical two-person social encounters where participants are instructed to describe what emotions they think they would feel in each scenario, and the feelings of the other person. Greater complexity in the described emotional experience is associated with higher levels of emotional awareness. However, as emotional awareness varies over time, Versluis and colleagues (2021) adapted the LEAS using Ecological Momentary Assessments (EMAs). In their study, participants would complete six EMAs per day for two consecutive days. In each EMA, participants were instructed to describe their current or most recent social interaction (online/offline), and were asked to describe how they felt during that social interaction, as well as indicate how the other person (or the most significant person to the participant) felt during the social interaction. Participants would complete these EMAs using their smartphone devices, and responses are scored using the LEAS scoring system, thereby collecting emotional awareness data from different social interactions over a period of time.

Between these two assessment strategies, we believe that the ERT is more appropriate, more specifically its short form, given its shorter administration time. Indeed, as already mentioned, the ERT presents dynamic stimuli through using both morphs and video clips of facial expressions. These two stimulus types offer unique advantages: while morphs allow for greater control in emotional state expression, thereby collecting finer grained data at the cost of experiment length, video-recorded facial expressions are more naturalistic than morphs. Furthermore, the ERT would be standardized between participants but only across different institutions, unlike using the LEAS with EMAs, which would describe too many different social interactions and parameters to the point of poor standardization. Furthermore, there is concern that forensic patients would not follow through such a long data collection procedure but are typically able to complete clinical tests over a short period of time. Therefore, although

both have their advantages, we come to the conclusion that the ERT paradigm is more appropriate for this context.

The Emotional Recognition Task has been validated with various clinical populations, including bipolar disorder (Gray et al., 2006), post-traumatic stress disorder (Poljac et al., 2011), schizophrenia (Scholten et al., 2005), and ASD (Smith et al., 2010). However, certain populations appear to make consistent within-group errors. For instance, individuals with schizophrenia appear to be less accurate in recognizing fearful and angry facial expressions (negative expressions), and make more fear-as-anger misattributions, compared to healthy controls (e.g., Kucharska-Pietura et al., 2005; Premkumar et al., 2008). However, Larøi and colleagues (2010) instead observed that schizophrenic patients were only significantly worse in identifying happy and surprised faces compared to healthy controls.

As for youth who have offended and youth with conduct problems and CU traits, these individuals have problems in recognizing negative emotions specifically (Bowen et al., 2014; Woodworth & Waschbusch, 2008). Note that, in some cases, these difficulties in negative emotion recognition might be linked with how much the young person attends to the person's eyes. Indeed, Dadds and colleagues (2011) found that, in male youth with Conduct Disorder and CU-traits who showed an impairment in eye contact as well empathy deficits, the latter could be reversed by asking them to look at the person's eye region.

As for individuals high on psychopathy, findings are mixed, with some studies observing impaired recognition of fear and/or sadness compared to those low on psychopathy, while other studies do not find an association between psychopathic traits and impaired recognition of facial expressions (Dawel et al., 2012; Deming et al., 2022). This could be explained by the Response Modulation Hypothesis: if the activity's goal aligns itself with that of the psychopathic individual, then they are believed to perform on par with healthy controls, but if the goals of the task and person do not align, then there is a deficit in performance (Baskin-Sommers et al., 2009).

Finally, adolescents with early-onset CU traits (i.e., cases where CU traits developed during childhood, before adolescence) showed marked deficits in the recognition of anger, disgust, and happiness, compared to matched healthy controls, whereas adolescent-onset CU-trait adolescents only showed impairments in recognizing fear compared to matched healthy controls, and to a lesser, but non-significant, degree than early-onset participants (Fairchild et al., 2009). Overall, therefore, it is expected that some specific forensic populations will show deficits in recognizing negative emotional expressions. As for individuals high on psychopathy, it is recommended to manipulate their

goal to either align, or not, with that of the task, perhaps through distraction to allow to test the Response Modulation Hypothesis.

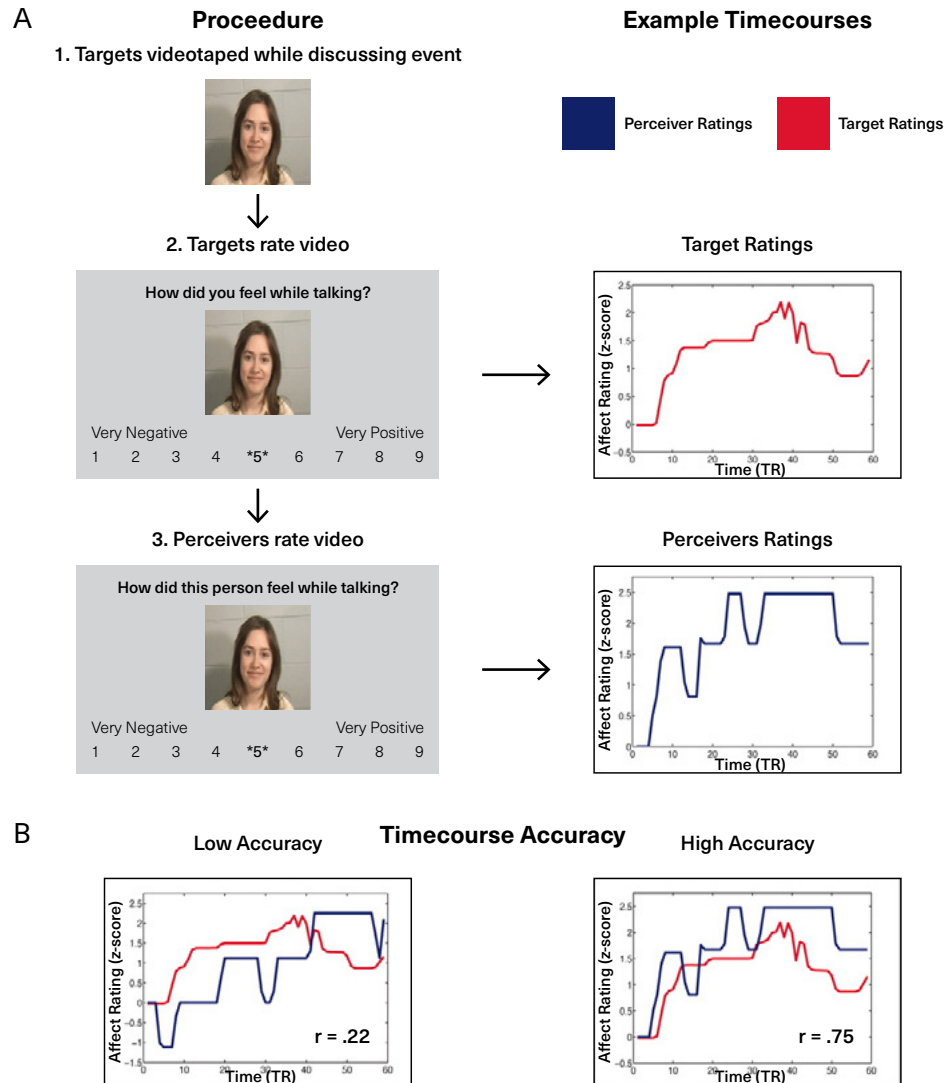
In sum, we propose to measure Emotional Recognition using the Emotion Recognition Task (more specifically the short form). This task presents several advantages compared to other considered tasks, such as standardization, task completion time, the use of dynamic stimuli and different levels of emotional expression intensity. Several forensic populations are expected to show marked deficits in recognizing and identifying negative facial expressions, notably anger and fear. Finally, we recommend manipulating the goal of the task from the participants' perspective by distracting them so that the clinical goal of the task does not match their expectations.

2.1.3 *Emotional Contagion*

Emotional contagion happens when an emotional reaction of the same valence is elicited in oneself when observing another person's emotions (in other words, an isomorphic emotional reaction). Emotional contagion is a crucial step in developing empathy and is considered the root of empathy by contemporary models (Bird & Viding, 2014; de Waal & Preston, 2017), with a minimal potential of affiliation and shared emotional meaning required for the emergence of emotional contagion (Hess & Fischer, 2014, 2022). In the example above, emotional contagion was experienced by John who started to cry quietly. To define the working definition of emotional contagion, one needs to distinguish between whether the emotional reaction is how a person feels subjectively or their associated bodily sensations. We will first focus on measuring subjective emotional valences here, and then go into depth with regards to physiological arousal.

To measure the subjective emotional valence within emotional contagion, we propose using an adjusted version of the Empathic Accuracy Task (EAT; Ickes, 1997). The EAT was developed as an assessment of accuracy in understanding another's emotions, i.e., emotional awareness. Speakers would be videotaped, asked to discuss an emotional autobiographical event, and were subsequently asked to rate how they felt while talking. Participants would then be shown the recording of story-telling and asked to rate the speakers' emotion in the story (Figure 2) (Ickes, 1997; Zaki et al., 2009).

In order to adapt the EAT to measure emotional contagion, instead of asking participants how the speakers felt, we would ask participants how they felt themselves, and compare it to the target's self-rating to see whether there



▲ **Figure 2. The Empathic Accuracy Task** Task design and sample behavior from Zaki and colleagues (2009). Outline of procedure. (1) Targets were videotaped while recounting an emotional autobiographical event. (2) Immediately after recounting their memory, targets rewatched their videos, and continuously rated how positive or negative they felt at that moment when telling their story. (3) Participants watched the videos and continuously rate how positive or negative they believe the targets had felt at each moment while recounting their story. From Zaki et al. (2009); figure used with permission.

was indeed contagion. The EAT is a continuous measure, which allows for comparison within-subjects, not between-subjects. Moreover, the EAT involves real people telling real stories, capturing dynamic states of emotional contagion, and is more naturalistic, especially when compared to other methods of self-report in assessing subjective feelings of contagion (e.g., Emotional Contagion Scale; Doherty, 1997).

Another suggestion for a measure of emotional contagion are physiological responses. This approach is founded on the idea that, while observing another's emotional state, this activates bodily sensations associated with that emotional state in the observer. Examples of methods that could be used to measure physiological arousal include galvanic skin conductance or heart rate variability (HRV), i.e., a measure of the variation in the time interval between heartbeats. We believe measuring HRV to be the more appropriate approach, since it is more insightful of the balance between the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS) (Appelhans & Luecken, 2006; Berntson et al., 1997).

These methods are more implicit compared to self-report tools such as surveys and harder for participants to influence, or to realize what the "desirable" answers would be, especially within forensic contexts (Schmidt et al., 2015). Ideally, these tools should be combined with other valid, convergent measures (e.g., adapted Empathy Accuracy task above) to increase the validity of emotional contagion assessment. Moreover, tools measuring emotional states isomorphic to the sender (i.e., emotional contagion) in real time highlight potential unconscious mechanisms (Bell et al., 2018; Herrando & Constantinides, 2021).

As far as we are aware, only one paper has studied the relationship between empathy accuracy and psychopathy, using a variant of Ickes' (1997) original task: Brook and Kosson (2012). They found that men in prison with higher scores on PCL-R rated psychopathy, performed worse on the Empathy Accuracy Task, with significant group differences between those high and low on psychopathy. Specifically, when analyzing the emotional content, psychopathy was only related to poorer cognitive empathic accuracy in emotions with negative valence (fear and sadness). Since Ickes' as well as Brook and Kosson's version of the Empathy Accuracy Task measures emotional awareness instead of our intended emotional contagion, we are unable to predict how psychopathy might vary with emotional contagion in the context of the adapted empathy accuracy task. This is especially when prior literature seems mixed as to whether there is a deficit of emotional contagion in people who have psychopathy (Bird & Viding, 2014; Lishner et al., 2012).

In terms of physiological measurements of autonomic nervous system activity, a recent meta-analysis showed that (1) the most robust biological correlate of antisocial behavior is resting heart rate (HR) and (2) samples of individuals who offended violently and those who are high on psychopathy have the largest effect size when using biological correlates as a predictor for differentiation (de Looff et al., 2022). In terms of heart rate specifically, De Wied and colleagues (2009) found reduced heart rate variability (HRV) in boys with disruptive behavior disorder (with or without CU traits). High CU individuals also showed less HR change from baseline than low CU ones (de Wied et al., 2012). Also, when measuring high-frequency HRV (HF-HRV) in healthy male students, greater HF-HRV was associated with increased self-reported empathy (Lischke et al., 2018). Hence, it could be argued that HRV could be used as a proxy for empathic functioning in studying psychopathy. In terms of galvanic skin response, participants high in fearless dominance domains of psychopathy had smaller skin conductance responses specifically to aversive pictures (from the IAPS, Lang et al., 1999) (Benning et al., 2005). Moreover, there is also experimental evidence demonstrating a robust effect in skin conductance while watching various forms of emotions (Folz et al., 2022). Overall, the use of physiological measures to study psychopathy seems sensible.

2.1.4 *Self-Other Orientation and Perspective Taking*

Perspective taking is the ability to understand and focus on another individuals' point of view. This is often split into the cognitive and affective components, with the former most commonly referred to as Theory of Mind (ToM) (Baron-Cohen et al., 1985; Healey & Grossman, 2018). This is largely defined as the ability to assign and attribute mental states to the self and others but has been the subject of vigorous debate in recent years, i.e., the proposal of understanding of ToM beyond false beliefs (Airenti, 2015; Apperly, 2012; Baron-Cohen et al., 1985; Wimmer & Perner, 1983). In our example, John showed that perspective-taking by automatically putting himself into Peter's shoes. The most contemporary definition comes from the Self to Other Model of Empathy (SOME), which defines ToM as a cognitive representation of self and others' mental states (Bird & Viding, 2014). Further incorporated in this 'level' of the Zipper Model of Empathy is spontaneous/automatic perspective taking, which is discussed further below.

A comprehensive ToM battery of tests is usually recommended instead of one single test due to the variety of social-cognitive tasks that measure ToM

different aspects of ToM (Blijd-Hoogewys et al., 2008; Quesque & Rossetti, 2020). Moreover, to measure perspective taking in adult forensic populations, we recommend ToM tasks that are more complicated in nature. Broadly speaking, there are a few suggested ways to measure advanced ToM, for example, non-literal communication tasks and Reading the Mind in the Eyes Task (RMET) (Hayward & Homer, 2017). For example, to encapsulate ToM beyond beliefs, Happé's Strange Stories task taps into a mentalistic understanding of non-literal communication (Beaudoin et al., 2020; Happé, 1994). The task presents participants with 24 short vignettes of 12 stories in daily-life situations where people say things they do not mean literally, e.g., white lies, jokes, or sarcasm, accompanied with a picture. At the end of the task, they would be asked about the intentions of the characters. A major benefit of the Strange Stories task is that it captures individual variance in mental state reasoning compared to false belief tasks, with subsequent replication (Kaland et al., 2005; White et al., 2009). The Faux Pas task is similar to the Strange Stories task, consisting of 10 short stories with the presence of a faux pas: an embarrassing blunder. Participants are asked to answer questions about whether they detected and understood the faux pas, alongside the associated mental state and feelings (Baron-Cohen et al., 1999). Both tasks were found to have acceptable levels of internal consistency, but with potential difficulties in comprehension for young children, and adolescents (Hayward & Homer, 2017).

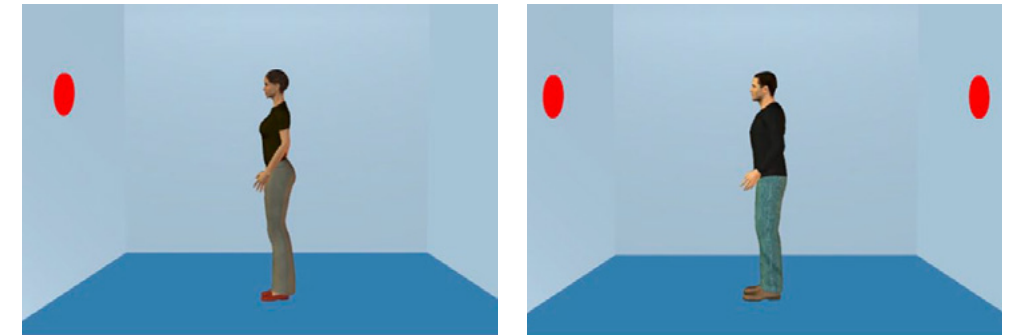
Furthermore, one of the most popular measures of measuring ToM is the RMET. It consists of 36 items, where participants are asked to view the eyes of a person, and select one of four items that describes the intention of the person best (Baron-Cohen et al., 2001). Despite its popularity, RMET has limited internal consistency, inadequate model fit, and uncertain validity of specific items (Higgins et al., 2022; Olderbak et al., 2015; Vellante et al., 2013). Moreover, there are also suggestions that RMET might not be measuring ToM, but rather emotion perception or recognition, casting doubt on the interpretations of related results (Kittel et al., 2022; Oakley et al., 2016). Due to the mixed literature in this regard, RMET is not recommended, as while Olderbak and colleagues (2015) recommend the use of a short-form RMET, this has not been subjected to empirical testing to the extent of the original RMET. An alternative to RMET, Reading the Mind in the Voice Task (RMVT), was also proposed in order to account for alternative modalities in ToM (Golan et al., 2007; Rutherford et al., 2002). The RMVT consists of 40 naturalistic speech segments that potentially include intonation contrary to word content (e.g., sarcasm) played to participants, who had to choose one of two words that describes the mental state of the speaker best. This is a step beyond the Vocal

Affect Recognition Test, where participants are asked to listen to words, and asked to name the type of emotion, ranging from happiness, disgust, anger, sadness, to fear (Scott et al., 1997). To our knowledge, there have only been two psychometric validation studies for the RMVT, both showing a satisfactory reliability and validity (Golan et al., 2007; Sánchez-Reales et al., 2019). Perhaps using a combination of these ToM tasks in conjunction with the RMVT could enhance the overall validity.

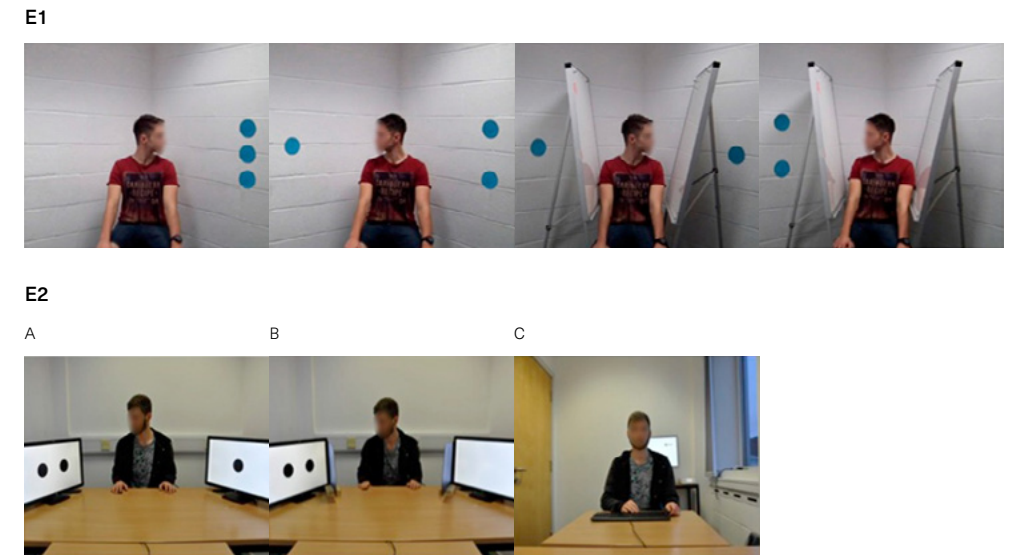
An often-neglected component of perspective taking is its spontaneity. Spontaneous perspective taking refers to the ability to rapidly and involuntarily understand and focus on another's point of view (O'Grady et al., 2020). The literature often uses the terms "spontaneous" and "automatic perspective taking" interchangeably, but there is a subtle difference. In order to distinguish spontaneous with automatic perspective taking, the following criteria were suggested (Carruthers, 2017; O'Grady et al., 2020; Westra, 2017):

- Automatic processes are reflexive, cannot be inhibited, rapid, and, importantly, goal-independent. An example of this would be asking what another person sees in optical illusions, e.g., the checker shadow illusion or the Thatcher effect (Thompson, 1980).
- Spontaneous processes are unconscious, rapid, and involuntary, and, importantly, are attention- and goal-dependent. In the context of perspective taking, they can be driven by whether the alternative perspective is made salient. For example, when viewing two people sitting opposite each other, looking at a picture of the number 6 on a table between them, the answer would differ depending on whether the goal is to view the image from your perspective (a 6), or the person opposite (a 9) (Zhao et al., 2016).

The Dot Perspective Task (DPT) is considered one of the classic tasks for measuring automatic/spontaneous perspective taking (Samson et al., 2010). Participants are asked to indicate how many dots appear on an image with an avatar, either (1) from their own perspective or (2) the avatar's perspective. These two perspectives may be congruent (same number of dots) or incongruent (different number of dots) (Figure 3). Participants typically respond slower in inconsistent trials, where their perspective is different to the avatar's. When participants respond slower on inconsistent trials when asked about the avatar's perspective, this is called egocentric interference, in contrast to altercentric interference, where they are asked about their own perspective.



▲ **Figure 3. The Dot Perspective Task** Stimuli from Samson and colleagues (2010), with an avatar in the middle of the "room". Left image illustrates a consistent trial, while the right image illustrates one that is inconsistent. Figure from O'Grady et al., 2020; figure used with permission.



▲ **Figure 4. The Dot Perspective Task** Stimuli from Langton (2018), with an avatar in the middle of the room. Left image illustrates photo-realistic stimuli in consistent/inconsistent trials, with/without barriers (E1), while the right image illustrates an in-person trial (E2). Figure from Langton et al., 2018; figure used with permission.

The altercentric interference effect led researchers to conclude that participants automatically take the perspective of the avatar, and the avatar's perspective is represented despite going against their goals of perspective taking involuntarily (Samson et al., 2010). However, this is largely critiqued by the submentalizing account, which suggests that attentional cueing is caused by directional gaze-cues from the avatar (Cole et al., 2016; Heyes, 2014). Indeed, Langton (2018) found that when either using photo-realistic stimuli presented on a screen (Figure 4, E1), or using an in-person confederate (Figure 4, E2), a consistency effect was observed regardless of whether there were barriers, going against the automatic perspective-taking account.

Taking this into account, O'Grady and colleagues (2020) created an adapted version of the DPT (DPT-Revised). The DPT-Revised included consistent/inconsistent trials for both line-of-sight and directionality, controlling for a potentially spurious directional effect (Figure 5). In manipulating the salience of the avatars, visual task complexity, and using the original DPT stimuli with/without occluders, they found that altercentric interference is dependent on salience to the avatar, stimuli, and complexity of scene. Specifically, humanoid/realistic avatars in tasks of sufficient visual simplicity lead to a perspective-taking effect when the avatar's perspective is congruent with task goals. Collectively, this suggests the original DPT (explicit tasks, where the avatar's perspective is explicitly relevant) does provide evidence for visual perspective-taking and not directional orienting. However, this process is not automatic, but spontaneous, as perspective-taking occurs only when it is goal-relevant (O'Grady et al., 2020). A meta-analysis by Holland and colleagues (2021) further reconciles this debate, stating that directional and perspective consistency both influence responses on the DPT, with the latter contributing to a smaller amount of variance. This means that the DPT can still be used, as the submentalizing account is not supported. However, one should still exercise caution in using DPT for clinical samples, as the effect of directionality is not primarily from taking the perspective of the avatar. They also agree with O'Grady and colleagues' (2020) conclusions that DPT taps into a spontaneous process that occurs when tracking another's perspective becomes a relevant-goal. We hence propose the use of O'Grady and colleagues' (2020) Lego avatar experiment, which we believe better accounts for explicit and implicit accounts of perspective-taking.

The use of ToM tasks within this test battery is essential in distinguishing individuals with psychopathy, ASD, and alexithymia. A deficit of ToM is often considered the core deficit of ASD, while the relationship of ToM and alexithymia is more complicated, with deficits centered in tasks that involve emotion recognition (Pisani et al., 2021; Yirmiya et al., 1998). Individuals high

Avatar sees:

- Line-of-sight consistent
- Directionally consistent



Avatar faces (central):

- Line-of-sight inconsistent
- Directionally consistent
- Balls in centre



Avatar faces (peripheral):

- Line-of-sight inconsistent
- Directionally consistent
- Balls on periphery



Behind avatar:

- Line-of-sight inconsistent
- Directionally inconsistent



▲ **Figure 5. The Dot Perspective Task - Revised** Stimuli from O'Grady and colleagues (2020), with a single avatar either on the left or right of the central table and a number of balls (maximum 4–5 possible positions and maximum 2 balls in any position). The four consistency conditions are illustrated from top to bottom. Figure from O'Grady et al. (2020); figure used with permission.





on psychopathy have largely been considered to have intact ToM. When using Happé's advanced test of ToM, the RMET, and a comprehensive battery of ToM tasks ranging from false belief to faux pas tasks, incarcerated offenders high on psychopathy were found not to have any deficits on these tasks when compared to incarcerated controls (Blair et al., 1996; Dolan & Fullam, 2004; Richell et al., 2003). However, in a recent study, primary and secondary psychopathy were found to correlate with deficits in ToM, using a collection of tasks indexing perspective taking in different ways, such as the RMET, the Situational Test of

Emotion Management, Situational Test of Emotion Understanding, the Hinting Task, and the Imposing Memory Test (Vonk et al., 2015). One explanation of this could be that Vonk and colleagues (2015) used a large variety of ToM tasks beyond false belief, indexing ToM further in depth than the older studies.

However, what should also be of note is the heterogeneity in samples and various measurements of psychopathy. Indeed, Vonk and colleagues (2015) used a largely female community sample, and a self-report form of psychopathy (Levenson self-report psychopathy scale; Levenson et al., 1995), whereas the older studies focused on forensic, male populations, who were rated by clinicians using the PCL-R/SV (Hare, 2003). A future direction in investigating ToM deficits within populations with psychopathy could be to apply Vonk and colleagues' methodology in a male, forensic, PCL-R assessed population (as in Blair et al.'s, 1996 study), and vice versa, to better delineate heterogeneous effects of ToM tasks, gender, and psychopathy assessment. This cross-validation of assessments across heterogeneous samples is essential in understanding psychometric tests and their relation to the construct of psychopathy and perspective taking.

One suggestion of why individuals high on psychopathy might succeed in ToM tasks is because they are not restricted in deliberate forms of cognitive or even affective perspective taking. Rather, they show reduced spontaneous perspective taking, due to lack of motivation or attention. The theoretical idea stems back to Newman's attention-based hypothesis of psychopathy, where he proposed psychopathic symptoms come from a deficit in cognitive-attentional processing that impairs inhibitory control and punishment learning (Patrick, 2022). Specifically, the response modulation hypothesis postulates that individuals with psychopathy have a deficit in response modulation, i.e. brief automatic shifts of attention from organization and implementation of goal-directed behavior to evaluate ongoing behavior (Vitale et al., 2016). In other words, they show less automatic, quick shifts from a preset goal to what is currently ongoing "unless it is an integral aspect of their pre-potent focus of attention" (Baskin-Sommers et al, 2009, p. 628). The current consensus in the field is that male psychopaths in forensic settings cannot automatically take the perspective of others, unless it suits their goals, but they do have an intact (deliberate) ToM, as established by Drayton and colleagues' (2018) key study. The researchers adapted Samson and colleagues' (2010) original DPT task to incarcerated offenders (Figure 6) and found that participants scoring high on the PCL-R showed a lower difference in response times between trials where the number of dots seen by the participant and on-screen avatar were consistent or inconsistent, compared to low PCL-R scoring participants.

In other words, this reduced difference (i.e., altercentric interference) suggests that psychopathic participants failed to automatically take the perspective of others. They also found a correlation in the reduced altercentric interference with the number of assaults charges, leading them to suggest a core cognitive deficit in psychopaths could originate from an automatic tendency to ignore the perspective of others when it does not help them reach their preset goals (i.e., when the task is not considered goal-relevant).

Trial Type	Fixation	Perspective	Content	Avatar
self/consistent	+	YOU	2	
Self/inconsistent	+	YOU	2	
avatar/consistent	+	HE	2	
avatar/inconsistent	+	HE	2	

▲ **Figure 6. Adapted Dot Perspective Task** Stimuli from Drayton and colleagues (2018), with an avatar in the middle of the room. Each image from top to bottom indicates the trial type, where participants were asked to view from their own perspective (YOU/self), or the avatar's perspective (HE/Avatar) in both dot-consistent and inconsistent trials. Figure from Drayton et al. (2018); figure used with permission.

However, as mentioned in the literature discussed above, one should exercise caution in interpreting results from the original DPT, especially when applied to clinical samples (Cole et al., 2016; Holland et al., 2021; Langton, 2018; O'Grady et al., 2020). As a theoretical definition, we believe that in contrast to automatic perspective taking, the core deficit of psychopathy could better lie in spontaneous perspective taking. This is because spontaneous perspective taking fits better with the response modulation hypothesis (as their performance depends on the relevance of the preset goals) and DPT is fundamentally a test of spontaneous and not automatic perspective taking. Moreover, in order to consider directional-gaze cue and stimulus effects, better methodology (such as the DPT-Revised in O'Grady et al., 2020) should be used and standardized for future experiments involving clinical samples.

As a final note, there are many other compelling ToM measures that could, and arguably should be included in this discussion, such as Sarfati and colleagues' (1997) Intention Comic Strip Task and Dziobek and colleagues' (2006) Movie of the Assessment of Social Cognition task for their non-verbal and naturalistic designs, respectively. However, a core aim of this paper is to start a discussion over how to assess empathy as modeled by the Zipper Model of Empathy. Therefore, it is more important here to select a few ToM assessments with a depth of literature behind them, and discuss these in depth, rather than briefly summarize many potential ToM measures without augmenting their validity in depth. However, with the hope that such a discussion is started, we of course encourage others to argue why their selection of measures are more appropriate, using both theory and empirical research.

2.1.5 *Other-Oriented Isomorphic Emotional Responsiveness*

Other-Oriented Isomorphic Emotional Responsiveness is defined as the emotional response directed to another person that is congruent with the perceived welfare or emotional state of that person, who is often in need (Decety et al., 2012; Feshbach, 1997). Note the similarity with empathic concern, sympathy and compassion, which is importantly unselfish by nature. In our example, this is what John shows by rushing to Peter to hug him when he breaks into tears. To measure Other-oriented Isomorphic Responsiveness, we suggest measuring the participant's tendency to act compassionately and through goodwill to another person often in need. Experimentally, these should be measured somewhat indirectly, to not make the goal of the test too obvious.

To do so, we propose using an adjusted Charity Task (Dapprich et al., in preparation).

The methodological procedure for the adjusted Charity Task is as follows. Patients are presented the story of Melany, a normally intelligent child with Down syndrome who grows up under challenging socioeconomic circumstances and ends up being severely bullied by fellow schoolchildren, with the story changing from optimistic to sad. At certain moments, the story is paused, and participants are asked to categorize what emotion they believe Melany to be feeling and rate the intensity of that emotion. Participants then also categorize and rate the intensity of what emotion they themselves feel. After rating emotions, participants are given the opportunity to donate a small amount of money (e.g., €2) to a foundation that organizes vacation trips for children with Down Syndrome but are simultaneously told that the donation will be deducted from their final participation payment. As there are five pauses throughout the story, participants can donate between €0 and €10, though are unaware that in the end they all receive full compensation for participating, whatever their previous donating actions were.

We also propose a handful of minor modifications to this experiment. There is the arguable problem of collecting data using forced choices when examining such a high-level manifestation of empathy that builds upon the aforementioned 'levels' of empathy maturity. Indeed, it might be preferable to instead ask patients to freely self-report what emotions they are feeling, how strongly these are felt, and why the participant decided to (not) donate. This would allow them to report information in higher detail and complexity than, for example, simply "emotion: sad; intensity: 4/10; no donation". However, such response data is highly qualitative, therefore poorly standardized and requiring significant interpretation. Moreover, though related to the first point, the emotion felt by the participant might not only mismatch that felt by the character Melany, but also lead to the same behavior (to donate or not) while differing from those felt by others. For instance, while patient 1 might feel pity for Melany, and therefore donate because of this strongly felt emotion, patient 2 might instead feel angry in response to the situation Melany is experiencing, and therefore also donate to reduce the number of future children who will experience Melany's same situation. Without gathering free self-report data, this nuance might be lost in the standardized data. Therefore, a more intuitive and streamlined way to measure the emotional valence and intensity felt by participants could function as follows. When prompted to select which emotion the participant is currently feeling, the length of time they keep that emotion selected represents the intensity to which they feel that emotion. This could

be visually represented by a red circle that increases in size and saturation to represent greater intensity.

Another important point to highlight with this task is that, while altruistic behavior is mature empathy, mature empathy is not limited to only altruistic forms of behavior (e.g., donations). Therefore, on top of collecting detailed qualitative information about the participant's self-reported emotions, we also propose to collect physiological data, e.g., HRV data. Indeed, it would serve as an indirect measure proxy for emotional valence (see Shi et al., 2017), which is often harder to mangle, especially when coupled with the self-report data described above. Note however that HRV presents a number of limitations. First, it must be compared to a baseline, which would require measuring the patient's HR throughout the entire assessment. Furthermore, the physiological responses will likely not cue clinicians as to exactly what 'level' of empathic maturity the participant is currently experiencing. However, by taking these limitations into account, the benefits of this indirect measure could help compensate for the limitations of the qualitative self-report measurements discussed above. Finally, of course, these converging suggestions are simply hypothetical proposals that require further empirical validation.

The described (adjusted) Charity Task is the only task that we know of that could measure Other-oriented Isomorphic Responsiveness. This task presents a number of important advantages. Most notably, individuals can only help another out-group in need by sacrificing personal gain (full payment), meaning that the altruistic action comes at a personal cost. This is thought to help minimize faking good, as according to the Zipper Model of Empathy, individuals who are not fully "zipped up" to this level will not be inclined, or able, to show empathy to an out-group member in need. However, if there was no personal cost to the action, and patients recognized that the clinical goal is to assess whether they donate or not, it would be easier to "fake good" with no personal cost. Furthermore, the real-world story and consequences for acting out of compassion increase the ecological validity of the task, similar to the Empathy Accuracy Task described above. Finally, the repeated data collection of speaker and patient emotion category and intensity increases the difficulty in consistently faking good, further increasing malingering detection.

In sum, we propose to assess other-oriented isomorphic emotional responsiveness - a high-level presentation of empathy - using the adjusted Charity Task, along with a number of modifications such as collecting qualitative self-report data and HRV. Currently, there is no research that we are aware of that uses this task, let alone our proposed modifications, so it is difficult to make predictions based on past research as to what forensic populations may struggle

with this task. However, given that certain aforementioned forensic populations are expected to struggle with tasks assessing lower levels of empathy, which are required to reach Other-oriented Isomorphic Emotional Responsiveness according to this model, we expect these same populations to show deficits as well, such as by donating less than healthy controls, and showing less accuracy in categorizing and assessing the intensity of the emotions felt by Melany compared to healthy controls.

3 Discussion

We have described the Zipper Model of Empathy outlining the necessary architecture that unifies components of empathy to build towards mature empathy. We also provided operationalized definitions and proposed assessments specific to each component, aiming to elucidate the complexity of multidimensional and bidirectional empathy. Moreover, this model has the potential to differentiate specific empathy deficits within different conditions and disorders and help integrate the field's understanding of behavioral, cognitive, and neurophysiological work. For example, in populations with psychopathy, alexithymia, and autism spectrum disorders. Specifically for psychopathy, we further identified measures that are sensitive to these populations and highlight neglected or debated literature in social cognition. The model and the checklist is also designed to be empirically tested, validated, and falsified, with its clear operational definitions.

One limitation of the proposed battery of tests indexing the Zipper Model of Empathy in forensic-clinical populations would be the length of the assessment. Patients in clinical settings might not be able to sustain attention in an assessment that is too long, and clinicians might also be worried that the assessment itself would be too time consuming to use in practice. There are a few suggestions that would reduce the time required. For example, a shortened form of empathy tasks could be used, e.g., for Happé's Strange Stories (Happé, 1994; White et al., 2009). A caveat for this approach is that most of these shortened versions are often not empirically tested as often, or show sufficient psychometric validity. A further review or more experiments might be needed with shortened tests before employing its use in a clinical checklist.

An alternative would be to combine tasks that measure two different components of empathy. For example, due to its similarities, the revised-Empathy Accuracy Task (EAT) could be combined with the adjusted Charity Task. In the EAT, instead of videotaping speakers, participants could be presented with “Melany’s story” discussing her experiences as described in the Charity task via tape or writing, asking participants to categorize Melany’s emotions, the intensity, their own emotions and respective intensity, and eventually the option to donate. The total time for the checklist can hence be significantly shortened. The donating behavior could be separately analyzed as a measure of Other-oriented Isomorphic Emotional Responsiveness, while the categorization of emotions a measure of emotional contagion.

Overall, we hope the paper can inspire the development and discussion on neuroclinical assessments, which incorporate neurophysiological variables into applied psychological assessments. As Iacono (1991) succinctly puts it: “Psychophysiological methods have been widely used in psychopathology research, but they have yet to be exploited as assessment techniques” (p. 309). Neuroclinical assessments like ours are able to tackle the problem of comorbid disorders by assessing core neurocognitive deficits (in this case empathy) and reduce the susceptibility to response biases (e.g., social desirability) by employing a multi-modal assessment. Furthermore, there is clear documentation on the procedure of developing neuroclinical assessments, its clinical utility, and illustrations of how this could be done in concepts relating to psychopathy. For example, Patrick and colleagues (2019) illustrated how self-report scales, brain-ERP, and task-performance measures could be integrated as a neuroclinical assessment of (dis)inhibition. Our paper has not touched upon the intricacies of neuroimaging research and its extensive connection with the amygdala, a concept central to understanding psychopathy (Blair, 2005; Marsh, 2016; but also see Deming et al., 2022, for evidence against). This is because the use of MRI in forensic-clinical settings is rather unrealistic in the context of clinical assessments. Perhaps future psychopathy research could benefit from the neuroclinical approach, where neurobiological evidence could be integrated with cognitive, behavioral, and self-report questionnaires where core deficits can be assessed and used within clinical settings. Similarly, empathy research could benefit from such a strategy, which could start with the Zipper Model of Empathy. Ultimately, we hope this paper serves as a starting point for discussion and debate on defining and assessing empathy, and the model to be falsified and continuously updated based on recent scientific findings.

Chapter 4
**Revealed masks:
Facial mimicry after oxytocin
administration in forensic
psychopathic patients**

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*equal contribution

Abstract

Facial mimicry serves as an evolutionarily rooted important interpersonal communication process that touches on the concepts of socialization and empathy. Facial electromyography (EMG) of the corrugator muscle and the zygomaticus muscle was recorded while male forensic psychopathic patients and controls watched morphed angry or happy facial expressions. We tested the hypothesis that psychopathic patients would show weaker short latency facial mimicry (that is, within 600 ms after stimulus onset) than controls. Exclusively in the group of psychopathic patients, we tested the hypothesis that a placebo-controlled administration of oxytocin would enhance short-latency facial mimicry. Compared with placebo, we found no oxytocin-related significant short-latency responses of the corrugator and the zygomaticus. However, compared with normal controls, psychopathic patients in the placebo condition showed significantly weaker short-latency zygomaticus responses to happy faces, while there was a trend toward significantly weaker short-latency corrugator responses to angry faces. These results are consistent with a recent study of facial EMG responses in adolescents with psychopathic traits. We therefore posit a lifetime developmental deficit in psychopathy pertaining short-latency mimicry of emotional facial expressions. Ultimately, this deficit in mimicking angry and happy expressions may hinder their processing of empathy, which is known to be impaired in psychopathy.

1 Introduction

With an estimated global prevalence of 0.5% to 1.2% in the general population (Hare, 1996; Neumann & Hare, 2008; Sanz-García et al., 2021), psychopathic persons are believed to be involved in 30% to 40% of violent crime in the United States (Kiehl & Sinnott-Armstrong, 2013). Psychopathy as a lifelong personality disorder is operationally defined by the Psychopathy Checklist-Revised (PCL-R; Hare, 2003). Its phenotypic expression is heterogeneous (Brinkley et al., 2004), but some core features are invariably present, like affective empathy deficits (Mullins-Nelson et al., 2006; Rijnders et al., 2021a). Based on the assumption that mimicry is a precursor to the empathy process (Hatfield et al., 1994, 2009; Rijnders et al., 2021a) we investigated mimicry responses to morphed pictures of emotional facial expressions in forensic psychopathic patients. In addition, we investigated whether the neuropeptide oxytocin contributes to enhancing mimicry.

Mimicry includes emotional postures, gestures or facial expressions (Chartrand & van Baaren, 2009) and is part of a highly dynamic interpersonal communicative process (Chartrand et al., 2005). Mimicking another person's emotional facial expression can elicit the same affective resonance and isomorphic emotional states in the observer (Adolphs, 2006; Olszanowski et al., 2019; Söderkvist et al., 2018) partly depending on the observer's social appraisal of the context and the relationship with the sender (Hess & Fisher, 2022). Blocked facial mimicry due to congenital facial paralysis in Moebius patients resulted in lower intensities in the perception of others' facial expressions of sadness, fear, anger and disgust (Schiano Lomoriello et al., 2023).

Mimicry of emotional facial expressions is often measured with facial electromyography (EMG), a sensitive technique for inferring subjective mood states or affective responses (van Boxtel, 2010). Watching a positive emotional facial expression can elicit zygomaticus major muscle activation, while inhibition of the corrugator supercillii muscle response (i.e., relaxation) may occur (van Boxtel et al., 2022). Looking at a negative emotional facial expression can induce an increased activation of the corrugator with simultaneously little or almost null effect on the zygomaticus (Dimberg, 1982). EMG studies of mimicry responses in adult psychopathic individuals or adolescents with callous-unemotional (CU) traits; see Frick & Morris, 2004) are scarce and inconsistent. CU traits are generally considered precursors to psychopathy in later life (McMahon et al., 2010). Nonpsychopathic and psychopathic male offenders compared with normal controls showed no significant differences in corrugator responses to both neutral and morphed angry, sad, or happy facial expressions

(Künecke et al., 2018). In contrast, weaker corrugator EMG responses to sad facial expressions were found in male adolescents with disruptive behavior disorders (DBD) compared with healthy controls, although no significant difference could be established between DBD adolescents with low or high CU traits (de Wied et al., 2012). Among incarcerated adult males, PCL-R scores showed no associations with mimicry of slowly evolving facial emotions during 6-s videos (Deming et al., 2022). However, a recent study revealed significant group differences in EMG responses to dynamic facial emotional expressions in male DBD adolescents with low vs. high CU traits (van Boxtel et al., 2022). These differences occurred in the 500-ms early rise time of dynamic expressions after stimulus onset, often even at very short latencies of 100 or 200 ms, and not during the 1,500 ms phase of maximal expression. Within this 500-ms rise time, high-CU adolescents showed both smaller inhibitory corrugator responses and weaker zygomaticus responses to happy expressions and weaker corrugator responses to angry and sad expressions compared with those with low CU traits and healthy controls. Interestingly, the amygdala is thought to be involved in early automatic responses to emotional facial expressions (Adolphs, 2006). Such emotional cues may reach the amygdala through several fast subcortical and cortical pathways (for a comprehensive overview, see: van Boxtel et al., 2022). Starting from the assumption that deficient empathy seen in psychopathic individuals is associated with amygdala dysfunction (Blair, 2005b), the current study examines early mimicry responses (i.e. faster than 600 ms) to dynamic emotional facial expressions in psychopathic individuals.

As it is thought that deficits in empathy processing in psychopaths are partly driven by impediments in mimicking others' expressed emotions (e.g., Bird & Viding, 2014; Rijnders et al., 2021a), the question arises whether facial mimicry can be enhanced in psychopathic individuals. Oxytocin (OT) may be a candidate in this regard, as this neuropeptide plays an important role in social understanding and interpersonal behavior (Caldwell, 2017; Domes et al., 2007; Landgraf and Neumann, 2004; Meyer-Lindenberg et al., 2011; Schiller et al., 2023), and empathy (Barchi-Ferreira & Osório, 2021). The social salience hypothesis of OT (Shamay-Tsoory & Abu-Akel, 2016) predicts that OT is of great importance in interpersonal relationships, as it is associated with attentional modulation depending on salience of external social cues, e.g., increased attention to emotional facial expressions, especially in men (Boyle et al., 2022). Moreover, in healthy men, OT resulted in increased mimicry of emotional facial expressions, especially angry children's faces (Korb et al., 2016), although the participants' responses were measured over a longer time and therefore cannot be considered automatic early mimicry responses. However, no positive effects

of OT on facial mimicry were found in healthy male participants (Trilla et al., 2020). To our knowledge, no studies have examined OT effects on early facial mimicry in people with high levels of psychopathy.

In this study, we examined PCL-R confirmed forensic psychopathic patients admitted to high-security forensic psychiatric hospitals, as well as normal controls. The first major objective was to examine early zygomaticus and corrugator mimicry responses (that is, the first 600 ms after stimulus onset) to morphed emotional facial expressions of happiness and anger. Since psychopathic patients are thought to have difficulties processing negative and positive emotions (Blair, 2005a; Dawel et al., 2012), we first hypothesized that compared with normal controls, they would exhibit weaker early corrugator activation to angry facial expressions and less corrugator inhibition to happy facial expressions. Second, we hypothesized that the increase in zygomaticus activity during happy expressions would be smaller in psychopathic patients compared with normal controls (second hypothesis).

Exclusively in the group of psychopathic patients, our second major objective was to investigate the effect of a single intranasal dose of 24 IU OT on the early zygomaticus and corrugator mimicry responses to morphed angry and happy facial expressions. Based on the OT social salience hypothesis (Shamay-Tsoory & Abu-Akel, 2016) and OT-associated increased attention to emotional facial expressions, especially in males (Boyle et al., 2022), we hypothesized that in the OT condition, compared with placebo, happy expressions would elicit a stronger zygomaticus activation as well as a stronger corrugator inhibition (third hypothesis). We also expected stronger corrugator EMG responses in the OT condition, compared with placebo, when looking at angry faces (fourth hypothesis).

2 Methods and materials

2.1 Participants

Psychopathy was diagnosed using Hare's Psychopathy Checklist-Revised (PCL-R; Hare, 1991) in which a maximum score of 40 point represents maximum psychopathy (see Table S1 in the Supplementary Information). Compared with a diagnostic cut-off score of 30 in North America, several European studies used lower cut-off scores (e.g., Cooke et al., 2005). Initially, 24 male forensic

psychopathic patients and 21 male normal control subjects were included in the present study, which was part of a larger study in this patient group (see Rijnders et al., 2021b). The psychopathic patients were selected if their PCL-R total score was 26 or higher. The normal control subjects were male security guards or nursing staff members recruited from two forensic psychiatric hospitals. Similar inclusion and exclusion criteria were applied to them, except that they could not be diagnosed with the PCL-R because this instrument is not appropriate for a non-forensic group. Instead, to check for psychopathic features, they completed the Psychopathic Personality Inventory-Revised (PPI-R; Lilienfeld & Widows, 2005).

Additional requirements for participation were a good physical health, an age between 18 and 60 years, a normal visual acuity, and a total IQ of 80 or above. Exclusion criteria were color blindness, illiteracy, insufficient knowledge of Dutch language, a current severe psychiatric disorder like a psychotic, a depressive, or a severe anxiety disorder, endocrine disorders or brain diseases, or the use of selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors, antipsychotics, and hormonal libido inhibitors.

Of the 24 patients who were enrolled in this OT study, four were eventually excluded from analysis, one because of missing EMG data, and three others due to their co-morbid DSM-IV-TR Pervasive Developmental Disorder Not Otherwise Specified (APA, 2000). In addition, two normal controls were excluded from analysis, one because of a psychopathic tendency according to the PPI-R, and the other as he turned out to be alexithymic (Bagby et al., 1994). The 20 remaining psychopathic patients were tested in two separate sessions with either OT or placebo. The 19 remaining normal controls did not receive either placebo or OT and were therefore tested in a single session. They served as the reference population. Detailed sample characteristics are presented in Table 1.

Participants provided written informed consent prior to their participation. The study was approved by the Medical Research Ethics Committee of the University Medical Centre Utrecht, The Netherlands (protocol number 12/056), and was carried out in accordance with the guidelines of the Declaration of Helsinki (World Medical Association, 2013). The participants received a monetary compensation of 30 Euros.

2.2 Study design

The 20 psychopathic patients followed a within-subject, double-blind, counterbalanced, cross-over design, which was in line with previous studies

(e.g. Andari et al., 2010; Guastella et al., 2010; Lischke et al., 2012). In two test sessions they received either a nasal spray containing 24 IU OT or a placebo nasal spray consisting of physiological saline. The mean time interval between self-administration of the intranasal spray and the start of the dynamic morphing task on both test days was 57.2 ± 6.5 minutes and 56.9 ± 5.3 minutes, respectively. All participants were instructed to refrain from cigarette smoking and caffeine consumption at least one hour before the start of the test session. The overall test procedure for the normal controls was similar to that of the patient group, except that they were tested on one day only, as they did not apply OT. All participants completed the entire test procedure. PCL-R scores including the PCL-R facet scores, and the mean T-scores of the PPI-R combined scales including the higher order PPI-R dimensions Fearless Dominance and Impulsive Antisociality are presented in Table 1.

2.3 Dynamic morphed facial pictures

The dynamic facial morphing task was programmed in E-Prime version 1.2 (Psychology Software Tools, Sharpsburg, USA) and presented on a 17-inch, 120 Hz TFT monitor. Pictures of four different human faces (two male and two female Caucasians) from two standardized photo sets were used (Ekman & Friesen, 1976; Lundqvist et al., 1998). Participants were instructed to look at a small white cross that appeared on a black computer screen for 1,000 ms, which served as baseline period. Then a neutral face appeared that immediately started linearly morphing into either an angry or a happy face (see Figure 1). In total 32 morphed pictures were presented in a random order: four happy faces and four angry faces, each type of expression being produced by two different females and two different males, and each stimulus being repeated four times.

2.4 Facial EMG recordings and quantification

Facial EMG activity was recorded from two facial muscles: corrugator supercillii (inducing a frown expression) and zygomaticus major (inducing a smile-like elevation of the mouth corner) (Hermans et al., 2006; Larsen et al., 2003; Sonnby-Borgström, 2002). Before attaching the EMG surface electrodes, the skin was cleansed with 70% isopropyl alcohol swabs. Two

	Psychopathic patients (N=20)	Normal controls (N=19)
<i>Age' (years)</i> (range)	39.4 ± 9.5 (23.7 – 54.9)	36.5 ± 9.0 (25.1 – 57.5)
<i>Ethnic-cultural and national origin</i> (all participants currently had a Dutch nationality)	18 Europeans and Mediterraneanans (viz 15 Dutch, 1 Belgian and 2 Turks), 1 Surinamese African and 1 Surinamese Chinese-African.	17 Europeans and Mediterraneanans (viz 14 Dutch, 2 Moroccanans, and 1 Turk), 1 Dutch Antillean, and 1 Surinamese - Hindu
<i>Duration of mandatory treatment</i> (months)	118 ± 84	
<i>PCL-R total score (range)</i>	30.9 ± 2.7 (26–36)	
<i>PCL-R facets</i>		
<i>Interpersonal facet (facet 1)</i>	5.6 ± 1.3	
<i>Affective facet (facet 2)</i>	7.4 ± .8	
<i>Lifestyle facet (facet 3)</i>	7.8 ± 1.3	
<i>Antisocial facet (facet 4)</i>	8.3 ± 1.4	
<i>Category "Other" (two items)</i>	1.9 ± 1.4	
<i>PPI-R total score (range)</i>		287.0 ± 28.3 (243–336)
<i>T-scores</i>		
<i>PPI-R total</i>		47.5 ± 10.1
<i>PPI-R Factor Fearless Dominance</i>		55.2 ± 8.8
<i>Social potency</i>		54.4 ± 11.5
<i>Fearlessness</i>		52.0 ± 11.7
<i>Stress immunity</i>		58.2 ± 8.7
<i>PPI-R Factor Impulsive Antisociality</i>		41.8 ± 10.6
<i>Machiavellian egocentricity</i>		41.6 ± 10.8
<i>Rebellious nonconformity</i>		48.0 ± 10.9
<i>Blame externalization</i>		43.8 ± 8.1
<i>Carefree nonplanfulness</i>		47.1 ± 11.3
<i>Coldheartedness</i>		51.0 ± 12.0

▲ **Table 1. Demographic information** For all variables the means ± standard deviations are reported. 1 No significant group differences in age ($t_{37} = 0.95$, $p = .35$). All patients and normal controls grew up and were educated in the Netherlands from an early age. There were no cultural barriers in either group that could eventually interfere with test instructions or test attitudes. PCL-R = Psychopathy Checklist-Revised (including four facets and two items that do not load on the four facets, i.e. category "Other"; see also Table S1 in the Supplementary Information). PPI-R = Psychopathic Personality Inventory-Revised (two factors and eight subscales, including the subscale Coldheartedness that does not load on the two PPI-R factors).

FLAT Ag/AgCl Active electrodes (Biosemi) were filled with Elefix Z-401CE paste (Nihon Kohden GmbH, Germany) and then attached to the skin above the left corrugator supercilii. Placement was parallel to the longitudinal direction of the muscle with a distance of about 1 cm between the centers of each sensor. The same procedure was applied to the placement of the two electrodes above the left zygomaticus major. Finally, two reference electrodes were placed on the central and right forehead skin with a distance of 6–8 cm between the centers of each sensor.

The raw EMG signals were digitized with an ActiveTwo AD-box amplifier (Biosemi, Amsterdam, 24 bit resolution) at a rate of 2048 Hz (with 24 times oversampling), anti-aliasing filtered at 400 Hz, and stored on a Windows notebook. The EMG signals were then further processed with homemade software. They were 20-Hz digitally high-pass filtered to remove low-frequency



▲ **Figure 1. Visualization of the sequential steps in dynamic facial morphing** A baseline period of 1,000 ms preceded the start of stimulus onset. Participants were instructed to look at the small white cross during this baseline period. Then a neutral face appeared that immediately started linearly morphing into either an angry or a happy face. Emotional expression from 0% to 100% took place in 40 steps of 40 ms each. The fully morphed emotional face was then statically portrayed for another 2,000 ms. Then a black screen appeared for 6,000 ms before the start of a new baseline period. The five pictures of the two protagonists shown here represent the total range of emotional expression. (From Hermans et al., 2006, Figure used with permission)

artifacts (cf. van Boxtel, 2010). EMG responses were then visually inspected by two authors (AvB, RJPR) for remaining technical artifacts or strong potentials caused by disruptive actions like coughing, sneezing, strong eyeblinks, etc. Responses affected by such actions were removed by consensus. Removing records during this inspection did not affect the analysis design since each stimulus was presented four times. Thus, deleting one or two (in a single case even three) EMG responses did not lead to an incomplete design. In the control group, the removal rate was 4.8%, while in the patient group it was 2.5% in the OT condition and 3.0% in the placebo condition.

For each morphed picture, EMG was recorded during a period of 4,600 ms: (1) the 0-1,000 ms baseline period before onset of dynamic facial morphing, (2) the 1,600-ms linear morphing period, and (3) the 2,000-ms period of maximal expression. For analysis purposes the entire 4,600-ms period was divided into intervals of 200 ms. The optimal morphing duration for processing happiness and anger expressions is several hundred milliseconds after stimulus onset (van Boxtel et al., 2022; Hoffmann et al., 2010; Sato & Yoshikawa, 2004). These short-latency facial mimicry responses are thought to be automatic, amygdala-processed preconscious responses that are by definition difficult to control voluntarily, and as such might have diagnostic value for psychopathy (van Boxtel et al., 2022). Therefore, we analyzed short-latency EMG responses during a 600-ms period following morphing onset. For each morphed picture, the mean rectified EMG value in the 1,000 ms baseline period was calculated and the average EMG value during the 600-ms periods was expressed as a percentage of baseline value.

2.5 Statistical Analyses

Statistical analyses were performed using Microsoft Excel 2016 and SPSS version 27. EMG responses after stimulus onset were expressed as a percentage of the 0-1,000 ms baseline activity. EMG responses were analyzed during the first 600 ms of the increasing emotional expression after stimulus onset (i.e., 1,000-1,600 ms). For greater temporal resolution, we also separately analyzed the three consecutive 200 ms periods within this 600-ms early rise time (i.e. 1,000-1,200 ms, 1,200-1,400 ms, and 1,400-1,600 ms).

Comparisons of early corrugator or zygomaticus EMG responses between the normal control group and psychopathic patients in the placebo condition were performed with independent samples t-tests (one-tailed),

assuming equal or unequal variances. Within the group of psychopathic patients, comparisons between EMG responses obtained during OT and placebo conditions were performed using paired samples t-tests (one-tailed). Finally, Pearson's correlations between psychopathy scores and EMG responses during the 600-ms early rise time were performed to further specify the effects regarding the relationship between psychopathic severity and EMG performance.

3 Results

3.1 Early rise time EMG responses of psychopathic patients in the placebo condition vs. those of normal controls

In agreement with expectations, psychopathic patients showed a marginally significant weaker corrugator EMG responses to angry faces in the 600-ms early rise time than controls ($p = .072$). On a more fine-grained scale, a trend towards a significantly weaker responses was also found during the first two consecutive 200-ms periods within this 600-ms period ($p = .074$ and $p = .098$, respectively). In contrast to expectations, corrugator inhibition during happy faces was not significantly different between groups.

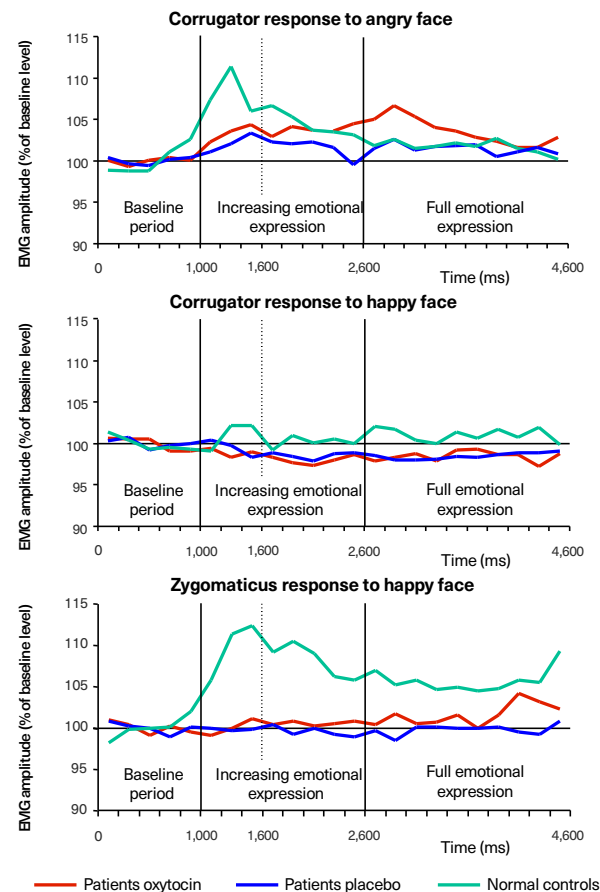
Also in agreement with expectations, psychopathic patients showed a significantly weaker zygomaticus 600-ms early EMG response to happy faces than controls. They showed a significantly weaker zygomaticus EMG response than controls during all three consecutive 200-ms periods (all p s < .05).

3.2 Early rise time EMG responses of psychopathic patients in OT and placebo conditions

No significant differences between OT and placebo conditions were observed in both corrugator and zygomaticus EMG responses during angry and happy expressions, which contradicted our third hypothesis. However, there was a trend toward a significant difference in corrugator inhibition when looking at happy faces during the first 200-ms period ($p = .074$).

3.3 Psychopathy scores and early rise time EMG responses

Analyses revealed no significant correlations between the PCL-R total scores and all corrugator and zygomaticus responses in the 600-ms early rise time (all p s > .424). The same was true for correlations between PPI-R total scores and all EMG performances in the early rise time (all p s > .391).



▲ **Figure 2. Facial EMG responses** to morphed emotional facial expressions in psychopathic patients and normal control subjects.

Time (ms)	1,000-1,600	1,000-1,200	1,200-1,400	1,400-1,600
Facilitatory corrugator response to angry face				
Patients oxytocin (% baseline)	103.4 (0.12)	102.3 (0.08)	103.6 (0.12)	104.4 (0.16)
Patients placebo (% baseline)	102.2 (0.04)	101.1 (0.03)	102.0 (0.04)	103.4 (0.07)
Normal controls (% baseline)	108.3 (0.17)	107.4 (0.18)	111.4 (0.30)	106.0 (0.12)
Placebo vs. normal controls	$t_{20}=-1.52$; $p=.072$	$t_{19}=-1.50$; $p=.074$	$t_{19}=-1.34$; $p=.098$	$t_{28}=-0.84$
Oxytocin vs. placebo	$t_{19}=0.47$	$t_{19}=0.59$	$t_{19}=0.60$	$t_{19}=0.27$
Inhibitory corrugator response to happy face				
Patients oxytocin (% baseline)	98.9 (0.03)	99.4 (0.03)	98.4 (0.04)	99.0 (0.04)
Patients placebo (% baseline)	99.5 (0.03)	100.4 (0.03)	99.7 (0.03)	98.4 (0.04)
Normal controls (% baseline)	101.1 (0.14)	99.1 (0.07)	102.2 (0.15)	102.1 (0.19)
Placebo vs. normal controls	$t_{19}=-0.52$	$t_{25}=0.78$	$t_{20}=-0.70$	$t_{19}=-0.84$
Oxytocin vs. placebo	$t_{19}=-0.86$	$t_{19}=-1.51$; $p=.074$	$t_{19}=-1.30$	$t_{19}=0.62$
Facilitatory zygomaticus response to happy face				
Patients oxytocin (% baseline)	100.0 (0.02)	99.1 (0.02)	99.9 (0.02)	101.1 (0.04)
Patients placebo (% baseline)	99.8 (0.01)	99.9 (0.02)	99.7 (0.03)	99.9 (0.02)
Normal controls (% baseline)	109.8 (0.21)	105.8 (0.13)	111.3 (0.24)	112.4 (0.28)
Placebo vs. normal controls	$t_{18}=-2.04$; $p=.028$	$t_{16}=-1.98$; $p=.031$	$t_{18}=-2.07$; $p=.027$	$t_{18}=-1.98$; $p=.032$
Oxytocin vs. placebo	$t_{19}=0.35$	$t_{19}=-1.80$	$t_{19}=0.28$	$t_{19}=1.09$

▲ **Table 2. Mean EMG responses** (SD) during the early dynamic phase of emotional facial expressions

4 Discussion

In the current study, we examined short-latency (that is, within 600 ms after stimulus onset) facial EMG responses to morphed angry and happy facial expressions in forensic psychopathic patients and normal controls. Psychopathic patients in the placebo condition showed significantly weaker short-latency zygomaticus responses to happy faces and a trend to significantly weaker short-latency corrugator responses to angry faces relative to normal controls. These results are consistent with a recent study of facial EMG responses in male DBD adolescents with high CU traits (van Boxtel et al., 2022). In that study, weaker short-latency responses to positive and negative dynamic emotional facial

expressions were demonstrated in adolescents with high CU traits compared to those with low CU traits and normal controls, with the latter two groups not showing significantly different responses among themselves.

Our hypotheses that OT in psychopathic patients enhances facial mimicry compared with placebo proved incorrect. The corrugator responses to angry faces (third hypothesis) did not differ between OT and placebo conditions. Similarly, OT did not induce a stronger corrugator inhibition (i.e., relaxation) to happy expressions, except for a trend during the first 200 ms within the early rise time. The zygomaticus response to happy faces (fourth hypothesis) did not differ either between OT and placebo conditions.

Psychopathic patients are impaired in their short-latency mimicry responses of emotional expressions. Both our study in adult male psychopathic patients and the above study by van Boxtel and colleagues (2022) in male adolescents with psychopathic traits together demonstrate short-latency mimicry deficits, which are believed to be automatic and unconscious. We therefore posit a lifetime developmental deficit in psychopathy regarding short-latency mimicry of emotional expressions. Whether this is an innate deficit or whether it stems from adverse experiences in early life, such as poor quality of parental care (Kraaijenhanger et al., 2017), is unknown. We assume that unraveling this lifetime developmental deficit in short-latency mimicry in psychopathic individuals will help to better understand their impaired empathy processing and ultimately lead to elucidating their maladaptive social interactions. Deficits in facial emotional information processing are thought to partly underlie empathy deficits (Rijnders et al., 2021a). There is debate as to whether deficits in facial emotional information processing stem from either a failure to allocate attention to stimuli deemed of secondary importance (according to the response modulation theory of psychopathy; see: Newman & Lorenz, 2003; Baskin-Sommers et al., 2009) or an innate deficient amygdala processing (Blair, 2001, 2005a). Amygdala dysfunction in psychopathy is thought to underlie impaired attention to the human eye region, reducing recognition of emotional facial expressions (Dadds et al., 2011). This forms the basis of integrated emotion systems theory (Blair, 2005b) that describes significant deficits in emotional face recognition as the root cause of a disrupted social interaction process in which facial expressions of fear and sadness are not understood as distress signals that should induce inhibition of aggressive behavior. The ultimate result is impaired empathic behavior. It is thought that amygdala subregions are of great importance in this process (cf. Rijnders et al., 2021a). However, it should be stipulated that it is not completely certain that attentional deficits to the eye region are actually amygdala-based, as Terburg and colleagues (2012) showed

improved fear recognition and longer attention to the eye region of fearful faces in nonpsychopathic subjects with bilateral basolateral amygdala damage. Response modulation theory and integrated emotion systems theory are not mutually exclusive, as both contextual factors and motivational forces could influence the likelihood and strength of psychopathic individuals' attentional gaze if it is in their best interest. If it matches their primary goal, they will focus their attention on the other person's eye region, which may lead to enhanced facial emotion recognition (Dadds, 2011). This could result in a boost in their empathy processing (Meffert et al., 2013; Rijnders et al., 2021a).

In this study, the effect of OT on facial mimicry is different than we had previously hypothesized. In fact, compared with placebo, OT has no significant effect on the corrugator responses to happy and angry faces, nor on the zygomaticus response to happy faces. We have no explanation for this null result, but perhaps attentional modulation as predicted by the social saliency hypothesis of OT (Shamay-Tsoory & Abu-Akel, 2016) does not apply to psychopathic individuals. Alternatively, the one-time administration of OT may be too little to bring about change and multiple OT applications should be followed to measure effects. There are a few limitations to the current study. First, although we used a within-patient design, the number of patients was still low, which potentially increased the risk of underpowering of this study (Walum et al., 2016). Second, due to practical reasons the group of normal controls did not administer OT. As a result, it was not possible to analyze whether OT has different effects in psychopathic patients compared with normal controls. Third, we used morphed facial expressions in which all aspects of facial muscle actions change linearly in a uniform manner, whereas this is not the case with natural expressions. As a result, morphed expressions may have a somewhat unnatural appearance compared with natural expressions (Bernstein & Yovel, 2015; Calvo et al., 2016; Krumhuber et al., 2013) and have been suggested to be inferior to facial motion captured in video recordings (Becker et al., 2023).

Furthermore, we analyzed mimicry responses during a 600-ms early rise time. The optimal duration in terms of the perceived intensity and naturalness of basic emotions is in the range of 500-740 ms (cf. van Boxtel et al., 2022). Since the refresh rate of the emotional pictures was 40 ms, only 15 of the 40 pictures were displayed during this 600 ms, so the maximum intensity of the emotional expression (apex) was not reached. It is possible that this relatively slowly evolving presentation of stimuli might have negatively affected the strength of the mimicry responses of both psychopathic patients and normal controls.

Notwithstanding these limitations, the current study provides several valuable insights into the relationship between psychopathy and facial mimicry.

A unique point of this study is that we investigated a clinically identified and PCL-R confirmed group of forensic psychopathic patients who were not treated with medication like selective serotonin reuptake inhibitors, selective noradrenaline reuptake inhibitors, antipsychotics, or hormonal libido inhibitors. This study showed reduced mimicry of corrugator and zygomaticus of angry and happy expressions, respectively. This finding is consistent with the results obtained in a study with male adolescents with disruptive behavior disorders and high CU traits (van Boxtel et al., 2022), which leads us to posit a lifetime developmental deficit in short-latency mimicry in psychopathy. This deficit may have negative implications for the evolvement of empathy in psychopathic individuals.

Cleckley (1941) originally described the psychopath's severe deficits in the behavioral, emotional, and interpersonal domains. He stated that psychopathic individuals have a "convincing mask of sanity" and are unable to attribute genuine affective meaning to important experiences, despite their intact rational processes. Although further research is warranted, we assume that our study of short-latency facial mimicry has revealed some insight behind the masks of our group of psychopathic patients. One might also ask whether deficiencies in short-latency facial mimicry are a biomarker of psychopathy. EMG is an interesting parameter in that regard and we advocate future research on that application.

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Supplementary Information

PCL-R facets	PCL-R facet domains	Items	PCL-R factor domains	PCL-R factor
<i>Facet 1</i>	<i>Interpersonal facet</i>	glib/superficial	<i>Interpersonal/ Affective factor</i>	1
		grandiose self-worth		1
		pathological lying		1
		conning/manipulative		1
<i>Facet 2</i>	<i>Affective facet</i>	lack of remorse or guilt		1
		shallow affect		1
		callousness or lack of empathy		1
		failure to accept responsibility		1
<i>Facet 3</i>	<i>Lifestyle facet</i>	stimulation seeking	<i>Impulsive lifestyle/ Antisocial factor</i>	2
		impulsivity		2
		irresponsibility	2	
		parasitic orientation	2	
		lack of realistic goals	2	
<i>Facet 4</i>	<i>Antisocial facet</i>	poor behavior controls		2
		early behavior problems		2
		juvenile delinquency		2
		revocation of conditional release		2
		criminal versatility		#
<i>Two items that do not load on any of the four facets</i>		promiscuous sexual behavior		#
		many short-term marital relationships		#

▲ **Table S1. The two-factor and four-facet model of the PCL-R (Hare, 1991, 2003).** The three items in the two-factor model marked with # do not load on these two factors, while in the four-facet model this is the case for two items. In Table 1, we refer to these last two items as PCL-R category "Other".

Chapter 5
Sniffing submissiveness?
Oxytocin administration
in severe psychopathy

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Abstract

Psychopathy is a personality disorder associated with criminal behavior and violent recidivism, and therefore a burden to society. Social dominance is one of the characteristics of psychopathy that might contribute to these problems. Nevertheless, only few studies have objectively measured the relationship between socially dominant behavior and psychopathy. Therefore, the current study assessed performance of 21 forensic PCL-R confirmed psychopathic patients and 24 normal controls on a gaze aversion task, in which slower gaze aversion from masked angry faces compared to masked happy faces is a measure of reactive dominance. Moreover, the current study assessed the potential beneficial effects of the neuropeptide oxytocin. The results showed that psychopaths were not more dominant on the gaze aversion task compared to normal controls. However, the severity of psychopathy was positively correlated with reactive dominance. Crucially, a single nasal spray administration of oxytocin abolished the connection between psychopathy and reactive dominance. This implies that socially dominant psychopaths might benefit from oxytocin administration.

1 Introduction

Psychopathy is a lifespan personality disorder characterized by disturbances in the emotional, interpersonal and behavioral domains and an increased tendency to antisocial behavior (Blair, 1995; Blair, 2003b; Hare, 1991; Hare, 2003). Psychopathy is operationally defined by Hare's Psychopathy Checklist-Revised (PCL-R), which is a diagnostic assessment tool that consists of 2 factors (or 4 facets) (Hare, 1991, 2003; zie Table 1 and § 3.3). In addition to predicting violent behavior, psychopathic characteristics are also strongly associated with criminal recidivism. (Dhingra & Boduszek, 2013; Hare, 1996; Hare, 2003; Harris et al., 1991; Hemphill et al., 1998; Skeem & Cooke, 2010). Due to this propensity for antisocial behavior, psychopathic individuals are over-represented in the forensic system (Hare, 1996; Coid et al., 2009; Nentjes et al., 2017).

Social dominance is one of the characteristics of psychopaths that might contribute to their problematic and aggressive behavior (Blair, 1995; Hare, 1991; Hare, 2003; von Borries et al., 2012). Social dominance is not explicitly defined in the PCL-R, but is related to the interpersonal factor (factor 1) of the PCL-R (Draycott et al., 2011; Hall et al., 2004; Murphy et al., 2016; Verona et al., 2001). In addition, the psychopath's nonsocial and noncooperative behavior is believed to be related to amygdala-based deficits in interpreting emotional signals (Blair, 1995; Blair, 2003a) or to an insensitivity to peripheral information with at the same time a prevailing tendency to focus superiorly on primary goals (Newman & Lorenz, 2003; Baskin-Sommers et al., 2009). In support of these theories, previous studies have shown that adult psychopaths as well as youngsters with callous-unemotional traits (CU traits; i.e. precursors of psychopathy) have a reduced gaze to the eye region (Boll & Gamer, 2016; Dadds et al., 2008; Rice & Derish, 2015; Gillespie et al., 2017). As a consequence of this reduced eye gazing, psychopaths may have altered social perceptions and a lack of inhibition of inappropriate social behavior, eventually resulting in social dominance. This theory is further supported by a study that found that psychopaths with high fearless dominance scores had lower levels of facial exploration (Boll & Gamer, 2016). Despite this theoretical basis for an association between a dominant personality trait and psychopathy, dominance behavior in psychopaths was measured in only a few studies. Lobbestael and colleagues (2018) demonstrated that psychopathic traits correlate with dominant behavior towards a dominant interviewer. Nentjes and colleagues (2017), however, were unable to find an association between psychopathy and both self-dominant associations and explicitly assessed dominance. These results may also reflect participants'

reluctance to explicitly reveal a dominant self-view or lack of self-awareness, which is believed to be insufficient in psychopaths (Fowler et al., 2009; Nentjes et al., 2017).

Considering the social impact of psychopaths' crimes and their high recidivism rates, as well as a lack of adequate treatment strategies, it must be concluded that psychopathic behavior is a burden to society (Draycott et al., 2011; Hare, 1996; Moul et al., 2012; von Borries et al., 2012; Kiehl & Sinnott-Armstrong, 2013). Hence, there is a need to explore future treatment options, including drug therapy. In that regard we point to the role of oxytocin (OT). This is a neuropeptide assumed to be involved in prosocial behavior (Caldwell, 2017) and whose expression is negatively associated with psychopathy (Moul et al., 2012; Verona et al., 2018). As social dominance is part of the behavioral repertoire of the psychopaths that negatively affects their social attunement and behavior, whereas a decrease in dominance behavior may be beneficial in treatment, we investigated whether OT can inhibit social dominance in favor of more submissive behavior.

The effect of OT on dominance behavior is not precisely known. In both animal and human studies it has been established that OT encourages social approach, increases eye contact, emotion recognition, trust, and empathy, influences amygdala function, and enhances submissive behavior in social groups (Caldwell, 2017; Guastella et al., 2008; Liu et al., 2012; Tillman et al., 2019; Timmer et al., 2011; Hellmann et al., 2015). The social salience hypothesis of OT predicts that OT is associated with attention modulation depending on the salience of external social cues, while individual aspects such as character, gender and psychopathological states still remain important (Shamay-Tsoory & Abu-Akel, 2016). In healthy subjects, intranasal OT administration resulted in a decreased gaze at angry faces, while the gaze at happy faces increased (Domes et al., 2012; Domes et al., 2013; Ellenbogen et al., 2012; Tollenaar et al., 2013). These findings emphasize that OT increases the salience of emotional cues, which is considered important in dominant or submissive behavior, as differentiation of perceived emotional valenced cues is important in eliciting reactive interpersonal responses (Domes et al., 2013). Since these behavioral, affective and cognitive processes touch upon the concept of psychopathy, one could assume a role for OT in psychopathy. Previous studies have further shown that OT receptor gene methylation (Aghajani et al., 2018; Dadds et al., 2014a) and OT receptor polymorphisms (Dadds et al., 2014b) as well as lower OT concentrations in saliva and blood plasma (Dadds et al., 2014b) positively correlate with high CU traits in children and adolescents. Conversely, Verona and colleagues (2018) found another association between OT and psychopathy, as

they showed that lower psychopathic traits in adults were negatively correlated with OT-related single-nucleotide polymorphisms (SNPs), including an SNP on the OT receptor. Furthermore, most studies on OT effects are done in (healthy) men, while studies in women are unfortunately scarce (Quintana et al., 2020). It is warranted to enroll more women in OT studies as it appears that the usual dose of OT (i.e. 24 IU) may lead to opposite effects in women compared to men (Lieberz et al., 2020).

Although until date no research has been done into the effects of OT on reactive dominance in psychopaths, in theory OT administration could become an additional treatment strategy aimed at reducing the psychopath's disruptive (e.g. dominant) behavior. Therefore, we examined OT effects on measures of dominance behavior in psychopaths. We used the gaze aversion task, developed by Terburg and colleagues (2011), which measures gaze aversion latencies of masked angry, happy, and neutral faces. They showed that slower gaze aversion from angry faces compared to happy faces is a strong indirect measure of reactive dominance, while more rapid gaze aversion from angry faces indicates submissiveness (van Honk & Schutter, 2007; Mazur & Booth, 1998; Putman et al., 2004; Terburg et al., 2011; Terburg et al., 2012; Terburg et al., 2016; Hortensius et al., 2014). This gaze aversion task could potentially provide an objective measure of reactive social dominance in psychopaths, especially since compared to healthy controls, psychopathic offenders avoid angry faces less in an approach-avoidance task (von Borries et al., 2012).

2 Current study

The gaze aversion task in the current study was part of a larger study in which the behavioral effects of intranasal OT in psychopathic patients were measured. Two groups were tested. One group consisted of male psychopathic patients who followed a within-subject, double-blind, counterbalanced, placebo-controlled, crossover design. They were tested on two days. A control group of male guards or nurses was tested on one day only, as the controls did not undergo any OT or placebo intervention (see Figure 1).

Three hypotheses were tested. First, it was hypothesized that compared to normal controls, psychopathic patients are more dominant and therefore have a slower gaze aversion of masked angry faces compared to happy faces

(Mazur & Booth, 1998; Terburg et al., 2011; Terburg et al., 2012; Hortensius et al., 2014; Terburg et al., 2016; von Borries et al., 2012). Second, in psychopathic patients OT was hypothesized to reduce their reactive dominance in the sense that they would have a faster gaze aversion from masked angry faces compared to happy faces (Domes et al., 2012; Domes et al., 2013; Ellenbogen et al., 2012; Tollenaar et al., 2013). Third, gaze aversion latency of all participants was hypothesized to correlate positively with measures of psychopathy, i.e. PCL-R (especially PCL-R factor 1) for the psychopathic patients and the Psychopathic Personality Inventory-Revised (PPI-R; Lilienfeld & Widows, 2005) for the normal controls, as previous studies had found strong associations between dominant behavior and PCL-R factor 1. For example, in a group of 310 inmates of a medium-security facility their PCL-R facet 1 related to social dominance, higher adaptive functioning and low stress reactivity (Hall et al., 2004), while in a non-clinical sample, those who scored high in PCL-R factor 1 showed increased dominant behavior when interacting with a dominant interviewer (Lobbestael et al., 2018). In addition, boldness measures that encompass terms as fearlessness, reduced anxiety, surgency, interpersonal poise, and emotional resilience, were positively associated with scores on PCL-R facet 1 in particular, albeit for men, not for women (Murphy et al., 2016). In addition, in a group of 313 male inmates, dominance and status seeking were strongly related to PCL-R factor 1 (Verona et al., 2001).

3 Method

3.1 Participants

Initially, a total of 24 male forensic psychiatric in-patients and 30 normal male controls were included in the current study. Patients were recruited from five maximum security forensic psychiatric hospitals in the Netherlands. They were selected if their PCL-R total score was 26 or higher. As this study was part of a larger study that also focused on empathy processing in psychopathy, the maximum score (i.e. 2) of PCL-R item “callousness / lack of empathy” (Hare, 2003) was required. The normal controls were male security guards or nursing staff members recruited from two forensic psychiatric hospitals. Similar inclusion and exclusion criteria applied to these participants, except that they could not

be diagnosed with the PCL-R. Instead, to check for psychopathic features, they completed the authorized Dutch translation of the PPI-R (Uzieblo et al., 2010). T-scores were calculated for the two PPI-R factors, i.e. Fearless Dominance (with its subscales Social potency, Fearlessness, and Stress immunity) and Impulsive Antisociality (with its subscales Machiavellian egocentricity, Rebellious nonconformity, Blame externalization, and Carefree nonplanfulness) as well as for the PPI-R subscale Coldheartedness that does not load on the two PPI-R factors (Benning et al., 2003).

Additional requirements for participation in this study were a good physical health, age between 18 and 60 years, a normal or corrected to normal visual acuity, and a total IQ of 80 or above. Exclusion criteria were color blindness, illiteracy, insufficient knowledge of Dutch language, or a current severe psychiatric disorder like a psychotic disorder, a depressive disorder, or a severe anxiety disorder. After screening by a psychiatrist (first author R.J.P. R.) it was concluded that these psychiatric disorders were not currently present in any of the participants. Other exclusion criteria were a history of endocrine disorders or brain diseases, including closed head injury with loss of consciousness exceeding 15 minutes. Selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors, antipsychotics, and hormonal treatments for libido inhibition were contraindicated due to a possible interference with the action of OT or with social dominant relationships (Yamaguchi et al., 2017; Malatynska & Knapp, 2005; Neshet et al., 2013). In case of a “runny nose”, currently or within the past seven days, participants were temporarily excluded from the test procedure. Participation was also temporarily suspended if they had used alcohol or recreational drugs in the past 24 hours before each test procedure (alcohol use and drug use were a priori prohibited in all hospitals). When in doubt an urine based screen test for immediate drug use detection was performed (Multi-Drug Rapid Test Cup; AKSA Medical, the Netherlands). Recent use of cannabis was revealed in one case, which led to postponement of the test procedure by one week.

Of the 24 patients with PCL-R cut-off scores of 26 or higher who were enrolled in this OT study, three were eventually excluded from analysis due to their co-morbid DSM-IV-TR (American Psychiatric Association, 2000) Pervasive Developmental Disorder Not Otherwise Specified. In addition, of the 30 normal controls two persons were excluded before analysis. One of them was excluded due to a total score of >2 SD above average on the PPI-R, indicating a psychopathic tendency. Another normal control was expelled as he turned out to be deficient in describing, identifying and processing emotions according to the Toronto Alexithymia Scale (Bagby et al., 1994).

The group of the remaining 21 psychopathic patients that complied with all inclusion and exclusion criteria was considered the “intervention group”. The 28 remaining normal controls did not apply either placebo or OT and were therefore tested for one session only.

Few normal controls had a different cultural background, but all had lived and were educated in the Netherlands from an early age. The same was true for the few psychopathic patients with a different cultural background, who all had extensive experience with Dutch society before they were arrested and convicted for their crimes. Therefore, it was concluded that no cultural barriers in either group existed that eventually could hinder test instructions or disrupt test attitudes. Detailed sample characteristics are presented in Table 1.

3.2 Study design

The 21 psychopathic patients of the intervention group followed a within-subject, double-blind, counterbalanced, placebo-controlled, cross-over design. Thus, these participants completed two test sessions, one in which they sniffed a nasal spray with a total of 24 International Units (IU) of the synthetic version of OT (registered product name Syntocinon®). This product is identical to the human pituitary version of OT. In the other test session, they received a placebo nasal spray consisting of a solution of physiological saline (NaCl; quality label PH.EUR; BUFA, Spruyt Hillen, The Netherlands). The mean time interval between the two sessions was 12.3 ± 3.6 days. Times of nasal spray administration on the two test days were kept as similar as possible within-subjects. Participants were instructed to refrain from cigarette smoking and caffeine consumption at least one hour before the start of the test session. During the wash-in period of OT to act in the central nervous system (Leng & Ludwig, 2016) the participants of the intervention group watched stress-free fragments of the documentary Planet Earth (BBC, 2006).

The overall test procedure for the normal controls was similar, except that they were tested on one day only, as they did not sniff intranasal spray. The clips from the BBC documentary were therefore not presented to them. An overview of the test procedures for both groups is shown in Figure 1. All participants have completed their test procedures.

Shortly before the start of the gaze aversion task the participants completed a computerized and Dutch version of the Profile of Mood States questionnaire (POMS; McNair et al., 1971) based on the short-form

	Psychopathic patients (N=21)	Normal controls (N=24)
<i>Age¹ (years)</i>	39.5 ± 9.3	36.1 ± 7.7
<i>Ethnic-cultural and national origin (all participants currently had a Dutch nationality)</i>	19 Caucasian (16 Dutch, 1 Belgian, 2 Turks), 1 African-Surinamese, and 1 Chinese-African Surinamese	23 Caucasian (20 Dutch, 2 Moroccans, 1 Turk), and 1 Hindustan-Surinamese
<i>Duration of mandatory treatment (months)</i>	112 ± 82	
<i>PCL-R total score</i>	31.1 ± 2.9	
<i>PCL-R facets</i>		
<i>Interpersonal facet (facet 1)</i>	5.8 ± 1.3	
<i>Affective facet (facet 2)</i>	7.4 ± .8	
<i>Lifestyle facet (facet 3)</i>	7.8 ± 1.3	
<i>Antisocial facet (facet 4)</i>	8.3 ± 1.4	
<i>Category “Other” (two items)</i>	2.0 ± 1.5	
<i>PPI-R total score</i>		286.6 ± 28.7
<i>T-score total</i>		47.5 ± 10.5
<i>Factor Fearless Dominance</i>		54.4 ± 9.8
<i>Social potency</i>		55.0 ± 11.5
<i>Fearlessness</i>		53.6 ± 12.1
<i>Stress immunity</i>		55.4 ± 8.0
<i>Factor Impulsive Antisociality</i>		42.1 ± 9.7
<i>Machiavellian egocentricity</i>		38.3 ± 12.5
<i>Rebellious nonconformity</i>		48.1 ± 10.1
<i>Blame externalization</i>		44.8 ± 8.4
<i>Carefree nonplanfulness</i>		48.1 ± 10.6
<i>Coldheartedness</i>		49.5 ± 10.8

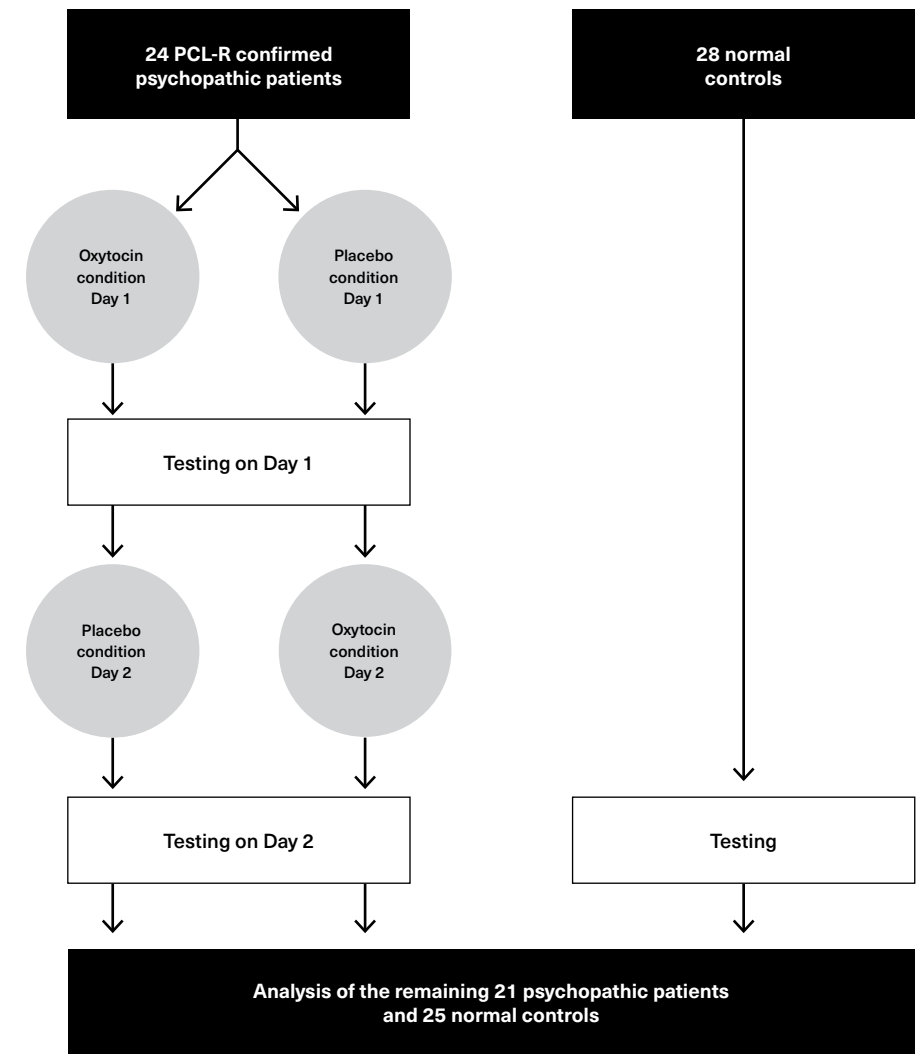
▲ **Table 1. Demographic information** For all variables the means ± standard deviations are reported. ¹ No significant group differences in age ($t=1.34, p=.187$). PCL-R = Psychopathy Checklist-Revised; PPI-R = Psychopathic Personality Inventory-Revised (two factors and eight subscales).

version (Shacham, 1983) and using a visual analog scale. In this self-report questionnaire, 35 adjectives were presented describing both the presence and perceived intensity of six mood state-related categories: tension-anxiety, anger-hostility, fatigue-inertia, depression-dejection, confusion-bewilderment, and vigor-activity. A Total Mood Disturbance (TMD) score was calculated for each participant by adding up the individual mean scores of the first five mood state-related categories and then subtracting from it the individual mean score of the last category (i.e., vigor-activity) (McNair et al., 1971). It was analyzed whether OT affected the TMD scores in the intervention group of psychopathic patients.

In order to control for blindness of drug administration, the psychopathic patients gave their estimate of the order of drug allocation at the end of the second test procedure. In line with reviewed placebo-controlled OT studies with OT dosages ranging from 18 to 40 IU (MacDonald et al., 2011) it was expected that participants were unable to accurately report on when they had received OT and placebo.

3.3 Psychopathy Checklist - Revised

Psychopathy can be diagnosed by Hare's Psychopathy Checklist-Revised (PCL-R). This checklist consists of 20 items with scores of 0, 1 or 2 per item, so a maximum score of 40 points represents the extreme end of the psychopathy score. In the revised form of the PCL, Hare (2003) proposed a four-factor model (also referred to as a four-facet model), comprising 1) an interpersonal facet, 2) an affective facet, 3) a behavioral lifestyle facet, and 4) an antisocial facet, leaving two PCL-R items (viz "promiscuous sexual behavior", and "many short-term marital relationships") separately as they do not load on any of the four facets. In the analysis below we will refer to these two separate PCL-R items as PCL-R category "Other". Note that PCL-R factor 1 in the original two-factor model (Hare, 1991) includes both PCL-R facet 1 and facet 2 in the four-facet model. PCL-R facet 3 and facet 4 are derived from the original PCL-R factor 2 plus PCL-R item "versatile criminality" which did not load on either factor 1 or factor 2 in the original two-factor model. The items, factors and facets of the PCL-R are presented in Table 1. Compared to North America, lower cut-off scores for psychopathy are used in various European countries (Cooke et al., 2005; Grann et al., 1998; Cooke, 1998; Rasmussen et al., 1999; Cooke & Michie, 1999; Mokros et al., 2013).



▲ **Figure 1. Flowchart of test procedures for both groups** The psychopathic patients sniffed nasal spray containing either OT or placebo in a cross-over within-design. They were therefore tested on two days. The normal controls did not undergo an experimental condition and were thus tested on one day. Of the group of psychopathic patients, 3 were excluded from analysis due to a co-morbid Pervasive Developmental Disorder Not Otherwise Specified. In addition, 4 normal controls were excluded from further analysis: 2 because of missing GA data, and an additional 2 because according to the awareness check, they appeared to be aware of the facial stimuli presented in the GA task.

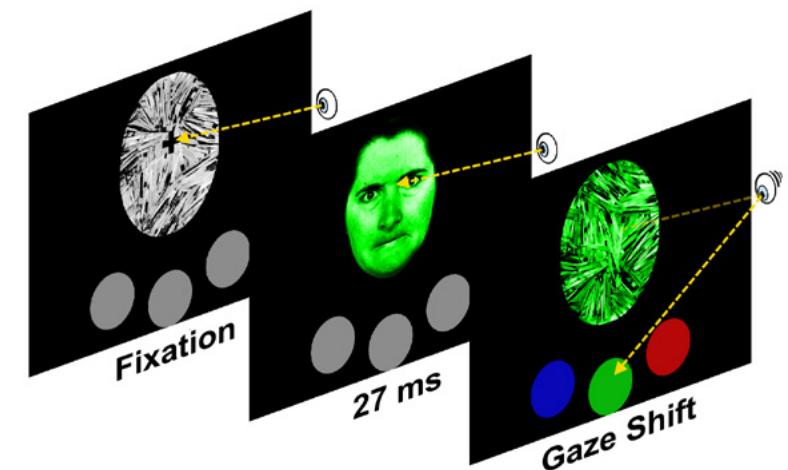
PCL-R facets	Domains	Items
Facet 1	Interpersonal facet	glib/superficial; grandiose self-worth; pathological lying; conning/manipulative
Facet 2	Affective facet	lack of remorse or guilt; shallow affect; callousness or lack of empathy; failure to accept responsibility
Facet 3	Lifestyle facet	stimulation seeking; impulsivity; irresponsibility; parasitic orientation; lack of realistic goals
Facet 4	Antisocial facet	poor behavior controls; early behavior problems; juvenile delinquency; revocation of conditional release; criminal versatility
Category "Other"	Two items that do not load on any of the 4 facets	promiscuous sexual behavior; many short-term marital relationships

▲ Table 2. The four-facet model of the PCL-R (Hare, 2003)

3.4 Gaze Aversion Task

Participants performed a slightly modified version of the gaze aversion task developed by Terburg and colleagues (2011). This response time task reflects reactive dominance to masked facial stimuli (see Figure 2). Participants had to focus on a fixation cross projected on a gray oval premask that suddenly changed in an either blue, green, or red colored facial image with an either neutral, happy, or angry facial expression. This facial stimulus was presented for 27 ms, and was then followed by an oval postmask with an identical color and similar luminance.

Participants were instructed that from the moment the central gray stimulus turned color, they should avert their gaze as quickly as possible from the original fixation cross to the smaller circle of the same color as the mask. Gaze aversion latency was defined as the reaction time between the onset of the masked colored facial stimulus and the first gaze at the circle with the identical color. The task started with 10 practice trials with only neutral faces. A total of 90 facial stimuli with either neutral, angry, or happy facial expression were then presented in a semi-random order (NxxNyyxNNyyxNxxN; N = neutral; x and y = angry and happy faces; this fixed sequence was repeated five times and counterbalanced across the two sessions; Terburg et al., 2012). As soon as a participant had focused on the circle with the identical color, the next trial began. The stimuli consisted of subliminally presented neutral or emotional (angry, happy) faces with similar luminance. They were from 5 different Caucasian men and 5 different Caucasian women who were derived from a standardized photo set (Ekman & Friesen, 1971).



▲ Figure 2. The Gaze Aversion Task A trial started with a fixation cross that appeared on a gray oval. After this gray premask turned color, the participant had to avert his gaze as quickly as possible to the smaller circle with the same color. Shortly (27 ms) before the postmask appeared a colored facial stimulus with an either neutral, happy, or angry facial expression was presented with identical color and similar luminance. The next trial began as soon as the participant had focused on the circle with the identical color. Gaze aversion latency was defined as the reaction time between the onset of the masked colored facial stimulus and the first gaze at the circle with the identical color.

3.5 Awareness check

An awareness check was performed at the end of the one-day test procedure (normal controls) or at the end of the second test day (psychopathic patients). The aim was to determine whether the facial stimuli in the gaze aversion task had been successfully masked. A total of 30 masked facial stimuli with above-mentioned emotions and colors were randomly assigned in a way that each color was presented 10 times. Contrary to the instructions prior to the gaze aversion task, the participants were now explicitly informed of the briefly displayed (27 ms) emotional facial expressions and instructed to indicate the emotion of the masked facial stimuli (either angry, happy, or neutral) by pressing numbers on the keyboard.

3.6 Materials

All tasks were programmed in E-Prime version 1.2 (Psychology Software Tools, Sharpsburg, USA) and presented on a 17-inch TFT monitor with a sampling rate of 75 Hz, in combination with a Tobii-120 infrared eye-tracker, which recorded participants' eye movements (Tobii AB, Danderyd, Sweden).

3.7 Ethics

Participants provided written informed consent prior to their participation. The study was approved by the medical ethics committee of the University Medical Centre Utrecht, Netherlands, and was carried out in accordance with the guidelines of the Declaration of Helsinki (World Medical Association, 2013). The participants received a monetary compensation.

4 Statistical Analyses

Statistical analyses were performed using Jamovi (v1.2.27) (The Jamovi Project, 2020) using the GAMLj toolbox (v2.0.5) (Gallucci, 2019). First, independent-sample t-tests were used to assess differences in demographic variables between the participants in the intervention group and the normal controls. To analyze whether the facial stimuli in the gaze aversion task were masked successfully, the total number of correctly recognized emotions on the awareness check was scored per participant. A score of 15 or higher was considered significantly higher than the chance level of 10 correctly recognized emotions, and was therefore defined as unsuccessful masking (binomial upper limit, $\alpha = .05$, $n = 30$, probability of correct responses = 1/3) resulting in exclusion of the participant.

Thereafter, the performance on the gaze aversion task was analyzed. First, reaction time (RT) outliers needed to be removed from the data. For each participant, RTs were deleted if they were less than 100 ms, or longer than 1,000 ms, or if they were more than 2 standard deviations above or below the mean RT. After this outlier removal procedure, the mean RTs of the angry and happy face trials were scaled to the mean RTs of the neutral face trials using subtraction, creating Angry–Neutral and Happy–Neutral contrast scores. For post-hoc analyses the mean RTs on the happy face trials were subtracted from the mean RTs on the angry face trials to create Angry–Happy contrast scores, which is the main contrast of interest for this study. High Angry–Happy contrasts represent a slower gaze aversion from angry compared to happy faces, which has been shown to be a measure of reactive dominance across multiple studies (Terburg et al., 2011; Terburg et al., 2012; Hortensius et al., 2014; Terburg et al., 2016). Vice versa, low Angry–Happy contrasts reflect a propensity for submission.

The Angry–Neutral and Happy–Neutral contrasts were then entered in a linear mixed model to assess emotion differences in gaze aversion latencies between the psychopathic patients (placebo condition) and the normal controls. Subsequently, a linear mixed model was used to test for the influence of intranasal OT administration on gaze aversion latencies from both emotions in the intervention group, i.e. psychopathic offenders. Finally, PCL-R total scores, followed by PCL-R facet scores, were entered in this linear mixed model as continuous predictor. In case of significant PCL-R effects, simple-slope analyses were used to specify the effect. Finally, follow-up Pearson's correlations between PCL-R (and PPI-R) scores and Angry–Happy contrast scores were performed to further specify the effects with regard to our hypotheses on the

relation between reactive dominance and psychopathic severity. All linear mixed models were estimated using the Satterthwaite method for degrees of freedom and all continuous predictors were entered as standardized scores.

5 Results

5.1 Demographic information and preliminary analyses

Of the 28 normal controls, two were excluded from analysis due to missing data on the gaze aversion task. In addition, two other normal controls were also excluded from further analysis as they had more than 15 correct answers on the awareness check, indicating an awareness of the facial stimuli presented in the gaze aversion task. As a result, the final sample size that was analyzed consisted of 21 psychopathic patients and 24 normal controls. The mean age of the psychopathic patients (39.5 ± 9.3 yrs) and the normal controls (36.1 ± 7.7 yrs) did not differ significantly from each other ($t(43)=1.34$, $p=.187$). The number of correct responses on the awareness check of psychopathic patients (9.5 ± 1.8) and the normal controls (10.0 ± 1.9) were also not significantly different ($t=-.79$, $p=.435$). For the psychopathic patients, the mean time interval between self-administration of the intranasal spray and the start of the gaze aversion task on both test days was 46.0 ± 5.9 minutes and 45.9 ± 6.3 minutes, respectively. The 24 IU dose and this time period were considered adequate. Although intranasal OT administration does not result in a linear dose-response curve, most human intranasal OT studies use doses between 20 and 48 IU, preferably 24 IU, while the time window for measuring OT-related neurobehavioral effects varies between 20 – 90 minutes after OT administration (Quintana et al., 2020). Furthermore, Spengler and colleagues (2017) found effective amygdala responses in a time window of 45 – 70 minutes after 24 IU OT administration in their functional magnetic resonance imaging study. OT administration did not affect current mood state ($F(1,20)=-.274$, $p=.607$). Furthermore, the expectation that the psychopathic patients could not accurately report on which day they received OT or placebo turned out to be true. The correct estimate of drug allocation was made by 13 participants (61.9%). The difference from chance was not significant (Fisher's exact test, $p=.181$), so it was concluded that the psychopathic patients did not know in which session they received OT or placebo.

5.2 Gaze Aversion Task

5.2.1 Group differences between psychopathic patients and normal controls

Angry–Neutral and Happy–Neutral contrasts of normal controls and psychopathic patients group (placebo condition) were entered in a linear mixed model including EMOTION, GROUP and their interaction as factors (see SI-Model1 in Supplementary Information). Data were clustered by participant and a random effect for the intercept across participants was included to account for general between-subjects variance. No significant effects emerged (EMOTION: $F(1,43)=.085$, $p=.772$, GROUP: $F(1,43)=.654$, $p=.423$, EMOTION by GROUP: $F(1,43)=.217$, $p=.644$) indicating that the psychopathic patients after sniffing placebo were not more dominant in the gaze aversion task than the normal controls.

5.2.2 Oxytocin intervention

Angry–Neutral and Happy–Neutral contrasts from the placebo and oxytocin conditions of the psychopathic patients group were entered in a linear mixed model including EMOTION, DRUG and their interaction as factors (see SI-Model2 in Supplementary Information). Data were clustered by participant and a random effect for the intercept across participant was included to account for general between-subjects variance. No significant effects emerged (EMOTION: $F(1,60)=.136$, $p=.713$, DRUG: $F(1,60)=.239$, $p=.627$, EMOTION by DRUG: $F(1,60)=.072$, $p=.789$), indicating that oxytocin administration in general did not affect reactive dominance.

5.2.3 PCL-R and PPI-R scores

PCL-R total score was added as continuous predictor to the oxytocin intervention linear mixed model. All possible interactions were modelled and data were clustered by participant (see SI-Model3a in Supplementary Information). In addition to the random effect for the intercept across participants we also added random effects of EMOTION and DRUG as we focus on the three-way interaction.

The three-way interaction of EMOTION, DRUG and PCL-R total score was significant ($F(1,19)=5.364, p=.032$), but all other effects were not (all $ps>.56$). Simple-slope analyses testing the DRUG effect in low PCL-R (-1SD) and high (+1SD) PCL-R groups were inconclusive showing no effects on the separate emotions (all $ps>.38$) and a marginal decrease of the angry-happy contrast in the high PCL-R group ($t(19)=-1.954, p=.066$, estimated in a separate model using Angry-Happy contrast data, see SI-Model3b in Supplementary Information).

To further specify this PCL-R effect we repeated the previous final linear mixed model, but the PCL-R total score was replaced by the five PCL-R categories (i.e. four PCL-R facets and PCL-R category "Other"; see for an explanation of this last category § 3.3) as continuous predictors (see SI-Model4a in Supplementary Information). All possible interactions between the factors EMOTION and DRUG, and each facet score, were modelled and data were clustered by participant. The three-way interactions for PCL-R facet 1 ($F(1,14)=7.248, p=.018$) and PCL-R facet 4 ($F(1,14)=7.556, p=.016$) were significant, but all other effects were not (all $ps>.25$). Simple-slope analyses testing the DRUG effect in low PCL-R (-1SD) and high (+1SD) PCL-R facet groups showed no effects on the separate emotions (all $ps>.17$), but interestingly, oxytocin administration significantly decreased reactive dominance in the high PCL-R facet 1 ($t(14)=-2.742, p=.016$) as well as in the high PCL-R facet 4 ($t(14)=-2.575, p=.022$) groups (both estimated in a separate model using Angry-Happy contrast data, see SI-Model4b in Supplementary Information), while there was no effect in the low groups (all $ps>.07$).

Finally, we used correlational analyses to evaluate the relation of the PCL-R scores with the Angry-Happy contrasts in the separate DRUG conditions. In the placebo condition a positive correlation was found between Angry-Happy contrasts and PCL-R total ($r=.456, p=.038$), PCL-R facet 1 ($r=.444, p=.050$) and PCL-R category "Other" ($r=.516, p=.020$). No such correlations existed for PCL-R facet 2 ($r=-.046, p=.847$), PCL-R facet 3 ($r=-.146, p=.539$), and PCL-R facet 4 ($r=.102, p=.668$). Thus, reactive dominance is related to higher levels of psychopathy, which is mainly driven by PCL-R facet 1 and PCL-R category "Other".

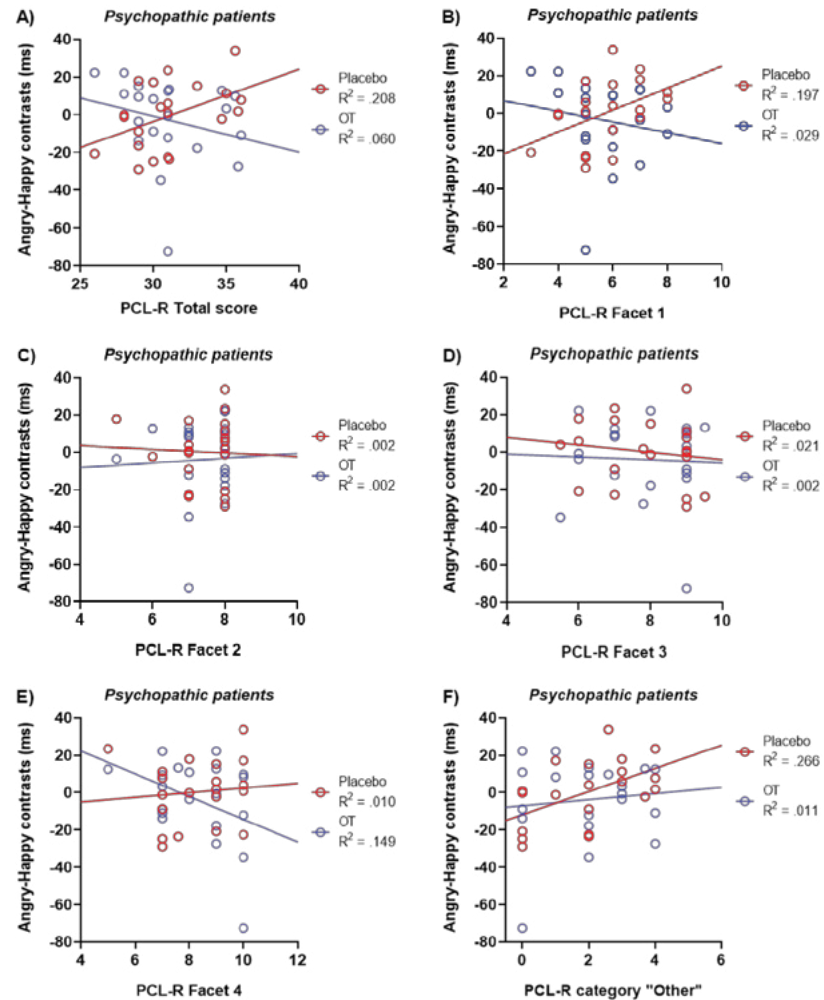
After oxytocin administration the significant relations between Angry-Happy contrasts and PCL-R total, PCL-R facet 1 and PCL-R category "Other" were abolished (respectively: $r=-.246, p=.283$; $r=-.168, p=.478$; $r=.106, p=.657$, see Figures 3A, 3B, & 3F). PCL-R facet 2, PCL-R facet 3 and PCL-R facet 4 (respectively: $r=.045, p=.849$; $r=-.044, p=.855$; $r=-.386, p=.093$, see Figure 3C, 3D, & 3E) were non-significant as well. We also tested for similar relations in the normal control group by correlating the Angry-Happy contrast with PPI-R

scores, but this was unexpectedly neither the case for the total PPI-R score ($r=-.015, p=.945$) and its two factors nor for any of its subscales (all $ps>.087$).

In sum, psychopathic severity (PCL-R total, PCL-R facet 1 and PCL-R category "Other") is related to higher reactive dominance, and oxytocin administration significantly reduces reactive dominance in psychopaths with severe PCL-R facet 1 and PCL-R facet 4 symptoms.

Normal controls	A - N	H - N	A - H			
PPI-R Factor 1: Fearless Dominance	.257	.247	.042			
Social potency	.355	.263	.149			
Fearlessness	-.077	-.077	-.010			
Stress immunity	-.030	.279	-.365			
PPI-R Factor 2: Impulsive Antisociality	.078	.125	-.045			
Machiavellian egocentricity	.304	.173	.189			
Rebellious nonconformity	-.043	-.068	.024			
Blame externalization	-.041	.159	-.238			
Carefree nonplanfulness	-.004	.115	-.140			
Coldheartedness	.330	.362	.002			
Total of 8 subscales	.214	.249	-.015			
Psychopathic patients	A - N	H - N	A - H	A - N	H - N	A - H
	Placebo			OT		
PCL-R total	.243	-.100	.456*	-.073	.233	-.246
PCL-R facet 1	.141	-.196	.444*	.018	.245	-.168
PCL-R facet 2	.388	.415	-.046	-.256	-.354	.045
PCL-R facet 3	.056	.164	-.146	-.016	.04	-.044
PCL-R facet 4	-.131	-.205	.102	-.129	.367	-.386
PCL-R category 'Other'	.134	-.257	.516*	.262	.160	.106

▲ **Table 3. Correlations of Emotion x Psychopathy scores (PCL-R or PPI-R) in the intervention group and normal controls.** A - N: Angry-Neutral contrasts; H - N: Happy-Neutral contrasts; A - H: Angry-Happy contrasts. Correlations with T-scores of the two PPI-R factors and the eight subscales (all $ps>.087$). Correlations with the PCL-R total score, its four facets and the category "Other". * $p<.05$



▲ **Figure 3. Emotion x Drug x PCL-R scores interaction effect in the intervention group.** A significant interaction effect existed between Emotion x Drug x PCL-R total scores. PCL-R facet 1 and PCL-R category “Other” contributed predominantly to this significant interaction effect. PCL-R facet 2, PCL-R facet 3 and PCL-R facet 4 did not show significant interaction effects. Note: even if the Angry–Happy contrast score of -72.46 in the OT condition is to be considered as an outlier and thus should lead to exclusion of this participant from analysis, then the main effects described would continue to exist (all p 's < .05 except the univariate relation between Angry–Happy contrasts and PCL-R facet 1 in the placebo condition would then turn to: $r = .449$, $p = .054$).

6 Discussion

In conclusion, contrary to our first hypothesis male psychopathic patients did not demonstrate higher levels of reactive dominance on the gaze aversion task compared to normal controls. However, contrary to normal controls, in the psychopathic patients, reactive dominance correlated significantly with measures of psychopathy (third hypothesis). Crucially, consistent with our second hypothesis, compared to placebo, a single nasal spray administration of OT abolished the relationship between severe psychopathy and reactive dominance, suggesting that OT can reduce reactive dominance in severe psychopathy. The mechanism behind this finding is unknown and needs further investigation. It can be hypothesized that the bidirectional interaction between OT and testosterone (Crespi, 2016) may be of significance in this reduced reactive dominance. Testosterone is known as a hormone associated with dominant behavior (Terburg et al., 2009), possibly only in the context of a concomitant low cortisol concentration (“dual-hormone hypothesis”; however, see for a critical discussion of this hypothesis: Dekkers et al., 2019). Since OT and testosterone appear to act opposite (Procyshyn et al., 2020), reduction of reactive dominance in severe psychopathy may then be due to OT counteracting the dominance-inducing effect of testosterone.

In the group of psychopathic patients significant positive correlations were found between reactive dominance and psychopathy PCL-R total scores as well as for PCL-R facet 1 (i.e. the interpersonal facet). These results are in line with previous studies (Hall et al., 2004; Lobbetael et al., 2018; Murphy et al., 2016; Verona et al., 2001). The PCL-R items “promiscuous sexual behavior” and “many short-term marital relationships” (referred to by us as PCL-R category “Other”), also correlated positively with reactive dominance. Not much is known about the link between social dominance and these two PCL-R items that touch upon concepts such as interacting with others in a sexual or intimate way. Although further research is warranted, social dominance can be a disruptive factor in establishing and perpetuating intimate relationships, so in this sense these two PCL-R items may reflect proxies of dominant behavior.

As stated above, according to the social salience hypothesis OT is associated with attention modulation depending on the salience of external social cues, while individual aspects such as character, gender and psychopathological states still remain important (Shamay-Tsoory & Abu-Akel, 2016). As observed by Ebitz and colleagues (2013) in rhesus monkeys, OT appears to weaken social threat vigilance when looking at images of dominant

conspicuous, by inhibiting information about negative social cues and thus allowing prosocial behavior that otherwise would not emerge. In everyday life, this can improve interpersonal attunement and ultimately reduce aggressive behavior. It might also result in a greater cooperation with the dominant other (de Dreu et al., 2012). In terms of therapy benefits, we assume that OT administration to patients with the most severe form of psychopathy will lead to a reduced sensitivity to dominance signals, which will result in better treatment alignment, ultimately allowing for faster and better therapy outcomes.

It is difficult to answer why no group differences were found in reactive dominance between normal controls and psychopathic patients. It could indicate different underlying mechanisms of reactive dominance in psychopaths and in normal controls. However, we hypothesize that specific group characteristics may also have been a determining factor. The psychopathic patients in the current study were recruited from several Dutch maximum security forensic psychiatric hospitals in which they underwent involuntary treatment on court order with the aim to reduce the risk of reoffending. Collaboration with hospital staff and patient's progress in therapy defined whether, and if so, when, they could start a reintegration phase in society and eventually discontinue their mandatory treatment program. All patients were aware that in case of an unsatisfactory treatment outcome, they ran the risk of ending up in a long-stay forensic psychiatric hospital with no prospect of release. So cooperation in these behavior-restricted environments is key and with it submission to the hospital staff and the rules of the hospital (Daffern et al., 2013; Draycott et al., 2011). Logically, it can therefore be understood that dominant behavior is not accepted, on the contrary, it might even prove counterproductive in terms of their chances of re-entering society. Therefore, a more submissive attitude might pay off. The study by Hornsveld and colleagues (2014) pointed in the same direction by showing that admission to a Dutch forensic psychiatric hospital leads to gradual changes in social behavior over the years, including changes in dominant behavior. As shown in Table 2, the psychopathic patients studied spent a considerable time in a forensic psychiatric hospital, on average 112 ± 82 months. Thus, it is possible that they have gradually become less dominant in line with the aforementioned considerations regarding mandatory therapy. Nevertheless, the foregoing consideration does not necessarily apply to the patients with the highest psychopathy scores, as they apparently still exhibit reactive dominance.

There are a few limitations to the current study. First, despite of the used dose of 24 IU OT intranasal spray, which was consistent with numerous other studies, it cannot be determined which proportion of OT actually substantially

entered the central nervous system (CNS) and induced intracerebral effects, as pharmacokinetic studies showed highly contradictory results of OT distribution in plasma, extravascular fluid, cerebrospinal fluid and CNS in terms of peak concentrations and the corresponding wash-in and wash-out time periods (Churchland & Winkielman, 2012; Leng & Ludwig, 2016). As a consequence, it cannot be ruled out either that the sniffed 24 IU of OT was too low for the group of psychopaths as a whole and that only the reactive dominance in the highest psychopathic patients decreased in the sense that they became more submissive. This hypothesis could not be explored in this study. Future studies should therefore include different concentrations of OT nasal spray as well as repeated administration rather than a single dose administration. Second, due to practical reasons the group of normal controls did not sniff nasal spray. As a result, it was not possible to analyze whether OT administration has different effects in psychopaths compared to normal controls. Consequently, it is not possible to interpret whether OT in a normal control group without psychopathy would also affect dominance.

Third, the normal control group was selected from male guards and nurses of two maximum-security forensic psychiatric hospitals. The question is whether personnel working in a forensic hospital environment in which continuous attention must be paid to safety problems and possible hostile behavior of the patient is the correct comparison group. It is possible that selection bias has occurred and that the normal controls work in a maximum-security forensic environment precisely because of their natural or acquired dominance. The individual balance in dominance measures specified with the GA task determines whether a person tends to be submissive or instead to be dominant towards an angry face. One would expect a continuum on this balance under normal controls. However, unexpectedly for us, as can be seen in Table 3, both PPI-R factors Fearless Dominance and Impulsive Antisociality and the eight PPI-R subscales did not show significant correlations between psychopathic traits and all reactive dominance measures in the control group, as they might have developed insensitivity for, or a better control over their reactions to, facial dominance signals. Therefore, in future research, it may be preferable to include a non-forensic community sample as a control group.

Notwithstanding these limitations, the current study provides several valuable insights into the relationship between psychopathy, reactive dominance and OT. We have demonstrated that OT abolished the relationship between severe forms of psychopathy and reactive dominance. More research is warranted and we suggest studying OT treatment applications, for example as adjunctive treatment in psychopathic patients with problematic dominant behavior.

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Supplementary Information

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Chapter 6

Would you? Effects of oxytocin on moral choices in forensic psychopathic patients

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*equal contribution

^equal contribution

Abstract

Psychopaths seem more likely to favor utilitarian outcomes over non-utilitarian (i.e., deontological) choices. Here we re-test this hypothesis and investigate whether oxytocin, a hormone associated with empathy, can counter this utilitarian effect. Forensic psychopathic patients and non-psychopathic controls participated in a sacrificial moral decision-making paradigm. Psychopathic patients performed the task in a double-blind cross-over placebo-controlled oxytocin administration paradigm. We found no evidence for psychopathic patients to act more utilitarian (or sacrificial) nor any effect of oxytocin administration. Psychopathic traits within the control group, particularly traits associated with lack of empathy and failure to consider consequences, were however associated with more utilitarian choices, but only when these actions were low in emotion. In contrast, psychopathy severity in psychopathic patients, particularly impulsivity-related traits, predicts deontological choices, but only in highly emotional actions. Thus, although psychopathic traits do predict utilitarianism when emotional investment is low, this is not the case in full-blown psychopathy. Instead, there is a link between impulsivity and deontological choices in psychopathic patients, but only when emotional investment is high, and self-interest is not at stake. These explorative results are discussed in relation to subregion amygdala processing and whether utilitarian outcomes align with the personal goals of psychopathic individuals.

1 Introduction

Psychopathy is a lifelong personality disorder characterized by deficits in interpersonal, emotional and behavioral functioning. Among other clinical features, psychopathic individuals exhibit a tendency to disrespect personal boundaries of others, are prone to antisocial behavior and instrumental aggression, and are known for their high criminal recidivism rates (Blair, 2001, 2003; Hare et al., 1991, 1996; Kiehl & Hoffman, 2011; Raine & Yang, 2006). The estimated lifetime prevalence of psychopathy worldwide in the general population would range from 0.5% to 1% (Hare, 1996; Neumann & Hare, 2008), although a recent meta-analysis estimated a higher prevalence rate in the general adult population of 4.5%, albeit only 1.2% when the Psychopathy Checklist-Revised (PCL-R; Hare, 2003) was used as a diagnostic tool (Sanz-García et al., 2021). The disruptive behaviors of psychopathic individuals, such as disrespecting the boundaries of others, make them disproportionately common among forensic patients and in prison populations (Coid et al., 2009; Dhingra & Boduszek, 2013; Guay et al., 2018; Hare, 1996; Hildebrand et al., 2004; Nentjes et al., 2017; Nicholls et al., 2005). Psychopathic individuals constitute 27.8% to 34.4% of homicide offenders (Fox & DeLisi, 2019). Given the extreme societal costs associated with this forensic overrepresentation (Kiehl & Hoffman, 2011), it is crucial to better understand why psychopaths violate social and legal norms and whether this can be treated. To that end, it is important to study how psychopathic individuals cope with situations in which their sense of morality is called upon.

In the most basic sense, morality can be described as reasoning about what is considered right and wrong, involving intuitive and emotional processes and taking calculative and social consequences into account (Greene et al. 2001). Moral reasoning is often studied through so-called moral dilemmas, i.e., specific situations in which the morality of an action is not evident (Whiteley, 1970). Moral dilemmas are typically defined in terms of mutually exclusive choices where an assumed rational response to maximize total welfare (i.e., the utilitarian judgment) is pitted against an emotional aversion to harm (i.e., the non-utilitarian or deontological judgment) (Gleichgerricht & Young, 2013). Sex differences exist, as women make fewer utilitarian decisions than men, thus favoring deontological choices, but only in cases of personally inflicting harm, not when the harm is indirectly inflicted (Capraro & Sippel, 2017; Friesdorf et al., 2015). We emphasize that utilitarian decisions should not be considered morally superior to deontological choices, and vice versa. Both mutually exclusive phenomena are rooted in distinct paradigms, each of

which may have evolutionary benefits in different contexts.

The dual-process theory of moral judgment (Greene et al., 2001) proposes that controlled cognitive and automatic emotional processes are normally competing while making moral judgments (Greene et al., 2001, 2004). In general, these cognitive processes are reflected by deliberate cost-benefit analyses, resulting in utilitarian decisions (John Stuart Mill, 1863/1998) that violate societal norms “for the greater good”. In other words, the calculated outcome of an action that harms others determines whether that action is considered right or wrong.

In contrast, emotion is reflected by an automatic aversive emotional reaction that results in deontological decisions (Immanuel Kant, 1785/2005) that avoid actively and intentionally inflicting harm (Koven, 2011; Patil & Silani, 2014). In other words, the nature of the action itself determines whether that action is considered right or wrong. In this case, the aversive emotional reaction to the utilitarian action would result in a passive stance, since it is wrong to intentionally harm people regardless of the outcome. Due to emotional deficits (e.g., Blair, 1995; Rijnders et al., 2021a), in psychopathic individuals such moral dilemmas arguably evoke only little emotional aversion against inflicting harm, so their focus would predominantly be on achieving positive net outcomes. Less empathic concern leads to making more utilitarian than deontological decisions (Gleichgerrcht & Young, 2013).

Psychopathic individuals exhibit emotional deficiencies (e.g., Blair, 1995) that disturb these processes. It is argued that these deficiencies diminish the automatic emotional processes, causing a bias towards the controlled cognitive processes, favoring utilitarian choices. This is however only confirmed in relation to psychopathic traits in community samples (Bartels & Pizarro, 2011; Glenn et al., 2010) while studies in confirmed psychopaths show mixed results (Koenigs et al., 2012; Young et al., 2012), which is arguably due to the different levels of emotion associated with utilitarian behavior in these studies.

Interestingly, the emotionality of the utilitarian action in moral dilemmas can be varied in a controlled manner. Moral dilemmas are classified as either personal or impersonal. The former describes acts where harm is caused by direct physical contact and the latter where harm is inflicted in an indirect, non-physical way. In this classification the utilitarian actions in personal dilemmas are associated with a stronger emotional value. Personal dilemmas are further divided into dilemmas in which the victim’s harm is either inevitable or evitable (Greene et al., 2009). Inevitable harm assumes that regardless of whether and what action is taken, the person involved will eventually suffer harm, whereas the latter is not the case with evitable harm if the action is waived. For example, in the

submarine dilemma, a personal inevitable dilemma is given. In this dilemma, you are the captain of a military submarine traveling underneath an immense iceberg. An onboard explosion has caused you to lose most of your oxygen supply and has injured one of your crew who is quickly losing blood. This injured crew member is going to die from his wounds no matter what happens. The remaining oxygen is not sufficient for the entire crew to make it to the surface. The only way to save the other crew members is to sacrifice the injured crew member so that there will be just enough oxygen for the rest of the crew to survive. Is it appropriate for you to kill the fatally injured crew member in order to save the lives of the remaining crew members? (Greene et al., 2001). Would you? In comparison, in personal-avoidable dilemmas, the victim will not suffer harm or die unless the utilitarian action is performed, giving that action an even stronger emotional response. In general, actions such as the captain’s in the latter personal inevitable dilemma are considered more morally permissible compared to harm inflicted in personal avoidable dilemmas (Huebner et al., 2011). Therefore, moral dilemmas can be ordered from impersonal to personal-avoidable to personal-avoidable in terms of increasing emotionality of the utilitarian action.

In the present study we will therefore explore moral decision-making in psychopathic patients and healthy controls using a strict separation of moral dilemmas based on the emotional value of the utilitarian action. We will thereby focus on the question whether moral judgment in psychopathy can be altered by administration of oxytocin (OT). This neuropeptide is a logical research candidate for influencing moral judgment, as it is known for its role in empathy processing (Barchi-Ferreira & Osório, 2021; Hurlemann et al., 2010), in generosity (Zak et al., 2007) and in social understanding and interpersonal behavior (Caldwell, 2017; Domes et al., 2007; Landgraf & Neumann, 2004; Meyer-Lindenberg et al., 2011). Furthermore, OT is involved in discriminating between outgroup and ingroup members (de Dreu & Kret, 2016). Effects of OT administration on moral decision-making are however mixed, possibly due to not taking account of the emotionality of the utilitarian actions (Goodyear et al., 2015; Preckel et al., 2014; Scheele et al., 2014; see for an overview Freitas & Osório, 2022).

To the best of our knowledge this is the first study in PCL-R-confirmed psychopathic individuals to investigate the influence of OT on moral judgments. We hypothesized that OT will reduce psychopathic patients’ choice of more utilitarian than deontological choices (hypothesis 1). We further hypothesized that psychopathic patients make more utilitarian choices compared to normal controls (hypothesis 2). In hypothesis 3, we stated that the percentage of utilitarian choices is positively related to psychopathy severity (Glenn et al., 2009; Koenigs et al., 2012).

2 Methods and materials

2.1 Participants

Initially, 24 male forensic psychiatric patients and 28 normal male controls were included in the current study. Patients were recruited from five maximum-security forensic psychiatric hospitals in the Netherlands. Compared with the diagnostic cut-off score of 30 in North America, lower cut-off scores for psychopathy are used in various European countries (Cooke et al., 2005; Grann et al., 1998; Cooke, 1998; Rasmussen et al., 1999; Cooke & Michie, 1999; Mokros et al., 2013). We selected patients if their PCL-R total score was 26 or higher. As this study was part of a larger study that also focused on empathy processing in psychopathy, the maximum score (i.e., 2) of PCL-R item “callousness / lack of empathy” (Hare, 2003) was required. The normal controls were male security guards or nursing staff members recruited from two forensic psychiatric hospitals. Similar inclusion and exclusion criteria applied to these participants, except that they could not be diagnosed with the PCL-R. Instead, to check for psychopathic features, they completed the Psychopathic Personality Inventory-Revised (PPI-R; Lilienfeld & Widows, 2005). Their raw scores were linearly converted into standardized T-scores allowing comparison with norm groups. T-scores were calculated for the two PPI-R factors, i.e., Fearless Dominance and Impulsive Antisociality as well as for the PPI-R subscale Coldheartedness that does not load on either of the two PPI-R Factors (Benning et al., 2003).

As the current study was part of a larger study in this group of psychopathic patients, we refer for an extensive description of additional requirements for participation in this larger study to Rijnders and colleagues (2021b). In short, inclusion criteria were male sex, good physical health, age between 18 and 60 years, and a total IQ of 80 or above. A current severe psychiatric disorder like a psychotic disorder, a depressive disorder, or a severe anxiety disorder, the current use of selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors, antipsychotics, and hormonal libido inhibitors as well as the current use of alcohol or recreational drugs constituted a contraindication to participation in this study. Of the 24 patients with PCL-R cut-off scores of 26 or higher who were enrolled in this OT study, three were eventually excluded from analysis due to their co-morbid DSM-IV-TR (APA, 2000) Pervasive Developmental Disorder Not Otherwise Specified. In addition, two normal controls were excluded from analysis as well. One was excluded because of a total score of >2SD above average on the PPI-R total

score, indicating a psychopathic tendency. The second was excluded as he turned out to be deficient in describing, identifying and processing emotions according to the Toronto Alexithymia Scale (Bagby et al., 1994).

The group of the remaining 21 psychopathic patients that complied with all inclusion and exclusion criteria was tested with OT vs. placebo. The 26 remaining normal controls did not apply either placebo or OT and were therefore tested in one session only. Seven normal controls participated only in this morality study and thus not in the larger study. There was no difference in mean age between the other 19 normal controls and this subgroup of seven ($t(24) = 1.698, p = .102$), nor did their ethnic-cultural and national origins differ. Exclusion of these seven in preliminary analyses yielded the same results. Therefore, we decided to fully include this subgroup in the final analyses. It was concluded that there were no cultural barriers in either group that could eventually interfere with test instructions or test attitudes. Detailed sample characteristics are presented in Table 1.

Participants provided written informed consent prior to their participation. The study was approved by the Medical Research Ethics Committee of the University Medical Centre Utrecht, The Netherlands (protocol number 12/056), and was carried out in accordance with the guidelines of the Declaration of Helsinki (World Medical Association, 2013). The participants received a monetary compensation of 30 Euros.

2.2 Study Design

The 21 psychopathic patients of the intervention group followed a within-subject, double-blind, counterbalanced, placebo-controlled, cross-over design, which was in line with previous studies (e.g., Guastella et al., 2010; Andari et al., 2010; Lischke et al., 2012). Thus, they completed two test sessions, one in which they self-administered a nasal spray with 24 IU of the synthetic version of OT (registered product name Syntocinon®). This product is identical to the human pituitary version of OT. In the other test session, they received a placebo nasal spray consisting of a solution of physiological saline (NaCl; quality label PH.EUR; BUFA, Spruyt Hillen, the Netherlands). The mean time interval between the two sessions was 12.3 ± 3.6 days (range 7 to 21 days). Starting times at which the nasal spray was administered on the two test days, was $1:14 \text{ pm} \pm 2.16 \text{ hrs}$ and $1:17 \text{ pm} \pm 2.1 \text{ hrs}$, respectively. The participants were instructed to refrain from cigarette smoking and caffeine consumption at least one hour before the

start of the test session. During the wash-in period of OT to act in the central nervous system (Leng & Ludwig, 2016; Spengler et al., 2017) the participants of the intervention group watched stress-free fragments of the documentary Planet Earth (BBC, 2006). The overall test procedure for the normal controls was similar, except that they were tested on one day only, as they did not use OT. The clips from the BBC documentary were therefore not presented to them. All participants completed the entire test procedure.

In order to control for blindness of drug administration, the psychopathic patients gave their estimate of the order of drug allocation at the end of the second test procedure. In line with reviewed placebo-controlled OT studies with OT doses ranging from 18 to 40 IU (MacDonald et al., 2010) it was expected that participants would not be able to accurately indicate when they had received OT and placebo.

2.3 Moral Dilemmas Task

Greene and colleagues (2001, 2004) previously described the moral dilemmas used in this study. The texts of 24 moral dilemmas were translated from English to Dutch, and then translated back from Dutch to English and checked for consistency by a native English speaker (see Montoya et al., 2013). Two sets of twelve different moral dilemmas were created that were similar in emotional intensity and content (Koenigs et al., 2012). The proportions of impersonal, personal evitable and personal inevitable were also similar across the two sets. For each dilemma, participants were asked to indicate the moral permissibility of the proposed action which were presented in forced-choice questions (i.e., “Would you...?”) that could only be answered “yes” or “no”. Participants who were tested twice (i.e., the psychopathic patients) answered two sets of twelve different dilemmas each whereas the normal control group answered one randomly assigned set of twelve dilemmas. The English and Dutch texts of all 24 moral dilemmas are listed in Table S1 in Supplementary Information.

2.4 Statistical Analyses

Statistical analyses were performed using IBM SPSS statistics version 27. Before testing the hypotheses, data were checked for outliers and missing data. Data

of one healthy control were incomplete (i.e., only nine out of twelve dilemmas were answered). Therefore, it was decided to use the percentage of utilitarian choices for every participant, which meant that the data of this participant could still be used. The data showed no outliers. Independent sample t-tests were conducted to determine whether there were significant differences in demographic variables between the psychopathic patients and normal controls. Descriptive and exploratory analyses were conducted to test the normality of all continuous variables. To analyse whether participants knew whether they were receiving OT or a placebo, a Fisher’s exact test was conducted.

To test our first hypothesis that OT will reduce utilitarian moral decision-making in psychopathic patients, we performed a 3 (Dilemma type) x 2 (Drug) repeated-measures ANOVA. Our second hypothesis that psychopathic patients make more utilitarian moral choices than normal controls was tested using a 3 (Dilemma type) x 2 (Group) repeated-measures ANOVA, in which we compared psychopathic patients in placebo condition with normal controls. Finally, our third hypothesis about a positive relationship between psychopathy severity and the percentage of utilitarian choices was tested using Spearman’s one-tailed correlational analyses.

3 Results

3.1 Demographic information

The final sample consisted of 21 psychopathic patients and 26 normal controls. The mean age of the psychopathic patients (39.5 ± 9.3 years) and the normal controls (36.7 ± 8.0 years) did not differ significantly ($t(45) = 1.130$, $p = .264$). For the psychopathic patients, the mean time interval between self-administration of the intranasal spray and the start of the moral dilemmas task on both test days was 77.8 ± 6.5 minutes and 81.5 ± 5.5 minutes, respectively. These time intervals were considered adequate, as in most human intranasal OT studies the time window for measuring OT-related neurobehavioral effects varies between 20 - 90 minutes after OT administration (Quintana et al., 2020). It was expected that the psychopathic patients could not accurately report in which session they received OT or placebo. Thirteen participants (61.9%) correctly assigned the correct drug to the session. The difference from chance

was not significant (Fisher's exact test, $p = .656$).

PCL-R scores of all psychopathic patients, including the PCL-R facet scores, are presented in Table 1. Among normal controls, mean T-scores of the combined PPI-R subscales and mean T-scores for the higher-order PPI-R factors Fearless Dominance and Self-Centered revealed no indication of psychopathic personality (Table 1).

3.2 Utilitarian choices in psychopathic patients and effect of OT on dilemma type

To test our first hypothesis that OT reduces utilitarian choices in psychopathic patients, a repeated-measures ANOVA was first conducted using a 3 (Dilemma type) \times 2 (Drug) design. Mauchly's test indicated that the assumption of sphericity had been violated for the dilemma type effect, $\chi^2(2) = 6.52$, $p = .038$, therefore the Huynh-Feldt correction was applied to the degrees of freedom ($\epsilon = .83$). No corrections were made on the tests for the main effect of drug as well as the interaction effect. There was a significant main effect of dilemma type on utilitarian choices, $F(1.66, 33.11) = 50.19$, $p < .001$. Post-hoc contrasts revealed a significant difference in utilitarian choices between the impersonal and personal inevitable dilemmas, implying that impersonal dilemmas were judged more utilitarian ($F(1, 20) = 45.44$, $p < .001$; Figure 1). There was also a significant difference between personal evitable and personal inevitable dilemmas, the psychopathic patients chose more utilitarian in personal inevitable dilemmas ($F(1, 20) = 5.69$, $p = .027$; Figure 1). The main effect of drug on utilitarian choices was not significant, $F(1, 20) = 0.14$, $p = .715$. The interaction effect between dilemma type and drug was also not significant, $F(2, 40) = 1.29$, $p = .286$.

3.3 Utilitarian choices in psychopathic patients and normal controls

To analyze any differences in utilitarian choices between normal controls and psychopathic patients in the placebo condition we performed a repeated-measures ANOVA with dilemma type as the within-subjects factor and group membership as the between-subjects factor. Mauchly's test indicated that the assumption of sphericity had not been violated, $p = .091$, therefore no corrections were applied. The results show a main effect of dilemma type, $F(2,$

	Psychopathic patients (N=21)	Normal controls (N=26)
<i>Age in years¹</i> (range)	39.5 \pm 9.3 (23.7 – 54.9)	36.7 \pm 8.0 (24.5 – 51.9)
<i>Ethnic-cultural and national origin</i> (all participants currently had a Dutch nationality)	19 Caucasians (viz 16 Dutch, 1 Belgian, and 2 Turks), 1 African-Surinamese, and 1 Chinese-African Surinamese	24 Caucasians (viz 20 Dutch, 3 Moroccans, and 1 Turk), 1 Dutch Antillean, and 1 Hindustan-Surinamese
<i>Duration of mandatory treatment</i> <i>in months</i>	112 \pm 82	n.a.
<i>PCL-R total score (range)</i>	31.1 \pm 2.9 (26 – 36)	n.a.
<i>PCL-R facets (ranges)</i>		
<i>Facet 1: Interpersonal facet</i>	5.8 \pm 1.3 (3 – 8)	
<i>Facet 2: Affective facet</i>	7.4 \pm .8 (5 – 8)	
<i>Facet 3: Lifestyle facet</i>	7.8 \pm 1.3 (5.5 – 9.5)	
<i>Facet 4: Antisocial facet</i>	8.3 \pm 1.4 (5 – 10)	
<i>Category "Other" (two items</i> <i>that do not load on any of the</i> <i>four facets)</i>	2.0 \pm 1.5 (0 – 4)	
<i>PPI-R total score (range)</i>	n.a.	287.3 \pm 28.1 (243 – 336)
<i>T-scores (ranges)</i>		
<i>PPI-R total</i>		47.7 \pm 10.3 (29 – 65)
<i>PPI-R factor Fearless Dominance</i>		54.6 \pm 9.8 (31 – 68)
<i>Social potency</i>		55.4 \pm 11.3 (19 – 78)
<i>Fearlessness</i>		52.1 \pm 13.0 (25 – 80)
<i>Stress immunity</i>		56.1 \pm 8.5 (44 – 82)
<i>PPI-R factor Impulsive Antisociality</i>		42.3 \pm 9.5 (26 – 61)
<i>Machiavellian egocentricity</i>		39.5 \pm 12.8 (4 – 61)
<i>Rebellious nonconformity</i>		48.3 \pm 9.8 (34 – 74)
<i>Blame externalization</i>		44.5 \pm 8.3 (34 – 64)
<i>Carefree nonplanfulness</i>		47.6 \pm 10.3 (27 – 65)
<i>Coldheartedness</i>		50.7 \pm 11.5 (24 – 70)

▲ **Table 1. Demographic information** For all variables the means \pm standard deviations are reported. PCL-R = Psychopathy Checklist-Revised; PPI-R = Psychopathic Personality Inventory-Revised (with two Factors and eight subscales, including the subscale Coldheartedness that does not load on the two PPI-R factors). ¹No significant group differences in age ($t(45) = 1.130$, $p = .264$).

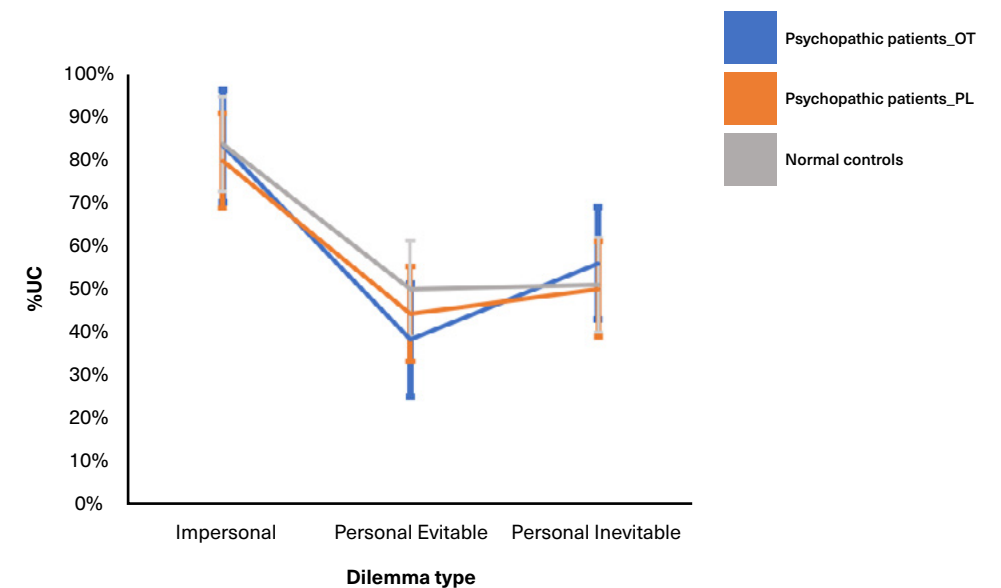
90) = 42.46, $p < .001$. Post-hoc comparisons indicated significant differences between impersonal and personal evitable ($p < .001$) and impersonal and personal inevitable ($p < .001$) dilemmas. Impersonal dilemmas were judged significantly more utilitarian across the two groups. For all dilemma types, no significant differences existed between psychopathic patients in the placebo condition and the normal controls ($F(1, 45) = 0.63$, $p = .435$; see Figure 1).

3.4 Correlations between psychopathy severity and utilitarian choices

We used Spearman's correlations to test our third hypothesis that the percentage of utilitarian choices is positively related to psychopathy severity. Because of multiple measurements, we adjusted the significance interval so that $\alpha = .05/3 = .0167$. A significant negative correlation existed between the PCL-R total score and the percentage of utilitarian choices when assessing personal evitable dilemmas in the placebo condition ($r = -.54$, $p = .011$; see Figure 2). For this dilemma type, highly psychopathic patients in the placebo condition showed fewer utilitarian choices (i.e., more deontological moral choices).

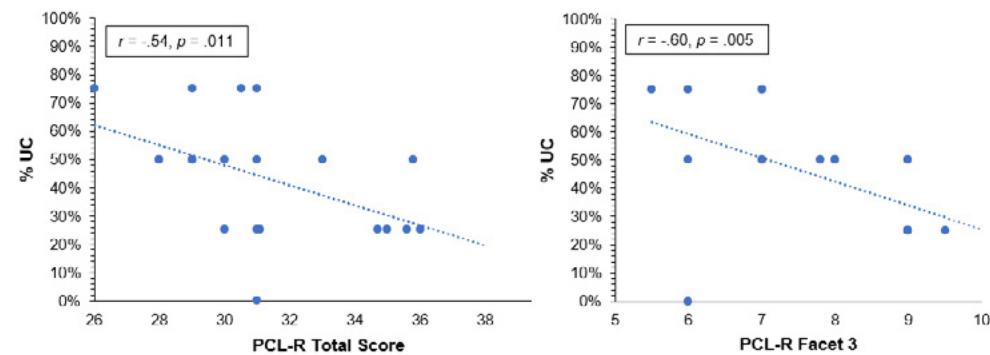
Further exploration of this unexpected finding that contrasted sharply with our third hypothesis, revealed that PCL-R facet 3 was negatively correlated with the percentage of utilitarian choices in personal evitable dilemmas ($r = -.60$, $p = .005$; see Figure 2). PCL-R facet 3 includes the lifestyle items stimulation seeking, impulsivity, irresponsibility, parasitic orientation, and lack of realistic goals (Hare, 2003). A higher score on this PCL-R facet was thus correlated with more deontological (i.e., less utilitarian) choices. No significant correlations were found between the other PCL-R facets including Category "Other" and the three types of moral dilemmas (all $ps > .133$).

For the normal controls, we further performed Spearman's correlation analyses for the PPI-R total score and the percentage of utilitarian choices on the three dilemma types. Because of multiple measurements, we also adjusted the significance interval so that $\alpha = .05/3 = .0167$. A significant positive relation existed between PPI-R total T-score and the percentage of utilitarian choices when judging impersonal dilemmas ($r = .47$, $p = .016$; see Figure 3). Further exploration showed that only PPI-R factor Impulsive antisociality was significantly correlated with the percentage of utilitarian choices ($r = .59$, $p = .002$). Within this PPI-R factor Impulsive antisociality (see Table 1), the subscale Machiavellian egocentricity (i.e., willingness to exploit others for personal gain and a lack of empathy (Lilienfeld & Widows, 2005)) showed a significant

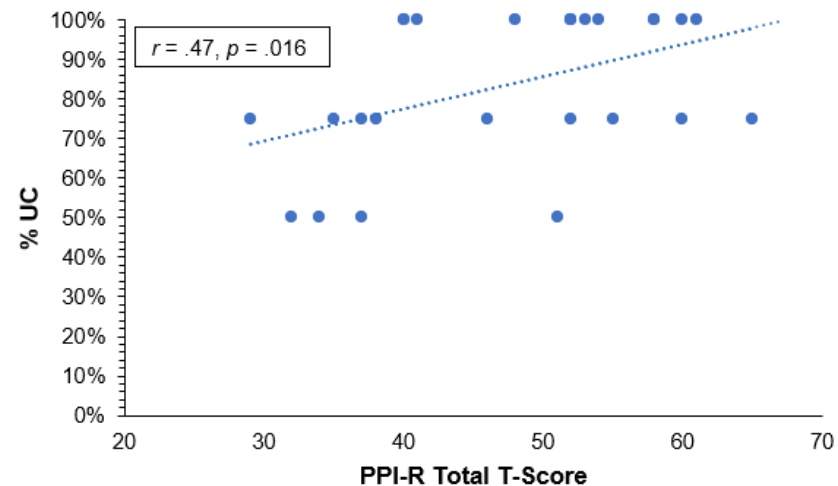


▲ **Figure 1. The main effect of moral dilemma type on the percentage utilitarian choices for both normal controls and patients in the OT and placebo conditions.** Using drug condition as a covariate in the psychopathic patient group, significant differences existed between impersonal and personal inevitable dilemmas, $F(1, 20) = 45.44$, $p < .001$ and between personal evitable and personal inevitable dilemma types, $F(1, 20) = 5.69$, $p = .027$. There were no significant differences between normal controls and psychopathic patients in the placebo condition for all dilemma types ($F(1,45) = 0.63$, $p = .435$). %UC: percentage of utilitarian choices.

correlation with the percentage of utilitarian choices ($r = .50$, $p = .010$). The subscale Carefree nonplanfulness, which is the lack of long-term planning and lack of consideration of consequences (Lilienfeld & Widows, 2005) was also significantly positively correlated with the percentage of utilitarian choices ($r = .53$, $p = .006$). However, this was not the case with the other two subscales of PPI-R factor Impulsive antisociality, i.e., Rebellious nonconformity and Blame externalization ($p = .045$ and $p > .100$, respectively). No follow-up correlation analyses were performed for the other dilemma types and the PPI-R subscales as the PPI-R total T-score showed no significance.



▲ **Figure 2. Relationship between PCL-R scores and the percentage of utilitarian choices for personal evitable dilemmas in psychopathic patients in the placebo condition.** The PCL-R Total Score was significantly negatively correlated with the percentage of utilitarian choices ($r = -.54, p = .011$). This significance was driven by the PCL-R facet 3 score ($r = -.60, p = .005$), not by the other PCL-R facets (all $ps > .266$). %UC: percentage of utilitarian choices.



▲ **Figure 3. Relationship between the PPI-R Total T-score and the percentage of utilitarian choices for impersonal dilemmas in normal controls.** The PPI-R total T-score was significantly positively related with the percentage of utilitarian choices ($r = .47, p = .016$). %UC: percentage of utilitarian choices.

4 Discussion

In this study of PCL-R confirmed psychopathic patients admitted to forensic psychiatric hospitals and normal controls, we examined their willingness to make utilitarian choices, i.e., assumed rational responses to maximize well-being for all, as opposed to deontological judgments, i.e., an emotional aversion to harming other people. Contrary to our first hypothesis, a single nasal administration of OT did not reduce utilitarian moral decision-making in psychopathic patients. Moreover, contrary to our second hypothesis, we found no differences in the percentage of utilitarian choices between psychopathic patients and normal controls. There is a history of conflicting results on this topic, as several other studies similar to the current study reported no differences between psychopathic individuals and normal controls (Blair, 1995; Cima et al., 2010; Glenn et al., 2009; Tassy et al., 2013). However, other studies showed a positive association between psychopathy severity and utilitarian decision-making as opposed to deontological judgment (Bartels & Pizarro, 2011; Glenn et al., 2010; Koenigs et al., 2012; Young et al., 2012). A recent meta-analysis revealed a small to moderate positive relationship between psychopathy and utilitarian choices (Marshall et al., 2018). One possible explanation for the mixed results is the way psychopathy is measured and in which populations the research is conducted. For example, Bartels and Pizarro (2011) and Glenn et al. (2010) used self-report instruments in their non-forensic samples, while in our study we identified our clinically admitted group of forensic psychopathic patients by deploying the PCL-R, as is common in forensic and clinical settings. Furthermore, the use of different diagnostic cutoffs of psychopathy may partially explain the contrasting results. Koenigs and colleagues (2012) used a PCL-R cutoff of 30 points, while the cutoff in our study was 26 points, as is common in European countries.

Our third hypothesis stated that in both groups psychopathy severity was positively related to the percentage of utilitarian choices. This could not be confirmed for the group of psychopathic patients. In contrast, we found that psychopathy severity was negatively related to the percentage of utilitarian choices, meaning that the higher the PCL-R total score, the more non-utilitarian (i.e., deontological) responses the psychopathic patients gave. This unexpected finding was observed only in the case of personal evitable dilemmas (i.e., where one can choose to waive action to avoid harm). Understandably, because of the direct physical action to be taken, a personal evitable moral choice carries a greater emotional burden than a personal

inevitable dilemma, and probably even much more than an impersonal dilemma. Follow-up analyses revealed that PCL-R facet 3 specifically was negatively associated with the percentage of personal evitable choices. This PCL-R facet 3 encompasses lifestyle items such as stimulation seeking, impulsivity, irresponsibility, parasitic orientation, and a lack of realistic goals (Hare, 2003). A priori, there is no reason to assume that psychopathic individuals will not opt harm aversion, especially in situations where their self-interest is not at stake. PCL-R facet 3 reflects high levels of impulsivity. It is conceivable that high PCL-R facet 3 scoring psychopathic individuals, due to their high impulsivity, may be inclined to make a harm-aversive choice in the personally evitable dilemma, more so than is the case in the less emotion-laden personally inevitable and impersonal dilemmas. This inclination seems to contradict what has been described above about the dual-process theory of moral judgment (Greene et al., 2001, 2004) in which psychopathic individuals, who are known to have disturbed emotional processing (Blair, 1995; Rijnders et al., 2021a), tend to choose utilitarian solutions. We believe that the combination of high impulsivity, absent self-interest, an emotionally charged decision that is harmful to the other person and must be carried out by direct physical force can tilt the response toward a deontological choice. Choosing the emotion-laden use of evitable harm may immediately be considered “too hot” and then impulsively rejected.

The above relationship may well be a chance finding not previously discovered in other studies. Therefore, a replication study is warranted. Nevertheless, we believe that the relationship is interesting enough to further explore this deontological preference. We hypothesize that an explanation can be found when comparing highly impulsive psychopathic individuals and subjects with Urbach-Wiethe disease (UWD) in which a genetic mutation causes selective bilateral calcification of the basolateral amygdala (BLA), while the central-medial amygdala (CMA) remains functional and intact (van Honk et al., 2022). UWD subjects make impulsive social-emotional decisions due to the loss of the regulatory effects of the BLA on structures required for moral decision-making, namely the CMA, nucleus accumbens and ventral medial prefrontal cortex (vmPFC) (Schoenbaum et al., 2003). As a result, they lack outcome-oriented decision-making, preventing them from making instrumental utilitarian decisions in conflict situations. Therefore, they impulsively and rigidly tend strongly toward deontological choices (van Honk, et al., 2022). In violent and high-risk to violence psychopathic individuals, regional reductions in gray matter were demonstrated in several paralimbic and limbic regions, including the bilateral amygdala (Ermer et al., 2012),

with up to 30% reduction in BLA tissue and a 10% to 30% enlargement of the central and lateral nuclei of the amygdala (Boccardi et al., 2011), while amygdala volume reductions showed significant correlations with PCL-R scores with the strongest correlations with PCL-R facets 1 and 2 scores, i.e., the interpersonal and affective facets, respectively (Yang et al., 2009). These findings indicate abnormal functioning of the amygdala in psychopathy, likewise they have been linked to motivational aspects (Moul et al., 2012). BLA input is mandatory for the vmPFC to acquire motivational value in decision-making (Schoenbaum et al., 2003). Moreover, the CMA promotes automatic emotional reactivity and general motivation, while these processes can be inhibited by the BLA, resulting in more instrumental goal-directed motivation and behavior (Balleine & Killcross, 2006; Terburg et al., 2018). In short: the BLA is fueling instrumental (i.e., utilitarian) decisions by suppressing the automatic affective processing from the CMA. We hypothesize that when their self-interest is not at stake, highly impulsive psychopathic individuals tend to respond impulsively deontologically to strong aversive dilemmas due to BLA deficits. In terms of moral decision-making, the difference between impulsive psychopathic individuals and UWD subjects may be that the former may reach an instrumental decision when contextual information favorable to them prompts them to do so. Of course, a time factor is involved in considering this contextual information that is at odds with the high levels of impulsivity of the psychopathic individual. Future research should ask high PCL-R factor 3 scoring psychopathic subjects whether they stand by their choice after further consideration and reflection.

Similar correlation analyses using the PPI-R total score were performed for the normal controls. We emphasize that none of the normal controls reached the clinical level of psychopathy; on the contrary, one of them was excluded from analysis because of a total score of >2SD above average on the PPI-R total score, indicating a psychopathic tendency. Here, a positive relationship was found between psychopathy severity and the percentage of utilitarian choices ($r = .47$), which was consistent with our third hypothesis. This moderate effect was only present in case of judging impersonal dilemmas (i.e., where harm is inflicted in an indirect, non-physical way). As can be inferred from the definition, impersonal dilemmas, because of the non-physical contact with the other person during the chosen action, presumably bear less burden than personal evitable and personal inevitable dilemmas. These findings were consistent with both a meta-analysis (Marshall et al., 2018) and recent research by Paruzel-Czachura and Farny (2023). In conclusion, psychopathic patients showed an unexpected preference for nonutilitarian judgments in dilemmas

with greater emotional strain, while the responses of normal controls were in line with previous research.

There are a few limitations to the current study. First, although we used a within-patient design, the number of patients was still low, which potentially increased the risk of underpowering of this study (Walum et al., 2016). Second, due to practical reasons the group of normal controls did not administrate OT. As a result, it was not possible to analyse whether OT has different effects in psychopathic patients compared with normal controls. In addition, since the normal controls did not use a nasal spray themselves, there is a potential risk in comparing this group with psychopathic patients in the placebo condition, as the placebo effect of an intervention on outcome measures may be significant. Third, Koenigs and colleagues (2012) included anxiety levels in their analysis and found that only psychopaths with low anxiety responded significantly more utilitarian than normal controls. In our study, anxiety was not measured directly, so it is unknown whether anxiety levels may have affected the results.

Notwithstanding these limitations, the current study provides insight into the relationship between psychopathy and moral decision-making. A unique point of this study is that we investigated a clinically identified and PCL-R confirmed group of forensic psychopathic patients who were not treated with medication like selective serotonin reuptake inhibitors, selective noradrenaline reuptake inhibitors, antipsychotics, or hormonal libido inhibitors. This study showed no effects of the neuropeptide OT on moral decision-making and we further could not demonstrate a significant difference between psychopathic patients and normal controls in their moral choices. However, we found an intriguing association between highly impulsive psychopathic traits and an aversion to make utilitarian choices in a dilemma type that is thought to be more negatively emotion-laden than other dilemma types.

Future research on moral decision-making in psychopathy should measure reaction time to questions so that it can be used to determine a proxy measure of impulsivity. Future research should also focus on the distinction between moral choices and moral judgments, since while psychopathy may predict utilitarian choices, it does not predict utilitarian judgment per se, the latter being a self-assessment of morality. In this sense, psychopathic individuals tend not to differ from normal people (Tassy et al., 2013).

Supplemental information

Table S1. English and Dutch text of 24 moral dilemmas including the classification of the different dilemma types

The psychopathic patients were presented with two sets (Set 1 or Set 2) of 12 different moral dilemmas in random order during their two test sessions.

The normal controls were presented with a randomly assigned set during their one test session. Questions must be answered “yes” (i.e., a utilitarian choice) or “no” (i.e., a deontological choice).

Nr	Dilemma – English / Dutch	Type	Set
1	<p>Burning House One day you are walking home and you see a house on fire. In a room in the house are six people. If you don't do something quickly, these six people will die from the fire. The only way to get all six people out of the house safely is to force the thick door to this room. But if you force the door, it blocks the way to the exit for one person in an adjacent room, killing that person by fire. If you do nothing, the six people will die, but this one person will be able to escape. <i>Question: Would you force the door to save the six people?</i></p> <p>Brandend huis Op een dag loop je naar huis en je ziet een huis dat in brand staat. In een kamer in het huis zijn zes mensen; als je niet snel iets doet, zullen deze zes mensen sterven door het vuur. De enige manier om alle zes mensen veilig uit het huis te krijgen, is door de dikke deur naar deze kamer te forceren. Maar als je de deur forceert, zal hij de route naar de uitgang blokkeren voor één persoon in een aangrenzende kamer, waardoor deze persoon door het vuur wordt gedood. Als je niets doet, zullen de zes mensen sterven, maar deze ene persoon zal kunnen ontsnappen. <i>Vraag: Zou je de deur forceren met het doel de zes mensen te redden?</i></p>	Impersonal	2

2 River raft

Impersonal 2

You are returning from a kayaking trip when you see that an upstream dam has been damaged and, as a result, the river is about to flood. You know that everyone still in the water will die if the river floods. Downstream, five people are sitting on a large raft. In a nearby drainage channel, someone is fishing. There is a lock nearby that can be opened to divert the flow of water into the drainage canal. If you do nothing, the river will flood and the five people on the raft will perish. If you open the lock to divert the water to the drainage canal, the one person sitting fishing will be killed.

Question: Would you open the lock to divert the water and save five people?

Vlot

Je keert terug van een kajaktocht als je ziet dat er stroomopwaarts een dam is beschadigd en hierdoor de rivier op het punt van overstromen staat. Je weet dat iedereen die nog in het water is, zal sterven, als de rivier overstroomt. Stroomafwaarts bevinden zich vijf mensen op een groot vlot. In een nabijgelegen waterafvoerkanaal zit een persoon te vissen. Er is een sluis dichtbij die geopend kan worden om de waterstroom om te leiden naar het waterafvoerkanaal. Als je niets doet zal de rivier overstromen en zullen de vijf mensen op het vlot gedood worden. Als je de sluis opent om het water om te leiden naar het waterafvoerkanaal, zal die ene persoon die zit te vissen worden gedood.

Vraag: Zou je de sluis openen met het doel het water om te leiden en vijf mensen te redden?

3 Speedboat

Impersonal 1

While vacationing on a remote island, you are fishing at a shipyard. You see a group of tourists boarding a small boat and setting sail for a nearby island. Shortly after their departure, you hear on the radio that a severe storm is coming. This storm will definitely get them into big trouble. The only way you can make sure they are safe from the storm is to warn them by borrowing a nearby speedboat. The speedboat belongs to a mean, rich man who will get very angry if he were to know that you are borrowing his property.

Question: Would you borrow the speedboat for the purpose of warning the tourists about the storm?

Speedboot

Tijdens een vakantie op een afgelegen eiland ben je aan het vissen op een scheepswerf. Je ziet een groep toeristen aan boord gaan van een kleine boot en uitvaren naar een nabijgelegen eiland. Vlak na hun vertrek hoor je op de radio dat er een hevige storm op komst is, een storm die hen zeker in grote problemen zal brengen. De enige manier waarop u ervoor kunt zorgen dat ze veilig zijn voor de storm is hen te waarschuwen door een nabijgelegen speedboot te lenen. De speedboot is van een gemene, rijke man die heel erg kwaad zal worden als hij zou weten dat je zijn eigendom leent.

Vraag: Zou je de speedboot lenen met het doel de toeristen te waarschuwen voor de storm?

4 Guarded Speedboat

Impersonal 2

While vacationing on a remote island, you are fishing at a shipyard. You see a group of tourists boarding a small boat and setting sail for a nearby island. Shortly after their departure, you hear on the radio that a severe storm is coming. This storm will definitely get them into big trouble. The only way to protect them is to borrow a nearby speedboat and warn them of the storm. The speedboat belongs to a mean old man, who has hired a very loyal guard to make sure no one uses his boat without permission. To use the speedboat, you must lie to the guard. *Question: Would you lie to the guard for the purpose of borrowing the speedboat and warning the tourists about the storm?*

Bewaakte speedboot

Tijdens een vakantie op een afgelegen eiland ben je aan het vissen op een scheepswerf. Je ziet een groep toeristen aan boord gaan van een kleine boot en uitvaren naar een nabijgelegen eiland. Vlak na hun vertrek hoor je op de radio dat er een hevige storm op komst is, een storm die hen zeker in grote problemen zal brengen. De enige manier waarop u ervoor kunt zorgen dat ze veilig zijn voor de storm is hen te waarschuwen door een nabijgelegen speedboot te lenen. De speedboot is van een gemene, oude man, die een zeer trouwe bewaker heeft ingehuurd om er zeker van te zijn dat zonder toestemming niemand zijn boot gebruikt. Om de speedboot te kunnen gebruiken zul je moeten liegen tegen de bewaker.

Vraag: Zou je liegen tegen de bewaker met het doel de speedboot te lenen en de toeristen te waarschuwen voor de storm?

5 Lost Wallet

Impersonal 2

You are walking down the street and see a wallet lying on the ground. You open the wallet and it contains several hundred euros in cash as well as the owner's driver's license. You can clearly see from the credit cards and other items in the wallet that the owner is wealthy. However, you have recently become tight on money and could use some extra cash. You are considering returning the wallet to the owner without the money in it and keeping the money yourself.

Question: Would you keep the money you found in the wallet to have more money yourself?

Gevonden portemonnee

Je wandelt over straat en je ziet een portemonnee op de grond liggen. Je opent de portemonnee en deze bevat enkele honderden euro's contant geld en bovendien het rijbewijs van de eigenaar. Aan de creditcards en andere dingen in de portemonnee kun je duidelijk zien dat de eigenaar rijk is. Jij zit sinds kort echter krap bij kas en kan wat extra geld echt goed gebruiken. Je overweegt om de portemonnee terug te sturen naar de eigenaar zonder het contante geld erin. Het contante geld houdt je zelf.

Vraag: Zou je het geld dat je in de portemonnee hebt gevonden, houden, met het doel zelf meer geld te hebben?

6 Standard Fumes

Impersonal 1

You are in charge during a night shift in a hospital. Due to an accident in the adjacent building, deadly smoke enters the hospital through the ventilation system. In one room of the hospital are three patients. In another room lies one patient. If you do nothing, the smoke will enter the room with the three patients and cause their death. The only way to prevent the death of these patients is to flip a certain switch, which will direct the smoke past the room with the three patients. As a result of this action, the smoke will enter the room with the one patient and lead to his death.

Question: Would you flip the switch to prevent the death of the three patients?

Rook

Je hebt de leiding tijdens een nachtdienst in een ziekenhuis. Door een ongeluk in het naastgelegen gebouw komt er dodelijke rook door het luchtventilatiesysteem het ziekenhuis binnen.

In een bepaalde kamer van het ziekenhuis liggen drie patiënten. In een andere kamer ligt één patiënt. Als je niks doet, zal de rook de kamer met de drie patiënten intrekken en voor hun dood zorgen. De enige manier om de dood van deze patiënten te voorkomen, is het omzetten van een bepaalde schakelaar, die ervoor zal zorgen dat de rook langs de kamer met de drie patiënten wordt geleid. Als gevolg van deze handeling zal de rook de kamer met de ene patiënt ingaan en tot zijn dood leiden.
Vraag: Zou je de schakelaar omzetten met het doel de dood van de drie patiënten te voorkomen?

7 Standard Trolley

Impersonal 1

You are driver of a runaway streetcar, rapidly approaching a fork in the track. The streetcar cannot be stopped. On the track that runs to the left is a group of five workers. On the track that runs to the right is one worker. If you do nothing, the streetcar will turn left and kill the five workers. The only way to avoid killing these five workers is to flip a switch on your dashboard, causing the streetcar to turn right. This will result in the death of that one workman.

Question: Would you flip the switch to avoid killing the five workers?

Tram

Je bent bestuurder van een op hol geslagen tram, die snel een splitsing in het spoor nadert. Op het spoor dat naar links loopt, staat een groep van vijf werklieden. Op het spoor dat naar rechts loopt, staat één werkman. Als je niets doet, zal de tram naar links gaan en de vijf werklieden doden. De enige manier om te voorkomen dat deze vijf werklieden gedood worden, is het omzetten van een schakelaar op je dashboard, waardoor de tram naar rechts zal gaan. Dit zal de dood van de ene werkman tot gevolg hebben.

Vraag: Zou je de schakelaar omzetten om te voorkomen dat de vijf werklieden worden gedood?

8 Resume

Impersonal 1

You've been trying to get good grades in math, without much success. You consider that if you do well on the final exam, it is possible to get your final grade up. You decide to sit next to the smartest girl in your math class during the final exam and

transcribe the answers from her test. As a result, you end up getting a good grade in math, better than many of your classmates.

Question: Would you copy someone else's answers to get a higher grade yourself?

Curriculum vitae

Je hebt geprobeerd goede cijfers te halen voor wiskunde, zonder veel succes. Je bedenkt je dat als je het goed doet op het eindexamen, het mogelijk is om je eindcijfer op te halen. Je besluit plaats te nemen naast het slimste meisje in je wiskundeklas tijdens het eindexamen en de antwoorden van haar toets over te schrijven. Door dit te doen lukt het je uiteindelijk om een goed cijfer te halen voor wiskunde, beter dan veel van je klasgenoten.

Vraag: Zou je de antwoorden van iemand anders toets overschrijven om zelf een hoger cijfer te halen?

9 Transplant

You are a physician. You have five patients, each about to die because of a non-functioning organ. You have another patient who is healthy. The only way you can save the lives of the first five patients is to transplant five organs from this young man (against his will). Those five organs will then be implanted in the bodies of the sick patients. If you do this, the young man will die, but the other five patients will live.

Question: Would you perform this transplant to save the lives of five of your patients?

Personal - 2
evitable

Organtransplantatie

Je bent een dokter. Je hebt vijf patiënten, die elk op het punt staan te sterven vanwege een niet-functionerend orgaan.

Je hebt een andere patiënt die gezond is. De enige manier waarop je de levens kunt redden van de eerste vijf patiënten is het transplanteren van vijf van de organen van deze jongeman (tegen zijn wil). Die vijf organen worden dan geïmplanteerd in de lichamen van de zieke patiënten. Als je dit doet, zal de jongeman sterven, maar de andere vijf patiënten zullen leven.

Vraag: Zou je deze transplantatie uitvoeren met het doel het leven te redden van vijf van je patiënten?

10 Traveler push

You are on vacation and traveling through a remote part of South America. You approach a group of tribesmen preparing for an execution of five tribesmen, who are lined up in a line. The executioner sees you and makes you the following offer based on his impression that you are a valued stranger. If you push one person present at the execution to the ground, that person will be shot, but then the five others will go free. If you do not push the one person to the ground, the five others will be executed as scheduled, and the person watching the execution will go free.

Question: Would you push the one person to the ground for the purpose of saving the lives of the other five tribal members?

Personal - 2
evitable

Reiziger

Je bent op vakantie en reist door een afgelegen deel van Zuid-Amerika. Je nadert een groep stamleden die bezig is met het voorbereiden van een executie van vijf stamleden, die in een rij staan opgesteld. De beul ziet je en doet je het volgende aanbod uitgaande van zijn indruk dat je een gewaardeerde vreemdeling bent. Als je een persoon, die bij de executie aanwezig is, tegen de grond duwt, zal deze persoon neergeschoten worden, maar dan zullen de vijf anderen vrijuit gaan. Als je de ene persoon niet naar de grond duwt, zullen de vijf anderen volgens planning worden geëxecuteerd, en zal de persoon die naar de executie kijkt vrijuit gaan.

Vraag: Zou je die ene persoon naar de grond duwen met het doel het leven te redden van de andere vijf stamleden?

11 Bomb

You are negotiating with a powerful and determined terrorist who is about to detonate a bomb in a crowded place. Your only advantage is that you are holding his teenage son captive. You can do only one thing to stop him from detonating the bomb, which will kill thousands of people. To stop him, you must contact him through a satellite link he has connected and right in front of the camera break his son's arm and threaten to break the other arm as well if he does not surrender.

Question: Would you break the arm of the terrorist's son to stop the terrorist from killing thousands of people with his bomb?

Personal - 2
evitable

Bom

Je onderhandelt met een machtige en vastberaden terrorist die op het punt staat een bom te laten ontploffen op een drukke plaats. Je enige voordeel is, dat je zijn tienerzoon in gevangenschap hebt. Er is maar één ding wat je kan doen om ervoor te zorgen dat hij de bom niet laat ontploffen, die duizenden mensen zal doden. Om hem te stoppen moet je contact met hem opnemen via een satellietverbinding die hij heeft aangesloten en recht voor de camera één van de armen van zijn zoon breken en dreigen de andere arm ook te breken als hij zichzelf niet overgeeft.

Vraag: Zou je de arm van de zoon van de terrorist breken, met het doel de terrorist te weerhouden van het doden van duizenden mensen met zijn bom?

12 Country road

You are driving on a country road and you hear someone begging for help from the bushes. You stop and find a man, whose legs are bloodied. The man explains that he had an accident while walking and asks you to take him to a nearby hospital. Your first inclination is to help this man, who will probably lose his legs if he does not get to the hospital quickly. But if you give this man a ride, his blood will ruin your leather car seats.

Question: Would you leave this man on the side of the road to save your leather car seats?

Landweg

Je rijdt op een landweg en je hoort uit de bosjes iemand smeken om hulp. Je stopt en vindt een man, wiens benen bebloed zijn. De man legt uit dat hij een ongeluk heeft gehad tijdens het wandelen en vraagt of je hem naar een nabijgelegen ziekenhuis wil brengen. Je eerste neiging is het helpen van deze man, die waarschijnlijk zijn benen zal verliezen als hij niet snel bij het ziekenhuis is. Maar, als je deze man een lift geeft, zal zijn bloed je leren autostoelen verpesten.

Vraag: Zou je deze man aan de kant van de weg achterlaten, met het doel je leren autostoelen te sparen?

Personal - 2
evitable

13 Footbridge

A runaway streetcar is traveling along a track toward five workers, who will be killed if the streetcar continues.

Personal - 1
evitable

You are standing on a footbridge above the track, between the approaching streetcar and the five workers. Next to you on the walkway is a stranger who happens to be very fat. The only way to spare the lives of these five workers is to push this stranger off the bridge so that his large body on the track below can stop the streetcar. This kills the stranger, but saves the five workers.

Question: Would you push the stranger onto the tracks, with the goal of saving the five workers?

Loopbrug

Een op hol geslagen tram rijdt op een spoorlijn richting vijf werklieden, die gedood zullen worden als de tram zijn richting voortzet. Jij staat op een loopbrug boven het spoor, tussen de naderende tram en de vijf werklieden. Naast je op de loopbrug staat een vreemde die toevallig erg dik is. De enige manier waarop de levens van deze vijf werklieden gespaard kunnen worden, is door deze vreemde van de brug af te duwen, zodat zijn grote lichaam op het beneden gelegen spoor de tram kan stoppen. Als je dit doet, dood je de vreemde, maar de vijf werklieden zullen worden gered.

Vraag: Zou je de vreemde op het spoor duwen, met het doel de vijf werklieden te redden?

14 Student

You are a young student and you are taking a trip to the countryside with the rest of your class and your teacher. Your teacher is mean and makes everyone's life miserable, including yours. You figure out that if you pushed your teacher off a very high bridge, he would fall to his death and everyone would think it was an accident.

Question: Would you push your teacher off the bridge so that he disappears from your life?

Student

Je bent een jonge student en je maakt een excursie naar het platteland met de rest van je klas en je docent. Je docent is een gemene persoon en maakt iedereen het leven zuur, inclusief dat van jou. Je bedenkt dat als jij je leraar van een hele hoge brug zou duwen, hij dood zou vallen en iedereen zou denken dat het een ongeluk was.

Vraag: Zou je je leraar van de brug te duwen zodat hij uit je leven verdwijnt?

Personal - 1
evitable

15 Vaccine Test

A horrific disease has spread around the world and is killing millions of people. You have made two substances in your home laboratory. You know that one of these is a vaccine that will prevent more people from getting the disease, but you don't know which one. You also know that the other one is lethal. Once you have determined which substance is the vaccine, you can use it and save millions of lives. You have two people with you under your care, and the only way to identify the vaccine is to inject each of them with one of the solutions. One person will survive, the other will die. In this way, it will be possible for you to start saving lives with your vaccine.

Question: Would you kill one of these individuals with a lethal injection for the purpose of identifying the vaccine that will save millions of lives?

Vaccintest

Een gruwelijke ziekte heeft zich over de wereld verspreid en doodt miljoenen mensen. Je hebt twee substanties gemaakt in je thuislaboratorium. Je weet dat één van deze een vaccin is, dat voorkomt dat er nog meer mensen de ziekte krijgen, maar je weet niet welke. Je weet ook dat de andere dodelijk is. Als je hebt bepaald welke substantie het vaccin is, kan je het gebruiken en miljoenen levens sparen. Je hebt twee mensen bij je, die onder jouw zorg staan en de enige manier om het vaccin te identificeren is door elk van deze personen één van de oplossingen te injecteren. Eén persoon zal overleven, de andere zal sterven. Op die manier zal het voor jou mogelijk zijn om levens te gaan redden met je vaccin.

Vraag: Zou je één van deze personen doden met een dodelijke injectie met het doel het vaccin te identificeren dat miljoenen levens zal redden?

Personal - 1
evitable

16 Lawrence of Arabia

You are the leader of a small army consisting of warriors from two tribes, the hill tribe and the river tribe. You belong to neither tribe. Last night a man from the hill tribe got into an argument with someone from the river tribe and killed him. The river tribe will attack the hill tribe unless the killer is killed, but the hill tribe refuses to kill one of its own warriors. The only way to prevent the war between the two tribes, which will cost hundreds of lives, is to publicly execute the murderer by beheading him with your sword.

Personal - 1
evitable

Question: Would you behead this man to prevent the two tribes from fighting a war that will cost hundreds of lives?

Lawrence of Arabia

Je bent de leider van een klein leger bestaande uit strijders van twee stammen, de heuvelstam en de rivierstam. Jij behoort tot geen van de stammen. Afgelopen nacht heeft een man van de heuvelstam ruzie gekregen met iemand van de rivierstam en heeft hem vermoord. De rivierstam zal de heuvelstam aanvallen, tenzij de moordenaar wordt gedood, maar de heuvelstam weigert een van zijn eigen strijders te doden. De enige manier om de oorlog tussen beide stammen te voorkomen, die honderden levens zal kosten, is het openbaar executeren van de moordenaar door hem te onthoofden met je zwaard.

Vraag: Zou je deze man onthoofden om te voorkomen dat de twee stammen een oorlog uitvechten die honderden levens zal kosten?

17 Lifeboat

You are on a cruise ship when there is a fire on board and everyone has to leave the ship. The lifeboats already have more people on board than they were designed for. Your lifeboat has too many people on it and it will soon sink. The sea begins to get wild and the boat fills with water. If nothing is done, it will sink before help arrives and everyone on board will die. But there is one injured person who will not survive anyway. If you throw that person overboard, the boat will stay afloat and the other people on the boat will be saved.

Question: Would you throw this person overboard to save the lives of the other people in the lifeboat?

Reddingsboot

Je bent op een cruiseschip als er brand is aan boord en iedereen moet het schip verlaten. De reddingsboten hebben al meer mensen aan boord dan waar ze voor zijn ontworpen. Op jouw reddingsboot zitten te veel mensen en hij zal weldra zinken. De zee begint wild te worden en de boot vult zich met water. Als er niets gebeurt, zal hij zinken voor er hulp komt en iedereen aan boord zal sterven. Maar er is een gewonde persoon die sowieso niet zal overleven. Als je de persoon overboord gooit, zal de boot blijven drijven en de andere personen op de boot zullen worden gered.

Vraag: Zou je deze persoon overboord gooien om de levens van de andere personen in de reddingsboot te redden?

Personal - 2
evitable

18 Crying baby

Enemy soldiers have taken over your village. They have been ordered to kill all remaining villagers. You and some other villagers are hiding in the basement of a large house. Outside, you hear the voices of soldiers who have come to search the house for valuables. Your newborn baby brother begins to cry loudly. You cover his mouth to muffle the sound. If you remove your hand from his mouth, his crying will attract the attention of the soldiers who will kill you, your baby brother and the others hiding in the basement. To save yourself and the others, you must choke your little brother to death.

Question: Would you suffocate your little brother for the purpose of saving yourself and the other inhabitants?

Huilende baby

Vijandige soldaten hebben je dorp overgenomen. Ze hebben het bevel gekregen om alle overgebleven dorpsgenoten te doden. Jij en sommige andere dorpsgenoten verbergen zich in de kelder van een groot huis. Buiten hoor je de stemmen van soldaten die gekomen zijn om het huis te doorzoeken naar waardevolle spullen. Je pasgeboren broertje begint hard te huilen. Je dekt zijn mond af om het geluid te dempen. Als je jouw hand van zijn mond afhaalt, zal zijn huilen de aandacht van de soldaten trekken die jou, je broertje en de anderen die zich in de kelder verschuilen, zullen doden. Om jezelf en de anderen te redden, moet jij je broertje verstikken tot de dood.

Vraag: Zou je je broertje verstikken met het doel jezelf en de andere inwoners te redden?

Personal - 2
evitable

19 Antidote

While on vacation in Southeast Asia, you and four of your friends are kidnapped and deliberately infected with a deadly disease. You will die if you don't get antidote before the next morning. One of the guards presents you with a choice, and he tells you that he has enough antidote to save four of you. He is willing to help you, but demands that in return you kill one of your friends whom he is beginning to get annoyed with. If you refuse his offer, you and your four friends will all die. If you accept his offer, you and your other three friends will be able to escape safely.

Question: Would you kill one of your four friends to save yourself and the other three?

Personal - 2
evitable

Antigif

Tijdens je vakantie in Zuidoost-Azië worden jij en vier van je vrienden gekidnapt en opzettelijk geïnfecteerd met een dodelijke ziekte. Je zult sterven als je niet voor de volgende ochtend tegengif krijgt. Eén van de bewakers stelt je voor een keuze en hij vertelt je dat hij genoeg tegengif heeft om vier van jullie te redden. Hij is bereid je te helpen, maar eist dat je als tegenprestatie één van je vrienden, waar hij zich aan begint te irriteren, doodt. Als je zijn aanbod afwijst, zullen jij én je vier vrienden allemaal sterven. Als je zijn aanbod aanvaardt, zullen jij en je andere drie vrienden in staat zijn om veilig te ontkomen.

Vraag: Zou je één van je vier vrienden doden met het doel jezelf en de andere drie te redden?

20 Sophie's Choice

It is wartime and you and your two younger sisters, aged eight and five, live in an area occupied by the enemy. In the enemy's headquarters is a doctor who conducts painful experiments on people that lead to their death. He plans to perform an experiment on one of your sisters, but gives you the opportunity to choose which sister he will perform the experiment on. You have 24 hours to bring one of your sisters to his laboratory. If you refuse to bring one of your sisters to his laboratory, he will perform his experiments on both of them.

Question: Would you bring one of your sisters to the laboratory to avoid killing them both?

Personal - 2
evitable

Sophie's Choice

Het is oorlogstijd en jij en je twee jongere zusjes van acht en vijf jaar leven in een gebied dat bezet is door de vijand. In het hoofdkwartier van de vijand bevindt zich een dokter die pijnlijke experimenten uitvoert op mensen, die tot de dood leiden. Hij is van plan een experiment op één van je zusjes uit te voeren, maar geeft je de mogelijkheid om te kiezen op welk zusje hij het experiment uit zal voeren. Je hebt 24 uur de tijd om één van je zusjes naar zijn laboratorium te brengen. Als je weigert één van je zusjes naar zijn laboratorium te brengen, zal hij op beiden zijn experimenten uitvoeren.

Vraag: Zou je één van je zusjes naar het laboratorium brengen om te voorkomen dat ze allebei worden gedood?

21 SubmarinePersonal - 1
evitable

You are the captain of a military submarine traveling underneath an immense iceberg. An onboard explosion has caused you to lose most of your oxygen supply and has injured one of your crew who is quickly losing blood. This injured crew member is going to die from his wounds no matter what happens. The remaining oxygen is not sufficient for the entire crew to make it to the surface. The only way to save the other crew members is to sacrifice the injured crew member so that there will be just enough oxygen for the rest of the crew to survive.

Question: Is it appropriate for you to kill the fatally injured crew member in order to save the lives of the remaining crew members?

Onderzeeboot

Je bent de kapitein op een militaire onderzeeboot die onder een enorme ijsberg vaart. Een explosie aan boord heeft ervoor gezorgd dat je het merendeel van je zuurstofvoorraad hebt verloren. Eén van je bemanningsleden is gewond geraakt en verliest in korte tijd veel bloed. Wat er ook gebeurt, het gewonde bemanningslid zal weldra overlijden ten gevolge van zijn verwondingen. De overgebleven zuurstof is niet genoeg voor de gehele bemanning om de oppervlakte te halen. De enige manier om de rest van de bemanningsleden te redden, is het doden van het gewonde bemanningslid, zodat er net voldoende zuurstof voor de rest van de bemanning is om te overleven.

Vraag: Zou je het dodelijk gewonde bemanningslid doden, met het doel de levens van de overgebleven bemanningsleden te redden?

22 EcologistsPersonal - 1
evitable

You are part of a group of tourists on vacation visiting a jungle. The entire group, including eight children has been taken hostage by a group of terrorists. One of the terrorists likes you. He tells you that his leader plans to kill you and the rest of the hostages the next morning. He is willing to help you and the children escape, but he then wants you to kill one of your fellow hostages whom he does not like. If you refuse to do this, all the hostages, including you and the children will be killed. If you accept his offer, the others will die in the morning, but you and the eight children will escape.

Question: Would you kill one of your fellow hostages for the purpose of escaping from the terrorists and saving the lives of the eight children?

Ecologen

Je maakt deel uit van een groep toeristen op vakantie die een jungle bezoekt. De gehele groep, inclusief acht kinderen is gegijzeld door een groep terroristen. Eén van de terroristen mag jou wel. Hij vertelt je dat zijn leider van plan is om jou en de rest van de gegijzelden de volgende morgen te doden. Hij is bereid jou en de kinderen te helpen ontsnappen, maar hij wil dan dat jij een van je medegegijzelden die hij niet mag, doodt. Als je weigert dit te doen, zullen alle gegijzelden, inclusief jij en de kinderen gedood worden. Als je zijn aanbod accepteert, zullen de anderen in de morgen sterven, maar jij en de acht kinderen zullen ontsnappen.

Vraag: Zou je één van je medegegijzelden doden met het doel te ontsnappen van de terroristen en de levens van de acht kinderen te redden?

23 SacrificePersonal - 1
evitable

You and your four older brothers trek over a mountain on your way back from a trip to your homeland. Without knowing it, you have set up camp on the sacred burial ground of a local gang. The leader of the gang says you and your brothers must be killed according to local laws. But he wants you and the other three brothers to live if you kill your oldest brother yourself.

Question: Would you kill your oldest brother to save the lives of yourself and the other three brothers?

Opoffering

Jij en je vier oudere broers trekken over een berg op de terugweg van een tocht naar je vaderland. Zonder het te weten heb je een kamp opgezet op de heilige grafgrond van een lokale bende. De leider van de bende zegt dat jij en je broers volgens de lokale wetten gedood moeten worden. Maar hij wil jou en de drie andere broers laten leven als je zelf je oudste broer doodt.

Vraag: Zou je je oudste broer doden om het leven van jezelf en de andere drie broers te redden?

24 Plane crashPersonal - 1
evitable

Your plane has crashed in the mountains. The only survivors are you, a man and a little boy. The three of you have been traveling for days, battling extreme cold and wind. Survival is only possible

by finding your way to a small village on the other side of the mountain, several days away. The boy has a broken leg and cannot walk very fast. The chances of him surviving this trek are virtually nil. Without food, you and the other man will probably die as well. The other man suggests that you sacrifice the boy and eat his leftovers over the next few days.

Question: Would you kill this boy so that you and the other man can safely survive the journey?

Vliegtuigongeluk

Je vliegtuig is neergestort in de bergen. De enige overlevenden zijn jij, een man en een klein jongetje. Jullie drieën reizen al dagen, strijdend tegen extreme kou en wind. Overleven is alleen mogelijk door het vinden van de weg naar een klein dorpje aan de andere kant van de berg, enkele dagen verderop gelegen. De jongen heeft een gebroken been en kan niet erg snel lopen. De kans dat hij deze tocht overleeft, is nagenoeg nihil. Zonder eten zullen jij en de andere man waarschijnlijk ook sterven. De andere man stelt voor dat je de jongen opoffert en de volgende dagen zijn restanten eet.

Vraag: Zou je deze jongen doden, zodat jij en de andere man de reis veilig kunnen overleven?

Chapter 7
Steroid hormones and
severity of psychopathy
in forensic patients

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Abstract

The steroid hormones testosterone and cortisol, high and low levels respectively, are suggested to drive status-relevant behavior like aggression and dominance. Therefore, these steroids have also been linked to psychopathy. It is however unclear to what extent basal steroid levels, or their (in)flexibility over time, can account for severity of psychopathy as most studies either compare psychopaths to healthy individuals or focus on psychopathic traits within a healthy population. We investigated whether steroid levels, their fluctuations over time and their ratio (i.e. the testosterone-cortisol ratio) are associated with the severity of psychopathy as assessed with the four facet-model of the Psychopathy Checklist Revised (PCL-R). Steroid saliva levels were assayed in 20 male psychopathic patients (PCL-R score > 26) before and after patients participated in a within-subjects oxytocin administration protocol. Steroid levels, particularly cortisol, decreased across the test-protocol, which was not affected by oxytocin administration. Interestingly, steroid levels remained stable in psychopaths with severely distorted narcissistic and manipulative behavioral interpersonal tendencies (PCL-R facet 1), and baseline testosterone levels were higher in psychopaths with severe antisocial tendencies (PCL-R facet 4). Together these results confirm that basal steroid levels, as well as their fluctuation over time, are associated with psychopathic severity. Future endocrine research in psychopathy should take account of its behavioral diversity and focus on a combination of basal steroid levels and their change over time.

1 Introduction

The link between the steroid hormones cortisol and testosterone and the personality disorder psychopathy with its disruptive, manipulative, aggressive and status-seeking behavior remains a topic of discussion. This study focuses on cortisol and testosterone levels in relation to the diagnosis of psychopathy as measured with the Psychopathy Checklist-Revised (PCL-R), in particular the four-facet model of the PCL-R (Hare, 2003) that refines the different behavioral, cognitive and emotional domains that emerge in the two-factor model of the PCL-R (Hare, 1991; see also § 3.3). This study further aims at examining the relationship between basal steroid levels and their change over time on the one hand and the severity of the psychopathy diagnosis in forensic patients on the other.

Although not uncontroversial, indications exist that aggressive behavior is associated with context-dependent low levels of cortisol as well as with high levels of testosterone (Archer, 2006; Terburg et al., 2009; Montoya et al., 2012; Glenn & Raine, 2014; Carré & Archer, 2018). Cortisol is a hormone that reflects the activity of the hypothalamic-pituitary-adrenal (HPA) axis which aims to maintain the stability and integrity of the individual by adaptation to stressful circumstances (Del Giudice et al., 2011). Testosterone is an androgen of the hypothalamic-pituitary-gonadal (HPG) axis that is related to status-relevant behavior, such as dominance and aggression, especially when the status is challenged (Carré & Archer, 2018). As testosterone facilitates approach and reward-seeking, cortisol is associated with withdrawal and fearfulness (Glenn et al., 2011). Cortisol and testosterone show reciprocal suppressive interaction: while cortisol inhibits the HPG axis activity at the level of the hypothalamus, pituitary gland and gonads (Johnson et al., 1992), testosterone, vice versa, exerts an inhibitory effect on the higher level of the HPA axis (i.e., the hypothalamus) but not on the pituitary gland or adrenal cortex levels (Johnson et al., 1992; Viau, 2002). High cortisol levels block testosterone-related dominant behavior while this is not the case in subjects with low cortisol levels. This interaction between low cortisol and high testosterone levels on status-seeking and hierarchy-driven behavior (e.g. dominance and aggression) underlies the so-called dual-hormone hypothesis (Mehta & Josephs, 2010; Sherman et al., 2016; see also the seminal work on this cortisol – testosterone interaction by Dabbs et al., 1991). According to Knight & Mehta (2014) the mechanism behind this model is unknown, but it is speculated that high cortisol levels block the pathway between testosterone and dominant behavior by androgen receptor downregulation, whereas low cortisol levels do not have such an inhibitory effect (see also: Mehta et al., 2015).

Mazur & Booth (2014) in their large study among army veterans, however, could not corroborate a cortisol – testosterone interaction on several measures of antisocial behavior, but they pointed to possible artifacts in their study (and other's as well) such as the discrepancy between the time of blood or saliva collection of these steroids and the time at which the dominant, antisocial or aggressive behavior occurred: “[I]n real life settings, hormones are continually adjusting to changes in psychophysiological state, nearly simultaneously with dominant or deferent social interaction “ (pag. 76).

Considering our population of PCL-R confirmed psychopaths convicted of serious aggressive felony crimes, we focus below on the relationship between the dual-hormone hypothesis and different forms of aggression in psychopathy. The overlapping definitions of aggression and violence lead to disputes about their distinguishing features and boundaries, while at a clinical level difficulty in disentangling their behavioral presentations is the rule. Both forms of noxious behaviour are intended to threaten or inflict either harm or pain to others (Reiss & Roth, 1993) or to cause damage or destruction of non-living entities (Fragkaki et al., 2018). Aggression, however, appears to encompass a broader repertoire of intent than violence, as some forms of aggression seem not so much aimed at threatening or causing harm to others, but rather to protect and preserve the individual (Liu, 2004; Berkowitz, 1983). Since aggression apparently includes violence and self-defensive acts, we therefore prefer to use the terms “aggression” and “aggressive behavior” in the text hereafter. According to Haller & Kruk (2006), species-specific communicative aspects between the aggressor and the opponent play a key role in context-dependent aggression. Aggression can be an impulsive and relatively unplanned hostile response to a perceived threat or dangerous situation, but it might also be instrumental or proactive, i.e., targeted and deliberate, so to speak premeditated (Cornell et al., 1996). Impulsive and premeditated forms of aggression are not mutually exclusive (Barratt et al., 1999), and certainly not in psychopaths (Porter & Woodworth, 2006).

In their triple balance hypothesis of emotions, van Honk & Schutter (2006) incorporated both types of aggression within what later became known as a dual-hormone perspective by focusing on the balance between punishment and reward sensitivity. They postulated three balanced circuits involved in punishment and reward that build up to socio-emotional functioning, namely a subcortical balance (especially at the amygdala level), a cortical balance (predominantly involving the medial orbitofrontal cortex), and an intermediate subcortico-cortical communication balance. So-called “crosstalk” between the cortical and subcortical circuits reciprocally influences either inhibitory or excitatory functioning of both these circuits. They argued that this crosstalk

relies heavily on the intracerebral concentrations of cortisol and testosterone. Under a high level of testosterone it is assumed that a cortical balance shift occurs in favor of reward sensitivity and to the detriment of punishment sensitivity. Cortisol, on the other hand, has an opposite effect on the cortical level: unlike testosterone, a high intracerebral cortisol concentration tends to shift the balance between reward sensitivity and punishment sensitivity towards the latter. So in the case of combined high testosterone and low cortisol levels, the propensity for reward seeking and concomitant punishment insensitivity will prevail.

As both callous-unemotional traits (CU traits; i.e. precursors of psychopathy; Frick & White, 2008) and the psychopathic personality are strongly related to antisocial and aggressive behavior (Blair, 1995; Blair, 2003; Hare, 2003; Frick & White, 2008, Popma et al., 2007), and psychopathy is known for its high criminal recidivism (Harris et al., 1991; Skeem & Cooke, 2010; Dhingra & Boduszek, 2013; Sohn et al., 2020), attempts were made to investigate whether the dual-hormone hypothesis also applies to psychopathy. As testosterone is thought to reduce cortical-subcortical crosstalk (van Honk & Schutter, 2006), cortical processing at high testosterone levels will then be less affected by the input of emotionally valenced information from the subcortical circuit, such as the output that stems from the balanced interplay between the basolateral and central subregions of the amygdala (Terburg et al., 2018). While testosterone is also associated with reduction in fear (Schutter & van Honk, 2004; Boissy & Bouissou, 1994) and is correlated with aggressive behavior in men with low trait anxiety (Norman et al., 2015), then as a consequence, the fearless psychopath (Fowles, 2000) will rely heavily on non-emotional cognitive processing that ultimately allows for instrumental, non-empathic behavior, and instrumental aggression when deemed necessary (von Borries et al., 2012).

Stålenheim and colleagues (1998) found in a forensic sample of 61 males who had committed severe crimes a positive association between direct and indirect measurements of testosterone and the PCL-R factor 2, the latter being a strong indicator of impulsive and antisocial behavioral problems in the psychopathy construct. However, Welker and colleagues (2014) found conflicting results in their study of baseline testosterone and cortisol levels in a non-clinical sample of 237 undergraduate students. In men, measures of psychopathy were positively correlated with testosterone levels when their cortisol levels were high. They noted that these high cortisol levels may be positively associated in non-clinical samples, but negatively associated with psychopathy in clinical samples. They further questioned the mutually inhibitory effect of the HPG and HPA axes in case of higher levels of psychopathy in men. In a study of 50 incarcerated male

adolescents with conduct disorder Johnson and colleagues (2014) found in a subgroup with high CU-traits an uncoupling of testosterone and measures of HPA axis, meaning that high testosterone levels were associated with low levels of dihydroepiandrosterone, which is a hormone of the HPA axis. In addition, Glenn and colleagues (2011) who examined a community sample of 178 predominantly male adults, could not find associations between psychopathy scores and baseline levels of either cortisol or testosterone, nor between psychopathy scores and the ratio of baseline testosterone to baseline cortisol. However, they did find a significant association between psychopathy scores and the ratio between baseline testosterone and cortisol reactivity to a stressor. PCL-R factor 2 predicted testosterone-cortisol reactivity ratio scores, although in their subsequent analysis neither of the PCL-R facets falling under PCL-R factor 2 did so. They concluded that the HPA axis and the HPG axis conjointly predispose toward psychopathic properties.

In summary, mixed results are reported, which may be partly due to different populations studied, ranging from community samples to prisoners convicted for aggressive interpersonal crimes, while not all participants met the PCL-R criteria of the psychopathy diagnosis. In their meta-analytic evaluation of the dual-hormone hypothesis, Dekkers and colleagues (2019) found a significant interaction between testosterone and cortisol, albeit with very small effect sizes. Interestingly, when excluding studies without psychopathy as an outcome measure, they found a slight increase in the interaction between testosterone and cortisol on status-relevant behavior such as aggression and dominance.

In order to investigate the dual-hormone hypothesis in PCL-R identified psychopaths without comorbid major psychiatric disorders, we used salivary testosterone and cortisol levels obtained from a group of forensic psychopathic patients convicted of severe aggressive felony crimes (see Table 2) who participated in a larger study in which the influence of oxytocin on social behavior was examined. Analyses of these steroid levels across four measures over two days, almost two weeks apart, will allow us to measure not only the relationship between basal steroid levels and psychopathic severity, but also to explore the influence of hormonal variation over time.

2 Current study

The aim of the study was to examine the interaction between cortisol and testosterone saliva levels (i.e., baseline levels and their change over time) on the one hand and the interaction of both cortisol and testosterone with the severity of the psychopathy as measured by the four-facet model of the PCL-R on the other. Two hypotheses were tested. First, following the dual-hormone hypothesis it was hypothesized that the testosterone-cortisol ratio would show a positive association with the PCL-R factor 2 (Stålenheim et al., 1998), thus with PCL-R facet 3 and, presumably even more prominent, PCL-R facet 4. Second, as strong associations have been described between dominant behavior and PCL-R factor 1 (Hall et al., 2004; Lobbestael et al., 2018; Murphy et al., 2016; Verona et al., 2001) it was hypothesized that testosterone levels would have a positive association with PCL-R facet 1, but not or to a lesser extent with PCL-R facet 2 as this last facet does not appear to influence dominance.

Firstly, however, the effect of oxytocin on cortisol and testosterone levels was explored, as the measurement of the testosterone and cortisol levels in saliva formed part of a larger study in which the behavioral and cognitive effects of intranasal oxytocin in psychopathic patients were assessed. Oxytocin is a nonapeptide known for its involvement in various social and interpersonal roles, as well as prosocial behaviour (Meyer-Lindenberg et al., 2011; MacDonald & MacDonald, 2010; Caldwell, 2017). In some studies a negative association between oxytocin and psychopathy was found (Moul et al., 2012; Verona et al., 2018). Although studies showed opposite effects of oxytocin and testosterone on various tasks (e.g. Procyshyn et al., 2020), thus implying antagonistic properties, no such mechanism have been demonstrated to date (Crespi, 2016). Oxytocin administration resulted in lower cortisol levels during laboratory tasks, but this effect was not always present (Fragkaki et al., 2018). We therefore formulated no hypothesis regarding the direction of the oxytocin effect on either testosterone or cortisol, following Caldwell (2017) who pointed to the mixed results in animal research, and Jurek & Neumann (2018) who stated in their extensive review “that a “hypo-oxytocinergic state” is associated with an elevated trait aggression and may even predict aggression (...), they do not equivocally support the theory that intranasal oxytocin treatment is capable of inhibiting aggressive behavior in humans” (pag. 1855).

3 Method

3.1 Participants

We report how we determined our sample size, all data exclusions (if any), all manipulations, and all measures in the study. The original sample-size (N=24) for this study was based on a within-subject substance administration protocol aiming to detect medium effect sizes ($\eta^2 > .06$) in 2 by 2 repeated measures design interactions with 80% power. Given that this sample-size also provides 80% power to detect between-within interactions with medium effect-size when using four repeated measures (four measures for each steroid hormone), we deemed our present sample size (N=20) on the low side, but suitable given the unique properties of our sample. Initially, a total of 24 male forensic psychiatric in-patients were included in the current study. Patients were recruited from five maximum-security forensic psychiatric hospitals in the Netherlands. They were selected if their PCL-R total score was 26 or higher (see § 3.3). As this study was part of a larger study that also focused on empathy processing in psychopathy, the maximum score (i.e. 2) of PCL-R item “callousness / lack of empathy” (Hare, 2003) was required.

Additional requirements for participation in this study were a good physical health, age between 18 and 60 years, a normal or corrected to normal visual acuity, and a total IQ of 80 or above. Exclusion criteria were color blindness, illiteracy, insufficient knowledge of Dutch language, or a concurrent severe psychiatric disorder like a psychotic disorder, a depressive disorder, or a severe anxiety disorder. After screening by a psychiatrist (first author R.J.P. R.) it was concluded that these psychiatric disorders were not present in any of the participants. Other exclusion criteria were a history of endocrine disorders or brain diseases, including closed head injury with loss of consciousness exceeding 15 minutes. Selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors, antipsychotics, and hormonal treatments for libido inhibition were contraindicated due to a possible interference with the action of oxytocin or with social dominant relationships (Yamaguchi et al., 2017; Malatynska & Knapp, 2005; Neshet et al., 2013). Since oxytocin was administered intranasally, participants with a “runny nose”, currently or within the past seven days, were temporarily excluded from the test procedure. Participation was also temporarily suspended if they had used alcohol or recreational drugs in the past 24 hours before each test procedure (alcohol use and drug use were a priori prohibited in all hospitals). When in doubt a urine based screen test

for immediate drug use detection was performed (Multi-Drug Rapid Test Cup; AKSA Medical, the Netherlands). Recent use of cannabis was revealed in one case, which led to postponement of the test procedure by one week.

Of the 24 patients with PCL-R cut-off scores of 26 or higher who were enrolled in this study, four participants were eventually excluded from analysis, one participant due to missing data, and three others due to their co-morbid DSM-IV-TR (American Psychiatric Association, 2000) Pervasive Developmental Disorder Not Otherwise Specified. The data from the remaining 20 psychopathic patients are presented and analyzed below. Their age and ethno-cultural origin, the duration of their treatment in the maximum-security forensic psychiatric hospitals, their PCL-R scores, as well as the felony crime categories for which they have been convicted are presented in Table 1. Although their cultural backgrounds differed, all patients had extensive experience of Dutch society before being convicted of their crimes. There were no cultural barriers that could ultimately hinder test instructions or disrupt test attitudes. All participants provided written informed consent prior to their participation. They received a monetary compensation of € 30.

3.2 Study design

The 20 psychopathic patients participated in a larger study in which they had to perform computer tasks measuring emotion recognition, facial mimicry of dynamic emotional expressions (which was measured with facial electromyography) moral dilemma's, as well as dominance (for this latter sub-study using eyetracking, see: Rijnders et al., 2021). With these tasks no stress elevation was sought. In the current study involving saliva concentrations of steroids, no interference occurred with these computer tasks, as saliva was collected 40 minutes before the start of the first task as well as after the completion of the test procedure.

The participants followed a within-subject, double-blind, placebo-controlled, cross-over design, and thus they completed two test sessions on two days. In one test session they sniffed a nasal spray with either a total of 24 International Units of the synthetic version of oxytocin (registered product name Syntocinon®) or physiological saline (NaCl; quality label PH.EUR; BUFA, Spruyt Hillen, The Netherlands). The results of oxytocin intervention on the different tasks of the larger study will be published elsewhere (e.g. Rijnders et al., 2021). Participants were instructed to refrain from cigarette smoking and consuming caffeinated beverages at least one hour prior to the start of the test session. Saliva was collected before participants sniffed the nasal spray

20 forensic PCL-R confirmed psychopathic patients

Age (years)	39.9 ± 9.3	(23.7 – 54.9)
Ethnic and national origin (all participants had the Dutch nationality)	1 Surinamese Chinese-African, 1 Surinamese -African-, and 18 Caucasians (15 Dutch, 1 Belgian, 2 Turks),	
Time from the start of the mandatory treatment (years)	9.6 ± 6.9	(2.3 – 20.8)
PCL-R total score	31.2 ± 2.9	(26 – 36)
<i>PCL-R facet scores</i>		
Facet 1: Interpersonal facet (8*)	5.8 ± 1.3	(3 – 8)
Facet 2: Affective facet (8)	7.4 ± .8	(5 – 8)
Facet 3: Lifestyle facet (10)	7.8 ± 1.3	(5.5 – 9.5)
Facet 4: Antisocial facet (10)	8.3 ± 1.4	(5 – 10)
Two separate items (4)	2.0 ± 1.5	(0 – 4)
<i>Number of patients convicted of</i>		
Homicide	8	
Manslaughter (2)		
Attempted manslaughter (3)		
Murder (3)		
Attempted murder (2)		
Sexual crimes	5	
Rape (3)		
Attempted rape (1)		
Sexual abuse of minor (1)		
Other interpersonal aggression	8	
Assault (5)		
Arson (2)		
Hostage (3)		
Larceny	12	
Robbery (6)		
Extortion (3)		
Theft (7)		

▲ **Table 1. Demographic information** For all variables the means ± standard deviations are reported, including their range (minimum – maximum). Two separate PCL-R items (i.e. “promiscuous sexual behavior” and “many short-term marital relationships”) do not load on any of the four PCL-R facets. Note that some patients have been convicted of crimes in various categories, and in addition, they may also have been convicted of different crimes within the same category. PCL-R = Psychopathy Checklist-Revised. *) maximum possible score per PCL-R facet.

(“pre-trial saliva”). After the test procedure was completed, saliva collection was repeated (“post-trial saliva”).

3.3 Psychopathy Checklist-Revised and Profile of Mood States questionnaire

Patients were approached primarily based on their scores on the Psychopathy Checklist-Revised (PCL-R; Hare 1991, 2003). The 20-item PCL-R is generally accepted as the gold standard for the psychopathy diagnosis. Symptoms are scored with a 0 (not present), 1 (partially present) or 2 (clearly present), so the extreme end of the psychopathy score corresponds to a score of 40 points. In his four-factor (also known as the four-facet) model Hare (2003) proposed 1) an interpersonal facet, 2) an affective facet, 3) a behavioral lifestyle facet, and 4) an antisocial facet, leaving two PCL-R items (namely “promiscuous sexual behavior”, and “many short-term marital relationships”) separately as they do not load on any of the four facets. The four-facet model builds on the original two-factor model of de PCL-R (Hare, 1991). The original PCL-R factor 1 includes both PCL-R facet 1 and facet 2 of the four-facet model. PCL-R facet 3 and facet 4 are derived from the original PCL-R factor 2 in the original two-factor model plus the PCL-R item “versatile criminality” which does not load on either factor 1 or factor 2. The items, factors and facets of the PCL-R are presented in Table 2. In North America, a score of 30 is considered the cut off score of psychopathy, while in several European countries lower cut-off scores (even 25, or higher) are sometimes used for psychopathy (Cooke et al., 2005; Grann et al., 1998; Cooke, 1998; Rasmussen et al., 1999; Cooke & Michie, 1999; Mokros et al., 2013).

At the start of the test procedure as well as after completion of the final task, participants completed a computerized and Dutch version of the Profile of Mood States questionnaire (POMS; McNair et al., 1971) based on the short-form version (Shacham, 1983) and using a visual analog scale. In this self-report questionnaire, 35 adjectives were presented describing both the presence and perceived intensity of six mood state-related categories: tension-anxiety, anger-hostility, fatigue-inertia, depression-dejection, confusion-bewilderment, and vigor-activity. A Total Mood Disturbance (TMD) score was calculated for each participant by adding up the individual mean scores of the first five mood state-related categories and then subtracting from it the individual mean score of the last category (i.e., vigor-activity) (McNair et al., 1971). Since the participants completed the questionnaire shortly after they had sniffed placebo or OT, the TMD pre-trial scores could not be influenced by the drug condition.

PCL-R facets	PCL-R facet domains	Items	PCL-R factor domains	PCL-R factor
Facet 1	Interpersonal facet	glib/superficial	Interpersonal/ Affective factor	1
		grandiose self-worth		1
		pathological lying		1
		conning/manipulative		1
Facet 2	Affective facet	lack of remorse or guilt		1
		shallow affect		1
		callousness or lack of empathy		1
		failure to accept responsibility		1
Facet 3	Lifestyle facet	stimulation seeking	Impulsive lifestyle/ Antisocial factor	2
		impulsivity		2
		irresponsibility	2	
		parasitic orientation	2	
		lack of realistic goals	2	
Facet 4	Antisocial facet	poor behavior controls		2
		early behavior problems		2
		juvenile delinquency		2
		revocation of conditional release		2
		criminal versatility		#
Two items that do not load on any of the four facets		promiscuous sexual behavior		#
		many short-term marital relationships		#

▲ **Table S1. The two-factor and four-facet model of the PCL-R (Hare, 1991, 2003).** The three items in the two-factor model marked with # do not load on these two factors, while in the four-facet model this is the case for two items.

3.4 Ethics

The study was approved by the medical ethics committee of the University Medical Centre Utrecht, Netherlands, and was carried out in accordance with the guidelines of the Declaration of Helsinki (World Medical Association, 2013). Participants provided written informed consent prior to their participation.

3.5 Saliva collection and measurement of testosterone and cortisol

Saliva was collected in plastic tubes containing a synthetic swab with neutral taste (Salivette®; Sarstedt AG & Co., Nümbrecht, Germany). Participants chewed the swab for at least 1 minute. Saliva and swab were temporarily stored at -20 °C. Before final storage at -80 °C the saliva was centrifuged at 1,500 per minute for four minutes. After completing the test procedures of the last participant all saliva samples were measured in one batch in the Central Diagnostic Laboratory of the University Medical Center Utrecht, the Netherlands (Mrs. Inge Maitimu-Smeele).

Testosterone in saliva was measured in duplicate using an in-house competitive radio-immunoassay employing a polyclonal anti-testosterone-antibody (Dr.Pratt AZG 3290). [1,2,6,7-3H]-Testosterone (NET370250UC, PerkinElmer) was used as a tracer following chromatographic verification of its purity. The lower limit of detection was 20 pmol/L. Inter-assay variation was 10.5 – 8.3% at 70 – 480 pmol/L respectively (n=33). Intra-assay variation was 7.2 – 2.5% at 38 – 92 pmol/L respectively (n=10). Normative values in men for testosterone levels in the morning and the evening are 190 – 480 pmol/L and 83 – 240 pmol/L, respectively.

Cortisol in saliva was measured without extraction using an in-house competitive radio-immunoassay employing a polyclonal anticortisol-antibody (K7348). [1,2-3H(N)]-Hydrocortisone (NET396250UC, PerkinElmer) was used as a tracer. The lower limit of detection was 1.0 nmol/L and inter-assay variation was <7% at 3.3 – 30 nmol/L (n = 80). Intra-assay variation was <4% (n = 10). Normative values for cortisol levels in the morning, the afternoon and the evening are 9-29 nmol/L, 4 – 12 nmol/L, and 1 – 6 nmol/L, respectively.

3.6 Data analyses

The data and code are available upon request. Hormone levels were converted to psychometric t-scores ($PMT\text{-score} = 50 + 10 * ((x - M) / SD)$), with x=Hormone value, M=overall mean and SD=overall standard deviation) resulting in average hormone values of 50 whereby a difference of 10 indicates 1 standard deviation difference. Subsequently, testosterone divided by cortisol ratios were computed.

We analyzed steroid levels and (POMS) TMD scores using repeated-measures ANCOVAs. The PCL-R facets were entered (z-transformed) as continuous variables. Significant main or interaction effects were followed by correlational analysis to specify effect-size and -direction. Covariates that were included were age and start-time of the test session. Due to practical

circumstances as well as hospital rules, it was not possible to keep start-times of the test procedures the same for all participants (mean start-time 13:05 (SD=2:05) hours. Most, but not all, of the measurements started in the afternoon. Considering the daily rhythm of cortisol and testosterone (Gostisha et al., 2014; Knight & Mehta, 2014; Brambilla et al., 2009), that could potentially cause difficulties in comparing steroid levels, we statistically controlled for the influence of the start-time.

4 Results

4.1 Preliminary analysis

Twenty psychopathic patients were analyzed. The mean time interval between the two test sessions was 12.5 ± 3.5 days. The mean time between pre-trial and post-trial saliva collection on the two test days did not differ significantly (Day 1: 92.2 ± 7.3 minutes, and Day 2: 94.6 ± 5.6 minutes; $t(19)=-1.601$, $p=.126$). The start-times of pre-trial saliva collection were also not significantly different on the two test days (Day 1: 13:05 (SD=2:10) hours, and Day 2: 13:06 (SD=2:03) hours). Although the intention was to keep the start-time of the pre-trial saliva collection for an individual participant the same on the two test days, due to practical circumstances this turned out not always possible (mean time difference 31.9 minutes, SD 37.5 minutes).

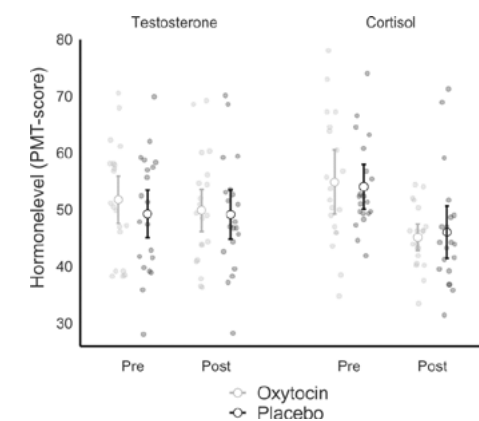
4.2 Hormone analysis

A 2 (HORMONE: testosterone and cortisol) by 2 (DRUG: oxytocin and placebo) by 2 (TIME: pre-trial and post-trial saliva) repeated-measures ANOVA controlled for age and start-time revealed a main effect of TIME ($F(1,17)=12.09$, $p=.003$, $\eta^2=.42$) and a TIME by HORMONE interaction ($F(1,17)=10.82$, $p=.004$, $\eta^2=.39$) indicating a drop in cortisol over time as expected according to its circadian rhythm (-8.875 , $p>.001$), but not in testosterone (-0.981 , $p=.606$) (see Figure 1). As expected the covariate age interacted with HORMONE ($F(1,17)=11.53$, $p=.003$, $\eta^2=.40$) indicating a significant negative relation with testosterone levels ($r=-$

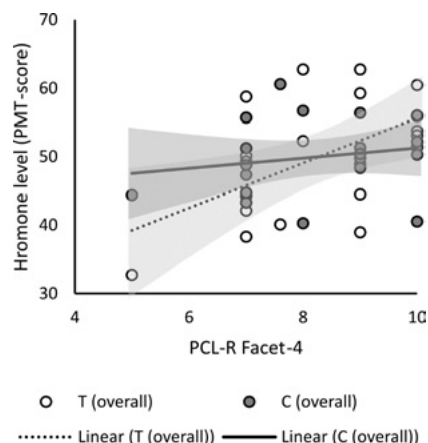
.573, $p=.008$), which was absent in relation to cortisol levels ($r=.078$, $p=.743$). All DRUG effects were non-significant (all $ps>.18$) thus oxytocin compared to placebo administration did not affect steroid hormone levels and we therefore collapsed the data across drug conditions for further analyses.

Separate 2 (HORMONE: testosterone and cortisol) by 2 (TIME: pre-trial and post-trial saliva) repeated-measures ANOVAs with the five z-transformed PCL-R categories (i.e., the four facets plus the two separate items) as continuous variables, controlled for age and start-time, revealed a main effect of PCL-R facet 4 ($F(1,13)=5.32$, $p=.035$, $\eta^2=.25$) and a TIME by PCL-R facet 1 interaction ($F(1,13)=8.30$, $p=.011$, $\eta^2=.34$). Other effects were non-significant (all $ps>.12$).

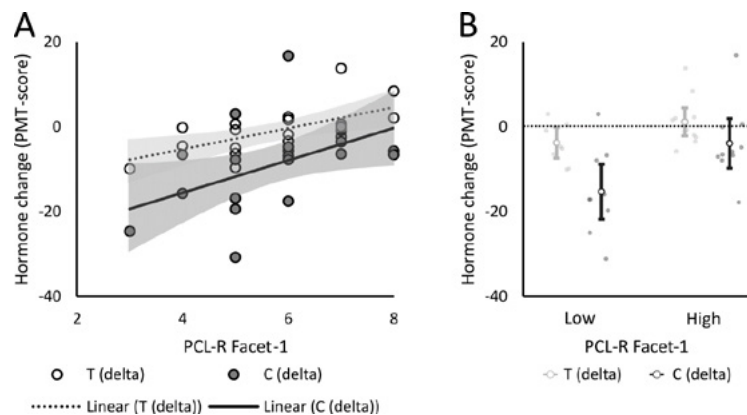
Follow-up correlations revealed that PCL-R facet 4 was positively correlated with testosterone levels ($r=.536$, $p=.015$), but this was not the case for cortisol ($r=0.192$, $p=.418$) (see Figure 2). Furthermore, PCL-R facet 1 was positively related to the decrease in testosterone ($r=.587$, $p=.007$) as well as cortisol ($r=.480$, $p=.032$) from pre-trial to post-trial (see Figure 3A). This suggests that high levels of PCL-R facet 1 protected against a decrease in both steroids which can be illustrated with an exploratory median-split analysis (PCL-R facet 1 scores 3-5: "low group", and facet 1 scores 6-8: "high group") showing that the low group had a significant decrease in testosterone (-3.64 , Student's $t(8)=-2.38$, $p=.045$, Cohen's $d=-0.792$) and cortisol (-15.07 , Student's $t(8)=-4.47$, $p=.002$, Cohen's $d=-1.491$), while this was not the case for the high group (both $ps>.16$), see Figure 3B.



▲ **Figure 1.** Pre- and post-trial testosterone and cortisol saliva levels in the oxytocin and placebo conditions. Error-bars represent 95% confidence intervals. PMT-score: psychometric t-score.



▲ **Figure 2.** PCL-R facet 4 was positively correlated with testosterone saliva levels ($r=.536$, $p=.015$), but not with cortisol ($r=0.192$, $p=.418$). Error-margins represent 95% confidence intervals. PMT-score: psychometric t-score.



▲ **Figure 3.** (A) PCL-R facet 1 was positively related to the decrease in testosterone level ($r=.587$, $p=.007$) and cortisol level ($r=.480$, $p=.032$) from pre-trial to post-trial saliva measurements (delta). Error-margins represent 95% confidence intervals. (B) The decrease in steroid levels was only significant in psychopaths scoring low (3-5 points) on PCL-R facet 1, and not in those scoring high on PCL-R facet 1 (6-8 points). Error-bars represent 95% confidence intervals. PMT-score: psychometric t-score.

4.3 Testosterone-cortisol ratio analysis

In line with the earlier hormone analysis, a 2 (DRUG: oxytocin and placebo) by 2 (TIME: pre-trial and post-trial saliva) repeated-measures ANOVA controlled for age and start-time revealed main effects of TIME ($F(1,17)=18.78$, $p<.001$, $\eta^2=.52$) and age ($F(1,17)=13.38$, $p=.002$, $\eta^2=.44$) reflecting the same decrease of cortisol saliva levels from pre-trial to post-trial and a negative relation between age and testosterone levels. All DRUG effects were non-significant (all $ps>.20$), thus we again collapsed the data across the two drug conditions for further analysis.

Separate 2 (HORMONE: testosterone and cortisol) by 2 (TIME: pre-trial and post-trial saliva) repeated-measures ANOVAs with the five z-transformed PCL-R categories (the four facets plus the two separate items) as continuous variables, controlled for age and start-time, revealed no significant relation between the PCL-R categories and testosterone / cortisol ratio (all $ps>.31$).

4.4 Total mood disturbance (TMD) by PCL-R facets analysis

The means and SDs of the TMD are presented in table 3. TMD measures were entered in a 2 (DRUG: oxytocin and placebo) by 2 (TIME: pre-trial and post-trial) repeated-measures ANOVA, but DRUG and TIME did not affect TMD (all $ps>.24$). TMD scores were collapsed into overall TMD for each participant and correlated with the five PCL-R categories (the four facets plus the two separate items). PCL-R facet 4 was negatively associated with TMD ($r=-.624$, $p=.003$), but the other facets and the two separate items were not related to TMD (all $ps>.38$). Given this relation of TMD and PCL-R facet 4 we tested whether TMD mediated the relationship between testosterone and PCL-R facet 4. In a mediation model with testosterone saliva levels as dependent variable, PCL-R facet 4 as predictor and TMD as mediator, the indirect effect (bootstrapped estimation method, 1,000 samples) mediated only 15.3% of the model ($p=.685$) indicating that TMD is not a relevant mediator in the relation between testosterone levels and PCL-R facet 4.

Condition	TMD pre-trial	TMD post-trial	
<i>Oxytocin</i>	-395.6 + 160.8	-387.8 + 147.6	$t(19)=-.471; p=.643$
<i>Placebo</i>	-410.3 + 146.7	-387.4 + 168.6	$t(19)=-1.20; p=.245$
	$t(19)=.693; p=.496$	$t(19)=-.015; p=.988$	

▲ **Table 3. Total Mood Disturbance (TMD)** Means and SDs of TMD scores of the Profile of Mood States questionnaire. TMD scores were calculated for each participant by adding up the individual mean scores of five mood state-related categories (i.e. tension-anxiety, anger-hostility, fatigue-inertia, depression-dejection, and confusion-bewilderment) and then subtracting from it the individual mean score of the category vigor-activity.

4 Discussion

In this oxytocin administration study among PCL-R-confirmed psychopathic patients convicted of highly aggressive felony crimes, the goal was to examine cortisol and testosterone saliva levels (i.e., baseline levels and their change over time) and their relation to the severity of the psychopathy diagnosis. Oxytocin administration did not affect steroid levels. Cortisol levels decreased during the test procedure, which was compatible with the circadian rhythm of cortisol. POMS mood states did not alter. Although we could not corroborate the expected positive association between PCL-R facet 1 scores and testosterone levels, our results suggest that PCL-R facet 1 partially protected against decrease in both cortisol and testosterone levels, i.e. in an explorative median-split analysis we illustrated that in psychopaths with a relatively low PCL-R facet 1 severity a significant decrease in cortisol as well as in testosterone levels occurred, while this was not the case for psychopaths with a relatively high PCL-R facet 1 severity. Furthermore, as expected testosterone levels were higher in psychopaths who scored high on PCL-R facet 4, but our hypothesis derived from the dual-hormone hypothesis, namely that the testosterone-cortisol ratio would be positively

associated with the PCL-R facet 3 and PCL-R facet 4, was not confirmed as no significant relationship was found with these facets nor with the other PCL-R categories. We conclude that the dual-hormone hypothesis as expressed in the testosterone / cortisol ratio appears to be incorrect in relation to psychopathic severity. As expected (see Feldman et al., 2002) age was significant negatively related with testosterone levels, but this did not mediate the associations found between steroid levels and PCL-R facets. We also controlled our analysis for differences in start-time of the saliva sampling.

Dutch criminal law allows the court to impose compulsory treatment on mentally ill offenders under the Entrustment Act. This means that involuntary admission to a maximum-security forensic psychiatric hospital can be enforced. Regular evaluations are done to determine whether or not psychiatric treatment can be safely terminated. Despite the mandatory treatment, there is no punitive intent on the part of hospital staff or authorities. Treatment takes place according to evidence-based medical treatment standards by highly trained health professionals. It is a commonly shared fact of experience that despite the coercive nature of their treatment, patients reside in a significantly less stressful environment compared to the stressful punitive ambiance in a correctional facility elsewhere. An important feature of our sample of PCL-R confirmed psychopathic patients is that their stay in the maximum-security forensic psychiatric hospitals lasted, on average, nearly ten years at the moment of the study (see Table 1). Nonetheless, we found that testosterone levels were still associated with psychopathic severity (PCL-R facet 4, i.e. the facet that includes both antisocial and, usually reactive, aggressive behavior). Cortisol, and consequently the testosterone / cortisol ratio, however, was not associated with psychopathic severity, which might reflect the long time of confinement to a predictable, safe and structured clinical environment. Their current hormonal balance, which is on average ten years older compared to the balance they had when they started their forensic psychiatric treatment, may therefore be less challenged (see also Knight & Mehta, 2014). Indeed, the dual-hormone hypothesis has been argued to particularly arise in relation to cortisol-reactivity to stressors (Glenn et al., 2011), which in the present data was clearly not the case as cortisol levels dropped in accordance with the circadian rhythm of cortisol over the course of our experiments. Furthermore, although oxytocin can be detected in saliva for a long time after intranasal administration (van IJzendoorn et al., 2012; Weisman et al., 2012), oxytocin is highly unlikely to exert a direct local oral effect on the salivary steroid levels. In addition, oxytocin administration is associated with a decrease in salivary cortisol levels during stress inducing interventions (Heinrichs et al., 2009; Ditzen et al., 2009; Cardoso

et al., 2013), but not when no stress is provoked (Wirth et al., 2015). Oxytocin is also associated with short-term (Weisman et al., 2014) and long-term elevations (Gossen et al., 2012) of salivary testosterone levels, but according to Wirth and colleagues (2015) not under nonstressful circumstances. Since in our study oxytocin did not affect steroid levels compared to placebo, and mood did not change between the moments of saliva collection, we assume that no exogenous alteration in steroid levels was induced and that the drop in cortisol level over time was caused by its diurnal rhythm.

Interestingly, this decrease in cortisol, as well as in testosterone, levels was not observed in psychopaths with high severity of the PCL-R facet 1, the facet that includes interpersonal behaviors such as dominance, narcissism, and manipulation (see Table 2). Given that steroid levels constantly adapt to the current (social) environment (Mazur & Booth, 2014), and blunted diurnal variation is associated with increased externalizing behavior (Adam et al., 2017), these data suggest that a lack of such hormonal flexibility underlies the extreme goal-directed tendencies in social conduct found in psychopaths scoring high on PCL-R facet 1. This facet is significantly associated with the instrumentality of the aggression displayed and also with the severity of aggressive crimes, while this is not the case for the other PCL-R facets (Laurell et al., 2010). In our study, it was unfortunately not possible to determine retrospectively from the criminal records whether the aggressive felony crimes of the high PCL-R facet 1 group were more instrumental or more severe compared to those of the low PCL-R facet 1 group. The question that arises, however, is whether, and if so to what extent, items of PCL-R facet 1 (i.e., glibness/superficiality, grandiose self-worth, pathological lying, and conningness/manipulation) fuel hormonal inflexibility or vice versa and whether hormonal inflexibility can be disrupted by e.g. drug interventions, that may eventually result in reduced aggressive tendencies and lower risk of violent recidivism. This is an interesting hypothesis that warrants more research, specifically focused on hormonal alterations by testing in changing (social) environments, and using larger samples to capture the effects and possible interactions of both steroids (Dekkers et al., 2019).

Lastly, testosterone levels were higher in psychopaths scoring high on PCL-R facet 4, which is in accordance with the study of Stålenheim and colleagues (1998) who found a close positive association of HPG axis functioning and PCL-R factor 2 (which encompasses PCL-R facet 3 and PCL-R facet 4). Within the PCL-R, the expression of antisocial, mostly reactive aggressive behavior is specifically linked to PCL-R facet 4. Furthermore, testosterone has been associated with reactive dominant behavior (Terburg et al., 2009; Terburg et al., 2016), which increases the likelihood of reactive aggressive behavior, albeit that

social contextual factors remain significant mediators. Psychopathy is however known for its involvement in both impulsive-reactive and instrumental forms of aggression (Porter & Woodworth, 2006). Combined with our observation that inflexibility of testosterone is positively linked to psychopathic patients who scored high in PCL-R facet 1, i.e. the facet associated with instrumental forms of aggression (Laurell et al., 2010), we therefore suggest that high testosterone levels might facilitate the actual expression of antisocial, mostly reactive aggressive behavior and that inflexibility over time of testosterone (and cortisol) could pave the way to instrumental aggression.

The long-standing debate on whether and how nasally administered OT can penetrate the brain seems to be gaining more clarity. Nasally administered OT enters the brain primarily through afferent olfactory and trigeminal nerves, rather than through the blood-brain barrier due to its molecular mass of 1007 Dalton (Quintana et al., 2021; Winterton et al., 2021). Although the dose-effect and dose-time relationships between nasally administered OT and its functional effects are not yet clear, there are indications that a dose of 24 IU and a time window between 45 and 75 minutes are the most effective (see, for example, Spengler et al., 2017).

Limitations of the current study are that it is not known whether higher doses than the single dose of 24 IU intranasal oxytocin still can affect steroid levels. Moreover, we cannot exclude that hormonal fluctuations in anticipation of substance administration affected our baseline hormone measures. A temporary aspect during the test procedure must also be taken into account, namely the time difference between pre-trial and post-trial saliva collection. On both test days this time gap was approximately one and a half hours (see § 4.1), so it is possible that by the end of the test procedure, the oxytocin concentration had dropped so low that the window of the oxytocin-induced systemic effect on the steroids had already closed. Furthermore, the absent effect of oxytocin on cortisol levels may also be due to the low challenges during the test procedure, as oxytocin has a greater impact on cortisol response when the HPA axis is vigorously stimulated than when little activation of the HPA axis occurs (Cardoso et al., 2014).

A word of caution should be mentioned here because of the rather small sample size ($n = 20$). Although we examined a unique group of illicit drug-free forensic psychopathic in-patients, with no major psychiatric comorbidity, who were not on significant psychopharmaceutical medication, and who were tested according to a within-design, we ran the risk that due to underpowerment our associations may not be replicated. Apart from the small sample size, another possible limitation may lie in the fact that we selected patients with a PCL-R total

score of 26 or higher. Non-psychopathic patients (those with a lower PCL-R total score) were not included in this study. In principle, testing one part of the PCL-R slope (i.e., the upper slope) might give rise to an overestimation of the relationship between PCL-R scores and steroid levels in the general population. Therefore, and given that this report specifically focused on the relation between steroid levels and PCL-R scores within the clinical range, our conclusions hold only for the group with a PCL-R > 26 and should not be extended to the general population.

Notwithstanding these limitations, the current study provides several valuable insights into the relationship between psychopathy and testosterone and cortisol. Hormonal inflexibility is positively linked to psychopathic patients who score high on the interpersonal PCL-R facet that represents narcissistic, dominant and manipulative tendencies. These individuals may not adapt to changing circumstances. This generates new hypotheses whether hormonal reactivity can be induced in the high scorers of PCL-R facet 1, and subsequently whether this can yield new treatment options.

Chapter 8
General discussion

It was not I that sinn'd the sin
 The ruthless body dragg'd me in
 Though long I strove courageously
 The body was too much for me

— Walt Whitman

1 General discussion

The dualism of René Descartes (1596-1650) shines through in Whitman's words, as if the body and mind are two different entities, with the body being will-less and thoughtless, as opposed to a conscious mind that can make free decisions. Descartes' dualism between matter (*res extensa*) and mind (*res cogitans*) is criticized to this day. Interestingly, perpetrators of all kinds sometimes refer to an automatically acting body as an explanation for their criminal acts, such as a decade ago Jasper S. who admitted to raping and murdering Marianne V. in a high-profile murder trial in the Netherlands. A newspaper account of the court hearing reflects the following: *S. again admitted during the trial that while threatening her with his pocketknife, he forced Marianne V. to have sex with him and then slit her throat. "Three times," he said in response to questions from the judge. S. acted, by his own admission, in a trance. "My body did it, it wasn't me," he said of it. "In full consciousness, I don't do something like that."* (www.nu.nl; 28 March 2013). Getting closer to Whitman's words is barely possible.

This dissertation is not about why people act criminally, nor about alleged automatic processes that seemingly circumvent free will when committing heinous crimes. Nonetheless, we describe a study with various tasks that examine subliminal bodily processes that are hardly controlled by consciousness, if at all. Central to this thesis is research into social-emotional behavior in psychopathy, such as empathy processing, and the domains of reactive dominance, facial mimicry, and moral choices. In psychopathic patients, we applied the neuropeptide oxytocin (OT) to investigate whether OT could bring about a positive development of psychopathic behavior in terms of less reactive dominance, stronger facial mimicry of emotional facial expressions of others and a preference for moral choices that could be considered less self-centered. Indirectly and with an eye to the distant future, we speculated that with positive results OT-application could increase the likelihood of improved empathic functioning and an increase in prosocial behavior in psychopathy.

In this General discussion first we discuss the empathy construct and empathy deficits in psychopathic individuals, as impaired empathy processing is thought to be the hallmark of psychopathy (Soderstrom, 2003). Then, we discuss a study in clinically admitted forensic psychopathic male patients performing various computer tasks after a placebo-controlled self-administered single nasal spray of OT. I briefly summarize the rationale for these sub-studies as well as the results as revealed in the various articles. Next, I will have final remarks about a possible relationship between empathic functioning in the

psychopathic patients examined and the research tasks used in this study. I then continue with Lennart's story and finally I conclude with future directions. In it, I will also speculate about possible future research on OT applications in psychopathic patients.

2 Empathy processing in psychopathy

In Chapter 2 we first focused on empathy and empathy processing. Empathy is a multidimensional construct with affective, cognitive, and behavioral characteristics and can be symbolically interpreted as the social glue in society (Chakrabarti & Baron-Cohen, 2011) that binds human beings. The empathy construct consists of conjointly operating distinct cognitive and emotional components, namely emotional mimicry, emotion awareness, emotional contagion, self-other orientation and perspective taking, and other-oriented emotional responsiveness that is isomorphic in nature. Note that emotional mimicry and emotional contagion are thought to be precursors of the empathy construct. Empathy processing is primarily shaped and maintained by constant mutual communication between the perceiver and the sender and is further based on the combination of appraisal of contextual variables as well as psychological aspects, such as attentional and motivational factors.

The main conclusion after reviewing the literature on empathy is that the whole construct of empathy should be seen as a highly dynamic two-way process rather than a static one-way phenomenon. To describe the conjointly interacting cognitive and affective components of the empathy construct, we developed the Zipper Model of Empathy (Figure 1). Note that “zipping up” represents approaching mature empathy and the expression of empathic behavior by combining the interacting cognitive and affective components. On the contrary, “unzipping” entails a looser collaboration between cognitive and affective processes and, as such, symbolizes either a reduction in empathy or its loss altogether. In this model, which is dynamic by definition, we defined “zipping” forces driving bidirectional changes in empathy processing, namely contextual factors and psychological (i.e., attentional and motivational) factors as they are symbolized by “hands” in Figure 1.

Facial emotional processing precedes the precursors of cognitive and affective empathy components, that is, facial mimicry and emotional contagion.

And this is where difficulties exist in psychopathic individuals, at least what we know so far. More broadly, during their instrumental actions, psychopathic individuals have serious difficulties in shifting their attention to initially less salient aversive conditions as they manifest (Patterson & Newman, 1993). These observations formed the basis of the response modulation theory of psychopathy (Newman & Lorenz, 2003). According to this theory, psychopathic offenders tend to pay little attention to processing peripheral information that they consider of secondary importance. Instead, in their response modulation, they have superior attention to a preset target of interest, ignoring all peripheral information that in normal circumstances might act as affective and inhibitory information necessary for normal individuals to decide whether or not to proceed with their goal-directed behavior (Baskin-Sommers et al., 2009). In a state of fundamental disinterest and lack of motivation to become involved with a person deemed of secondary importance, the psychopathic individual tends to ignore that person and therefore fails to explore the person's emotional facial expression (Boll & Gamer, 2016). According to the Zipper Model of Empathy, it follows that as a result of this aberrant response modulation, the precursors of the empathy construct are not set in motion, that is, facial mimicry and emotional contagion tend not to occur. Moreover, the “hand” of personal factors, i.e., motivation and attention (see Figure 1), does not become active, preventing mature empathy to emerge. This does not automatically mean that all components of the empathy construct are inactive, since psychopathic individuals are not necessarily impaired in their cognitive processing (Richell et al., 2003; Blair, 2007). For example, when it suits their own interests, they can perfectly focus their gaze on another person's eye region to “read” their emotional facial expressions. Although psychopathic individuals are able to interpret another person's emotional expressions, especially when their preset attentional focus is on that other person, the affective zipper components do not (fully) interact, so emotional contagion is not processed. The Zipper Model of Empathy explains that as a consequence of this incomplete processing of affective components a mature empathy state cannot be achieved.

In Chapter 2, we further explain that the neurobiological underpinnings of various theories on affect processing in psychopathy are according to the literature importantly amygdala-centered. The amygdala is not a single brain structure, but a heterogeneous collection of nuclei, most notably the basolateral (BLA) and central (CeA) subregions of the amygdala. In their mutual interplay, the BLA and CeA determine not only the level of emotional reactivity (Terburg et al., 2018), but also goal-directed motivation at the level



▲ **Figure 1. Zipper model of empathy** Conjointly interacting cognitive and affective components in two-way dynamic empathy processing, including mimicry and emotional contagion as precursors of the empathy process. The term emotional responsiveness stems from Feshbach (1997). Fully “zipping up” leads to mature empathic behavior while “unzipping” results in disappearing or hampered empathic behavior. The zipping direction and the strength of the zipper forces depend on both psychological states (hand 1) and contextual factors (hand 2). Original publication in: Rijnders et al. (2021a). *Neuroscience and Biobehavioral Reviews*, 131, 1116-1126.

of the striatum and prefrontal cortex (Balleine & Killcross, 2006). The BLA is necessary for learning and expressing calculative actions to make maximum profit, also at the expense of others (Rosenberger et al., 2019; van Honk et al., 2013). Although the CeA promotes automatic emotional reactivity and general motivation, the BLA can suppress CeA actions and redirect the amygdala output toward more instrumental goal-directed motivation and behavior. This redirection towards emotionally callous behavior may eventually block “zipping up” to mature empathic behavior. It is known that amygdala dysbalance is associated with impairments in the detection of and attention to the human eye region in youngsters with high psychopathic traits (Dadds et al., 2011). These findings contrast sharply with amygdala processing in subjects with Urbach-Wiethe disease (UWD), a genetic disorder in which the bilateral amygdala show focal calcifications in the basolateral subregion (BLA). UWD subjects with BLA damage look longer at the eye regions of persons with fearful facial expressions (Terburg et al., 2012) suggesting a regulatory mechanism within the amygdala. Therefore, the mechanism behind the impaired functioning of the amygdala in psychopathy warrants further research.

According to the response modulation theory of psychopathy (Baskin-Sommers et al., 2011; Newman et al., 2010) lack of motivational factors may result in a “downstream” face recognition deficit, especially when the other is thought to be of secondary interest while the psychopathic individuals are overwhelmingly attracted to achieve their primary goal. Amygdala processing in psychopathy also includes a motivational component (Moul et al., 2012), so if the other person is a part of their prepotent focus of attention, psychopathic individuals are able to focus their attention on the other’s affective facial information, and thus, according to “hand 1” of the Zipper Model of Empathy that represents attentional and motivational factors (see Figure 1), they might start to “zip up” parts of the empathy construct and come across as charming and empathic, although frequently in a clumsy and not entirely credible way.

In Chapter 3, we propose a neuropsychological battery for assessing empathy processing in psychopathy based on the Zipper Model of Empathy. Each component of the Zipper Model of Empathy can be measured using a multimodal approach. Based on non-systematic scientific literature search, we substantiated the use of the following validated clinical tasks. First, we propose the use of facial electromyography for measuring mimicry of facially expressed emotions, as facial mimicry is described as “the current psychophysiological gold standard of measuring emotional valence” of facial expressions (Höfling et al., 2020, p. 1). Second, the Emotion Recognition Task (Montagne et al., 2007) can be used to identify six expressed emotions,

namely happy, angry, disgust, sad, surprise and fear. We favor the use of dynamic facial stimuli over displaying static facial pictures because the former outperform the latter in terms of ecological validity (Calvo et al., 2016, 2018; Kamachi et al., 2013). Third, a modified version of the Empathic Accuracy task (Ickes, 1997) with an examination of self-perceived emotions combined with physiological measurements (e.g., heart rate variability) may touch on the principle of emotional contagion. Fourth, to examine self-other orientation and perspective taking, which are important cognitive components of the Zipper Model of Empathy, a selection of Theory of Mind tasks (e.g., Baron-Cohen et al., 1985; Burghart & Mier, 2022) and a modified Dot Perspective Task (Samson et al., 2010) can be employed. Fifth, finally in order to examine other-oriented isomorphic emotional responsiveness, which is defined as the emotional response directed to another person that is congruent with the perceived welfare or emotional state of that person (Feshbach, 1997, Rijnders et al., 2021a), we suggest measuring this high-level presentation of empathy in an indirect way by observing and rating the participant's tendency to act compassionately and through goodwill to another person in need. We therefore adapted the Charity Task (Dapprich et al., in preparation), in which while reading a sad story about an underprivileged child being severely bullied, participants can assess their own cognitive and affective empathy components along with those of the child. Meanwhile, an altruistic aspect is also measured, as participants are repeatedly invited over the course of the story to donate small amounts of money to an organization that provides assistance to underprivileged children like this one.

The description of the tasks above are intended as a starting point for discussion and debate on the definition and clinical assessment of various empathy components so that the Zipper Model of Empathy can be verified and falsified. Therefore, empirical test procedures are warranted both in psychopathy as well in in other psychiatric disorders known to be deficient in the processing of empathy. Indeed, after applying the Zipper Model of Empathy to schizophrenic patients with a history of severe interpersonal violence, it was found that lack of empathy was specifically associated with reduced facial emotion recognition, which, according to the authors, justified the conclusion that the results support the validity of this model (Vaskinn et al., 2023).

3 Intervention study with oxytocin

Intervention studies with medication in psychopathic individuals are scarce. Given the enormous social costs and interpersonal suffering among their victims caused by psychopathic individuals, there is a great need for intervention studies not only in the behavioral psychotherapeutic field but also in the field of treatment with psychotropic medication. The central question in this dissertation is whether the neuropeptide oxytocin (OT) can influence psychopathic symptoms in a group of hospitalized male forensic psychopathic patients, and if so, in what direction. We also examined a group of male security guards and nursing staff members who did not use OT and thus served as a reference population to the psychopathic patients in the placebo condition. Here we discuss the results of a study of social-emotional behavior in forensic psychopathic patients performing various computer tasks after placebo-controlled self-administration of a single nasal spray of OT. These tasks refer to likely proxies of the empathy construct, i.e., social dominance, moral choices and mimicry of facial expressions (see above and Introduction). Finally, we conclude with a sub-study among the psychopathic patients of their salivary concentrations of the steroid hormones testosterone and cortisol before and after the entire test procedure. Steroid hormones are suggested to drive status-relevant behaviors such as aggression and dominance, which are known to be abundant in psychopathic patients and may indirectly reflect empathy dysfunctioning. The rationale for this sub-study is that, although not uncontroversial, indications exist that aggressive behavior is associated with context-dependent low levels of cortisol as well as with high levels of testosterone (Archer, 2006; Carré & Archer, 2018; Glenn & Raine, 2014; Montoya et al., 2012; Terburg et al., 2009).

3.1 Participants

The patient group studied consisted of male psychopathic patients who had been involuntarily hospitalized in various forensic psychiatric hospitals in the Netherlands. They were diagnosed with psychopathy using the Psychopathy Checklist - Revised (PCL-R; Hare, 2003) and had been convicted of very serious crimes (see Table 1). All patients were involuntary hospitalized as part of a criminal justice measure according to the Dutch Entrustment Act (In Dutch: terbeschikkingstellingsmaatregel; tbs). During their stay in a high-security

forensic psychiatric hospital, psychiatric and psychotherapeutic treatment is offered, as well as sociotherapy. The main goal of the hospital staff is to reduce the risk of recidivism for crimes equivalent to the patients' index crime(s). In doing so, treatment efforts address all symptoms of their possible personality disorder, developmental disorder, intellectual disability and/or psychiatric disorder, including substance abuse disorders. In addition, interventions such as closely examining the offender's actions prior to and during the index crime take place so that a so-called crime scenario and crime analysis can be prepared aimed at clarifying dysfunctional criminal behavior that needs to be eliminated, especially with a view to future reintegration into free society. Although desirable, it is not necessary for all mental symptoms to disappear during treatment, as the main goal is to reduce the risk of recidivism in the future so that patients can eventually reintegrate gradually into society. Social support therefore also plays an important role in treatment. Independent psychiatric and psychological forensic evaluations are regularly conducted to determine whether termination of involuntary stay in the forensic psychiatric hospital is appropriate. A specialized Entrustment Act court decides and can possibly order an extension of forced stay for the next one or two years. Therefore, a court-imposed mandatory stay in a forensic psychiatric hospital can last for many years, as is the case in the group of the 21 forensic psychopathic patients in our study (average duration 112 ± 82 months).

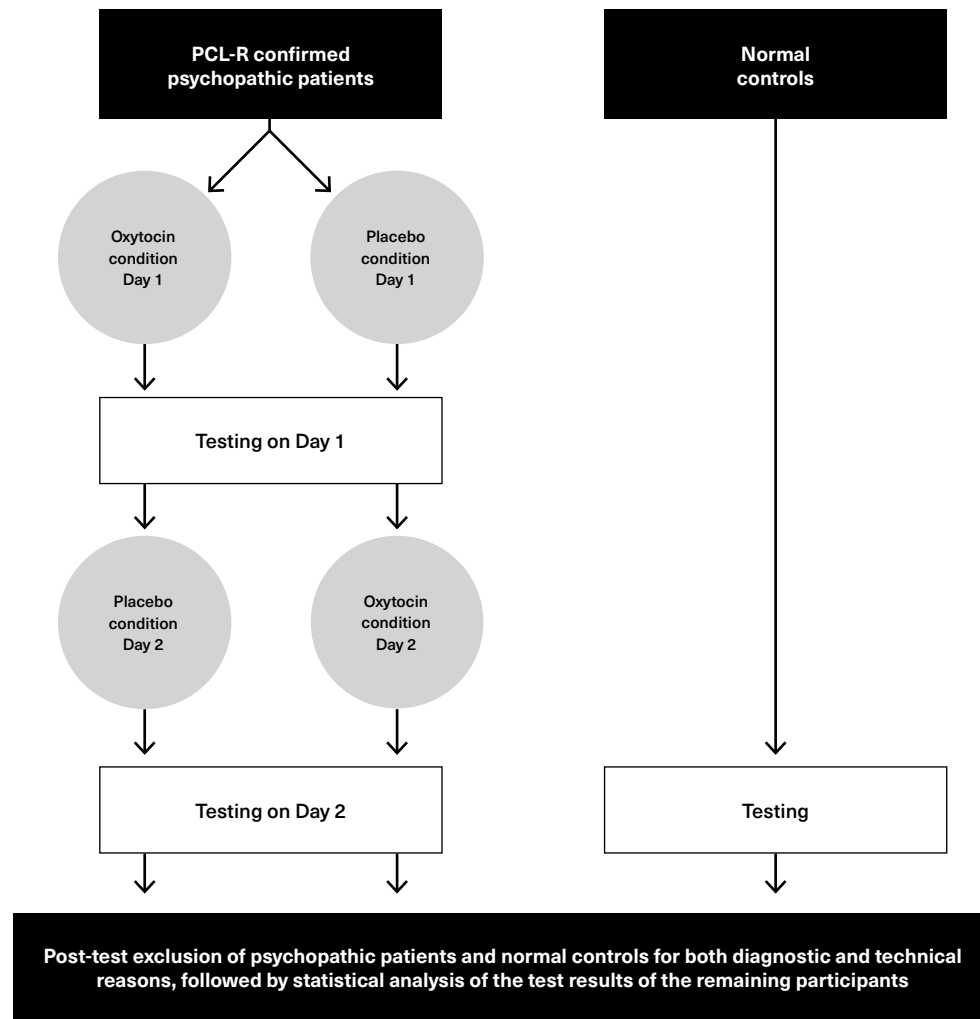
Participation in the study was possible with a PCL-R score of 26 or higher (the patients examined had a mean PCL-R score of 31.2 ± 2.9 ; range 26 - 36). In a group of 21 patients, a total of 8 convictions were for (attempted) murder or (attempted) manslaughter, 5 convictions were related to sexual crimes (i.e., (attempted) rape, or sexual abuse of a minor), 8 convictions were for other interpersonal aggressions (i.e., assault, arson, or hostage), and finally, 13 convictions were related to larceny (i.e., robbery, extortion, or theft) (Rijnders et al., 2022). A unique feature of this study is that this group of clinically admitted forensic psychopathic patients was not treated with medications such as selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors, antipsychotics or hormonal libido inhibitors, because these medications were also contraindicated. This is because these medications may interfere with OT or social (e.g., dominance) relationships (Galbally et al., 2021; Malatynska & Knapp, 2005; Neshet et al., 2013; Rich & Caldwell, 2015; Yamaguchi et al., 2017). The group of normal controls consisted of male security guards or nursing staff members recruited from two forensic psychiatric hospitals. Similar inclusion and exclusion criteria applied to these participants, except that they could not be diagnosed with the PCL-R. Instead, to

check for psychopathic features, they completed the Psychopathic Personality Inventory-Revised (PPI-R; Lilienfeld & Widows, 2005). Eventually, one of them was excluded from analysis because of a total score of $>2SD$ above average on the PPI-R total score, indicating a psychopathic tendency. As mentioned above, they did not use OT as technical reasons prevented administration of placebo-controlled OT nasal spray. Naturally, this design was not optimal, since it did not allow direct comparisons between OT and placebo applications between the two groups. However, the normal controls served as a reference population relative to the psychopathic patients in the placebo condition.

3.2 Study design

The psychopathic patients used a nasal spray of OT following a within-subject, double-blind, counterbalanced, placebo-controlled, cross-over design. Thus, they completed two test sessions, in which they randomly self-administered 24 IU of the synthetic version of OT, or a nasal spray with placebo consisting of a solution of physiological saline (NaCl). After a wash-in period of OT to act in the central nervous system the participants started with the test procedure with various tasks as described in the chapters 4, 5, and 6. For technical reasons, the normal controls did not use OT, so they were tested on one day only. We decided to use this group as a reference population. An overview of the test procedures for both groups is shown in Figure 2.

The first sub-study on oxytocin (OT) effects is described in Chapter 4 and involves a study of facial mimicry that is known to touch on the concepts of socialization and empathy. We recorded electromyography (EMG) of two facial muscles, namely the corrugator supercilii muscle and the zygomaticus major muscle while participants watched dynamically morphed angry or happy facial expressions displayed on a computer screen. EMG studies of mimicry responses in PCL-R confirmed adult psychopathic individuals or youngsters with callous-unemotional traits (CU traits; see Frick & Morris, 2004) are scarce and inconsistent. CU traits in youngsters are generally considered precursors to psychopathy in later life. We decided to specifically focus on short-latency facial mimicry within 600 ms after stimulus onset, as short-latency facial responses are thought to be automatic, amygdala-processed preconscious responses that are by definition difficult to control voluntarily, and as such might have diagnostic value for psychopathy (van Boxtel et al., 2022). The latter authors demonstrated significant group differences in short-latency EMG responses to



▲ **Figure 2. Flowchart of test procedures for both groups** The psychopathic patients sniffed nasal spray containing either OT or placebo in a cross-over within-design. They were therefore tested on two days. The normal controls did not undergo an experimental condition and were thus tested on one day. Of the group of psychopathic patients, 3 were excluded from analysis due to a co-morbid Pervasive Developmental Disorder Not Otherwise Specified. In addition, for each task, some normal controls and sometimes a psychopathic patient were excluded from further analysis because of missing data or because they did not meet all task criteria. Specification of those excluded is given in the respective articles in this dissertation. Adapted from the original publication in: Rijnders et al. (2021b), *Psychoneuroendocrinology*, 131, 1-11.

dynamic emotional facial expressions in youngsters with high CU traits. They showed both smaller inhibitory corrugator responses (i.e., less corrugator relaxation) and weaker zygomaticus responses to happy expressions and weaker corrugator responses to angry and sad expressions compared with those with low CU traits and healthy controls (van Boxtel et al., 2022).

Exclusively in the group of psychopathic patients, our hypothesis was that placebo-controlled administration of oxytocin (OT) would enhance the short-latency mimicry responses of both the corrugator and zygomaticus. This hypothesis could not be confirmed as no significant differences in short-latency responses were found between the two drug conditions. However, when post-hoc comparing psychopathic patients in the placebo condition with normal controls we found significantly weaker short-latency zygomaticus responses to happy faces, while there was a trend toward significantly weaker short-latency corrugator responses to angry faces. These interesting findings in this adult group and the above results in youngsters with CU traits combined suggest a lifetime developmental deficit in mimicking emotional facial expressions in psychopathy. We hypothesized that it could point to a biomarker of psychopathy. Ultimately, this deficit in mimicking angry and happy expressions may hinder their empathy processing, since mimicry like emotional contagion is thought to be a precursor to the empathy construct (Klimecki & Singer, 2013; Rijnders et al., 2021a). Unraveling this lifetime developmental deficit in short-latency mimicry in psychopathic individuals may therefore provide insight into their impaired empathy processing and their maladapted social interactions.

An important underlying factor of this hampered mimicry appears to be a deficit in the processing of emotional facial information (Rijnders et al., 2021a). There is debate as to whether deficits in emotional facial information processing stem from either a failure to allocate attention to stimuli deemed of secondary importance (according to the response modulation theory of psychopathy) or an innate deficient amygdala processing (Blair, 2001, 2005a; Newman & Lorenz, 2003; Baskin-Sommers et al., 2009). Although not precisely understood, it is thought that dysbalanced functioning of the amygdala in adolescents with high psychopathic traits underlies impaired attention to the human eye region, preventing undisturbed recognition of facial emotions (Dadds et al., 2011). This forms the basis of integrated emotion systems theory (Blair, 2005b) that describes significant deficits in emotional face recognition as the root cause of a disrupted social interaction process in which facial expressions of fear and sadness are not understood as distress signals that should induce inhibition of aggressive behavior. As predicted by our Zipper Model of Empathy, the ultimate result is impaired empathic behavior because absent or hampered facial mimicry

disrupts the joint processing of affective and cognitive empathy components, ultimately preventing the emergence of mature empathy. Response modulation theory and integrated emotion systems theory are not mutually exclusive. Both contextual factors and motivational forces of the Zipper Model of Empathy could influence the likelihood and strength of psychopathic individuals' attentional gaze if it is in their best interest. If it matches their primary goal, they will focus their attention on the other person's eye region, which may lead to enhanced facial emotion recognition (Dadds, 2011). This could also result in a boost in their empathy processing (Meffert et al., 2013).

Chapter 5 describes the second sub-study of oxytocin (OT) effects. In here we examined social dominance which is thought to be one of the characteristics of psychopathy that might contribute to problematic behavior including aggression and violent recidivism (Blair, 1995; Hare, 1991; Hare, 2003; von Borries et al., 2012). Social dominance is not explicitly defined in the PCL-R, but is related to the interpersonal factor (factor 1) of the PCL-R (Draycott et al., 2011; Hall et al., 2004; Murphy et al., 2016; Verona et al., 2001). We used a gaze aversion task developed by Terburg and colleagues (2011), in which slower gaze aversion from masked angry faces compared to masked happy faces is a measure of reactive dominance, while more rapid gaze aversion from angry faces indicates submissiveness (Hortensius et al., 2014; Mazur & Booth, 1998; Putman et al., 2004; Terburg et al., 2011; Terburg et al., 2012; Terburg et al., 2016; van Honk & Schutter, 2007).

First, we tested the hypothesis that compared to normal controls, psychopathic patients in the placebo condition are more dominant and therefore have a slower gaze aversion of masked angry faces compared to happy faces. Contrary to what we expected, the two groups did not differ significantly in gaze aversion, indicating that psychopathic patients were not more dominant than normal controls. Our second hypothesis held that exclusively in the group of psychopathic patients, OT would result in a faster gaze aversion from masked angry faces compared to happy faces (Domes et al., 2012; Domes et al., 2013; Ellenbogen et al., 2012; Tollenaar et al., 2013). In other words, we expected reduced reactive dominance in the OT condition. Again, contrary to our expectations, no significant statistic effects were found, suggesting that oxytocin administration in general did not affect reactive dominance. Finally, our third hypothesis held that gaze aversion latency of all participants correlated positively with measures of psychopathy, i.e., the PCL-R for the psychopathic patients and the PPI-R for the normal controls. For the latter group, this did not appear to be the case for the PPI-R total score and the two PPI-R factors, nor for any of the PPI-R subscales. For the group of psychopathic patients, the PCL-R

total score was added as continuous predictor to the oxytocin intervention linear mixed model. All possible interactions were modelled, and data were clustered by participant. We then replaced the PCL-R total score by the five PCL-R categories, i.e., the four PCL-R facets and PCL-R category "Other" (for an explanation of the latter category: see Table 3 in Chapter 1), as continuous predictors in this linear mixed model. We concluded that reactive dominance is related to higher levels of psychopathy, mainly driven by PCL-R facet 1 and PCL-R category "Other". Interestingly, these significant relationships were abolished after administration of OT. This gaze aversion task could potentially provide an objective measure of reactive social dominance in psychopathic persons. The mechanism behind the effect of OT on dominance reduction is unknown and needs further investigation. Testosterone is known as a steroid hormone associated with dominant behavior (Terburg et al., 2009). The reciprocal interaction between OT and testosterone (Crespi, 2016; Procyshyn et al., 2020) may be of significance, so we hypothesized that reduction of reactive dominance in severe psychopathy may then be due to OT counteracting the dominance-inducing effect of testosterone. Further research into this domain is warranted.

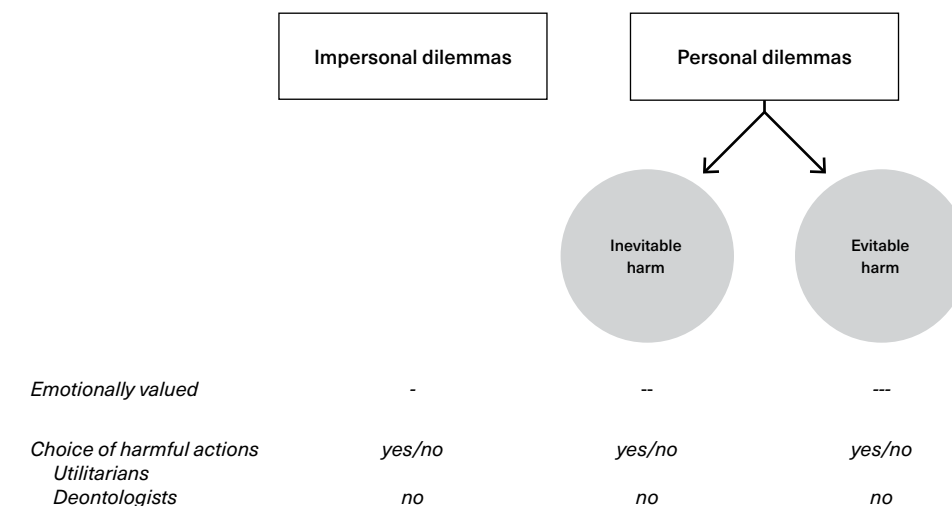
The third sub-study is described in Chapter 6 and deals with the topic of morality that is often studied through so-called moral dilemmas. The dual-process theory of moral judgment (Greene et al., 2001) posits that controlled cognitive and automatic emotional processes normally compete with each other while making of moral judgments (Greene et al., 2001, 2004). These judgments involve mutually exclusive utilitarian and deontological (i.e., non-utilitarian) choices. The emotionality of the utilitarian choice may vary depending on the so-called personal or impersonal action to be taken. The former describes actions where harm is caused by direct physical contact and the latter where harm is inflicted in an indirect, non-physical way. Compared to impersonal dilemmas, utilitarian actions in personal dilemmas are associated with stronger emotional value. Personal dilemmas are further divided into dilemmas in which the victim's harm is either inevitable or evitable (Greene et al., 2009; see also Figure 3). In their meta-analysis and systematic review of 34 studies on the role of empathy in moral decision-making (none of which included a forensic population or psychopathic individuals), Nasello and Triffaux (2023) found small to moderate associations between affective empathy and moral parameters, especially in personal moral dilemmas involving intentional harm, while most studies found limited or nonsignificant associations between cognitive empathy domains and moral judgments and choices. There is a history of conflicting findings on whether psychopathy leads to more utilitarian choices although a recent meta-

analysis revealed a small to moderate positive relationship between psychopathy and utilitarian choices (Marshall et al., 2018). Because of their emotional deficits (e.g., Blair, 1995; Rijnders et al., 2021a), psychopathic individuals are believed to experience little emotional aversion to inflicting harm and, due to their lower empathic concern, they prefer utilitarian choices over deontological ones (Gleichgerrcht & Young, 2013). However, studies in confirmed psychopathic individuals show mixed results (Koenigs et al., 2012; Young et al., 2012), which is arguably due to the different levels of emotion associated with utilitarian behavior in these studies.

We describe a forced-choice moral decision-making paradigm in which participants must make either a utilitarian or deontological decision. For the group of psychopathic patients only, we hypothesized that cross-over placebo-controlled administration of oxytocin (OT) would reduce utilitarian moral decision-making in favor of deontological choices. Moreover, compared with normal controls, psychopathic patients were expected to make more utilitarian than deontological choices. Finally, our third hypothesis held that for both groups a positive relationship existed between psychopathy severity and the percentage of utilitarian choices

Regarding the effects of OT in the psychopathic group, the main effect of drug on utilitarian choices was not significant. The interaction effect between dilemma type and drug was also not significant, but there was a significant main effect of dilemma type on utilitarian choices. Post-hoc contrasts revealed a significant difference in utilitarian choices between the impersonal and personal inevitable dilemmas, implying that in impersonal dilemmas more utilitarian answers were given. There was also a significant difference between personal evitable and personal inevitable dilemmas, namely, the psychopathic patients chose more utilitarian in personal inevitable dilemmas. When comparing normal controls with the psychopathic patients in the placebo condition for all dilemma types no significant differences existed between both groups. A main effect of dilemma type was observed while post-hoc comparisons indicated that across the two groups significantly more utilitarian answers were given for impersonal dilemmas. As described above impersonal dilemmas are associated with weaker emotional value. Further exploration in the control group, showed that only PPI-R factor Impulsive antisociality (Lilienfeld & Widows, 2005) was significantly correlated with the percentage of utilitarian choices. This result was consistent with our third hypothesis. However, and unexpectedly, within the group of psychopathic patients, we found a significant negative correlation between the PCL-R total score and the percentage of utilitarian choices when assessing personal evitable dilemmas (i.e., where one can choose to waive

action to avoid harm). For this dilemma type, highly-psychopathic patients in the placebo condition made fewer utilitarian choices, that is, more deontological choices. Further exploration of this unexpected finding that contrasted sharply with our third hypothesis, revealed that PCL-R facet 3 was negatively correlated with the percentage of utilitarian choices in personal evitable dilemmas. PCL-R facet 3 includes the lifestyle items stimulation seeking, impulsivity, irresponsibility, parasitic orientation, and lack of realistic goals (Hare, 2003). A higher score on this PCL-R facet was thus correlated with more deontological (i.e., less utilitarian) choices. No significant correlations were found between the other PCL-R facets including category "Other" and the three types of moral dilemmas. We concluded that although psychopathic traits predict utilitarianism when emotional investment is low (namely, in impersonal dilemmas), this is



▲ **Figure 3. Moral dilemmas and various choices** Following considered cost-benefit analyses, utilitarians decide to act or not to act depending on their assessment of whether a harmful action imposed on (an)other individual(s) is for "the greater good of all". Deontologists, on the other hand, choose not to act because they believe no intentional harm should be inflicted on (an)other individual(s), regardless of the (expected) outcome. The - sign symbolizes the assumed negative value related to the decision being asked to make.

not the case in highly-psychopathic patients when personal evitable dilemmas are assessed. Instead, a significant relationship exists between deontological choices and impulsivity as reflected in PCL-R factor 3, but only when emotional investment is high, since personal evitable dilemmas are associated with stronger emotional value. These explorative results may well be a chance finding not previously discovered in other studies. Therefore, a replication study is warranted. Nevertheless, we believe that the relationship is interesting enough to further explore this deontological preference.

We hypothesize that an explanation for this unexpected finding can be found when comparing highly impulsive psychopathic individuals with subjects with Urbach-Wiethe disease (UWD) in which a genetic mutation causes selective bilateral calcification of the basolateral amygdala (BLA), while the central-medial amygdala (CMA) remains functional and intact (van Honk et al., 2022). UWD subjects make impulsive social-emotional decisions due to the loss of the regulatory effects of the BLA on structures required for moral decision-making, namely the CMA, nucleus accumbens and ventral medial prefrontal cortex (vmPFC) (Schoenbaum et al., 2003). As a result, they lack outcome-oriented decision-making, preventing them from making instrumental utilitarian decisions in conflict situations (van Honk, et al., 2022).

Abnormal functioning and volume reductions of the amygdala have been found in violent and high-risk to violence psychopathic individuals, including up to 30% reduction in BLA tissue and a 10% to 30% enlargement of the central and lateral nuclei of the amygdala (Boccardi et al., 2011; (Ermer et al., 2012; Yang et al, 2009). BLA input is mandatory for the vmPFC to acquire motivational value in decision-making (Schoenbaum et al., 2003). Moreover, the CMA promotes automatic emotional reactivity and general motivation, while these processes can be inhibited by the BLA, resulting in more instrumental goal-directed motivation and behavior (Balleine & Killcross, 2006; Terburg et al., 2018). In short: the BLA is fueling instrumental (i.e., utilitarian) decisions by suppressing the automatic affective processing from the CMA. Although no research data exist on intra-amygdala processing in psychopathic individuals, it would be interesting to examine whether they respond impulsively deontologically to strong aversive dilemmas resulting from BLA deficits when their self-interest is not at stake. In terms of moral decision-making, the difference between impulsive psychopathic individuals and UWD subjects may be that the former may reach an instrumental decision when contextual information favorable to them prompts them to do so.

In Chapter 7 we describe a sub-study in which we measured salivary levels of the steroid hormones testosterone and cortisol in the group of psychopathic

patients who participated in the above study with various computer tasks (see Chapters 4, 5, and 6, respectively). As testosterone facilitates approach and reward-seeking, cortisol is associated with withdrawal and fearfulness (Glenn et al., 2011). Cortisol and testosterone show reciprocal suppressive interaction: while cortisol inhibits the hypothalamic-pituitary-gonadal axis activity at the level of the hypothalamus, pituitary gland and the gonads (Johnson et al., 1992). Testosterone, vice versa, exerts an inhibitory effect on the higher level of the hypothalamic-pituitary-adrenal axis (i.e., the hypothalamus) but not on the pituitary gland or the adrenal cortex (Johnson et al., 1992; Viau, 2002). High cortisol levels block testosterone-related dominant behavior while this is not the case in subjects with low cortisol levels. This reciprocal interaction between low cortisol and high testosterone levels on status-seeking and hierarchy-driven behavior (e.g. dominance and aggression) underlies the so-called dual-hormone hypothesis (Mehta & Josephs, 2010; Sherman et al., 2016; see also the seminal work on this cortisol – testosterone interaction by Dabbs et al., 1991). These steroids have also been linked to psychopathy, as this personality disorder is strongly associated with status-driven behaviors such as dominance and aggression. But again, mixed results are reported, which may be partly due to the different populations studied, ranging from community samples to prisoners convicted of aggressive interpersonal crimes, while not all the participants studied met the PCL-R criteria for the diagnosis of psychopathy.

Saliva was collected before the start of the cross-over placebo-controlled self-administration of oxytocin (OT) and after completing the entire test session. Mean start-times of the pre-trial saliva collection as well as the mean time between pre-trial and post-trial saliva collection on the two test days did not differ significantly. Two hypotheses were tested. First, following the dual-hormone hypothesis it was hypothesized that the testosterone / cortisol ratio would show a positive association with the PCL-R factor 2 (Stålenheim et al., 1998), thus with PCL-R facet 3 and, presumably even more prominent, PCL-R facet 4. Second, as strong associations have been described between dominant behavior and PCL-R factor 1 (Hall et al., 2004; Lobbestael et al., 2018; Murphy et al., 2016; Verona et al., 2001) it was hypothesized that testosterone levels would have a positive association with PCL-R facet 1, but not or to a lesser extent with PCL-R facet 2 as this last facet does not appear to influence dominance.

We found a drop in cortisol levels over time as expected according to its circadian rhythm, but not in testosterone levels. As expected the covariate age interacted with HORMONE, indicating a significant negative relation with testosterone levels, which was absent in relation to cortisol levels. Controlling for age and starting time, no significant relationship was found between the PCL-R

categories and testosterone – cortisol ratio. Administration of OT compared with placebo did not significantly affect steroid hormone levels. PCL-R facet 4 was positively correlated with testosterone levels, while this was not the case for cortisol levels. Furthermore, PCL-R facet 1 was positively related to a decrease in levels of testosterone and cortisol from pre-trial to post-trial. This suggested that high levels of PCL-R facet 1 protected against a decrease in both steroids, i.e. the low PCL-R facet 1 group had a significant decrease in testosterone and cortisol, while this was not the case for the high group. In conclusion, our hypothesis derived from the dual-hormone hypothesis, namely that the testosterone / cortisol ratio would be positively associated with the PCL-R facet 3 and PCL-R facet 4, was not confirmed as no significant relationship was found with these facets nor with the other PCL-R categories. We concluded that the dual-hormone hypothesis as expressed in the testosterone / cortisol ratio appears to be incorrect in relation to psychopathic severity. We hypothesized that this negative finding might partly due to the longtime confinement of our psychopathic patients in a predictable, safe and structured clinical environment as their forensic psychiatric hospitals can be considered. Their current hormonal balance, which is on average more than ten years older compared to the balance they had when they started their forensic psychiatric treatment, may therefore be less challenged (see also Knight & Mehta, 2014). Indeed, the dual-hormone hypothesis has been argued to particularly arise in relation to cortisol-reactivity to stressors (Glenn et al., 2011), which in the data was clearly not the case as cortisol levels dropped in accordance with the cortisol circadian rhythm over the course of our experiment. Since in this sub-study OT did not affect steroid levels compared to placebo, and mood did not change between the moments of saliva collection, we assumed that no exogenous alteration in steroid levels was induced and that the drop in cortisol levels over time was caused by its diurnal rhythm.

4 Final remarks

This dissertation focuses on empathy and disturbed empathy processing in psychopathy and, by extension, various computational tasks that may point to possible proxies for the empathy construct. Furthermore, the central question was whether the neuropeptide oxytocin (OT) can ameliorate psychopathic symptoms in psychopathic patients. Below, I will examine whether the research

tasks used reveal empathy processing in psychopathy.

Chapter 2 and Chapter 3, respectively, describe the empathy construct and a neuropsychological battery for assessing empathy processing in psychopathy based on the Zipper Model of Empathy. Empathy is a multidimensional construct that as a whole consists of separate cognitive and emotional components that conjointly interact in a highly dynamic bidirectional process. We developed the Zipper Model of Empathy (Figure 1), a dynamic model in which bidirectional changes in empathy processing are induced by “zipping” forces, namely contextual factors and psychological (i.e., attentional and motivational) factors as they are symbolized by the “hands” in Figure 1. Consequently, “zipping up” represents approaching mature empathy and the expression of empathic behavior by fully combining the interacting cognitive and affective components. “Unzipping,” on the other hand, entails a looser cooperation between cognitive and affective processes and as such symbolizes either a reduction of empathy or its loss altogether.

In our first sub-study of OT effects (Chapter 4), we examined facial mimicry, which is known to touch on the concepts of socialization and empathy (Hatfield et al., 1994, 2009; Klimecki & Singer, 2013; Rijnders et al., 2021a; Seibt et al., 2015), while deficits in empathy processing in psychopathy are thought to be partly driven by impediments in mimicking others’ expressed emotions (e.g., Bird & Viding, 2014; Rijnders et al., 2021a). We examined short-latency facial mimicry of both the *musculus corrugator supercilii* and the *musculus zygomaticus major* within 600 ms after stimulus onset, as short-latency facial responses are thought to be automatic, amygdala-processed preconscious responses that are difficult to control voluntarily, and as such may have diagnostic value for psychopathy (van Boxtel et al., 2022). The latter authors demonstrated significant group differences in short-latency EMG responses to dynamic emotional facial expressions in youngsters with high psychopathic traits. In our sub-study we could not confirm our hypothesis that placebo-controlled administration of OT would enhance the short-latency mimicry responses of both the corrugator and zygomaticus. However, when comparing psychopathic patients in the placebo condition with normal controls, we found significantly weaker short-latency zygomaticus responses to happy faces, while there was a trend toward significantly weaker short-latency corrugator responses to angry faces. Together, these interesting findings in our adult group and the above results in adolescents with high psychopathic traits suggest a lifetime developmental deficit in mimicking emotional facial expressions in psychopathy. We even suggest that deficiencies in short-latency facial mimicry may be considered a biomarker of psychopathy. Ultimately, this deficit in

mimicking angry and happy expressions may hinder their empathy processing, as facial mimicry, like emotional contagion, is thought to be a precursor to the empathy construct (Klimecki & Singer, 2013; Rijnders et al., 2021a), while both can ultimately facilitate the processing of affective forms of empathy (de Wied et al., 2006; Hermans et al., 2006; Hoffman, 2000; Sonnby-Borgström, 2002; Scheffer et al., 2011). So indeed, unraveling this lifetime developmental deficit in short-latency mimicry in psychopathic individuals may provide insight into their impaired empathy processing and their inappropriate social interactions.

Chapter 5 describes a sub-study of another form of inappropriate social interactions of psychopathic individuals, namely reactive social dominance, which is an expression of non-social and non-cooperative behavior. Psychopathic individuals with high fearless dominance scores have lower levels of facial exploration (Boll & Gamer, 2016), while both adult psychopathic individuals and adolescents with psychopathic traits have impaired gaze to the eye region where emotional facial expressions are abundant (Boll & Gamer, 2016; Dadds et al, 2008; Gillespie et al, 2017; Rice & Derish, 2015). As a result of this impaired gaze, psychopathic individuals may have altered social perceptions and a lack of inhibition of inappropriate social behavior, ultimately resulting in reactive social dominance. As follows from our Zipper Model of Empathy, facial exploration and facial affect processing form the basis of facial mimicry and emotional contagion, which are known to be precursors of the empathy construct. Taken together, it can be concluded that reactive social dominance of the psychopathic individual is associated with deficits in empathy processing.

In this sub-study, the results showed that psychopathic patients were not more dominant compared to normal controls on a task measuring reactive dominance. However, in the patient group the severity of psychopathy as measured by the Psychopathy Checklist - Revised (PCL-R) was positively correlated with reactive dominance while in the normal controls no such positive correlation was found on a measure of psychopathy.

Although OT yielded no effect on reactive dominance in general, OT was found to abolish the relationship between psychopathy severity and reactive dominance. Hypothetically, in highly psychopathic individuals, OT could attenuate social threat vigilance when looking at images of dominant others, by inhibiting information about negative social cues and thus enabling prosocial behavior that would not otherwise occur. This may improve interpersonal alignment and ultimately reduce reactive social dominance and, in its slipstream, aggressive behavior. Although unproven, I expect that lower reactive social dominance could give rise to reduced stressful exploration of others' facial

emotions, which, according to the Zipper Model of Empathy, could pave the way for improved empathy processing. In this sense, I postulate that reduced sensitivity to dominance signals after OT administration to individuals with the most severe form of psychopathy may lead to better treatment attunement, ultimately allowing for faster and better therapy outcomes.

In our third sub-study (Chapter 6) we explored moral decision-making that is often studied through so-called moral dilemmas, i.e., specific situations in which the morality of an action is not evident (Whiteley, 1970). Moral dilemmas are typically defined in terms of mutually exclusive choices where the utilitarian choice is pitted against the non-utilitarian (i.e., deontological) choice. Moral dilemmas can be ranked from impersonal to personal-inevitable to personal-avoidable in terms of increasing emotionality of the utilitarian action.

Contrary to our hypothesis, a placebo-controlled single nasal administration of OT did not reduce utilitarian moral decision-making in favor of deontological choices in psychopathic patients. Moreover, contrary to our expectations, we found no differences in the percentage of utilitarian choices between psychopathic patients and normal controls. Our hypothesis that in both groups psychopathy severity was positively related to the percentage of utilitarian choices was found to be partially true. It was confirmed in the group of normal controls, but not in the group of psychopathic patients. On the contrary, we found that the severity of psychopathy was negatively related to the percentage of utilitarian choices, meaning that the higher the PCL-R total score, the more non-utilitarian (i.e., deontological) choices the psychopathic patients made. This unexpected finding was observed only in the case of personal avoidable dilemmas (i.e., where one can choose to waive action to avoid harm). Understandably, because of the direct physical action to be taken, a personal avoidable moral choice carries a greater emotional burden than a personal inevitable dilemma, and probably even much more than an impersonal dilemma. In particular, the PCL-R facet 3 (see Chapter 1, Introduction, Table 3), which includes lifestyle items such as seeking stimulation, impulsivity, irresponsibility, parasitic orientation and lack of realistic goals, was negatively associated with the percentage of personal avoidable choices. We hypothesized that the combination of high impulsivity, absent self-interest, an emotionally charged decision that is harmful to another person and must be carried out by direct physical force may tilt the response toward a non-utilitarian (i.e., deontological) choice. Choosing the emotion-laden use of avoidable harm may then immediately be considered “too hot” and therefore impulsively rejected. Speculatively, such a non-utilitarian choice could stem from empathic cognitive considerations, after all, one refrains from harming another, but I will not go so far as to assume

this, since it is quite possible that this non-utilitarian choice arises primarily from the psychopathic individual's utterly egocentric tendency not to address major impactful problems involving others. Given the above, I believe that the conclusions cited in the Introduction should be reiterated, namely that both morality and empathy can be considered as evolutionarily rooted functions with the goal of thriving and surviving, and that there is no univocal relationship between these two, rather it is ambiguous and complex (Decety, 2014; Decety & Cowell, 2014; Decety, 2021).

Finally, the last sub-study (Chapter 7) involves the group of psychopathic patients only. The steroid hormones testosterone and cortisol, high and low levels respectively, are suggested to drive status-relevant behavior like aggression and dominance. Our goal was to examine cortisol and testosterone saliva levels (i.e., baseline levels and their change over time) and their relation to the psychopathy severity. In this sub-study, placebo-controlled administration of OT did not affect steroid levels. We further concluded that the dual-hormone hypothesis as expressed in the testosterone / cortisol ratio appears to be incorrect in relation to psychopathy severity. Both steroid levels, particularly cortisol, decreased across the test procedure, which was compatible with the circadian rhythm of both. Only in those who scored high on the PCL-R facet 1 (that includes severely distorted narcissistic and manipulative behavioral interpersonal tendencies; Hare, 2003) did steroid levels remain stable, while in agreement with a previous study (Stålenheim et al., 1998), baseline levels were higher in psychopathic patients with high scores on the PCL-R facet 4 that encompasses severe antisocial tendencies (see Chapter 1, Table 3). Together, these results confirm that basal steroid levels, as well as their fluctuation over time, can partially predict psychopathy severity. Although the following link was not examined in our research, it is known that PCL-R facet 1 is significantly associated with the instrumentality of aggression displayed and also with the severity of aggressive crimes, while this is not the case for the other PCL-R facets (Laurell et al., 2010). Lastly, testosterone levels were higher in psychopathic patients scoring high on PCL-R facet 4. Within the PCL-R, the expression of antisocial, especially reactive aggressive, behavior is specifically linked to PCL-R facet 4. Psychopathy is known for its involvement in both impulsive-reactive and instrumental forms of aggression (Porter & Woodworth, 2006). Combined with our finding that inflexibility of testosterone is positively linked to psychopathic patients who scored high in PCL-R facet 1, we therefore suggested that high testosterone levels might facilitate the actual expression of antisocial, mostly reactive aggressive, behavior and that inflexibility over time of testosterone (and cortisol) could pave the way to instrumental aggression.

An association between elevated steroid levels, particularly testosterone, and empathy processing in psychopathy was not investigated in our study. Indirect indications of this association emerged in the research by Procyshyn and colleagues (2020) who found through experimental empathy induction that salivary oxytocin and testosterone levels in healthy adults show antagonistic effects, meaning that oxytocin levels increase and testosterone levels decrease, with high diversity in individual responses. This association is very interesting, but does not yet prove a link between steroid levels, particularly testosterone, and empathic functioning in psychopathy. In my opinion, much more research on this relationship is needed.

4.1 *Summarizing the effects of oxytocin in our various sub-studies*

Contrary to our hypothesis the placebo-controlled administration of OT did not enhance the short-latency mimicry responses of both the corrugator and zygomaticus (Chapter 4). No significant differences in short-latency responses were found between the two drug conditions. In Chapter 5 we found that reactive dominance is related to higher levels of psychopathy, mainly driven by PCL-R facet 1 and PCL-R category "Other". Interestingly, these significant relationships were abolished after administration of OT. We therefore concluded that although OT yielded no effect on reactive dominance in general, OT was found to abolish the relationship between psychopathy severity and reactive dominance. The mechanism behind the effect of OT on dominance reduction is unknown and needs further investigation. Finally, Chapter 6 showed that, contrary to our hypothesis, OT did not reduce utilitarian moral decision-making in favor of deontological choices, as the main effect of drug on utilitarian choices was not significant. The interaction effect between dilemma type and drug was also not significant.

Thus, we must conclude that a single administration of nasal spray with OT has no effect on mimicking emotional facial expressions or on moral decision-making. There is a curious effect on reactive dominance, especially in the subgroup of psychopathic patients with a high PCL-R score. This seems to be a very interesting finding, which may also have future therapeutic implications. The reason why OT did not show more effects remains unclear. I do not rule out the possibility that a single administration of OT has too limited an effect on the neurocognitive and neurobehavioral systems of psychopathic patients. Perhaps more effects of OT can be found when OT is administered more frequently (i.e., several times in a day over several days). In "Future Directions" (see below) I describe my ideas about how OT research can be shaped in the future.

5 The story of Lennart (continued)

In Chapter 1, the Introduction, I described the forensic examination of Lennart that took place at the Pieter Baan Centrum (PBC) in 2008. Several years after the start of his mandatory treatment in a forensic psychiatric hospital under the Entrustment Act (in Dutch: *Beginnelsenwet verpleging terbeschikkinggestelden*), I suddenly bump into him in the courtyard of that forensic hospital. We are both completely surprised to see each other. We exchange a few pleasantries, after which I walk on to the ward of another patient whom I need to talk to about a report we have prepared on him at the PBC. After two hours I walk back to the exit and there it turns out Lennart is waiting for me. Immediately he steps up to me and inquires extremely kindly about my health and that of my colleagues of the former PBC examination team. He remembers their names and characteristics. He also recalls some anecdotes about me and mentions en passant some of my career details he had found on the Internet. His presentation is overwhelming and I feel discomfort and an emotional constriction rising. It is as if he clings to me and I cannot get rid of him. Lennart, on the other hand, seems extremely relaxed and charming as he talks about his time at the PBC and expresses deep respect for our expertise. He does not mention a single word about his previous opposition to both the diagnosis at the time and our advice to the criminal court. According to him, the current therapy is going well and there is a 99 to 100 percent chance that in about four months the judge will decide to end the mandatory stay in the forensic hospital, Lennart says, the only thing missing is a favorable report on him, prepared by an outside expert. Then he asks me to prepare a new report that can be submitted during that hearing, adding at the same time that he can convince me that there is nothing wrong with him in a psychological sense. As he suggests this, he looks at me piercingly while he has an extremely friendly smile on his mouth. I notice that when he smiles, his eye region muscles do not contract, giving him a Non-Duchenne smile (i.e., a non-genuine, often polite smile that can be perceived as fake, unlike the Duchenne smile in which the eye region muscles also fully participate). I interrupt his extremely slippery talk and point out that a report to the court is ordered through an official route and that we cannot just arrange it among ourselves. Furthermore, I tell him that, for various reasons, I will not be the one to make a new report on him. Lennart listens to me seemingly emotionless; I do notice however that his gaze becomes chillier, while the Non-Duchenne smile diminishes slightly. Then we say goodbye to each other. When I look back a moment later I see him staring at me with a dark gaze, tight facial expression and a tense body posture. Another failed attempt to use me for his purposes.

6 Future directions

Although the general perception among the lay public is that psychopathic persons constantly exhibit a happy go lucky attitude and commit their terrible crimes without conscience or remorse (see Introduction), this perception is, of course, grossly exaggerated. Psychopathic persons may also suffer from their disorder. Indeed, they repeatedly clash with society's norms, become entangled in social intercourse by failing to keep appointments, and continually experience interpersonal problems with loved ones, family, acquaintances and colleagues due to their behavior and emotional inaccessibility. Such frictions can cause them a lot of stress and thus overwhelming suffering. Hence, the term "Suffering Souls" may apply to them. That said, there is also suffering on the part of society, as explained at length in the Introduction, hence the term Suffering Society.

Psychopathic individuals are responsible for extreme social consequences and astronomical costs to society (Anderson, 1999; Kiehl & Hoffman, 2011). Extrapolated to 2024, this annual cost would now be approximately 680 billion US dollars (www.in2013dollars.com). This overwhelming figure does not include the cost of psychiatric treatment of psychopathic individuals themselves, nor other indirect costs, such as, for example, the treatment of victims or their unquantifiable emotional suffering. These tantalizing figures make it imperative to continue researching psychopathic individuals in the hope that a better understanding of their endophenotype and behaviors can be gained in the future so that better treatment strategies can consequently be developed. But before I continue, a comment on the diagnosis of psychopathy is in order. Caution should be exercised in diagnostic target group descriptions of psychopathic individuals and their psychological as well somatic characteristics. I believe that comparisons with different types of diagnostic questionnaires between different populations (in extremo: clinically hospitalized patients on the one hand versus online respondents completing questionnaires on the other) call for great caution. Diagnostic purity is also warranted in the area of neurobiological characteristics of psychopathy. For example, research by Jalava and colleagues (2021) provided evidence that structural magnetic resonance brain imaging studies in PCL-R confirmed psychopathic individuals show false-positive structural brain abnormalities that were in fact artifacts. Comparative studies should take this into account. It is recommended that results always be put in the perspective of possible differences in diagnostic procedure or that a warning be given about this. One should not make ultimate statements about psychological, somatic, and neurobiological characteristics

that one's own research cannot actually support or that are obtained through scientific research that is in fact not definitively standardized.

The question is whether there are treatment options that provide improved emotional and behavioral functioning of a psychopathic offender, which can lead to a low recidivism rate. This question has not been well answered to date. It is known that the combination of psychopathy and a psychiatric disorder, for example, a sexual disorder, produces a high recidivism rate. This means that psychopathic patients with paraphilia in a forensic psychiatric hospital usually undergo their mandatory treatment for much longer than non-psychopathic patients with paraphilia. The difference in mandatory stay can amount to years and sometimes it even proves impossible to reintegrate a psychopathic patient into free society at all since the risk of recidivism remains too high. Such a policy can be defended even in human rights terms, but only if every effort is made to understand and comprehend the psychopathic patient. This requires more scientific research that should focus on the emotional, cognitive and behavioral disorders within the psychopathy construct, including empathy deficits. This scientific approach should be multimodal, meaning that different scientific disciplines work together. Without opting for a limitation, it is important that research takes place in the fields of sociology, criminology, developmental psychology, trauma, addiction, psychotherapy, neurology and neurophysiology, endocrinology, (forensic) psychology, and (forensic) psychiatry. In the field of psychotherapy, much research is still needed, for example on Schema Focused Therapy, which may prove to be a positive intervention. Much attention should be paid to genetic, epigenetic and neurobiological aspects of the psychopathy construct. The quest for biomarkers of psychopathy must continue. In Chapter 4, we suggested that deficiencies in short-latency facial mimicry could be considered such a biomarker. I welcome other researchers to verify or refute this postulated lifetime developmental deficit in mimicking emotional facial expressions in psychopathy. Much research is being done on both structural and functional imaging of the brain, but so far no definitive conclusions can be drawn. Moreover, it is by no means expected that precise brain loci can be identified that are responsible for psychopathic behavior at large; rather, it is a matter of aberrant processing in different brain networks. That said, direct influence on one or a few brain parts of the psychopathic individual may have a positive cascading effect on brain activities downstream, and thus on the functioning of the psychopathic individual. I am thinking, for example, of an intervention such as repetitive transcranial magnetic stimulation. Perhaps deep brain stimulation will also be a possibility in the distant future.

Pharmacotherapy is also a factor to consider in the treatment of psychopathic patients, but so far there is no pharmacological new-kid-on-the-block. Pharmacotherapy to date has not produced decisive success in psychopathic patients. Treatment of co-morbid disorders, i.e. in addition to psychopathy, such as mood or affective disorder, paraphilia, psychosis, or aggression, can be treated with the appropriate medication. It is true that this does not substantially address the core concept of psychopathy, but the behavioral manifestation of the psychopathic patient can thus be mitigated, which should be considered an advantage.

Reflecting on one specific pharmacological intervention in particular, I would like to return to a key component of this dissertation, viz oxytocin. Most OT studies have been conducted in (healthy) men, leaving (healthy) women underrepresented (Quintana et al, 2020). This should be corrected, including in studies of psychopathy. It seems that OT-related studies in psychopathy are scarce. This means that much is still unknown about the effects of OT on psychopathic traits. We sought to fill this gap in our knowledge with our study of PCL-R confirmed forensic psychopathic patients who self-administered a single placebo-controlled nasal spray with OT. A unique feature of our study was that the group of clinically admitted forensic psychopathic patients was not treated with medications such as selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors, antipsychotics or hormonal libido inhibitors. These medications were contraindicated because they might interfere with the effects of OT.

The effect of this one-time administration of OT on various tasks of the psychopathic patient appears to be limited. Perhaps our one-time administration of OT was too little to produce significant changes and multiple OT applications should be applied to detect measurable effects. Here, I point to a recent study by Le and colleagues (2022) in young autistic children in which a 6-month follow-up showed long-term improvement in autistic symptoms. Their within-subject design consisted of a placebo-controlled application of nasal spray of OT in the early morning every other day during the 6-week treatment phases and having the child participate in a positive social interaction session for 30 minutes. The rationale for alternating OT every other day was to reduce presumed receptor desensitization. Although autism is clearly not similar to psychopathy, I can well imagine that more frequent administration over a longer period of time than occurred in our study will eventually produce measurable effects in psychopathic individuals. Such an approach should then of course be done in conjunction with a therapeutic intervention, for example cognitive behavioral therapy, but possibly other therapies as well. The reason is that administration of a hormone,

such as OT, by itself does not cause lasting behavioral changes. A hormone opens a “window of opportunity” during which a therapeutic intervention can produce an effect that persists and eventually leads to change. Such a process underlies the plastic brain.

Administration of long-acting OT agonists, such as carbetocin, may also be considered, although the latter drug can only be administered parenterally. Further research into oral OT agonists with longer duration of action is warranted. I advocate that future OT studies also exclude the concomitant use of the aforementioned psychotropic drugs like we did. Moreover, future researchers should bear in mind Leng & Ludwig's (2016) caution against common and essentially unfounded wishful thinking regarding the efficacy of peripherally administered OT on central brain processes.

With regard to the empathy construct and disrupted empathy processing, a core detail in psychopathy (Soderstrom, 2003), further research is warranted. We have developed the Zipper Model of Empathy and I cordially invite researchers to critically apply our model to psychopathy or perhaps other personality or psychiatric syndromes (as was done by Vaskinn et al. (2023) in the aforementioned study in aggressive schizophrenic patients). Further research on this core theme of psychopathy could perhaps be done using the neuropsychological battery we have described for assessing empathy processing (see Chapter 3), but of course other approaches can also shed light on this important topic.

A special note about future research on possible enhancement of empathy processing in psychopathic patients is in order here. As shown in the Zipper Model of Empathy, psychopathic individuals are usually able to adequately process cognitive aspects of empathy. Where they fail is in the processing of the affective aspects of the empathy construct. Pharmacotherapy, as well as all other possible interventions, aimed at improving empathy processing should focus on improving the latter aspects, because upgrading the cognitive aspects of empathy without improving affective aspects is only likely to make the psychopathic person in question more obnoxious of (criminally) dangerous.

I would like to end with a general remark. It is well known that a stress-free development in the perinatal period and subsequent phases of life in early childhood is preventive in terms of attachment problems and many psychiatric disorders in later life. In my work as a forensic psychiatrist, I therefore attribute great value to research on the entire life course. It has often struck me in psychopathic individuals that their early childhood was characterized by severe behavioral and attachment problems and that stressful and traumatic events were probably at the root of this. As I pointed out in the Introduction (Chapter 1),

there is a distinction between primary psychopathic individuals and secondary psychopathic individuals, the latter being thought to have disturbances in emotional processing because of a stressful or traumatic early socialization process that can lead to aberrant emotional states such as anxiety, depressive emotions and hostility (Thompson et al., 2014). Consistent with Birnbaum's (1909) assertions, Lykken's (1957) neurotic sociopathy shows diagnostic overlap with secondary psychopathy. So there is a world to be gained if a healthy pedagogical approach goes hand in hand with the prevention of stress and trauma in perinatal stages and in early childhood. The growing child can then establish significant attachment relationships, thereby reducing the likelihood that a secondary form of psychopathy will develop. Prevention is much better than cure. This is not only good for the growing child and his family, but also for society at large, especially with the following ominous quote in mind, namely that “psychopathy is probably the most expensive mental health disorder known to man” (Kiehl & Sinnott-Armstrong (2013, p. 1).

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There is nothing more hostile than water turning into ice.

Paul Klee (1930). Cited in: Ostendorf, B., Maiburg, B., & Schneider, M. (2004). [Scleroderma and Paul Klee: Metamorphosis of life and art?]. *Z Rheumatol.*, 63(4), 318-325. Article in German. English translation by Heberbrand VA PubMed.

I am not I: thou art not he or she: they are not they.

Evelyn Waughm (1945). Author’s note in: *Brideshead Revisited: The sacred & profane memories of Captain Charles Ryder*. Boston: Little, Brown and Company.

*It was not I that sinn'd the sin,
The ruthless body dragg'd me in;
Though long I strove courageously,
The body was too much for me.*

Walt Whitman (1891-1892). Singer in the Prison, in: *The Leaves of Grass (1891-1992)*. The Walt Whitman Archive: <https://whitmanarchive.org/>

*One sin, I know, another doth provoke
Murder's as near to lust as flame to smoke.*
Shakespeare, *Pericles, Prince of Tyre*, Act 1, scene 1

The past is a foreign country: they do things differently there.

Leslie Poles Hartley (1953). The opening line in *The Go-Between*

There is only one thing in the world worse than being talked about, and that is not being talked about.

Oscar Wilde (1890-1891). *The Picture of Dorian Gray*

List of publications

Articles in this dissertation

Rijnders, R. J. P., Terburg, D., Bos, P. A., Kempes, M. M., & van Honk, J. E. (2021). Unzipping empathy in psychopathy: Empathy and facial affect processing in psychopaths. *Neuroscience and Biobehavioral Reviews*, *131*, 1116-1126. <https://doi.org/10.1016/j.neubiorev.2021.10.020>

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Other publications

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Nederlandse samenvatting / Dutch summary

One sin, I know, another doth provoke
Murder's as near to lust as flame to smoke

— Shakespeare

1 Nederlandse samenvatting

Dit proefschrift is verdeeld in vier delen. Het bestaat uit (I) de Inleiding, met het verhaal over Lennart, een uitleg van het psychopathieconstruct en daarna van het neurohormoon oxytocine, (II) verschillende artikelen over empathie en de oxytocine-interventiestudie, (III) de Algemene discussie met een uitleg over de artikelen over het empathieconstruct bij psychopathie en de resultaten van de oxytocinestudie, het vervolgverhaal over Lennart, een vooruitblik wat betreft toekomstig onderzoek, en (IV) de literatuurreferenties, deze Nederlandse samenvatting, het dankwoord en mijn curriculum vitae.

1.1 Psychopathie

Etymologisch gezien komt de term psychopathie van de samenvoeging van de klassieke Griekse woorden ψυχή en πάθος (respectievelijk psyche en pathos) en staat voor 'lijdende ziel' (Suffering Soul). Psychopathie als levenslange persoonlijkheidsstoornis is geen unitair concept, maar wordt eerder gekenmerkt door verschillende intensiteiten van en diversiteit aan symptomen op interpersoonlijk, emotioneel en gedragsmatig niveau, wat uiteindelijk resulteert in een heterogene klinische expressie. Op interpersoonlijk niveau is de presentatie van psychopathische individuen glad en oppervlakkig, gelardeerd met uitspraken over hun eigen grandioze kwaliteiten. Hun acties bestaan ondertussen vaak uit liegen en bedriegen teneinde voordelen te behalen puur voor henzelf, terwijl zij de belangen van hun tegenhanger verwaarlozen en niet respecteren. Oplettende anderen voelen snel de opgelegde druk en manipulatie, terwijl naïevelingen het risico lopen door de gladde presentatie van psychopathische personen de manipulatie niet op tijd te doorzien. Op emotioneel niveau valt vooral hun gebrek aan empathie op, hoewel bij psychopathie de cognitieve aspecten van empathie meer intact zijn dan de affectieve empathieaspecten. Gedeeltelijk als gevolg van de gebrekkige affectieve empathie, is hun affect in emotioneel-gespannen situaties meestal oppervlakkig, en als het gaat om situaties waarin hun eigen fouten of schuld betrokken zijn, ervaren psychopathische personen een gebrek aan wroeging of schuldgevoel. Tot slot, op gedragsniveau, vertonen psychopathische individuen vaak egocentrische, parasitaire en impulsieve acties naar anderen. Hun remmende controle (inhibitory control) is zwak, waardoor ze snel betrokken

raken bij gevaarlijke of agressieve situaties of hun afspraken met anderen of wettelijke toezichthouders verbreken. Vooral vanwege deze gedragsproblemen zijn zij oververtegenwoordigd in het strafrechtelijk systeem en lopen zij een twee tot vijf keer hoger risico op recidive. Dit patroon bestaat zelfs al voordat zij volwassen zijn. Hun interpersoonlijke, emotionele en gedragsproblemen komen ook voor in partnerrelaties. Psychopathische individuen hebben daarom vaak losse, onpersoonlijke seksuele relaties en zijn niet goed in het onderhouden van duurzame liefdesrelaties.

Psychopathie is van alle tijden en alle culturen en is een persoonlijkheidsstoornis die astronomische kosten voor de samenleving met zich meebrengt. De precieze prevalentie van psychopathie in de algemene bevolking wereldwijd is niet bekend, maar schattingen lopen uiteen van 0,5% tot 1,2%, met een hoger percentage mannen dan vrouwen, hoewel dit deels te wijten zou zijn aan genderverschillen bij de verschillende psychometrische eigenschappen van de diagnostische test voor psychopathie. De persoonlijkheidskenmerken van psychopathie zijn pas relatief recent methodologisch bestudeerd. In zijn baanbrekende werk *Mask of Sanity* schreef Hervey Cleckley in 1941 vignettes van psychopathische individuen en toonde aan dat de psychopathiediagnose niet unitair was, maar veelzijdig in zijn presentatie. Naast enkele interpersoonlijk agressieve psychopathische individuen in zijn studie, beschreef hij ook sociaal-succesvolle psychopathische personen. Zijn resultaten zorgden voor een grote sprong voorwaarts in de studie van psychopathie. Het was uiteindelijk Robert Hare die, gebaseerd op de Cleckley-criteria, het hedendaags klinisch concept van psychopathie verder ontwikkelde - in het bijzonder bij criminele individuen. Hij nam deze op in de diagnostische criteria van wat later bekend werd als de Psychopathy Checklist - Revised (PCL-R). Deze lijst kent twee factoren of vier facetten. In ons onderzoek gebruiken wij de vier facetten. In tegenstelling tot Cleckley richtte Hare zich voornamelijk op de negatieve kenmerken van psychopathie, waardoor de positieve kenmerken van Cleckley's psychopathieconcept zwak zijn vertegenwoordigd in de PCL-R.

De termen primaire vs. secundaire psychopathie worden gebruikt voor een dichotomie in het psychopathiespectrum, hoewel een clear cut onderscheid tussen de twee zelden mogelijk is. De etiologie van deze verschillende fenotypes is waarschijnlijk het resultaat van een complexe gen-omgevingsinteractie, waarbij nature noch nurture alleen beide types kunnen veroorzaken. Van individuen met primaire psychopathie wordt gedacht dat zij aangeboren (nature) tekortkomingen in de emotionele verwerking hebben, waardoor ze geen negatieve emoties kunnen ervaren zoals ernstige angst, paniek of depressie. Mede door deze tekortkoming hebben zij er geen

probleem mee dominant, superieur en gewetenloos te zijn. Van personen met secundaire psychopathie wordt daarentegen gedacht dat ze verstoringen hebben in de emotionele verwerking als gevolg van een stressvol of traumatisch socialisatieproces (nurture) in de vroege jeugd die kunnen leiden tot afwijkende emotionele toestanden zoals angst, depressie en vijandigheid. Het begrip sociopathie kent een diagnostische overlap met secundaire psychopathie.

1.2 Oxytocine

De naam oxytocine is etymologisch geworteld in het klassieke Griekse woord *ὄκυτόκος* (*ōkutókos*), dat 'snelle bevalling' betekent. Het is een neuropeptide of neurohormoon dat de baarmoeder doet samentrekken waardoor de bevalling op gang komt en ook zorgdraagt voor het toeschieten van moedermelk. Oxytocine wordt voornamelijk in de kernen van de hypothalamus (hersenstructuur) gesynthetiseerd en uiteindelijk in de hypofyse opgeslagen, waarna het in de bloedbaan wordt afgegeven. De regulerende rol van oxytocine op sociaal gedrag is divers en gecompliceerd. Het is betrokken bij intieme gehechtheidsrelaties, altruïsme en competitie, beloning, agressie, maar ook bij pijnbestrijding, eetlust, angst en bezorgdheid. Doorgaans wordt in menselijk gedragsonderzoek een dosis van 24 internationale eenheden (IE) van de synthetische versie van oxytocine via neuspuffjes toegediend, waarna het uiteindelijk in de hersenen terecht komt. Deze dosis komt overeen met ongeveer het totale gehalte aan oxytocine in de menselijke hypofyse. De effecten van oxytocinetoediening zijn onderzocht bij verschillende psychische stoornissen, zoals autismespectrumstoornis, persoonlijkheidsstoornis, schizofrenie, angststoornissen en posttraumatische stressstoornis. Volgens de social salience hypothesis van oxytocine is dit neurohormoon geassocieerd met modulatie van de aandacht, en daarmee afhankelijk van de saillantie (in het oog springend) van externe sociale signalen. Hiermee kan worden aangenomen dat oxytocine van groot belang is in interpersoonlijke relaties. In zowel dier- als menssonderzoek is vastgesteld dat oxytocine sociale toenadering en oogcontact stimuleert, emotieherkenning en vertrouwen verhoogt, de amygdala-functie beïnvloedt en onderdanig gedrag in sociale groepen verbetert. Oxytocine is ook positief geassocieerd met empathie, ingroup social binding en zorgzaam gedrag, en is verder betrokken bij het discrimineren tussen outgroup- en ingroup-leden. Er moet echter een voorbehoud worden gemaakt. Recentelijk kwamen er zorgwekkende berichten dat veelbelovende studies naar oxytocine-interventies niet reproduceerbaar

blijken, mogelijk komt dit omdat dergelijke studies vaak te kampen hebben met een lage power.

Oxytocinestudies naar bovenstaande psychische aandoeningen zijn meestal uitgevoerd bij (gezonde) mannen, waardoor (gezonde) vrouwen ondervertegenwoordigd zijn. Verder blijken oxytocinestudies bij psychopathie heel schaars. Hoogpsychopathische trekken bij kinderen en adolescenten zijn positief gerelateerd aan methylering van het oxytocinereceptorgen en polymorfismen van de oxytocinereceptor, evenals lagere oxytocineconcentraties in speeksel en bloedplasma. Omgekeerd zijn laagpsychopathische trekken bij volwassenen negatief gecorreleerd met oxytocinegerelateerde single-nucleotide-polymorfismen (SNP's), waaronder een SNP op de oxytocinereceptor. Ik ben niet op de hoogte van eerder onderzoek naar de toediening van oxytocine bij psychopathie, met uitzondering van een recent functionele-MRI-onderzoek. Daarin wordt beschreven dat toediening van 40 IE oxytocine de verschillen in de verwerking van angstige gezichtsuitdrukkingen bij gewelddadige mannelijke daders met een antisociale-persoonlijkheidsstoornis die ook voldoen aan de criteria van psychopathie, opheft.

1.3 Artikelen over empathie en de oxytocine-interventiestudie

In ons onderzoek richt ik mij op delen van het psychopathieconstruct. De centrale vraag hierbij is of oxytocine psychopathische symptomen in een patiëntengroep met PCL-R-bevestigde psychopathie kan beïnvloeden, en zo ja, in welke richting. De onderzoekspopulatie betreft mannelijke psychopathische patiënten die op last van de rechtbank met een tbs-maatregel zijn opgenomen in verschillende strengbeveiligde Nederlandse tbs-klinieken. Een belangrijk onderdeel van de studie is onderzoek naar het empathieconstruct en in het verlengde hiervan de gestoorde empathieverwerking in psychopathie, belangrijk omdat empathiegebrek mogelijk hét centraal kenmerk is van psychopathie. Het is in testonderzoek niet mogelijk directe empathieveranderingen door oxytocine te meten. Daarom kozen wij bij de psychopathische patiënten ervoor de effecten van oxytocine op enkele afgeleiden van het empathieconstruct te onderzoeken, te beginnen met mimicry van emotionele gezichtsuitdrukkingen, ook wel op te vatten als de onwillekeurige nabootsing van andermans mimiek. Van mimicry wordt aangenomen dat het een voorloper is van het empathieproces. Verder onderzochten wij reactieve dominantie en het maken van morele keuzes bij psychopathische patiënten. Hoewel niet onomstotelijk bewezen, zijn deze twee

mogelijk ook afgeleiden van het empathieconstruct, zij het op meer afstand dan mimicry. Het effect van oxytocine op zowel mimicry, reactieve dominantie en moraliteit bij psychopathische personen is bij mijn weten nooit onderzocht, en derhalve niet bekend.

Als eerste starten wij met het beschrijven en ontrafelen van het empathieconstruct en vervolgens de gestoorde empathieverwerking in psychopathie. In hoofdstuk 2 bespreken wij de huidige theorieën over het empathieconstruct. Vervolgens presenteren wij een nieuw model van empathieverwerking, het Zippering Model of Empathy (ritsmodel van empathie) genaamd. Dit model beschrijft de interactie van verschillende cognitieve en affectieve componenten van empathie, inclusief mimicry en emotionele besmetting (emotional contagion), die beide als voorlopers van het empathieconstruct kunnen worden opgevat. Belangrijke drijvende krachten achter dit ritsmodel zijn zowel persoonlijke als contextuele factoren. Met behulp van ons Zipper Model of Empathy proberen wij vervolgens licht te werpen op de gestoorde empathieverwerking van psychopathische individuen. Hiervoor grijpen wij terug op de gelaatsemotieverwerking bij hen. Deze gelaatsemotieverwerking gaat voorafgaat aan mimicry en emotionele besmetting. Wij veronderstellen daarbij een disfunctionele gelaatsemotieverwerking in de basolaterale en centrale subregio's van de amandelkernen (amygdala).

In hoofdstuk 3 beschrijven wij een neuropsychologische testbatterij voor het beoordelen van empathieverwerking bij psychopathie. Wij proberen empirische fysiologische en gedragsmaatregelen te identificeren die nodig zijn voor het testen van de verschillende componenten van het empathieconstruct zoals beschreven door het Zipper Model of Empathy. Speciale aandacht wordt besteed aan verminderde empathieverwerking bij psychopathische personen.

Vervolgens beschrijven wij een oxytocine-interventiestudie met drie verschillende computertaken bij de genoemde groep mannelijke psychopathische patiënten. Bovendien bestudeerden wij speekselconcentraties van de steroïden testosteron en cortisol voorafgaand aan en ná de testprocedure. De psychopathische patiënten hadden allen een PCL-R-totaalscore van 26 of hoger. De oxytocine-interventiestudie volgde een dubbelblind, gebalanceerd, placebogecontroleerd, cross-over design. Patiënten werden daarom op twee dagen getest. Wij testten ook een controlegroep van mannelijke bewaarders en groepsleiders die niet voldeden aan de criteria van psychopathie. Om praktische redenen ondergingen zij geen oxytocine-interventie, zodat zij slechts op één dag werden getest. Volledige vergelijking met de psychopathische patiënten was door dit design niet helemaal mogelijk, daarom besloten wij deze controlegroep als referentiepopulatie te gebruiken.

De eerste oxytocine-interventiestudie wordt beschreven in hoofdstuk 4. Wij onderzochten mimicry van twee gelaatsspieren op computermatig veranderde (morphed) emotionele gezichtsuitdrukkingen van blijheid en boosheid. De twee gelaatsspieren waren respectievelijk de musculus corrugator supercilii (de fronsspier) en de musculus zygomaticus major (deze loopt van het jukbeen naar de mondhoek en is actief bij lachen). De corrugator wordt geactiveerd bij het kijken naar een negatieve emotionele gelaatsuitdrukking; de zygomaticus doet dan niet mee. Bij het kijken naar een positieve emotionele gelaatsuitdrukking vindt er een activering van de zygomaticus plaats en tegelijkertijd ontspanning van de corrugator.

Mimicry maakt deel uit van een zeer dynamisch interpersoonlijk communicatieproces meer oude evolutionaire wortels. Er wordt verondersteld dat de gestoorde empathieverwerking bij psychopathie (gedeeltelijk) wordt veroorzaakt door stoornissen in de mimicry van andermans emotionele mimiek. Daarom is mimicryonderzoek bij psychopathie belangrijk. Zoals te doen gebruikelijk in dergelijk onderzoek werd mimicry door ons gemeten met elektromyografie van de twee genoemde gelaatsspieren. Omdat verschillen in mimicry kunnen optreden met een zeer korte latentietijd van 100 tot 200 ms na de start van de stimulus (stimulus onset), onderzochten wij de mimicry tijdens de eerste 600 ms na stimulus onset.

Zoals beschreven kreeg alleen de groep psychopathische patiënten oxytocine en placebo toegediend. In deze patiëntengroep was onze hypothese dat placebogecontroleerde toediening van oxytocine de mimicry in de korte latentietijd van zowel de corrugator als de zygomaticus zou versterken. Wij verwachtten dat blijge gezichtsuitdrukkingen in de oxytocineconditie, vergeleken met placebo, een sterkere activatie van de zygomaticus en een sterkere ontspanning van de corrugator zouden uitlokken. Bij het kijken naar boze gezichten werd in de oxytocineconditie, vergeleken met placebo, ook een sterkere corrugatorrespons verwacht. Deze hypothesen konden niet worden bevestigd omdat er geen significante verschillen in de kortelatentieresponsen werden gevonden tussen de twee medicatiecondities.

Wij verwachtten tevens dat in vergelijking met normale controles, psychopathische patiënten binnen de eerste 600 ms een zwakkere corrugatorrespons op boze gezichtsuitdrukkingen zouden vertonen en juist minder corrugatorontspanning op blijge gezichtsuitdrukkingen. Verder verwachtten wij dat bij psychopathische patiënten vergeleken met normale controles de vroege zygomaticusrespons op blijge gezichtsuitdrukkingen binnen de eerste 600 ms kleiner zou zijn. In de post-hoc vergelijking van psychopathische patiënten in de placeboconditie met normale controles vonden we inderdaad significant

zwakkere kortelatentietijdresponsen van de zygomaticus op blijge gezichten, terwijl er een trend was naar significant zwakkere kortelatentietijdresponsen van de corrugator op boze gezichten. Deze interessante bevindingen in deze volwassen patiëntengroep gecombineerd met vergelijkbare resultaten uit een eerder onderzoek bij jongeren met hoogpsychopathische trekken suggereren dat in psychopathie een ontwikkelingsstoornis in mimicry van emotionele gelaatsuitdrukkingen aanwezig is. Wij stellen zelfs dat dit kan wijzen op een biomarker van psychopathie. Uiteindelijk kan deze deficiëntie in mimicry van boze en blijge uitdrukkingen de empathieverwerking in de psychopathische persoon belemmeren, zoals dat ook uit het Zipper Model of Empathy volgt. Nader onderzoek naar deze ontwikkelingsstoornis in mimicry bij psychopathische individuen kan daarom inzicht geven in hun verminderde empathieverwerking en hun onaangepaste sociale interacties.

In hoofdstuk 5 gebruikten wij een gaze aversion task, dat wil zeggen een reactietijdtaak die reactieve dominantie op gemaskeerde gezichtsstimuli weerspiegelt. Zonder dat de proefpersonen zich hiervan bewust waren, kregen zij gemaskeerde neutrale, blijge of boze gezichten te zien. De verschillen in reactietijd op blijge en boze gezichten geven de mate van dominantie aan. Wij testten de hypothesen dat psychopathische patiënten dominantier zijn dan normale controles en dat oxytocine in de groep psychopathische patiënten hun reactieve dominantie causaal zou verminderen. Verder hadden wij als hypothese dat dominantie-uitkomsten op de gaze aversion task positief zouden correleren met psychopathiematen in beide groepen deelnemers, lees: hoe hoger de scores op psychopathielijsten, hoe hoger de dominantie.

In tegenstelling tot wat wij verwachtten, verschilden de twee groepen niet significant in gaze aversion, wat aangeeft dat psychopathische patiënten niet dominantier zijn dan normale controles. Ook onze tweede hypothese over het effect van oxytocine in de groep van psychopathische patiënten kon niet worden bevestigd. Vergeleken met placebo was er na toediening van oxytocine geen snellere gaze aversion bij gemaskeerde boze gezichten in vergelijking met blijge gezichten. Dit resultaat suggereert dat toediening van oxytocine in het algemeen geen invloed heeft op reactieve dominantie. Tot slot bleek dat onze derde hypothese gedeeltelijk te kunnen worden bevestigd, een hoger niveau van psychopathie in de groep van psychopathische patiënten positief correleerde met reactieve dominantie, terwijl dat voor de controlegroep niet het geval was. Verder onderzoek hiernaar bij de psychopathische patiënten volgde. Hieruit concludeerden wij dat de reactieve dominantie bij de hoogpsychopathische patiënten voornamelijk werd gedreven door PCL-R facet 1 (dit omvat items die een arrogante en bedrieglijke interpersoonlijke stijl vertegenwoordigen) en

PCL-R categorie "Overig" (dit omvat twee items die met relaties en seksualiteit van doen hebben). Interessant genoeg werden deze significante verbanden opgeheven na toediening van oxytocine, met andere woorden de subgroep hoogpsychopatische patiënten werd onder oxytocine submissiever. Het geheel overziend suggereerden wij dat de gaze aversion task een objectieve maatstaf kan zijn voor reactieve dominantie bij psychopatische personen.

Hoofdstuk 6 betreft het maken van morele keuzes. Moreel redeneren is in wezen denken over goed en fout en omvat intuïtieve en emotionele processen, terwijl ook calculatieve en sociale gevolgen in overweging worden genomen. Het meten van moreel redeneren wordt vaak gedaan door middel van morele dilemma's, d.w.z. specifieke vignetten waarin de moraliteit van een handeling niet duidelijk is. Volgens de dual-process theory van morele oordeelsvorming kunnen gecontroleerde cognitieve en automatische emotionele processen worden geïdentificeerd die elkaar meestal uitsluiten. Aan de ene kant kunnen cognitieve processen resulteren in zogenoemde utilitaristische beslissingen waarbij de berekende uitkomst van het schaden van de ander bepaalt of die actie als goed of fout dient te worden bestempeld. Het resultaat kan zijn dat for the greater good of all wordt gehandeld en individuen worden geslachtofferd. Aan de andere kant kan een automatische aversieve emotionele respons resulteren in zogenoemde deontologische beslissingen waarbij de aard van de handeling zelf bepaalt of die handeling als goed of fout dient te worden beschouwd. Dit kan leiden tot het niet-nemen van een beslissing die minder schade of minder slachtoffers zou opleveren. Een verder onderscheid kan worden gemaakt in zogenoemde personal dilemmas (persoonlijke dilemma's) en impersonal dilemmas (onpersoonlijke dilemma's). De eerste categorie beschrijft handelingen waarbij schade wordt veroorzaakt door direct fysiek contact en de tweede categorie omvat handelingen waarbij schade wordt toegebracht op een indirecte, niet-fysieke manier. De utilitaristische handelingen in persoonlijke dilemma's worden geassocieerd met een sterkere emotionele waarde. Persoonlijke dilemma's worden verder onderverdeeld in dilemma's waarin de schade voor het slachtoffer inevitable (onvermijdelijk) of evitable (vermijdbaar) is. Onvermijdelijke schade veronderstelt dat ongeacht of een actie wordt ondernomen, de betrokken persoon uiteindelijk schade zal lijden, terwijl dit laatste niet het geval is bij vermijdbare schade als van de actie wordt afgezien.

Van psychopatische personen wordt over het algemeen gedacht dat zij utilitaristische keuzes verkiezen boven deontologische beslissingen. Dat veronderstelden wij in onze studie ook. Wij onderzochten verder de invloed van oxytocine op morele keuzes en hadden als hypothese dat oxytocine de voorkeur van psychopatische patiënten voor utilitaristische keuzes zou verminderen

ten gunste van deontologische keuzes. Bovendien verwachtten wij dat het percentage utilitaristische keuzes positief gerelateerd zou zijn aan de ernstmaat van de psychopathie, zoals vastgesteld met de PCL-R voor psychopatische patiënten en de PPI-R voor de normale controles.

Wij vonden geen verschillen in het percentage utilitaristische keuzes tussen psychopatische patiënten en normale controles. In tegenstelling tot onze hypothese verminderde een eenmalige nasale toediening van OT de utilitaristische morele besluitvorming bij psychopatische patiënten niet. Onze laatste hypothese dat in beide groepen de ernst van de psychopathie positief gerelateerd was aan het percentage utilitaristische keuzes, kon niet worden bevestigd voor de groep psychopatische patiënten. Integendeel, wij vonden dat de ernst van de psychopathie negatief was gerelateerd aan het percentage utilitaristische keuzes, wat betekent dat hoe hoger de PCL-R-totaalscore, hoe meer niet-utilitaristische (d.w.z. deontologische) antwoorden de psychopatische patiënten gaven. Deze onverwachte bevinding werd alleen waargenomen bij personal evitable dilemmas (d.w.z. waarbij men kan kiezen om af te zien van actie om schade te voorkomen). Het is begrijpelijk dat, vanwege de directe fysieke actie die moet worden ondernomen, een personal evitable moral choice voor de beslisser een grotere emotionele last met zich meebrengt dan een personal inevitable dilemma, en waarschijnlijk zelfs veel meer dan een impersonal dilemma. Follow-up analyse liet zien dat dat PCL-R facet 3 specifiek negatief geassocieerd was met het percentage personal evitable choices. Dit facet weerspiegelt hoge niveaus van impulsiviteit. Het is denkbaar dat op dit facet hogescorende psychopatische individuen, door hun hoge impulsiviteit, geneigd zijn een schade-aversieve keuze te maken in personal evitable dilemmas, meer dan het geval is in de minder emotioneel beladen personal inevitable en impersonal dilemmas. Deze neiging lijkt in tegenspraak te zijn met wat de hierboven beschreven dual-process theory van morele oordeelsvorming, waarin psychopatische individuen, van wie bekend is dat ze een verstoorde emotionele verwerking hebben de neiging hebben om utilitaristische oplossingen te kiezen. Wij geloven dat de combinatie van hoge impulsiviteit, afwezig eigenbelang, een emotioneel geladen beslissing die schadelijk is voor de ander en uitgevoerd moet worden met direct fysiek geweld, de respons kan kantelen in de richting van een deontologische keuze. Kiezen voor het emotioneel beladen gebruik van vermijdbare schade kan onmiddellijk als "te heet" worden beschouwd en dan impulsief worden afgewezen.

In hoofdstuk 7 onderzochten wij de relatie tussen de ernstmaat van psychopathie en speekselconcentraties van de steroïden testosteron en cortisol. Alleen psychopatische patiënten namen deel aan deze studie. Bovendien

onderzochten wij het effect van oxytocine op de speekselconcentraties van zowel cortisol als testosteron. Mogelijk heeft oxytocine op indirecte wijze een verlagend effect op plasmatestosteronspiegels. Testosteron is gerelateerd aan statusrelevant gedrag, zoals dominantie en agressie, vooral wanneer de status wordt uitgedaagd. Het vergemakkelijkt verder het benaderen en zoeken naar beloning, terwijl cortisol juist wordt geassocieerd met terugtrekking en angst. Beide hormonen vertonen een wederkerige onderdrukkende interactie. Hoge cortisolniveaus blokkeren testosterongerelateerd dominant gedrag, terwijl dit niet het geval is bij personen met lage cortisolniveaus. In de triple balance theory van emoties wordt een wisselwerking (crosstalk) beschreven tussen corticale en subcorticale circuits die wederzijds ofwel remmend ofwel prikkelend functionele invloeden hebben op beide circuits. Deze wisselwerking is sterk afhankelijk van de hersenconcentraties van cortisol en testosteron. Bij een hoog testosteronniveau wordt verondersteld dat er een corticale balansverschuiving plaatsvindt ten gunste van beloningsgevoeligheid en ten nadele van strafgevoeligheid. Cortisol heeft daarentegen een tegenovergesteld effect op het corticale breinniveau: in tegenstelling tot testosteron heeft een hoge hersencortisolconcentratie de neiging de balans tussen beloningsgevoeligheid en strafgevoeligheid te verschuiven in de richting van de laatste. Kortom, in het geval van een combinatie van hoge testosteron- en lage cortisolconcentraties zal de neiging tot het zoeken naar beloning en de daarmee gepaard gaande ongevoeligheid voor straf, de overhand krijgen. De reden dat wij de speekselconcentraties van deze steroïden bestudeerden is dat psychopathie wordt geassocieerd met een hogere incidentie van agressieve handelingen en dat psychopathische individuen daarom oververtegenwoordigd zijn in het forensisch systeem. Wij maten de speekselconcentraties voorafgaand aan de testprocedure met de bovenbeschreven taken én na afloop daarvan, zodat wij speekselconcentraties in de loop van de tijd konden observeren. Naast het meten van zowel testosteron- als cortisolspeekselconcentraties, bepaalden wij ook de zogenoemde testosteron-cortisol-ratio omdat deze positief gerelateerd zou zijn aan impulsiviteit en antisocialiteit, aspecten die in de PCL-R-facetten 3 en 4 zijn opgenomen. Als hypothese stelden wij dat de testosteron-cortisolratio inderdaad een positieve associatie met de PCL-R-factor 2 zou vertonen. Omdat sterke associaties zijn beschreven tussen dominant gedrag en PCL-R-factor 1 (deze omvat PCL-R-facetten 1 en 2), hadden wij bovendien de verwachting dat testosteronspiegels een positieve associatie zouden vertonen met PCL-R-facet 1, maar niet of in mindere mate met PCL-R-facet 2, omdat dit laatste facet geen invloed lijkt te hebben op dominantie.

De hypothese over de testosteron-cortisol-ratio werd niet bevestigd, aangezien er geen significante relatie werd gevonden met deze facetten noch met de andere PCL-R-categorieën. Wij concludeerden dat de zogenoemde double-hormone hypothesis zoals uitgedrukt door de testosteron-cortisol-ratio onjuist lijkt te zijn in relatie tot de ernstmaat van psychopathie. Speekselconcentraties van de steroïden, met name cortisol, daalden gedurende het testprotocol, wat niet werd beïnvloed door toediening van oxytocine. Interessant is dat de speekselconcentraties stabiel bleven bij psychopathische patiënten met ernstig verstoorde narcistische en manipulatieve gedragsmatige interpersoonlijke neigingen (hoge scores in PCL-R facet 1), en dat de speekselconcentratie van testosteron op baseline niveau hoger waren bij de psychopathische patiënten met ernstige antisociale neigingen (hoge scores in PCL-R facet 4). Samen bevestigen deze resultaten dat basale speekselconcentraties van de steroïden, evenals hun fluctuatie in de tijd, geassocieerd zijn met psychopathische ernst. Toekomstig endocrien onderzoek naar psychopathie zou rekening moeten houden met de gedragsdiversiteit en zich moeten richten op een combinatie van steroïdenconcentraties en hun verandering in de tijd.

1.4 Toekomstperspectief

Gegeven de enorme lijdensdruk van de slachtoffers van psychopathische personen in combinatie met de duizelingwekkende maatschappelijke belasting en de kosten door hun handelen, is het noodzakelijk dat meer wetenschappelijk onderzoek plaatsvindt naar hun gedrag en hun cognitieve en emotionele processenverwerking. Zonder een opzettelijke limitering dient dergelijk onderzoek plaats te vinden op het gebied van sociologie, criminologie, ontwikkelingspsychologie, trauma, verslaving, psychotherapie, neurologie en neurofysiologie, endocrinologie, (forensische) psychologie en (forensische) psychiatrie. De zoektocht naar biomarkers voor psychopathie moet doorgaan. In hoofdstuk 4 opperden wij dat tekortkomingen in de snelle mimicry van de gelaatsspieren als zo'n biomarker kan worden beschouwd. Meer onderzoek hiernaar is aangewezen.

Psychopathische patiënten hebben vaak co-morbide stoornissen, d.w.z. naast psychopathie bestaat er dan bijvoorbeeld een stemmings- of affectieve stoornis, parafilie, psychose of agressie. Deze co-morbide stoornis kan worden behandeld met de daarvoor aangewezen medicatie. Het is waar dat dit het kernconcept van psychopathie niet wezenlijk aanpakt, maar de

gedragsuiting van de psychopathische patiënt kan zo worden verzacht, wat als een voordeel moet worden beschouwd.

Wat betreft het beperkt effect van de eenmalige toediening van OT in onze studie, kan worden opgemerkt dat deze eenmalige toediening wellicht te weinig was om significante veranderingen teweeg te brengen en zouden meerdere OT-toepassingen moeten worden toegepast om meetbare effecten te detecteren. Nader onderzoek hiernaar is welkom.

Farmacotherapie, evenals alle andere mogelijke interventies, gericht op het verbeteren van de empathieverwerking moeten zich richten op het verbeteren van de laatstgenoemde aspecten, omdat het verbeteren van de cognitieve aspecten van empathie zonder het verbeteren van de affectieve aspecten de psychopathische persoon in kwestie waarschijnlijk alleen maar onaangener of (crimineel) gevaarlijker maakt.

Een laatste opmerking: het is algemeen bekend dat een stressvrije ontwikkeling in de perinatale periode en de daaropvolgende levensfasen in de vroege kindertijd preventief werkt met betrekking tot hechtingsproblemen en veel psychiatrische stoornissen in het latere leven. Door goede algemene gezondheidszorg en de juiste pedagogische surveillance in de begeleiding van zwangeren en kinderen in hun eerste levensjaren, kan daarmee het percentage secundaire psychopathie mogelijk worden verlaagd. Voorkomen is immers beter dan genezen.

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There is only one thing in the world
worse than being talked about,
and that is not being talked about.

— Oscar Wilde

Promoveren is een kronkelig pad. In mijn geval was dat pad soms glibberig en het was lang. Voor een zogenaemde buitenpromovendus is het promotieproces niet alleen interessant, maar met regelmaat ook lastig. Klinisch-psychiatrische werkelijkheden, immers, concurreren om de aandacht en hebben vaak de eigenschap gillende urgentie te hebben. Keuzes maken is dan ook voortdurend aangewezen. Toch ben ik blij het promotiepad te hebben gelopen, want er waren weliswaar diepe dalen, maar bovenal heb ik genoten van mijn medereizigers en de wonderschone uitzichten op de materie waarover dit proefschrift handelt.

Als praktiserend psychiater ben ik altijd van mening geweest dat wetenschapsbeoefening een significant onderdeel van mijn werk dient te zijn. Dat geldt mijns inziens ook andersom: wetenschappers zouden hun theorieën en modellen eveneens aan de klinische patiënt moeten toetsen, zodat wetenschappelijke uitspraken mogelijk worden over 'de échte patiënt' die artsen in hun dagelijkse praktijk tegenkomen. Ik ben blij dat wij dat ideaal in de samenwerking tussen de vakgroep Experimentele Psychologie van de universiteit Utrecht en de afdeling Wetenschap van het Nederlands Instituut voor Forensische Psychiatrie en Psychologie (NIFP) voor een groot deel hebben benaderd.

Trots ben ik op mijn eerste promotor, Jack van Honk; scherp, altijd in voor een kritisch, volslagen contrair standpunt en genietend van een stevige discussie. Jack, jij bent een man die zagezegd op zijn eigen eigenwijze wijze in het leven staat, maar jij hebt wel degelijk een subtiel oog en oor voor echtheid in persoonlijke relaties. Jou ontmoeten was niet alleen boeiend maar ook plezant. Jouw kennis van de neurohormonen en de neurobiologie is indrukwekkend en ik dank jou voor de hulp en het vertrouwen dat jij in mij stelde.

Rara, waar kwam zij vandaan? Plots was zij er: Maaïke Kempes, mijn latere tweede promotor. Maaïke heeft een enorme ausdauer en straalt immer energievolle bezigheid uit. Het prettige van bioloog Maaïke is dat zij goed weet wat de grenzen van haar vak en kennis zijn en dus ook serieus luistert naar de opinie van psychiaters en psychologen. Dat betekent niet dat zij alles voor zoete koek aanneemt, want bij Maaïke geldt dat schrandereheid wordt ingezet om via antithesen een synthese te bereiken. Maaïke, jij hebt mij onder andere bijgestaan in een fase waarin de patiëntselectie uitermate traag verliep en bleef daarin optimistisch. Jouw principiële standpunten, interesse voor goede intermenselijke verhoudingen en nieuwsgierigheid zijn mij dierbaar. Ik dank jou voor jouw sleephulp. Nu zal ik nooit een boot kopen - en al helemaal geen sleepboot, maar bij dezen: ik beloof dat mocht ik ooit een sleepboot kopen, ik die de 'Maaïke I' zal dopen.

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Chances are everywhere. Suddenly there were Raymond Ho and Ben Kemp, two international students from Maastricht University who had become excited by the article on the Zipper Model of Empathy and wondered how the various components of the empathy construct could then be operationalized. With admiration, I witnessed their clever and extraordinarily quick approach to the difficult subject matter. Guys, I thank you for the pleasant way of working together. Our project was further accelerated by the involvement of Hedwig Eisenbarth, Associate Professor at Victoria University of Wellington, New Zealand. Hedwig, your knowledge of the subject is very impressive and I would also like to thank you for the pleasant and open way of collaboration. I am so proud of our joint article in this dissertation.

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niveau. Ton, dank je voor onze komische en interessante ontmoetingen en jouw onontbeerlijke inbreng in ons gezamenlijk artikel. Op naar het volgende?

Als ik aan wetenschap in het NIFP denk, dan komt de naam van Thomas Rinne direct naar voren. Thomas, ik leerde jou kennen via jouw echtgenote, kinderen jeugdpsychiater Mirjam Rinne-Albers, met wie ik in De Vonk/Centrum '45 samenwerkte in een project voor kinderen van getraumatiseerde asielzoekers en vluchtelingen. Op een onbevagen manier besloten jij en ik de Werkgroep Trauma en Neurobiologie op te richten, een werkgroep van allerlei (beginnende) trauma-onderzoekers met uiteindelijk veel wetenschappelijke spin-off. Via jou kwam ik naar het Pieter Baan Centrum (PBC), een stap die ik toentertijd moeilijk maakte, maar tot op de dag van vandaag prijs. Jij stond - samen met Edwin de Beurs - aan de wieg van mijn promotieproject en ik ben dan ook blij jou als paranimf bij de verdediging aan mijn zijde te hebben. Naast jouw wetenschappelijke interesses stip ik hier ook jouw aandacht voor mensenrechtenkwesties aan. Het is fijn op dat vlak verder met jou samen te werken.

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parate kennis waarbij je je heel kleintjes voelt afsteken. Een onvolprezen man ook die veel heeft betekend voor de wetenschap, onder andere voor de neurobiologie van agressie. Menno, ik herinner mij onze interessante discussies waarbij wij trachtten jouw fundamentele wetenschappelijke inzichten te projecteren op mijn klinische kennis van posttraumatische stress-psychopathologie - en andersom. Het was heel fijn om te bemerken dat jij openstond voor vragen en inzichten uit de klinische praktijk en ook dat jij met jouw didactische gaven bij mij allerlei kennisluiken hebt geopend.

Als jarenlange vriend wil ik psychiater Horst van Renesse graag een ereplaats in dit dankwoord geven. Wij waren PBC-collega's en ik heb veel gehad aan zijn ervaring met en visie op zowel de psychoanalyse en de psychiatrie in het algemeen, als de forensische psychiatrie. Horst kan smakelijk verhalen over zijn bijzondere levensloop en de inzichten die hij daarbij heeft verworven. Horst = humor en Horst zonder zelfspot is als een eitje zonder zout. Reizen, dromen, fantaseren, sporten, niets van dit alles is deze jeugdige krasse knar vreemd. Zijn belezenheid en geheugen worden door veel collega's geroemd, en terecht. Horst, jij hebt mij mede gevormd in de forensische psychiatrie. Oog voor de observandus en relativering van diens en onze procespositie, naast de daarbij behorende psychodynamische, politieke en maatschappelijke context, alles kwam in onze genoeglijke gesprekken aan bod. Vaak lardeerde jij deze met vroegere casuïstiek en geschiedkundige of literaire verwijzingen, liefst in de vorm van aforismen of maximes. Ontmoetingen met jou waren (zijn) een ontdekkingsreis. Ik dank jou voor jouw onvoorwaardelijke steun bij wrijvingen rondom een patiënt. Dat jij paranimf wilt zijn, beschouw ik als een eer.

Narcistische trekken kunnen ook voorkomen bij psychiaters. Zo kan het gebeuren dat je als psychiater met veel klinische ervaring aanneemt dat de forensische psychiatrie in een vloek en een zucht te leren valt. Tja. Nu nog bloos ik als ik terugdenk aan mijn eerste schreden op dit pad. Zonder hulp van PBC-collega's zou ik nooit zover zijn gekomen. Ik ben dan ook dank verschuldigd aan tal van leermeesters in het PBC, bijvoorbeeld psychiater Pieter Ronhaar en klinisch psycholoog Berend Seinen. Pieter, jij was mijn eerste werkbegeleider en zette direct heldere piketpaaltjes uit. Via jouw onvermoeibare verificatie en falsificatie van de inhoud van het geschrevene leerde ik van jou rapporteren. Berend, ons bède veleije in en ompstreiks ut Haagse zorragde voâh un onùitgesprauke gevoel van vebinding. Ik hep veil vaje geleâhd. Jâh slimhèd, vebluffende taalvaahdighèd, diagnostiese kwalitète ware stuk voâh stuk kadeijautjes, net as jâh relativeringsvemaugè en besmùikte humoâh. Jâh beschèdehèd was nerreges voâh naudag. Dankkie, âhwe gènpaunem. Het is niet mogelijk hier de vele andere psychiaters en psychologen bij naam te

noemen, maar ook hen dank ik van harte voor hun aandeel in mijn vorming tot forensisch psychiater. GZ-psychologen Clemens Salet, Jildou Heerschop en Inge Schilperoord wil ik roemen om hun prettige omgang in de afgelopen jaren, waarbij aandacht voor inhoud en een betrokkenheid op het PBC en het vakgebied hand in hand gingen. Psychiatrie op het snijvlak van het strafrecht is een wonderlijk vak en vergt dus tevens kennis van het juridisch domein. Binnen het PBC prijzen wij ons gelukkig met juristen die een grote kennis van het strafrecht hebben en niet te beroerd zijn die herhaaldelijk aan de op dat vlak relatief onnozele gedragskundigen uit te leggen. Veel geleerd heb ik van Jos van Mulbregt, een man die net zo snel schrijft als hij denkt (en dat is echt snel) en een indrukwekkende catalogische kennis van het strafrecht bezit. Ik dank hem voor het voor mij openen van het strafrecht domein en zijn visie op het Utrechts gedachtegoed waarin het PBC is verankerd. Ik dank tevens de andere juristen, waaronder Hanneke Beekman en Asmaâ Ghonedale, beiden niet alleen keien in hun vak maar ook keihardwerkend. Ik denk in dezelfde bewoordingen aan de inmiddels vertrokken juristen Mascha de Boer en Eline van Poecke. Voor alle vier geldt dat hun geduldige hulp, wijsheid en humorvol vliegen afvangen veel voor mij hebben betekend - en nog.

Je zou kunnen denken dat het in het NIFP en het PBC draait om gedragskundigen en juristen. Niets is minder waar. Dergelijke organisaties draaiend houden terwijl tegelijkertijd de belangen van het politiek-maatschappelijk Umfeld dienen te worden meegewogen, is op zijn zachtst gezegd een lastige klus. Ik dank Agaath Cleyndert, algemeen directeur van het NIFP, Marrit de Vries, directeur Inhoud van het NIFP, en Arjan van den Nagel, PBC-directeur, voor hun geduld met mij en hun vertrouwen dat het goed zou komen. Ook ben ik dank verschuldigd aan de vele, vele groepsleiders van het PBC waarmee ik in de loop der jaren heb samengewerkt. Hun participerende observaties zijn van onmisbare waarde voor het PBC-onderzoek, zij schragen immers de eindconclusies van de rapportages. Onderzoek in het PBC kan alleen plaatsvinden wanneer de context veilig is. Gelukkig wordt daarvoor zorggedragen door een groot team bewaarders; zonder hen zouden wij nergens zijn. Dank hiervoor, jullie assistentie blijft niet onopgemerkt. De vrijwilligers onder de groepsleiders en de bewaarders die aan het wetenschappelijk onderzoek hebben meegewerkt in de zin van controlegroep ben ik natuurlijk extra dank verschuldigd. Jullie inbreng was van eminent belang. Naast dankzegging aan de collega's van de gedragskundige administratie voor hun titanenstrijd om de PBC-rapportages foutloos en op tijd naar de rechter te versturen, wil ik ook een woord van dank richten aan mijn collega's van het forensisch milieuonderzoek, een andere pijler onder het PBC-onderzoek, en

onontbeerlijk voor het in kaart brengen van de maatschappelijke context en het verleden van een onderzochte. Met velen van hen heb ik intensief en prettig samengewerkt, ik dank hen daarvoor hartelijk. Speciaal dank ik forensisch milieurapporteur Daniël van der Heide, een man die, als associatief denken aan een snelheidslimiet zou zijn gebonden, voortdurend in overtreding is.

Ook talrijke collega's buiten het PBC hebben mij in de loop der jaren gesteund door simpelweg een luisterend oor te zijn. Ik denk bijvoorbeeld aan mijn intervisiegroep of oud-collega's van GGZ Delfland en De Vonk/Centrum '45. Dank hiervoor. Mijn waardering voor het meelesen van menig manuscript in wording door Horst van Renesse, Clemens Salet, Johan Schinkelshoek en Michiel Westenberg is eveneens groot. Dank ook familieleden, vrienden en kennissen voor jullie belangstelling in de loop der jaren. Daniel Dittmar heeft de vormgeving van zowel het proefschrift als het PromotieMagazine verzorgd. Daniel, always interesting to notice that someone from deep Down Under can reach such impressive heights. Above all, besides being a very nice guy, you are a true professional. Thank you very much for the wonderful design.

Uiteraard wil ik als laatste mijn dankwoord richten tot mijn gezinsleden. De belangrijkste stut & steun in dit promotietraject is 'mijn betere ik', mijn vrouw Patricia Simon. Lieve Ptries, in de 45 jaren van ons gezamenlijk levenspad hebben wij lief en leed gedeeld. Menigeen heeft zich in bewonderende woorden uitgelaten over jouw betekenisvolle rol in mijn leven. En die rol is onmiskenbaar. Jij hebt veel geaccepteerd, moeten ontberen en ook eigen belangen aan de kant gezet. De laatste jaren vierde jij vakanties zonder mij. Jij hebt mij in wezen steeds vrijgelaten. Ik kan niet uitdrukken hoeveel dat voor mij heeft betekend. Ik heb dan ook in de tekst van dit dankwoord een - speciaal voor jou bedoelde - boodschap verweven die uitdrukt wat ik voor jou voel. Lees maar, er staat écht wat er staat. En dan onze kids, Daan, Nina Lucía en Broeno, jullie zijn ons intens dierbaar, net als de aanhang, Max en Jildou. Onze relatie is vrij, liefdevol en vol dynamiek - en bedoeld voor altijd.

Curriculum vitae



The past is a foreign country:
They do things differently there

— Leslie Poles Hartley

Ronald Rijnders is geboren en getogen in Rijswijk, gelegen onder de rook van Den Haag. Hij is psychiater en psychotherapeut.

Ronald behaalde zijn artsenbul (cum laude) aan de universiteit Leiden. Hierna volgde hij postuniversitair onderwijs aan het Prins Leopold Instituut voor tropische geneeskunde te Antwerpen. Hij werd door de Franse hulpverleningsorganisatie Médecins Sans Frontières uitgezonden naar oorlogs- en conflictgebieden in Honduras (vluchtelingenkamp voor Salvadoranen), Mozambique (regeringsgebied) en Afghanistan (opstandelingsgebied).

Uiteindelijk startte hij zijn opleiding tot psychiater. In zijn tweede specialisatiejaar was hij op verzoek van de Johannes Wier Stichting voor Gezondheidszorg en Mensenrechten lid van een geheime fact finding mission naar de lichamelijke en psychische gezondheidstoestand van overlevenden van de geheime militaire gevangenis Tazmamart in Marokko. Zij hadden achttien jaar incommunicado en in totale duisternis gedetineerd gezeten, met de toenmalige zekerheid daar voor de rest van hun leven te moeten verblijven. Dit onderzoek is beslissend geweest voor Ronalds verdere beroepsvorming. Hij specialiseerde zich in psychotrauma en transculturele psychiatrie in De Vonk/Centrum '45, een kliniek voor getraumatiseerde asielzoekers en vluchtelingen. Na elf jaar maakte hij de overstap naar het Pieter Baan Centrum, onderdeel van

het Nederlands Instituut voor Forensische Psychiatrie en Psychologie (NIFP) en werd vervolgens opgenomen in het Nederlands Register voor Gerechtelijk Deskundigen. Vervolgens startte hij zijn promotieonderzoek bij professor Jack van Honk, van de afdeling Experimentele Psychologie van de Universiteit Utrecht.

Ronald werkt(e) naast zijn werkzaamheden in De Vonk/Centrum '45 en het Pieter Baan Centrum ook in andere takken van de psychiatrie: ouderenpsychiatrie, verslavingszorg, psychotherapie, crisisdienst en forensisch-psychiatrische behandeling. Hij was deelnemer aan de Medische Beroepsgroep van Amnesty International, de werkgroep Marokko van de Johannes Wier Stichting voor Gezondheidszorg en Mensenrechten, stichting Forum Levenslang, Antares Foundation Amsterdam (een organisatie voor psychosociale hulpverlening aan humanitaire en hulpverleningsorganisaties wereldwijd) en aan het instituut voor Mensenrechten en Medisch Onderzoek (iMMO).

Ronald: "Het thema interpersoonlijk geweld loopt als een rode draad door mijn beroepsleven. Ik ben geboeid door de vraag waarom mensen en instituties bereid zijn zover te gaan in hun agressie-uitingen, soms verder dan zichzelf aanvankelijk voor mogelijk hielden. Tijdens mijn werk als transcultureel traumapsychiater zag ik de psychische gevolgen van geweld in de zin van psychiatrische symptomen bij de slachtoffers, maar ook extreem, niet-psychiatrisch leed dat volkomen invoelbaar was. Verbaasd was ik de enorme veerkracht te aanschouwen die getraumatiseerden ook kunnen hebben. In dat perspectief raad ik dan ook iedereen aan Tahar Ben Jallouns 'Een verblindende afwezigheid van licht' te lezen. Overleven behoort tot de mogelijkheden, vrijwel altijd ten koste van veel, niet zelden met posttraumatische groei. Als forensisch psychiater onderzoek ik - al of niet psychisch gestoorde - verdachten van misdrijven die in hun eigen voorgeschiedenis vaak grote psychosociale stress hebben gekend en daardoor in hun persoonlijkheidsontwikkeling zijn ontspoord. Ook zij hebben een verhaal. Traumatische gebeurtenissen kunnen niet ongedaan worden gemaakt; mogelijk wel de gevolgen. Mijn hoop is dat het leed verzacht kan worden, net als toekomstig gevaar kan worden ingedamd. Een humane samenleving wordt in mijn ogen gekenmerkt door een waarlijke erkenning van het leed van het slachtoffer, in samenhang met het op een veilige manier toewerken naar terugkeer in de maatschappij van de leedtoebrenger. Dit vergt een overheid die beide aspecten van de gevolgen van geweld serieus neemt."

