On the Inference of Agency in Operant Action:

An Examination of the Cognitive and Neural Underpinnings in Health and Schizophrenia

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Het infereren van zelf-causatie tijdens operante acties:
Een zoektocht naar de cognitieve en neurale substraten in gezondheid en schizofrenie

(met een samenvatting in het Nederlands)

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Chapter 1

Introduction and overview

When I was a little boy, my father and I competed in a match of soccer on an arcade machine in a diner. We used an analogue stick and buttons to move, tackle, pass and shoot. I played my heart out and I was defeating him in a humiliating fashion, like Germany would humiliate Brazil nearly 20 years later in 2014's World Cup semi-finals. Throughout the game, I felt in total control of my actions and their outcomes—an experience called *self-agency*. The players ran when I moved the stick, and they passed, tackled, and shot when I pressed the buttons. But I was tricked by my mind's best trick. Near the end of the match, I discovered that my father did not insert enough coins to play with two players, and he was not playing against me but against the computer. For more than 5 minutes, we were both fully immersed in the game and felt continuously in control over our actions and their consequences.

This consciously accessible sensation of control—the immediate experience of oneself as an agent during action control and execution—is pervasive, sometimes subtle, and can be even illusory in nature. Furthermore, the experience of self-agency is socially well-shared and considered to be fundamental to human social functioning. The experience of agency helps people (including my father and me) to make sense of the physical and social world around them, to guide and direct them in their goal-directed actions, and to make sense of who does what when they act and react in a social context. Understanding the roots and occurrence of the experience of agency, then, has become an important target in recent psychological and neuroscientific research. The present dissertation aims to contribute to this endeavor by setting out research that examines how—through which cognitive and neural processes—humans produce the conscious experience of agency.

How does the experience of self-agency arise? What are the processes that tell us whether we are in control of our own actions and their outcomes? Contemporary research into self-agency experiences recognizes two complementary processes: motor-prediction and a non-motor prediction mode of processing. Most research to date has focused on self-agency as a product of comparator processes described in models of motor control (Frith, Blakemore, & Wolpert, 2000; Wolpert & Flanagan, 2001). According to this account, people experience self-agency when there is an unambiguous and reliable relationship between their actions and the outcomes (e.g., between pressing a button and seeing one's player shoot the ball). We experience this automatically via motor-predictive mechanisms that anticipate and process incoming sensory (e.g., visual, auditory or haptic) information about the outcome. This is how my father experienced agency over his soccer team's actions. The actions he performed with the joystick and the buttons directly translated into actions and consequences of his soccer players. However, when the relationship between actions and outcomes is more ambiguous, such as in complex social situations and situations where our actions might lead to multiple outcomes, we can still experience agency by using non-motor predictive cues. Indeed, agency can be *inferred* when a specific outcome is matched by pre-activated information that is related to the outcome (Wegner & Wheatley, 1999). This is what happened when I pushed buttons for my soccer team, and I wanted my players to tackle, pass and score… and they did, by coincidence—allowing me to establish an immediate experience of self-agency even though I was not actually in control.

In self-agency inferences, pre-activated information can either be goal-based, when people engage in goal-oriented behavior, and prime-based, where information can be subtly pre-activated in people's mind by our environment. The present dissertation builds on the recent advancements in agency inference research, and means to gain further understanding of this phenomenon by focusing on the cognitive and neural underpinnings of agency inferences in health and schizophrenia. The main foci of this dissertation may be summarized in three research questions: 1) does the experience of agency arise differently as a function of goals and subtly presented information? 2) how are inferences of agency neurally represented in the brain? and 3) how do agency inferences operate in patients with schizophrenia, who as a part of their disease often show disturbances in self-agency processing?

Goal-based versus prime-based self-agency inferences

People see themselves as the author of their actions when they produce outcomes that match their goals. For example, if you have the goal to make people laugh, and the joke you produce succeeds in doing so, you infer it was you who brought about this laughter. But if they start laughing before you've told the joke, you known it wasn't your joke that made them laugh. However, in our busy everyday lives, one does not always have the time or the capacity to formulate explicit goals for our behavior, and we generally act in a spontaneous way. Recent findings suggest that self-agency experiences can also arise from a more implicit source of information. Indeed, when we are primed with a certain action outcome (e.g., the light switched on), and this action subsequently occurs, we feel that we caused this outcome to occur. Thus, in this so-called implicit route, agency inferences arise from information outside of conscious awareness. Importantly, both goal-setting and mere priming have been found consistently to contribute to agency inferences (Aarts et al., 2005; van der Weiden et al., 2013b; Wegner & Wheatley, 1999).

Recent research has suggested that both goals and primes *increase* agency experiences when the outcome information matches the actual outcome, whereas only goals *decrease* agency experiences when the actual outcome is not matched (van der Weiden, Ruys, & Aarts, 2013b). The present dissertation aims to build on this research, by exploring the possibility that this pattern of results with regards to increase and decrease of agency experiences is due to the mechanism of *attentional control*—a mechanism that allows people to focus on a specific outcome, to shield themselves from distracting information, and to learn from expected and unexpected results (Baddeley, 2007; Conway et al., 2005). It was proposed that attentional control is implicated in goal-based inferences (i.e., goals must be held in one's mind during the performance of actions), but that prime-based inferences rely mostly on implicit cognitive accessibility processes that follow the principles of automatic spreading of activation.

Neural substrates of self-agency inferences

To date, most research on agency inferences looks at the cognitive processes underlying self-agency. However, there has been no previous research that has focused on the neurobiological implementation of self-agency inferences. Indeed, previous research exploring the neural substrates of agency has solely focused on motor-predictive processes, identifying brain regions that were involved in signaling a mismatch between action and outcome (for an overview, see Sperduti et al., 2011). This lack of a neurobiological model of agency inferences is a significant gap in our understanding of this phenomenon, as understanding the way agency inferences are represented in the brain may shed light on potential cognitive mechanisms that underlie agency inferences, and could provide a basis for investigating models of perturbed agency processing. To that end, the present dissertation provides a first exploratory functional magnetic resonance imaging (fMRI) study into the neural substrates of goal-based agency inferences.

Self-agency inferences in schizophrenia

One way to investigate the mechanisms underlying self-agency inferences is by studying people whose self-agency is disturbed, as is the case in patients with schizophrenia. Schizophrenia is a severe psychiatric disorder in which people interpret reality abnormally – it may result in hallucinations, delusions, and disordered thinking and behavior. Patients with schizophrenia often exhibit difficulties in distinguishing their own actions and outcomes from those of others as part of their symptoms, leading to severely impaired autonomy and problems in social interactions (Walker et al., 2004). These abnormalities can, at least partly be explained by abnormalities in using motor-predictive cues to experience agency (e.g., Shergill et al., 2015). However, they may be able to compensate for this inability by inferring self-agency from goal-based processes (Voss et al., 2010). The present dissertation builds on this research and investigates goal-based and prime-based agency inferences in patients with schizophrenia. Furthermore, the neural underpinnings of these processes is also explored in these patients with the use of fMRI.

In sum, the present dissertation studies the cognitive processes underlying goal-based and prime-based agency inferences. Furthermore, it explores the neural implementation of goal-based agency inferences, and assesses how agency inferences operate in patients with schizophrenia.

Overview

Chapter 2 – Theoretical background and discussion.

This chapter provides an overview of research on agency processing. I discuss both motor and non-motor accounts of agency processing. In discussing inference accounts of agency, I describe goal-based and prime-based agency processing, the neural substrates of agency inferences, and elaborate on potential disturbances in agency processing. This chapter integrates the empirical data of the present dissertation in the existing body of research. The chapter ends with an elaborate discussion by providing some general conclusions, identifying unresolved issues, and suggesting directions for future research.

Chapter 3 – Attentional control and inferences of agency: working memory load differentially modulates goal-based and prime-based agency experiences.

In this chapter, I investigate to what extent goal-based and primed-based agency inferences rely on different underlying cognitive mechanisms, by focusing on their dependency on attentional control. First, the chapter introduces a novel agency inference task that replicates previous findings, showing that whereas both goal-based and prime-based agency inferences are strengthened when an outcome matches the pre-activated outcome information, only goal-based agency inferences are weakened when outcomes mismatch such information. Then, two studies demonstrate that taxing participants' working memory dwindles their goal-based, but not prime-based agency inferences, suggesting that goal-based agency inferences rely on attentional control, rendering them prone to conditions that modulate goal-directed control processes.

Chapter 4 – An exploratory fMRI study into inferences of self-agency.

To date, most research into the neural underpinnings of agency processing has focused on motor-prediction processes, while agency inferences have received little attention. This chapter presents a first test to explore the neural underpinnings of goal-based agency experiences. Participants performed a well-tested agency-inference task, while an MRI scanner captured the blood oxygen level dependent (BOLD) response of the brain at the very moment participants perceived the outcome of their action. When participants experienced agency over their outcomes, the frontal and parietal areas of the brain became active. The identified regions have previously been implicated in self-referential processing and the integration multi-sensory information. These findings are compared to research into neural underpinnings of agency experiences informed by motor-prediction, and implications for the mechanism of self-agency inferences are proposed.

Chapter 5 – Abnormalities in the establishment of feeling of self-agency in schizophrenia.

In this chapter, I examine self-agency inferences in patients with schizophrenia, a group that often exhibits problems in experiencing or establishing agency. Both healthy controls and patients performed two versions of an agency inference task: one tapping into goal-based agency inferences, another examining prime-based agency inferences. Results showed that for goal-based agency inferences, both groups experienced more agency when outcomes matched (rather than mismatched) previously set goals. However, in prime-based agency inferences, only healthy controls experienced more agency when outcomes matched (rather than mismatched) previously primed outcome information. This suggests that patients with schizophrenia are able to infer agency from an explicitly set goal (the explicit route) but not from implicitly primed information (the implicit route). These findings constitute the first demonstration of disturbed implicit information processing underlying inferences of agency in schizophrenia.

Chapter 6 – Abnormalities in the experience of self-agency in schizophrenia: a replication study.

An important question is: might the dysfunctions in implicit agency processing among patients with schizophrenia be due to impaired visual processing of primed information? This chapter provides a replication of the findings in chapter 4, again showing impairments in prime-based agency inferences in schizophrenia. In addition, it was found that patients demonstrate the same level of accuracy in visually detecting agency-relevant primes. Thus, patients with schizophrenia detect the implicitly primed information, but they do not rely on this implicit information to arrive at self-agency experiences.

Chapter 7 – Impaired frontal processing during agency inferences in schizophrenia.

So far, the studies (chapters 2-5) have focused on agency processing in healthy participants as well as in patients with schizophrenia, and have uncovered neural underpinnings of self-agency inferences. Chapter 6 integrates these approaches by conceptually replicating the findings in Chapter 3 in healthy controls with a new agency inference task, and to explore the neural substrates of goal-based agency inferences in patients with schizophrenia.

Findings in Chapter 4 did not show any impairments in goal-based inferences for patients with schizophrenia, so I predicted that these patients might show similar brain activation as controls during goal-based agency inferences. An alternative hypothesis proposes, however, that patients with schizophrenia would not show clear activation in frontal regions, due to impairments in frontal processing that is often found in patients with schizophrenia (e.g., Lee et al., 2006). The findings demonstrate that controls and patients with schizophrenia showed similar goal-based agency inference effects on a behavioral measure. However, in patients, frontal regions were not associated with goal-based self-agency inferences. Given that such frontal regions are generally associated with self-awareness and self-referential processing, the lack of activation in these regions may be related to broader self-disturbances in schizophrenia. The intact agency experiences, but lack of frontal brain activation lend credence to the notion that the problems in agency inference processing in patients with schizophrenia stem from brain dysfunctions that may be overcome in simple goal-oriented actions (e.g., tool-use), but likely not in everyday social interactions where agency experiences need to arise quickly and easily. In such interactions, planning and executing goal-directed behavior is more complicated and taxing (e.g., due to the attentional control required to shift priorities or to inhibit routinized modes of responding), and information about causes and outcomes is often implicit and ambiguous.

Together, the multidisciplinary nature of the chapters advance the understanding of the cognitive mechanisms of self-agency inferences, and provide an important stepping stone for the further investigation of the neural underpinnings of agency inferences in health and schizophrenia.

Chapter 2

Theoretical background and discussion

Humans are considered to be social animals that regulate each other's behaviors in simple as well as complex social structures based on past experiences. Whereas a larger part of social behavior is habitual and driven by stimulus–response links, an important faculty typically associated with successful regulation and social prosperity pertains to the human ability to plan action on the basis of anticipated outcomes and to act accordingly. Specifically, people are said to represent their action in terms of their results, and hence, such operant actions can take on voluntary features that control behavior independent of stimuli. Humans thus can time, select or veto their own courses of action in the service of individual and social functioning, rendering behavior flexible, adaptive and strategic (Brass & Haggard, 2008).

The capacity to act voluntarily is fundamental to self-perception and communication. First, because people are able to voluntarily regulate our own behavior, they experience control, freedom of choice, and more generally, wellbeing (Taylor & Brown, 1988; but see Colvin & Block, 1994). Furthermore, the degree of experienced agency is associated with the ascription of causation to one's own behavior and the behavior of others, allowing people to hold each other responsible (Synofzik, Vosgerau, & Newen, 2008). We praise others and ourselves for performing good deeds, and honor and respect those who voluntary contribute to our society. On the other hand, we punish and have disdain for those who are to blame for crimes and transgressions, forming the cornerstone of our legal system (Bandura, 2001). Also, those who are ascribed less agency and control over their actions, e.g., due to stages of maturation (infants), or the presence of mental illness (psychosis), are often judged less harshly for their misbehaviors (Gray, Gray & Wegner, 2007), suggesting that people are held responsible for contributing to society to the degree they are perceived to be able to do so.

The essence of voluntary action has been generally conceptualized in terms of the self – an active agent capable of becoming aware of thoughts, feelings and actions, willfully setting and pursuing goals, making decisions and choices, selecting and maintaining actions and adapting behavior when discrepancies with previously set goals emerge (Bandura, 1977; Baumeister, 1998; 2000; Carver & Scheier, 1998; Locke & Latham, 1990; Markus & Ruvolo, 1989; Metzinger, 2003). Importantly, whereas the active agent of the self is proposed to do most of the labor, most research on the self has addressed substance questions. A wealth of studies in several domains indicates that the self is formed and colored by introspecting and reflecting on past experiences with others, allowing people to gain knowledge about who they are (self-concept; Neisser & Fivush, 1994), what they are capable of (self-efficacy; Bandura, 1977), and how they feel about themselves (self-esteem, Rosenberg, 1965). This so-called *narrative self* (Gallagher, 2000; Gallagher & Frith, 2003) is strongly represented in language and communication, and manifests itself when one presents oneself while interacting with others. In terms of the sense of agency, the narrative self refers to intentions and traits that people explicitly convey in pronouncing what they want, do or feel responsible for in social context (Synofzik, Vosgerau, & Newen, 2008).

Whereas the concept of the narrative self as a (re)construction of personal experiences is well-accepted, the notion that a person's 'self' is the controller of one's own behavior seems to be more problematic –it suggests there is an entity in the human mind that determines behavior, also known as the 'homunculus problem' (Dennett, 1991; Minsky, 1986; Nørretranders, 1991; Prinz, 2004; Wegner, 2005). The issue here is that the homunculus itself must be explained. However, following the same logic that creates the homunculus, one would posit another (smaller) homunculus within itself, and another homunculus would inhabit the smaller one, leading to an infinite regression. To discover the roots of our sense of self, researchers have begun to explore the potential origin of the narrative self, which has been called the *minimal self* (Gallagher, 2000). The minimal self is the immediate subject of experience of oneself as an agent[1]. This sense of self, stripped from all knowledge of the past-self and future-self, is generated by motor-sensory processes of operant action that interact with the direct environment. Examining the self from this embodiment perspective, then, might offer insights into the underlying processes that have been remained hidden so far in the study on the self, action-control, well-being and health.

The present chapter analyses these motor-sensory processes in relation to the sense of agency. Specifically, I discuss the primary processes that play a role in the experience of agency over operant actions (i.e., actions followed by consequences). I depart from the notion that the voluntary control of an action associated with a specific outcome (i.e., operant), simultaneously generates an internal signal that predicts the sensory consequences of this action. This motor-prediction process forms the basis of agency experiences in voluntary (internally) generated behavior. When motor-prediction processes are not available or reliable, non-motor prediction processes can inform the feeling of agency. Non-motor prediction processes are thought to develop later during maturation in childhood (Hommel & Elsner, 2009; Tomasello, 1999). They are mainly governed by predictive cues (e.g., stimuli or thoughts) that coincide with

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[1] The minimal self includes a second component, i.e., the sense of ownership referring to the immediate subjective experience of the fact that is it one's own body that is moving (Gallagher, 2000). Because the present chapter focuses on the sense of agency, I will not further discuss the sense of ownership here.

subsequent sensory experiences during the execution on an action, thereby allowing individuals to consciously experience agency and to attribute causes to the proper agent (Wegner, 2002). Both motor and non-motor agency processes thus form the potential basis of our conscious desires and beliefs about autonomy, freedom and responsibility (Synofzik et al., 2008).

In the remaining part of this chapter, I will first provide a brief account of motor-prediction processes and their relationship to the experience of self-agency. Next, I address non-motor-prediction processes, with a special focus on the role of goals and primes in the context of agency experiences over operant behavior. Finally, I will elaborate on specific cases where agency processing is perturbed, and show how this is related to well-being and health – specifically in the context of psychiatric disorders such as schizophrenia.

Motor-prediction processes in the sense of agency

Our sense of agency over operant actions is primarily driven by motor-prediction processes. These processes arise as a product of consistent action-effect-registration, something that is readily available at birth. Infants readily engage in spontaneous movements, and their brains are inherently able to detect changes in the environment (Gergely & Watson, 1999; Hebb, 1949; Kellman & Arterberry, 1998; Piaget, 1952; Rochat, 1998; Rovee-Collier, 1987). When specific movements and sensory consequences coincide frequently and consistently, simple learning effects allow infants to create an action-effect association (Kray, Eenshuistra, Kerstner, Weidema, & Hommel, 2006; for an overview, see Hommel & Elsner, 2009). Indeed, between two and five months of age infants readily monitor and control their reaching and kicking behavior on the basis of such associations, as illustrated by the finding that they pedal longer if this behavior leads to a systematic and consequent movement of a mobile (Rovee & Rovee, 1969; Watson & Ramey, 1972).

When the action-effect coupling is reliable, subsequent goal-directed action is accompanied by a prediction of the associated sensory consequence of this action, the so called 'efference copy' (Von Holst & Mittelstaedt, 1950). The efference copy pertains to signals sent *out* from the brain, typically implicated in motor commands, and its informational value is short-lived (up to a few hundred milliseconds); long enough to allow for a comparison with the actual sensory feedback of action. When incongruence is detected, the sensory effect is generally registered as externally caused. However, as long as they are similar, agency over the outcome is experienced (Frith, Blakemore, & Wolpert, 2000). Due to the congruence of the predicted and actual sensory consequences, the resulting sensation following an action is perceived as less intense.

This sensory attenuation thus is the result of the smaller difference between the activation of the sensory cortex and the predicted incoming information (vs. non-predicted or incongruent information). Therefore, we cannot tickle ourselves (Blakemore, Wolpert & Frith, 1998), and we experience a stable visual world when moving our eyes. Similarly, in a demonstration of this effect, Shergill and colleagues (2003) showed that when participants had to reproduce tactile stimulation applied to their finger, they consistently overestimated the force that was applied due to the reduced sensory experience of their own actions.

The finding that self-produced effects are perceived differently from externally caused effects allows for a systematic measurement of self-causation. According to a pre-activation account of sensory attenuation, predicting an outcome increases the baseline activation of the representation of the sensory outcome in the brain (Roussel, Hughes, & Waszak, 2013).

When the predicted outcome actually occurs, the increased activation causes the outcome to be perceived sooner, as the increased baseline gives the perception of the outcome a head start in reaching the threshold of consciousness (Waszak, Cardoso-Leite & Hughes, 2013).

An important way to examine this shift in perception as a window to the sense of agency is the intentional binding task (Haggard, Clark, & Kalogeras, 2002). In this task, participants judge the timing of their own action (e.g., a key press) and an outcome (e.g., the occurrence of a tone) of their action with the help of a concurrently rotating clock hand on a computer screen. While performing operant actions intentionally, participants perceive the time of their actions as later in time, and the effect of their action as sooner in time. In other words, the occurrence of the action and the effect is perceived as closer in time, hence, the term intentional binding. Crucially, when the action is induced involuntarily by means of transcranial magnetic stimulation (TMS) over the primary motor cortex, and no efference copy can predict the outcome, the binding effect vanishes or even reverses. This latter finding has been taken as evidence that binding of action and effect in terms of perceived time is indeed a result of voluntary operant action and the operation of an efference copy, and hence, represents a measure of the sense of agency.

Building on this work, several studies have examined qualifiers of the motor-prediction process (i.e., efference copy effect) in yielding the sense of agency, such as manipulating the predictability of the action-effect (Sato & Yasuda, 2005), the time delay between action and effect (Blakemore, Frith, & Wolpert, 1999), externally induced action movement (Dogge et al., 2012; Moore, Wegner & Haggard, 2009; Wegner & Wheatley, 1999) and motivational boosting of operant action by reward signals (Aarts et al., 2012). In short, intentional binding occurs when operant action follows from a voluntary (internally) generated movement, and the efference copy accompanying the preparation of action is strong and reliable enough to render a comparison with the actual sensory feedback of the action possible.

As previously noted, taking away the voluntary (internally)-generated inducement of an action effect is suggested to decrease self-agency experiences, as no efference copy is produced by an internal signal (e.g., derived from a need or motivation) to cause an effect. However, apart from being absent, motor-prediction processes can also be unreliable. Such unreliability is at hand, for example, when people perform operant actions for which outcomes are unpredictable or actions can have multiple causes and outcomes. For instance, in a situation where two persons simultaneously press a separate light switch and only one lamp turns on, they cannot exclusively rely on motor predictions to establish an agency experience over the outcome. However, there is research to suggest that in the absence of motor prediction processes or when these processes are unreliable, intentional binding and agency experiences can still occur. Specifically, this is the case when task instructions imply self-causation (Dogge et al., 2012), or in the presence of action-outcome cues that accompany the execution of an action and resulting outcome (Moore, Wegner, & Haggard, 2009). This indicates that motor prediction signals are not the sole source of self-agency, and that agency processing also relies on non-motor prediction cues implicating cognitive processes.

Below I address this issue by focusing on beliefs and agency cues when motor prediction processes are present but unreliable, and information about action outcomes in situations where motor prediction processes are fully absent.

Non-motor prediction processes: Beliefs and agency cues

One way in which the role of non-motor cues has been studied pertains to testing whether specific task instructions induces beliefs about causation in intentional binding tasks. For example, Desantis, Roussel and Waszak (2011) had participants produce a tone with a button press. They were manipulated to believe that in some trials, they were the author of the tone and in other trials a confederate would cause the tone. Thus, participants were placed in a context where motor prediction processes were unreliable. Interestingly, stronger intentional binding was found when participants believed they caused the tone themselves as compared to when they believed the confederate caused the tone. These results suggest that high-level contextual cues can modulate the contribution of sensorimotor processes in generating intentional binding. Similar effects of task-related beliefs have been observed in other studies (Moore, Wegner, & Haggard, 2009; Dogge et al., 2012).

Furthermore, more general beliefs about causation and control, such as believing in a free will, can influence agency experiences by changing the functionality and inclination to rely on sensorimotor processes underlying operant action. First, research indicates that people with stronger beliefs in free will tend to be more concerned with controlling and accounting for their own action outcomes before deciding on a course of action (e.g., Vohs & Schooler, 2008). Furthermore, undermining beliefs in free will by persuasive messages seems to disturb sensorimotor processes that are normally involved in the voluntary preparation and initiation of operant action (Rigoni et al., 2011). Consistent with this notion, correlational and experimental work suggests that participants who held determinist beliefs show a weaker intentional binding effect as compared to those who believe in a free will (Aarts & van den Bos, 2011; Lynn et al., 2014).

Aside from the influence of general and more task specific beliefs about causation and control on the sense of agency, people can also rely on specific agency cues (i.e., causes for effects) to establish a sense of agency. In one study, priming participants with agency-relevant cues that refer to the self (e.g., words such as "I" or "me") or to external agents (e.g., words such as god or computer) influence experienced agency in a computer task (Dijksterhuis, Preston, Wegner, & Aarts, 2008). Here, priming participants with self-primes before performing an action increased experienced self-agency, whereas god-primes decreased such experiences, particularly among religious individuals. In addition, in a further demonstration that agency cues can influence experienced agency, participants were found to show a smaller intentional binding effect when they retrieved from memory a personal causation instance where they had low power, as compared to when they recalled a situation where they had much power (Obhi, Swiderski, & Brubacher, 2012).

The non-motor agency cues alluded to above have in common that they do not directly speak to the relationship between action and outcome. That is, these cues bring to mind whether or not one might be the cause of an action and resulting outcome, and hence, allowing people to establish experienced agency over action-outcomes by relying on these thoughts. In cases where the relationship between action and outcome is reliable, and action performance can produce an efference copy, motor-prediction cues and non-motor agency cues might be weighted according to a specific rule to inform the sense of agency (Sato, 2009; van der Weiden et al., 2011; see for a theoretical account, Synofzik, Vosgerau, & Voss, 2013). However, and perhaps more strikingly, even when both (motor and agency) cues are absent or unreliable, the sense of agency can result from non-motor processes that inform people about potential outcomes of our actions, that is, non-motor cues that trigger thoughts about the potential outcome of an action and allow people us to retrospectively infer agency once these outcomes occur (Wegner, 2002).

Goal-based inferences of agency

The inference account of agency suggests that we experience ourselves as the author of outcomes due to sense-making processes upon perceiving the outcome of our actions (Wegner, 2002). In other words, we quickly deduce whether we caused an outcome to occur or not. It seems self-evident that when we set goals, and subsequently achieve these goals by executing the relevant actions, we experience ourselves as the cause of this achievement. Indeed, in several psychological models of goal-directed behavior, goals are usually conceptualized as mental representations of desired outcomes that precede and accompany the performance of action and resulting outcome and thus allow people to arrive at goal-based inferences of agency (e.g., Carver & Scheier, 1998; Deci & Ryan, 1985). Accordingly, the inference account of agency suggests that we attribute agency to ourselves when outcomes match our goals or intentions, while outcomes that mismatch our intentions are generally ascribed to other causes.

Importantly, it is not a requirement that *our* actions indeed lead to desirable outcomes to experience agency over them. That is, whereas the human attainment of goals is commonly considered to follow from the performance of instrumental actions, goal-based agency inferences can occur even in the absence of motor prediction processes. According to the theory of mental causation (Wegner, 2002), agency is readily inferred when our thoughts about outcomes exist before the action is executed (priority principle), this thought is consistent with the action (consistency principle) and is not accompanied by other potential causes (exclusivity principle). The relative unimportance of the actual relationship between the action and the outcome is illustrated by an experiment where participants did not perform actions at all (Wegner, Sparrow, & Winerman, 2004). Here, participants watched themselves in a mirror while a confederate extended her hands forward on each side where the participants' hands would normally be. The hand movements were accompanied by instructions broadcast via a headphone. These instructions describing the movements were either given before or after each movement. When instructions previewed movements, participants reported increased agency experiences over the movements as compared to when the instructions followed the movements –which violated the priority principle.

Further demonstration that agency experiences can emerge for outcomes that we desire to attain but are not necessarily caused by our own actions comes from experiments where the cause of action-outcomes is ambiguous (Aarts, Custers, & Wegner, 2005; van der Weiden, Ruys, & Aarts, 2013b; Renes et al., 2013; 2015c; 2015b). In these studies, participants were always in doubt whether a presented outcome was caused by their own action, or by another agent (e.g., the computer). Moreover, the participant's action and subsequent observed outcome were independent. However, when action outcomes corresponded with consciously formulated goals, participants reliably reported more experienced agency than when actions did not yield the intended outcome. Thus, matches between a person's goal and observed outcome leads to the experience of agency in the absence of motor prediction cues, suggesting that, in principle, humans heavily rely on goal-based agency inferences to make sense of the situation at hand.

Prime-based inferences of agency

The role of goals in establishing a sense of agency might have evolved from the human capacity to foresee and anticipate future consequences of actions; a capacity that involves cognitive processing and requires mental resources to consciously formulate goals, to reduce the impact of interfering information processing (e.g., other irrelevant thoughts, distracting stimuli) and to focus attention on the goal (Miyake & Shah, 1999). Importantly, there is ample research indicating that the reliance on such conscious cognitive processing dwindles with practice, such that goal-directed behavior becomes automatized and sensitive to environmental cues or primes that instigate behavior directly (Aarts & Custers, 2009). This raises the intriguing question of whether agency experiences can also emanate from the mere exposure to cues or primes that pertain to information about action-outcomes and modulate prime-based agency inferences implicitly.

In a first demonstration of this possibility, Wegner and Wheatley (1999) devised an experiment where participants moved and stopped a cursor over an array of objects (e.g., ball, car) presented on a computer-screen by using a mouse together with a confederate. On each trial while moving the mouse –but before stopping– the participants heard an object name through their headphones. Unbeknownst to the participants, the confederate forced the mouse to stop at the location of the named object in some trials, and in others the confederate let the participant stop the cursor. After each trial, the participant rated the stop for personal agency. Participants reported increased agency over stopped outcomes (e.g., cursor stopped at the ball on the screen) that corresponded with the outcome prime (the word ball heard through the headphone) as compared to when it did not.

This demonstration of prime-based agency inferences has been conceptually replicated in a variety of studies, showing that pre-activated outcomes increase experienced agency across different tasks (Aarts et al., 2005; van der Weiden, Aarts, & Ruys, 2010; 2011; Linser & Goschke, 2007; Renes et al., 2013; 2015b) in western (individualistic) and eastern (collectivistic) cultures (Aarts, Okaiwa, & Okaiwa, 2010; Sato, 2009). Whether outcome-primes pertain to objects (Wegner & Wheatley, 1999), spatial information (e.g., Aarts et al., 2005), color words (Renes et al., 2015b) or even more socially meaningful information such as emotional facial expressions (Ruys & Aarts, 2012), the findings converge on showing that people readily rely on implicit processes to arrive at a sense of agency.

In sum, research has shown that people infer agency when information about action outcomes are mentally accessible before they perform actions and observe outcomes that match these accessible outcomes. Interestingly, these agency inferences occur no matter how the outcome information is activated: either by explicitly setting goals or implicitly presenting primes. Although this suggests that both type of agency inferences are equally produced, in the next section I will explore and show that they might differ.

Goal-based versus prime-based inferences of agency

Our analyses on agency inferences suggests that both goal-setting and mere outcome-priming contribute to the sense of agency in a similar fashion. However, recent research has suggested that goals and primes might affect agency experiences differently. Both goal-setting and mere priming increase agency experiences when the outcome information matches the actual outcome, whereas only goals decrease experienced agency when the actual outcome does not match the goal (van der Weiden, Ruys, & Aarts, 2013b).

Goal-based inferences of agency are argued to rely on attentional control that allow a person to attend to a specific outcome (s)he wants to obtain; by actively maintaining the goal in mind, one can check the progress towards it, process feedback regarding this progress, and learn from expected and unexpected results (Baddeley, 2007; Conway et al., 2005; Carver & Scheier, 1998; Custers & Aarts, 2007; Frith et al., 2000). The effect of primes on agency inferences, however, is proposed to rely on a more implicit cognitive accessibility process that follows principles of automatic spreading of activation and does not necessarily engage attentional control processes (van der Weiden, Ruys, & Aarts, 2013b).

In order to further examine differences between goal-based and primed-based agency inferences, Renes, van Haren, and Aarts (2015b) conducted a series of experiments in which they taxed participants' ability to employ attentional control in an agency inference task. In order to do so, participants were either prompted with a goal to produce a specific outcome, or were exposed to outcome-primes. Before each trial, participants were shown a sequence of digits, which they had to remember during each trial. If the proposed differences between goal-based and prime-based agency inferences are correct, then taxing participants' working memory would strain goal-based inferences, but leave prime-based agency inferences intact. Indeed, it was shown that goal-based, but not prime-based agency inferences dwindled under a higher working memory load (retaining 2 vs. 5 digits). These findings thus indicate that attentional control is more involved in goal-based agency inferences than in prime-based agency inferences.

Recent work has also begun to explore the neural implementation of goal-based and prime-based agency inferences. First, a recent fMRI study provides evidence that goal-based agency inferences indeed make use of higher order cognitive processes (Renes, van Haren, Aarts, & Vink, 2015c). Specifically, this study showed activity in frontal and parietal regions such as the medial prefrontal cortex, bilateral superior frontal gyrus and inferior parietal lobule that was associated with participants' experienced agency over outcomes that matched previously set goals. The frontal regions found in this study had previously already been associated with goal- and social inferences (e.g., van Overwalle & Baetens, 2009) and self-referential processing (e.g., van Buuren et al., 2010; Northoff et al., 2006), whereas the inferior parietal lobule is often associated with comparing intended and actual outcomes (e.g., O'Connor et al., 2010). These findings were replicated in another agency inference study, again showing the involvement of parietal and frontal regions in goal-based agency inferences (Renes et al., 2016). Furthermore, in an electroencephalography (EEG) study into agency inferences, a measure of brain connectivity was computed to assess the potential communication route in cortical areas during goal-based agency inferences (Dogge, Hofman, Boersma, Dijkerman, & Aarts, 2014). In line with the findings obtained in the fMRI studies, clear connectivity between frontoparietal regions was established when participants experienced agency over outcomes matching previously set goals (Dogge et al., 2014).

For prime-based agency inferences, characterized by its implicit nature, the neural implementation turns out to be harder to capture. In an exploratory effort to examine the cortical processes involved in prime-based agency inferences, region of interest analysis showed the implication of frontal cortical regions similar to goal-based agency inferences, although to a lesser extent and in a less clear-cut way (Renes, van Haren, Aarts, Vink, unpublished data). Furthermore, an EEG study into prime-based inferences of agency also showed connectivity between frontal and parietal regions, but this was considerably weaker and more diffuse than the connectivity during goal-based inferences (Dogge et al., 2014).

In short, in the absence of motor prediction cues, goals and primes can guide agency inferences. Furthermore, they differ in that goals more strongly rely on attentional control to track progress towards achieving the goal, whereas primes rely on more automatic cognitive accessibility processes that do not necessarily rely on attentional control. These differences are corroborated by behavioral data where working memory was taxed. Furthermore, psychophysiological data acquired via fMRI and EEG also showed differences in the way goals and primes were neurally implemented, showing heavier reliance on higher cortical areas in goal-based than prime-based agency inferences.

Disruptions of healthy agency processing

So far, I have focused on agency inferences in individuals who are blessed with a healthy mental state. However, as has been evidenced in mental diseases, agency processing can be disturbed. That is, several mental disorders show deficits in agency processing, potentially leading to the symptoms that characterize these disorders. For example, a study with dysphoric participants –who are characterized by subclinical depression and negative self-concept– showed that priming the concept of self decreased dysphoric participants' feelings of causation in an action-outcome task (Aarts, Wegner, & Dijksterhuis, 2006). These effects were explained by assuming that self-primes trigger self-schemata of uncontrollability in dysphoric people (Bargh & Tota, 1988; Kuiper & MacDonald, 1982), thereby decreasing their experience of agency. Interestingly, priming with outcome information alleviated the effect of self-primes, such that agency inferences were raised to an equal level as in non-dysphoric participants who received an outcome-prime.

Another example of a disorder that is characterized by disturbances in agency processing is Obsessive-Compulsive Disorder (OCD). Here, patients generally exhibit symptoms that often include an inner sense of imperfection and incompleteness, leading to the impulse to redo an action or double-check (Coles, Frost, Heimberg, & Reaume, 2003). Research into motor-prediction processes in OCD has revealed that patients tend to be unable to sufficiently predict and suppress sensory consequences of their own actions, potentially explaining the persistent feelings of incompleteness even after properly executed action (Gentsch, Schütz-Bosbach, Endrass, & Kathmann, 2012). Furthermore, research has also suggested that OCD patients tend to focus too much on the actions they perform, forgoing attention to the outcomes of their actions, leading to deficits in prime-based inferences of self-agency (Belayachi, & van der Linden, 2010; see also van der Weiden et al., 2010; for similar effects as a function of manipulating attention to actions or outcomes).

The most prominent mental disorder that is characterized by disturbances in agency processing is schizophrenia. Because of this inherent link between agency problems and schizophrenia I will elaborate on it in more detail.

The case of schizophrenia. Patients with this debilitating disease often exhibit difficulties in distinguishing their own actions and outcomes from those of others. As a consequence, patients' autonomy and their professional and personal achievements are reduced and they experience problems in social interactions and relationships with family and peers (Walker et al., 2004). Initial research into agency disturbances in schizophrenia has identified deficits in motor-prediction processing

(Haggard, Martin, Taylor-Clarke, Jeannerod, & Franck, 2003; Shergill, Samson, Bays, Firth, & Wolpert, 2005; Voss et al., 2010). For example, one study (Haggard et al., 2003) yielded excessive intentional binding in patients with schizophrenia, potentially causing the tendency of some patients to overattribute outcomes to themselves.

Interestingly, research suggests that (over)attribution of agency in schizophrenia despite deficits in motor-prediction processes might follow from a compensating cognitive inferential mechanism that one has learned to apply during goal-based processing; however, this mechanism might operate more noisily and less accurately than in healthy individuals (Voss et al., 2010). A recent test specifically designed to investigate goal-based agency inferences in patients with schizophrenia, established that patients indeed show the ability (comparable to healthy controls) to infer agency in a goal-directed context (Renes et al., 2013; 2016). However, a neuroimaging study investigating goal-based agency inferences in patients with schizophrenia showed that despite their reported agency experiences, patients did not show the pattern of brain activation observed in healthy controls associated with these experiences (Renes et al., 2016). Appreciating the behavioral effects on agency inferences, it is likely that patients utilized a (hitherto unknown) compensatory mechanism that was not detected with fMRI, enabling them to experience agency in a highly controlled goal-based processing task.

The lack of a clear pattern of cortical activation during agency inferences in patients with schizophrenia might suggest inefficient neural processing, rendering patients vulnerable for misjudgments of agency in more complex (real-life) situations, where patients often experience difficulties in social functioning and communication. In such situations, where people often do not have the opportunity or time to form goals, healthy people can rely on prime-based agency inferences to successfully ascribe agency. Conversely, recent work has demonstrated that patients with schizophrenia are unable to rely on pre-activated outcome information to ascertain self-agency (Renes et al., 2013; 2015a). Indeed, when patients with schizophrenia encountered outcomes after action performance that matched previously primed outcomes, they did not experience more self-agency than when the outcome mismatched the prime, even after controlling for potential visual processing deficits of the primes (Renes et al., 2015a).

The impaired prime-based agency inference processing that characterizes schizophrenia is likely due to neurobiological impairments. This is not only suggested by the potentially inefficient goal-based agency inference processing, but also due to compromised white matter tract integrity related to schizophrenia (de Weijer et al., 2011; Ellison-Wright & Bullmore, 2009; Voineskos et al., 2010; Whitford, Kubicki, & Shenton, 2011). Previous research has suggested that primed information generally does not directly recruit frontal cortical structures (Baars, 1998; Dehaene & Naccache, 2001), rendering the integrity of frontoparietal fibers that transfer outcome-information potentially vital for agency inferences. Given the inherent diffuse cortical connectivity involved in prime-based agency inferences (Dogge et al., 2014), even subtle impairments to the integrity of these fibers could perturb such inferences. These abnormalities might underlie poor social interactions that often unfold rapidly and implicitly, posing a daily struggle for patients with schizophrenia.

In short, disturbances in agency processing are associated with severe mental disorders, often causing a devastating effect on a patient's autonomy, social interactions and well-being (Walker et al., 2004). In the special case of schizophrenia, research seems to indicate that predictive processes based on the motor system are impaired, potentially contributing to the disease's symptoms. However, as long as patients can operate in a goal-directed setting, they seem to overcome this impairment by applying cognitive inference to ascertain self-agency. Nevertheless, whereas healthy people can rely on subtle and implicit action-outcome information to infer self-agency in a context where goals cannot be readily formed, patients with schizophrenia show an inability to do so. This impairment might lead to difficulties in more complex social interactions, where information about causes and outcomes is often implicit and ambiguous.

Conclusions and discussion

The present chapter reviewed research aimed at addressing the processes that yield a sense of minimal self, i.e., the acute subjective experience of oneself as an agent. An understanding of the minimal self has been proposed to offer clues about the sources of the narrative self – the (re)construction of our personal experience. Specifically, the minimal self provides a window into the way the mind produces a sense of agency over operant action, and hence, how people might get to know and to express themselves by building further knowledge about what they want, can and how they feel about themselves when navigating through the physical and social world.

Our analysis indicates that when people engage in movements with a clear outcome in mind, the motor system can generally signal a sense of agency over sensory outcomes. However, motor-prediction processes can become unreliable or even absent, such as in more complex, ambiguous social situations. Self-agency can then readily be experienced through non-motor prediction processes, such as cognitive inferences of agency. The most prominent input for such inference process derives from information about action-outcomes itself. Indeed, such information has been clearly found to produce a sense of agency upon a match with the pre-activated information. Importantly, action-outcome information results from learning, that is, when one knows that an action can lead to a specific outcome. Accordingly, activating the representation of the outcome enhances experiences over controlling the action and resulting outcome, even though the action is not performed or leads to the outcome. The exact mechanism of how these experiences have evolved and are produced is an essential problem in its own right, and remains a topic of intriguing theorizing and empirical scrutiny (Dennett, 1991; Nørretranders, 1991; Prinz, 2004; Wegner, 2002). However, it is clear from the literature in psychology that these experiences are generally considered to form the basis for setting goals (e.g., Locke & Latham, 1990), assessing one's abilities (e.g., Bandura, 1977), feelings of worth (Rosenberg, 1965), and responsibility (Duval & Silvia, 2001). Thus, changes in these experiences might affect the way people consider and talk about themselves.

The research discussed in the present chapter points to multiple potential influences on the sense of agency. One central factor pertains to the individual's focus of attention when preparing and executing behavior. Specifically, the level at which people represent their behavior plays an important role in the matching process underlying experiences of self-agency (Pacherie, 2008). Take, for example, the act of turning on the light in a room. A person may represent this act in terms of moving her finger, pushing the light switch, or illuminating a room, and the level of attention to behavior determines whether she perceives the outcome of an action (e.g., tactile perception versus an illuminated room) to match with a pre-activated outcome representation (e.g., the room will be illuminated), several studies have indeed yielded results to suggest that when people identify or attend to their actions at a lower level (e.g., motor movements) rather than to the outcomes they produce, experiences of agency over action-outcomes are reduced (Damen et al., 2014; Dannenberg et al., 2012; van der Weiden et al., 2010).

Interestingly, the level at which individuals identify their behavior has also been related to psychological states, such as perceptions of social power, fear of failure and beliefs in a free will (Aarts & van den Bos, 2011; Dannenberg et al., 2012; Lynn et al., 2014; Obhi et al., 2012; Vallacher & Wegner, 1986). For instance, people who are inclined or made to believe that their behavior is predetermined rather than freely chosen are less inclined to take the outcomes of their actions into account and experience less agency over operant actions. Furthermore, a person who thinks he will fail on a task is likely to attend to the specifics of the task, and hence, experiences less agency when pre-activated task-outcome information and the actual outcome matches (Dannenberg et al., 2012). The general gist, then, is that setups that encourage people to (chronically) focus on the details of their actions, rather than the outcomes they produce, may decrease experiences of agency over action-outcomes in everyday life. It is not known, yet, how this weakening of the sense of agency affects the relation of the minimal self and narrative self, but it is possible that it forms the basis for breeding weaker beliefs of self-efficacy and self-worth and, as a consequence, discourage people to engage in action-control. Because this line of thought is speculative, it might be intriguing to examine how this relationship evolves and sustains as part of human development and socialization.

Furthermore, apart from the focus of attention, research suggests that people’s ability to rely on goal-based inferences to arrive at the experience of agency is diminished when their attentional control processes are heavily taxed, while prime-based agency inferences (due to their automatic nature of operation) are less sensitive to such cognitive load. Importantly, given that distraction and mental load are omnipresent in modern life, this observation may have implications for situations where individuals operate in a goal-directed fashion. In the context of law, moral judgments and human conduct, the experience of agency and responsibility are often assumed to be intertwined (Frith, 2014; Greene et al., 2009; Haggard & Tsakiris, 2009). Hence, discrepancies between instant personal experiences of agency and norms and rules about personal responsibility might occur when people are distracted or preoccupied during action performance. In other words, people might feel less responsible for goal-directed actions (either good or bad) while being distracted from the matter at hand. Whereas research suggests that people link their actions to social norms and rules by attributing causes of consequences of behavior to themselves or others (Tetlock, 1985; Weiner, 1985), little is known about whether and how this occurs when instant experiences of agency are attenuated or even absent. Future research thus might address this issue by examining how people learn to relate their capacity to act voluntarily to the feeling of responsibility and morality when agency experiences are substantially reduced.

A special group of people who suffer from such reduced (or at least distorted) experiences of agency are patients with schizophrenia. Research into self-agency experiences in these patients have yielded insight in both disturbances caused by the disease and in the mechanisms of how people experience agency in general. For schizophrenia, it is becoming increasingly clear that motor-predictive processes are disturbed (Haggard et al., 2003; Shergill et al., 2005), but that this can be compensated by patients' ability to infer agency in a goal-driven context (Renes et al., 2013;

2016). However, it is important to note that, similar to healthy individuals, such goal-based agency inferences are likely to be impaired under mental load. Furthermore, whereas healthy individuals are still able to sense agency in a context where only primed outcome information is at work (a situation that is rather common during everyday social interaction), patients are less capable of doing so (Renes et al., 2013; 2015a). Because goal- and prime-based inferences both contribute to the experience agency and social functioning, it is important to further examine how goal-based agency inferences can be elevated under cognitive load, and prime-based agency inferences in schizophrenia in particular.

To conclude, the present chapter addressed recent developments in the study of the minimal self. Specifically, I discussed how the acute subjective experience of oneself as an agent of behavior is generated by motor and non-motor prediction processes, provides input for subsequent action-control and can have downstream consequences for well-being and health. I am confident that the interest in the role of the self in action-control continues to surge, and I hope that the present analysis offers a point of departure to generate new insights into the foundation and capacity of volitional action and self-control.

Chapter 3

Attentional control and inferences of agency: Working memory load differentially modulates goal-based and prime-based agency experiences

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Abstract

Previous research indicates that people can infer self-agency, the experience of causing outcomes as a result of one's own actions, in situations where information about action-outcomes is pre-activated through goal-setting or priming. We argue that goal-based agency inferences rely on attentional control that processes information about matches and mismatches between intended and actual outcomes. Prime-based inferences follow an automatic cognitive accessibility process that relies on matches between primed and actual information about outcomes. We tested an improved task for a better examination of goal-based vs. primed-based agency inferences, and examined the moderating effect of working memory load on both types of inferences. Findings of four studies showed that goal-based, but not prime-based agency inferences dwindled under working memory load. These findings suggest that goal-based (vs. primed-based) agency inferences indeed rely on attentional control, thus rendering goal-based agency inferences especially prone to conditions that modulate goal-directed control processes.

Introduction

The sense of agency – the feeling that one causes one's own actions and their subsequent outcomes – is a pervasive and fundamental aspect of human self-perception and social functioning. The sense of agency has been explained in two separate, but complementary models. Initially, self-agency has been studied as a product of comparator processes described in models of motor control (Frith, Blakemore, & Wolpert, 2000; Wolpert & Flanagan, 2001). The execution of a goal-directed action is accompanied by the prediction of sensory action-outcomes based on internal copies of movement-predicting signals (i.e., efference copies) generated by the sensorimotor system. These internal motor predictions are generally short-lived but very reliable, and sensory outcomes are readily perceived as self-produced until this prediction no longer corresponds with the actual outcomes. However, some situations are too ambiguous for motor predictions to be reliable. Interestingly, people still experience self-agency in these situations, for example when there is no causal link between action and following event (Moore & Haggard, 2008), when people move involuntarily (Dogge, Schaap, Custers, Wegner, & Aarts, 2012; Moore, Lagnado, Deal, and Haggard, 2009) or when actions have multiple causes and outcomes (van der Weiden, Ruys, and Aarts, 2013b; Wegner, 2002). This recent work points to an additional –non-motor prediction– process of agency experiences. This so-called inference account of agency suggests that when motor signals are absent or unreliable, agency can still be established when there is a match between the actual outcome and pre-activated information that is related to the outcome (Aarts, Custers, & Wegner, 2005; Wegner & Wheatley, 1999).

Whereas the motor-prediction process of agency has received much theoretical and empirical attention (see Hughes, Desantis, & Waszak, 2013), research on the mechanism underlying agency inferences has been relatively limited. The present research aims to further the understanding of agency inferences by examining how two distinctive sources of information shape the experience of self-agency (Aarts et al., 2005; van der Weiden et al., 2013b). Firstly, the experience of self-agency can emerge from *goal-based* inferences, which is the case in situations where people engage in goal-oriented behavior and their attention is directed towards subsequent outcomes they intend to attain. Additionally, other situations can give rise to *prime-based* self-agency inferences, for example when people engage in actions that are more spontaneous and prepared without much attention, and observe outcomes that are in line with information that is merely pre-activated in mind. Both types of agency inferences can occur independent of motor predictions, and contribute to a sense of selfhood, feeling of control and social behavior during daily social interaction (Frith, 2013). Despite the importance of both types (goals and primes) of agency inferences for human functioning, little is known, however, about whether and how goal and prime-based inferences differ in shaping self-agency experiences. Here, we report a set of studies that (a) tested an agency inference task that allows for a clear examination of goal-based vs. primed-based agency inferences, and (b) explored whether the occurrence of goal-based agency inferences vs. primed-based agency inferences differ as a function of attentional control processes that are installed by goal-directed thought and action.

As alluded to above, research on agency inferences distinguishes two routes to the experience of agency that are based on the pre-activation of outcome information. Based on whether actual outcomes match or mismatch with the mental preview of the outcome, self-agency is inferred. In daily life this is often experienced as a result of our explicitly set goals as part of intentional behavior. That is, if one had the goal of bringing about a specific outcome and that outcome actually occurred, one must have caused it. If there is a mismatch, one may infer that one was not the cause. However, recent findings suggest that self-agency experiences can also arise from a more implicit source of information. Specifically, observing action-outcomes that were previously primed also provides the feeling we caused the outcome to occur. This implicit route pertains to agency inferences that can result from instances in which the source of the experience of agency is likely to remain outside of awareness, as is, for example, often the case during social interactions. Both goal-setting and mere priming have been found to contribute to agency inferences across various tasks (e.g., Aarts et al., 2005; Linser & Goschke, 2007; Sato, 2009; van der Weiden, Aarts, & Ruys, 2011; van der Weiden et al., 2013b; Wegner & Wheatley, 1999), suggesting that agency experiences result from a cognitive process that relies on agency-relevant outcome information, irrespective of whether this information is pre-activated by goal-setting or priming.

However, recent research suggests that goals and outcome-primes impact self-agency experiences differently. Specifically, whereas explicitly set goals to produce an action-outcome and implicit priming of the action-outcome both increase agency experiences when the actual outcome matches the pre-activated outcome, only goals substantially decrease agency experiences when outcomes mismatch the goal. This finding has been taken to suggest that the underlying mechanism of goal-based agency inferences and prime-based agency inferences differ (van der Weiden et al., 2013b). Building on the proposed distinctive effects of goal-setting and mere priming on information processing and behavior (Aarts, 2012; Dehaene, Changeux, Naccache, Sackur, & Sergent, 2006; Fishbach & Ferguson, 2007), goal-based effects on agency inferences are considered to involve attentional control in which the person attends to specific outcomes she wants to obtain. However, outcome-priming effects on agency inferences are proposed to rely on a more automatic cognitive accessibility process that follows principles of spreading of activation and, in principle, does not heavily engage attentional control processes (van der Weiden et al., 2013b). Accordingly, goal-setting (but not outcome-priming) causes individuals to focus attention on the attainment of the intended outcome and to process feedback information and learn from expected (matches) and unexpected (mismatches) results (Baddeley, 2007; Conway et al., 2005; Carver & Scheier, 1998; Custers & Aarts, 2007; Frith et al., 2000).

If this notion about the difference between goal-based and prime-based agency inferences is correct, then taxing attentional control (i.e., by working-memory load) should differentially affect these inferences. Increasing working-memory load has been demonstrated to diminish the ability to freely focus attention on secondary tasks and process feedback information, showing impaired performance in goal attainment (e.g., Baddeley, 1986; 2007; Hester & Garavan, 2005; Lavie, Hirst, de Fockert, & Viding, 2004; Lavie, 2010; Ward & Mann, 2000). Accordingly, taxing attentional control should deteriorate goal-based, but not prime-based agency inferences, as outcome-priming effects are suggested to not heavily rely on attentional control. There is some preliminary evidence supporting this notion (Hon, Poh, & Soon, 2013). Hon and colleagues (2013) asked their participants to set goals to produce an outcome in an action-outcome dependency task (pressing an up and down arrow to move a dot in the direction consistent or not with the arrow) and required them to maintain either two or six consonants in memory while performing the task. Results showed that a higher working-memory load (i.e., remembering six consonants) caused decreased experiences of agency of matching (but not mismatching) outcomes. Although these findings suggest that working-memory load affects experiences of agency, this study is unclear in delineating motor prediction from cognitive inferences. Moreover, participants only set goals and were not primed with outcome information. Accordingly, this study does not directly speak to the issue of whether goal-based and prime-based agency inferences differ in the way they materialize.

The present study

The present study serves two main goals. First, we present two experiments to replicate the differential effects of goal-based and prime-based agency inferences as a function of matching and mismatching outcomes by using a new and improved agency task in which action and outcome are independent. Previous studies (Aarts et al., 2005; Renes, Vermeulen, Kahn, Aarts, & van Haren, 2013; van der Weiden et al., 2013b) addressing this issue have all been employing a specific procedure, one that does allow goal-setting to differ from outcome-priming in terms of preparation before performing an action and observing an outcome. Specifically, in goal trials participants first think about which outcome they aim to attain (for 3 seconds) and formulate their action-goal accordingly (e.g., pressing a key to stop the rapid alternation of words on a computer screen at a specific word), and then engage in the stimulus alternation task before performing an action (pressing a key) and observing the well-prepared outcome. In the prime trials, participants engage directly in the stimulus alternation task, and are primed with the outcome (e.g., a word) just before they press a key and observe the outcome. In other words, goal-based inferences were tested in a setting where goals could be prepared in an unconstrained way, whereas information is not processed as freely in prime-based inferences. This poses the question whether goals only impact self-agency experiences when processed extensively and without interruption, and whether the way primes are presented might prevent them from impacting self-agency experiences like goals do. Therefore, the present study aims to first demonstrate the robustness of the current ideas by testing a more internally valid task, where information about both goals and primes is presented amidst the alternation of information and at the same moment in time, thereby ensuring a more equal empirical test for the impact of goals and primes on agency inferences.

The second goal of the present study is to employ the new agency inference task to explore whether goal-based agency inferences rely more on attentional control than prime-based inferences do. For this purpose, we examined the occurrence of goal-based and primed-based agency inference under different levels of working memory load. If goal-based agency inferences indeed rely on attentional control, then the impact of goals on agency experiences should diminish when working memory is taxed. Because primed-based agency inferences are suggested to not engage much attentional control processing, taxing working memory are expected to not (or to a lesser extent) modulate the impact of primes on agency inferences.

Experiment 3.1a

In order to test the differential effects of goal-based and prime-based self-agency inferences, we used a task in which participants perform an action (pressing a key) that is followed by an outcome (the color word red or blue presented on the computer screen) that either matches or mismatches the goal or primed outcome. Importantly, goals and primes are presented at a similar time within the same distractive task before performing the action, ensuring participants had equal opportunity to process this information and prepare the action.

Methods

Participants

Experiment 3.1a included twenty-five right-handed participants (M_{age} = 22.24, *SD* = 3.24; 15 females). All participants received course credit or a monetary reward in exchange for their participation.

Procedure

The agency inference task was adapted from van der Weiden and colleagues (2013b, experiment 2). Before starting the experiment, participants were told that the task was designed to assess how experiences of self-agency come and go, and were asked to indicate how these experiences vary during the task. Similar to playing a slot machine, this task required participants to stop a sequence of rapidly presented information to produce a particular outcome (i.e., the color word red or blue) on the computer screen. Specifically, participants pressed a key in response to a cue while viewing alternating letter strings. Upon pressing this key, the stream of letter strings stopped and the color word ‘red’ or ‘blue’ was presented. This outcome could either match or mismatch with prior knowledge regarding the action-effect (i.e., goals or outcome primes; see below). In addition, participants learned that the computer could have caused the presented outcome as well. In other words, the cause of the observed effect was ambiguous (Aarts et al., 2005; Sato, 2009). After viewing the effect following their key press, participants reported their feelings of agency over causing the perceived effect.

Each trial consisted of five different phases: an exposure phase, a filler phase, an action phase, an outcome phase and a rating phase (see Figure 3.1). The last four phases were identical for all trials. During the filler phase, participants attended to rapidly alternating letter strings. This interval served as a delay between exposure to pre-activated information and the action that was also present in previous work on agency inferences (e.g., van der Weiden et al., 2013b). In the action phase, participants responded to a circle that was presented above or below the letter strings by pressing the corresponding upper or lower key on a response box with their right index finger (required upper and lower key presses were evenly distributed and randomly selected across all experimental trials). The interval in which a response could be given lasted 800 milliseconds. If participants pressed the key within this interval, the strings continued to alternate until the end response interval, whereas if they pressed too late, an error message occurred and the trial was processed as missing.

Following the action phase, the color word ‘red’ or ‘blue’ (counterbalanced between trials) was shown for 1500 milliseconds. A 100 milliseconds delay was added between the action and outcome phase to make the two phases more distinguishable. To ensure that participants would maintain looking at the letter strings, participants were told that pressing the key during the presentation of a string containing the letter R (e.g., MTFR) would cause the word ‘red’ to appear, whereas a key press during the presentation of a string containing the letter ‘B’ (e.g., NXBCZ) was followed by the word ‘blue’. Letter strings were presented for 2 cycles on a 60 Hz LCD screen (thus, presentation time was ±33 ms). In reality, the computer determined the presentation of color words. Thus action and outcome were independent, ruling out the potential contribution of motor-prediction cues.

After each trial, experienced agency was assessed during a rating phase by asking participants to what extent they felt their key press caused the presented color word to occur. They could respond by moving a square on an 8-point analogue scale ranging from ‘*not me*’ (1) to ‘*me*’ (8). The square was positioned in the middle of the scale and participants had to provide their response by moving the square to the left (not me) or the right (me) of the scale.

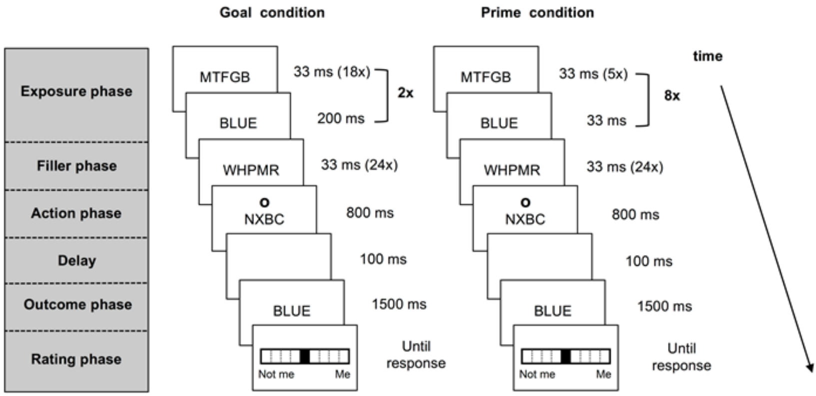

Figure 3.1. Schematic presentation of a match trial in the agency inference task for the goal condition and the prime condition. Presentation times are rounded based on a 60 Hz monitor (e.g., 33 ms. equals 2 cycles).

Pre-activated information about outcomes. As mentioned earlier, the exposure phase was not identical for all trials. Specifically, in this phase information regarding the outcome was activated by either goals or by primes.

In goal trials, participants were exposed to a series of 18 letter strings followed by a color word that was clearly presented on the screen for 200 milliseconds. This sequence was repeated twice, such that participants were two times exposed to the goal within a 1600 milliseconds period (see Figure 3.1). Participants were instructed to form the goal to produce the color word that appeared within the series of letter strings.

In outcome prime trials, participants were exposed to a series of 5 letter strings followed by a briefly presented color word (±33 ms). This sequence of events was repeated eight times, resulting in a total of 8 primes within a 1600 milliseconds period (see Figure 3.1). Note that the duration of the exposure phase was identical for both types of pre-activation. Importantly, participants were not instructed to formulate a goal in the prime trials.

The goal trials and outcome prime trials were presented in two separated (counterbalanced) blocks which each consisted of 64 randomly presented trials. In half of the trials, pre-activated color words corresponded with the actual outcome, whereas in the other half of the trials they did not correspond with this outcome. Before the critical trials of the first block, participants first practiced (eight trials) both blocks in counterbalanced order. Additionally, the second block was preceded by four practice trials to ensure participants' understanding of the task. In between the two blocks participants were allowed to have a break. Furthermore, participants paused for thirty seconds after completing the first half (i.e., 32 trials) of each block.

Results

Due to the absence of a key press within the interval of the action phase, 5.7% of the total number of trials were excluded from the analyses. Mean agency experiences were calculated for matches and mismatches in the goal trials and in the prime trials. Averaged self-agency experiences were subjected to a 2 (Type of pre-activation: Goal vs. Outcome prime) by 2 (Matching: Match vs. Mismatch) repeated-measures ANOVA. See Figure 3.2 for an overview of the results. The analysis yielded no main effect for Type of pre-activation, $F(1,24) = 0.43$, $p = .52$, $\eta\rho^2 = .02$, showing equal average self-agency experiences in both the goal and outcome prime trials. As expected, the main effect of Matching was significant, $F(1,24) = 10.43$, $p = .004$, $\eta\rho^2 = .30$, indicating that when outcome-information matched the actual outcome, more self-agency was experienced than when it mismatched the actual outcome. Furthermore, a Type of pre-activation by Matching interaction was found, $F(1,24) = 8.91$, $p = .006$, $\eta\rho^2 = .27$. To gain more insight into this interaction, follow-up analyses were performed. In both tasks the main effect of Matching was significant (Goal: $F(1,24) = 10.18$, $p = .004$, $\eta\rho^2 = .30$; Outcome prime: $F(1,24) = 7.38$, $p = .012$, $\eta\rho^2 = .24$), where the difference in effect size between the tasks qualifies the interaction between Type of pre-activation and Matching. Furthermore, order of the type of trials (i.e., a block of goal trials first, or prime trials first) did not influence these patterns (interaction of Type of pre-activation and Matching and Order: $F(1,23) = 1.22$, $p = .281$, $\eta\rho^2 = .05$).

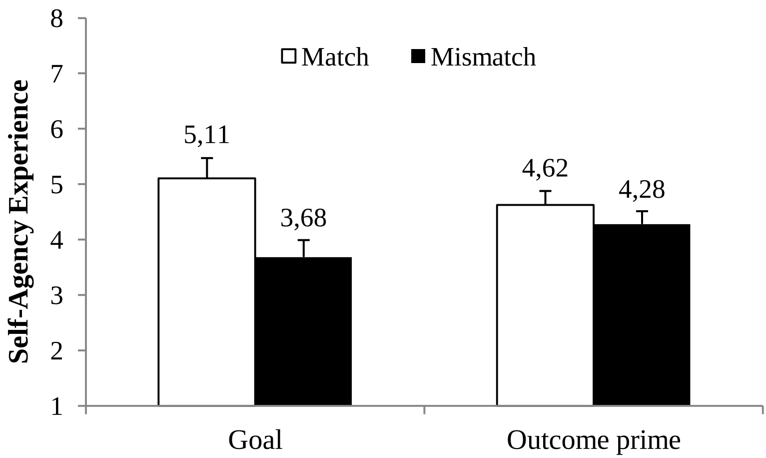

Figure 3.2. Self-agency experiences as a function of Type of pre-activation and Matching for experiment 3.1a. Error bars indicate the standard error of the mean.

Discussion

In line with expectations, the data indicate that participants experienced stronger self-agency when outcomes matched pre-activated outcome information as compared to when outcomes mismatched such information. Furthermore, the effect of matching was more pronounced for goal-based than for prime-based agency inferences. Supported by the results of Experiment 1a, we aimed to provide an independent direct replication of these findings in Experiment 1b.

Experiment 3.1b

Methods

Participants

Based on the effect size of the interaction effect observed in Experiment 3.1a (Cohen's d_z = 0.60), and a power of 0.80 (α = 0.05), we calculated that we needed at least 25 participants to replicate the effect. We recruited thirty-two undergraduates to take part in Experiment 1b. One participant did not follow instructions, as this person did not vary on agency ratings across the trials. This participant was therefore excluded from analyses. After the exclusion, 31 participants (M_{age} = 23.48, *SD* = 3.83; 16 females) were included in the analyses. All participants received course credit or a monetary reward in exchange for their participation.

Results

Due to the absence of a key press within the interval of the action phase, 2.5% of the total number of trials were excluded from the analyses. Participants' self-agency experiences were averaged and subjected to a 2 (Type of pre-activation: Goal vs. Outcome prime) by 2 (Matching: Match vs. Mismatch) repeated-measures ANOVA (see Figure 3.3). Overall, the analyses yielded very similar results as in the previous experiment. No main effect was found for Type of pre-activation, $F(1,30) = 0.90$, $p = .350$, $\eta\rho^2 = .03$, showing equal average self-agency experiences in both the goal and outcome prime trials. Again, the main effect of Matching was significant, $F(1,30) = 16.05$, $p < .001$, $\eta\rho^2 = .35$, showing stronger self-agency experiences when outcome-information matched the actual outcome than when it mismatched the actual outcome. Additionally, the Type of pre-activation by Matching interaction was found to be significant, $F(1,30) = 14.61$, $p < .001$, $\eta\rho^2 = .33$. The follow-up analyses demonstrated a similar difference in effect size of the (significant) goal and outcome prime effects of Matching (Goal: $F(1,30) = 17.55$, $p < .001$, $\eta\rho^2 = .37$; Outcome prime: $F(1,30) = 5.57$, $p = .025$, $\eta\rho^2 = .16$). Finally, the order of the trials did not influence these patterns (interaction of Type of pre-activation and Matching and Order: $F(1,29) = 1.50$, $p = .230$, $\eta\rho^2 = .05$).

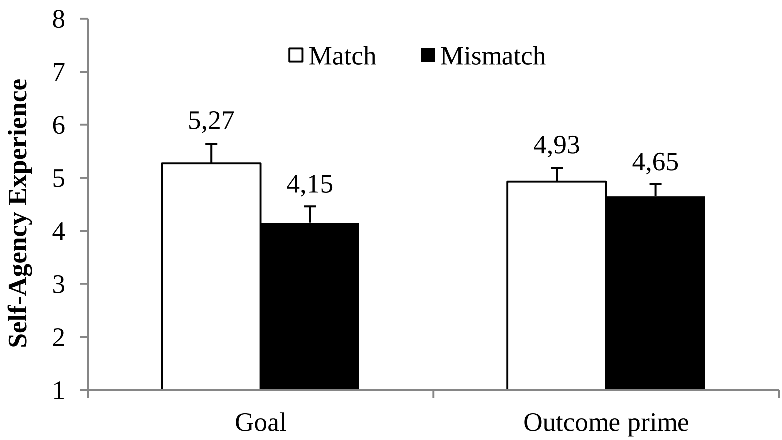

Figure 3.3. Self-agency experiences as a function of Type of pre-activation and Matching for experiment 3.1b. Error bars indicate the standard error of the mean.

Combined results of Experiments 3.1a and 3.1b

To assess the combined effects across the two studies, averaged self-agency ratings of all 56 participants were subjected to a 2 (Type of pre-activation: Goal vs. Outcome prime) by 2 (Matching: Match vs. Mismatch) by 2 (Experiment: 3.1a vs. 3.1b) repeated-measures ANOVA. The analysis yielded no main effects of Experiment, $F(1,54) = 1.72$, $p = .196$, $\eta\rho^2 = .03$, or Type of pre-activation, $F(1,54) = 1.18$, $p = .282$, $\eta\rho^2 = .02$, indicating that average self-agency experiences did not differ between the separate experiments or Types of pre-activation. However, the main effect of Matching was significant, $F(1,54) = 25.47$, $p < .001$, $\eta\rho^2 = .32$, showing that overall, outcomes that matched pre-activated information induced stronger agency experiences than when the outcomes mismatched this information. Furthermore, this effect was moderated by the Type of pre-activation, as indicated by the significant interaction of Type of pre-activation and Matching, $F(1,54) = 22.25$, $p < .001$, $\eta\rho^2 = .29$. Mean agency experiences are presented in Figure 3.4.

The interaction shows a larger difference between match and mismatch conditions in goal than in outcome prime trials (Goal: $F(1,54) = 25.72$, $p < .001$, $\eta\rho^2 = .32$; Outcome prime: $F(1,54) = 12.94$, $p = .001$, $\eta\rho^2 = .19$). Furthermore, differences in agency experiences between the goal and prime trials are more pronounced in the mismatch condition, $F(1,54) = 16.20$, $p < .001$, $\eta\rho^2 = .23$, than in the match condition, $F(1,54) = 9.71$, $p < .001$, $\eta\rho^2 = .15$ (cf. van der Weiden et al., 2013b).

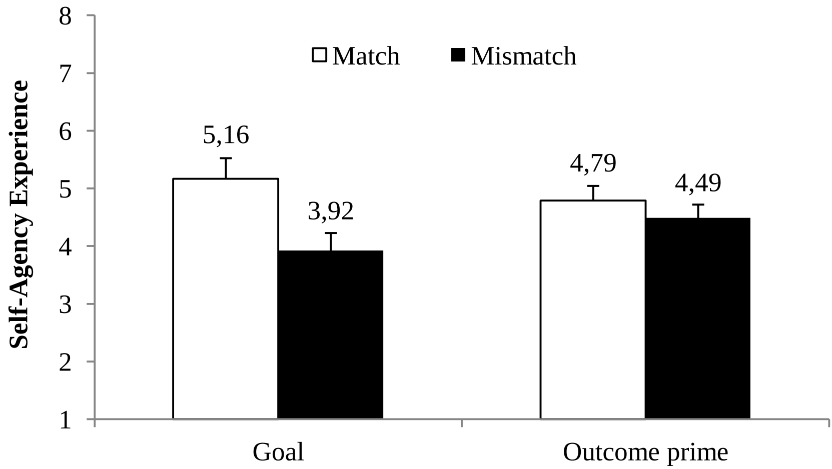

Figure 3.4: Self-agency experiences as a function of Type of pre-activation and Matching, collapsed across Experiments 3.1a and 3.1b. Error bars indicate the standard error of the mean.

Discussion

The findings of two studies show the robustness of goal-based and prime-based agency inferences in a paradigm devoid of previous shortcomings in timings and exposure times. In Experiments 3.1a and 3.1b, both goals and outcome primes are presented in equivalent time windows before the presentation of the action-outcome, ensuring that both sources of information have equal opportunity to affect self-agency experiences. Results showed that, whereas both goals and primes affected experiences of agency, goal-based agency inferences more strongly relied on matching and mismatching information than prime-based agency inferences. These findings replicate previous investigations into goal-based and prime-based self-agency inferences (Aarts et al., 2005; Renes et al., 2013; van der Weiden et al., 2013b), lending credence to the idea that the differential effects for both routes are likely no artefacts of the specific paradigm employed in these studies.

However, in order to examine whether attentional control processes modulate these differential effects, more evidence is needed. Accordingly, Experiment 3.2 and 3.3 will add a working memory load manipulation to the task. Specifically, based on earlier work (Hon et al., 2013) we created a low working memory load condition in Experiment 3.2 by asking participants to remember two digits for the duration of a self-agency trial, after which they had to recall a specific digit of the digit span. This low load of working memory is expected to not affect goal-based and prime-based agency inference. However, as we had no prior knowledge about how heavy the digit span load would be in this specific agency inference task for more than two digits, we decided to explore the effects of both four and five digits. A next study (Experiment 3.3) would then serve to replicate the effects of working memory load on goal-based vs. prime-based agency inferences. As we argued in the introduction, applying a heavier working memory load was expected to reduce goal-based agency inferences, but not (or to a lesser extent) prime-based agency inferences.

Experiment 3.2

Methods

Participants

Due to the exploratory nature of this experiment, and the lack of knowledge about the size of the specific interaction effect between Type of pre-activation and Working memory load, no power analysis could be performed and participant recruitment erred on the side of caution. Accordingly, 75 undergraduates were recruited to participate in this experiment and received a monetary reward or course credit for participation. One participant’s data was lost due to a technical failure. Furthermore, one participant’s data was excluded from further analysis because (s)he failed to respond to any of the digit span retrievals. Finally, like in Experiment 3.1b, three participants did not follow instructions, as they did not vary on agency ratings across the trials. These participants were also excluded from analyses. After exclusions, 70 participants (45 females; M_{age} = 22.06, SD = 3.13) were included in the analyses.

Procedure and self-agency task

The agency task was identical to the one in the previous experiments, with one exception. A working memory load manipulation was introduced in the goal and outcome-prime self-agency trials. Before each trial, participants were required to remember two (low load condition), four (medium load condition) or five (high load condition) digits for the remainder of the trial. The agency part of the trial then proceeded as in Experiments 3.1a and 3.1b, until the participant provided a self-agency rating. Then, participants were probed for free recall of one of the digits.

Events in a trial

With the addition of a digit encoding phase at the beginning of each trial and a digit retrieval phase at the end, each trial now consisted of seven phases. In the encoding phase, participants were presented with either two, four or five digits at the center of the screen, each digit separated with a space from the next. Digits ranging from 0 to 9 were randomly selected each trial, allowing no duplicates to maintain a similar level of difficulty across trials of each condition. The duration of this phase was dependent on the number of digits, allowing one second of exposure for each digit (i.e., two seconds in the low load condition, four in the medium load condition, and five in the high load condition).

In the digit retrieval phase, one of the digits was probed with a randomly selected question, querying a digit before or after another digit (e.g., in a digit span of 3 5, "what digit was presented before 5?" Or "what digit was presented after 3"). Irrespective of condition, the retrieval phase lasted a maximum of four seconds or until a response was given. After this, participants received one second of feedback regarding the accuracy of their answer. If no answer was given, the answer was classified as incorrect and the feedback instructed participants to respond faster.

In order to accommodate the increased length of the trials and the potential additional fatigue of the participants, the number of trials was reduced. Accordingly, the goal trials and outcome prime trials were presented in two separated (counterbalanced) blocks which each consisted of 48 randomly presented trials. In half of the trials, pre-activated color words corresponded with the actual outcome, whereas in the other half of the trials they did not correspond with this outcome. Furthermore, the working memory load levels were also evenly divided over the trials. Participants first practiced both types of trials in the counterbalanced order before the onset of the experiment (8 trials per practice block without the working memory load manipulation, then 4 trials including working memory load for the first block). After completing these practice trials participants completed the first type of pre-activation trials, followed by the second type of pre-activation trials (4 practice trials including the working memory conditions preceded this second block). In between the two blocks participants were allowed to have a break. In addition, participants paused for thirty seconds after completing every third (i.e., 16 trials) of each block of trials.

Manipulation checks

To ascertain a difference in working memory load between the low, medium and high load condition conditions, several measures were collected for analyses. First, upon completion of the task, participants received three questions probing the difficulty of each digit spans (i.e., “how difficult was it to remember two (or four/five) numbers throughout the trials?”; 9-point likert scale, ranging from ‘*not at all’* [1] to ’*very’* [9]), in order to establish participants’ subjective difficulties of engaging in the three different working memory load conditions. Furthermore, the response time to the working memory probes and the proportion of accurate working memory performance were assessed for each load condition (see also Hon et al., 2013).

Results

Manipulation checks

The subjective difficulty of remembering the digit spans, the response time to the working memory probes and the proportion of accurate working memory performance were subjected to a repeated measures ANOVA with Working memory load (Low vs. Medium vs. High) as a within-subjects factor. All analyses examined a linear trend effect of Working memory load. First, the ANOVA yielded differences on the subjective measure of difficulty, $F(1,68) = 19.26$, $p < .001$, $\eta\rho^2 = .22$; participants reported that remembering 5 digits was more difficult ($M_{High} = 3.96$, $SD = 2.42$) than remembering 4 digits ($M_{Medium} = 3.07$, $SD = 1.85$) and that remembering 4 digits was more difficult than 2 digits ($M_{Low} = 2.64$, $SD = 2.13$); $t(69) = -4.10$, $p < .001$, and $t(69) = -1.94$, $p = .056$, respectively. Furthermore, there were strong differences between the load conditions on the response time to the working memory probes, $F(1,68) = 497.88$, $p < .001$, $\eta\rho^2 = .88$; participants were slower in the higher (5 digits) load condition (M_{High} = 2166 ms, $SD = 270$) than in the medium (4 digits) condition (M_{Medium} = 2038 ms, $SD = 280$) and they were slower in the medium condition than in the low (2 digits) load condition (M_{Low} = 1413 ms, $SD = 298$); $t(69) = -4.92$, $p < .001$, and $t(69) = -19.58$, $p < .001$, respectively. Finally, the ANOVA on the accuracy measure showed differences between conditions, $F(1,68) = 10.42$, $p = .002$, $\eta\rho^2 = .13$; participants were equally accurate in the high load condition (M_{High} = 83.6%, $SD = 15.2$) and in the medium load condition (M_{Medium} = 83.9%, $SD = 13.1$), but they clearly were less accurate in the medium load condition than in the low load condition (M_{Low} = 89.2%, $SD = 8.4$); $t(69) = 0.26$, $p = .79$, and $t(69) = 3.28$, $p = .002$, respectively. Thus, whereas the 4 and 5 digit load conditions resulted in statistically indistinguishable effects on the accuracy measure, overall the pattern of findings on the three checks indicates that our working memory load manipulation was successful.

Self-agency Experiences

Due to the absence of a key press within the interval of the action phase, 3.9% of the total number of trials was excluded from the analyses. Averaged self-agency experiences were subjected to a 2 (Type of pre-activation: Goal vs. Outcome prime) by 2 (Matching: Match vs Mismatch) by 3 (Working memory load: Low vs. Medium vs. High) repeated-measures ANOVA. The results yielded no main effect of Type of pre-activation, $F(1,69) = 0.44$, $p = .51$, $\eta\rho^2 = .01$, nor a main effect of Working memory load, $F(1,68) = 1.71$, $p = .20$, $\eta\rho^2 = .02$. The main effect of Matching was significant, $F(1,69) = 19.08$, $p < .001$, $\eta\rho^2 = .22$, prompting stronger self-agency experiences when pre-activated outcome information matched rather than mismatched action outcomes. This main effect of matching was qualified by a significant interaction with Type of pre-activation, $F(1,69) = 14.89$, $p < .001$, $\eta\rho^2 = .18$. In line with the previous findings, the effect of Matching was more pronounced for the goal-based agency inferences, $F(1,69) = 20.27$, $p < .001$, $\eta\rho^2 = .23$, than for the prime-based agency inferences, $F(1,69) = 4.01$, $p = .049$, $\eta\rho^2 = .06$.

Simple main effect analyses revealed that within the goal trials, there was a significant effect of Matching in Low, $F(1,69) = 20.65$, $p < .001$, $\eta\rho^2 = .23$, Medium, $F(1,69) = 21.21$, $p < .001$, $\eta\rho^2 = .24$, and High load conditions, $F(1,69) = 13.23$, $p = .001$, $\eta\rho^2 = .16$. With respect to our specific hypothesis, higher Working memory load reduced the effect of Matching at trend level as indicated by the interaction of Matching and Working memory load, $F(1,68) = 3.42$, $p = .069$, $\eta\rho^2 = .05$. The outcome prime trials also yielded an interaction of Matching and Working memory load, $F(1,68) = 4.25$, $p = .043$, $\eta\rho^2 = .06$. However, the pattern was found to be reversed: the high load condition showed a significant effect of Matching, $F(1,69) = 7.89$, $p = .006$, $\eta\rho^2 = .10$, whereas both the Medium, $F(1,69) = 1.94$, $p = .168$, $\eta\rho^2 = .03$, and Low levels, $F(1,69) = 0.29$, $p = .592$, $\eta\rho^2 = .00$, did not. These differential effects of working memory load on agency experiences within goal and prime conditions were corroborated by the three-way interaction between Type of pre-activation, Matching and Working memory load, $F(1,68) = 6.38$, $p = .014$, $\eta\rho^2 = .09$. Figure 3.5 presents this three-way interaction effect on agency ratings. For clarity of interpretation, differences scores between match and mismatch trials for each condition are displayed.

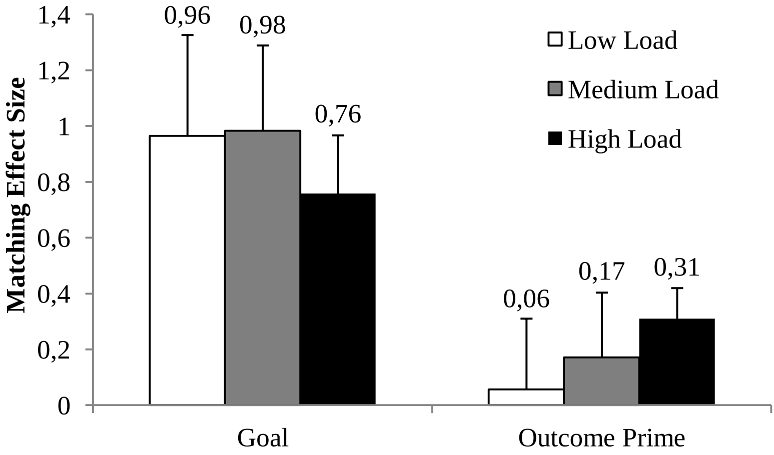

Figure 3.5. Self-agency experiences of Experiment 3.2 as a function of Type of pre-activation and Working memory load. For clarity of interpretation, differences scores between match and mismatch trials for each condition are displayed. Error bars represent standard errors of the mean.

Discussion

The findings in Experiment 3.2 show that goals have a larger impact on self-agency inferences than primes. These findings replicate the results of Experiment 3.1. Furthermore, working memory load modulated self-agency experiences differently for both goals and primes. In the goal condition, high working memory load reduced the effect of matching compared to low working memory load, as was hypothesized. In the outcome prime condition, however, the data suggest that while the effect of matching is significant in the high load condition, the effect of matching is diminished in the medium and low load conditions. In light of the findings of Experiment 3.1, in which outcome priming shows an effect without load, this is an unexpected result. Importantly, the effect of matching in the high working memory load condition is significant, as is congruent with our hypothesis. We do not know yet whether the decline effect of matching in the low and medium conditions effect is a fluke, or an effect of our specific working memory manipulation in the agency task at hand. However, we have no other explanations that can be supported by the data. Instead of speculating about the origin of this unexpected finding, it is more important to verify whether this pattern holds in Experiment 3.3. Experiment 3.2 showed that contrasting the low and high working memory load conditions provided the clearest demonstration of the effects (both on the manipulation checks and self-agency ratings), therefore Experiment 3 will only include the low and high load conditions.

Experiment 3

Methods

Participants

Based on the effect size of the three-way interaction effect observed in Experiment 3.2 (Cohen's $d_z = 0.30$), and a power of 0.80 ($\alpha = 0.05$), we would need 89 participants to replicate the effect. However, because we reduced the working memory load manipulation to two levels, we were also able to increase within participant power by doubling the number of trials (from 8 to 16) in each cell of the 2 (Type of pre-activation: Goal vs. Outcome prime) by 2 (Matching: Match vs. Mismatch) by 2 (Working memory load: Low vs. High) in the within participants design. Accordingly, we recruited 81 undergraduates who participated in the study and received a monetary reward or course credit for participation. In line with the previous experiments, six participants did not follow instructions and had to be excluded from analyses, as they did not vary on agency ratings across the trials. Hence, 75 participants (46 females; $M_{age} = 20.73$, $SD = 3.44$) were included in the final analyses.

Procedure and self-agency task

The working memory load manipulation was brought down to two levels, i.e., two or five digits (low vs. high working memory load, respectively). The number of trials per type of pre-activated outcome information was increased to 64 to increase power and allow for an equal distribution of trials per cell of the full design. This resulted in 32 trials per working memory load condition in each block, half of which had outcomes that matched pre-activated outcome-information, whereas the other half did not.

Results

Manipulation checks

The subjective difficulty of remembering the digit spans, the response time to the working memory probes and the proportion of accurate working memory performance were subjected to a repeated measures ANOVA with Working memory load (Low vs. High) as a within-subjects factor. All analyses yielded the expected main effect of Working memory load. First, participants reported that remembering five digits was more difficult than remembering two digits (M_{Low} = 2.92, *SD* = 1.98; M_{High} = 4.08, *SD* = 2.23; $F(1,74) = 21.46$, $p < .001$, $\eta\rho^2 = .23$). Response times to digit probes were slower in the high load condition than in the low load condition (M_{Low} = 1321 ms, *SD* = 245 ms; M_{High} = 2166 ms, *SD* = 256 ms; $F(1,74) = 848.61$, $p < .001$, $\eta\rho^2 = .92$). For the accuracy, participants were less accurate in the high load condition than in the low load condition (M_{Low} = 88.9%, *SD* = 9.1%; M_{High} = 83.4%, *SD* = 12.7%; $F(1,74) = 16.42$, $p < .001$, $\eta\rho^2 = .18$). These findings thus indicate that attentional processes were more taxed in the high working memory condition than in the low working memory condition.

Self-agency experiences

Due to the absence of a key press within the interval of the action phase 3.8% of the total number of trials were excluded from the analyses. Averaged self-agency experiences were subjected to a 2 (Type of pre-activation: Goal vs. Outcome prime) by 2 (Matching: Match vs. Mismatch) by 2 (Working memory load: Low vs. High) repeated-measures ANOVA (see Figure 3.6). The analyses yielded a main effect of Working memory load, $F(1,74) = 4.29$, $p = .042$, $\eta\rho^2 = .06$, showing slightly lower self-agency experiences in the high load condition (see also Hon et al., 2013). Type of pre-activation did not show a main effect, $F(1,74) = 0.12$, $p = .732$, $\eta\rho^2 = .00$. The main effect of Matching was significant, $F(1,74) = 47.4$, $p < .001$, $\eta\rho^2 = .39$, showing stronger self-agency experiences when outcomes matched pre-activated information than when they mismatched such information. Furthermore, this pattern was stronger for goals than for primes, as indicated by the Type of pre-activation by Matching interaction, $F(1,74) = 37.1$, $p < .001$, $\eta\rho^2 = .33$. Working memory load did not interact with neither Type of pre-activation, $F(1,74) = 2.47$, $p = .120$, $\eta\rho^2 = .03$, nor Matching, $F(1,74) = 0.20$, $p = .653$, $\eta\rho^2 = .00$.

With regard to our specific hypothesis for goal trials, it was found that while the effect of matching was significant in both low, $F(1,74) = 60.6$, $p < .001$, $\eta\rho^2 = .45$, and high load conditions, $F(1,74) = 51.54$, $p < .001$, $\eta\rho^2 = .41$, the higher working memory load did significantly reduce the effect of Matching as indicated by the interaction effect of Matching and Working memory load, $F(1,74) = 5.01$, $p = .028$, $\eta\rho^2 = .06$. Within the outcome prime trials, no such interaction effect was found, $F < 1$; in both the low, $F(1,74) = 9.59$, $p = .003$, $\eta\rho^2 = .12$, and high load condition, $F(1,74) = 10.05$, $p = .002$, $\eta\rho^2 = .12$, the effect of Matching was significant.

This pattern was corroborated by a marginal three way interaction between Type of pre-activation, Matching, and Working memory load, $F(1,74) = 3.15$, $p = .080$, $\eta\rho^2 = .04$.

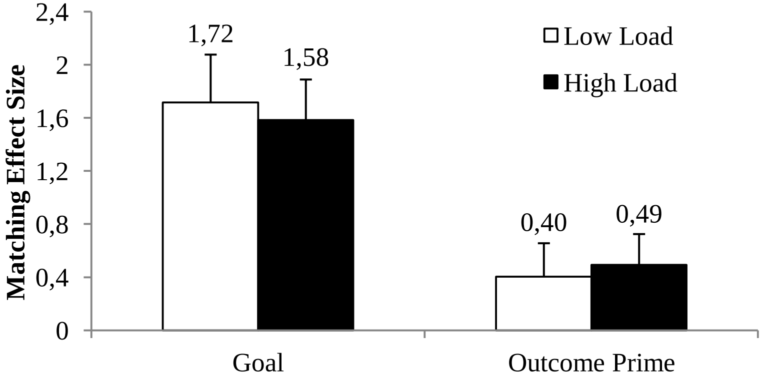

Figure 3.6. Self-agency experiences of Experiment 3.3 as a function of Type of pre-activation and Working memory load. For clarity of interpretation, differences scores between match and mismatch trials for each condition are displayed. Error bars represent standard errors of the mean.

Discussion

Experiment 3.3 largely replicated the findings of Experiment 3.2. As expected, higher working memory load reduced goal-based inferences of self-agency. Furthermore, this reduction was not found in prime-based self-agency inferences.

In Experiment 3.2, the outcome prime condition showed unexpected results, where the effect of matching was reduced in the low load condition. In Experiment 3.3 however, the effect of matching showed comparable results to Experiment 3.1. This suggests that the unexpected finding in Experiment 3.2 might have been a fluke or may have been an artifact of the specific working memory manipulation (three levels) that we used in comparison to Experiment 3.3 (two levels). Most importantly, closer scrutiny of both goal and prime conditions in Experiment 3.3 showed the expected patterns in support of our hypotheses.

General Discussion

Building on previous research that investigated self-agency experiences as a function of goals and primes, the present research was set out to examine whether goal-based agency inferences follow from a different process than prime-based agency inferences. Specifically, we suggested that goals (operationalized as sufficient amount of input of action-outcome information to form an explicit goal to produce the outcome) facilitates the recruitment of attentional control processes that monitor and process feedback about the progress of achieving the goal. Therefore, both matching and mismatching of the pre-activated action-outcome information with the actual action-outcome influences self-agency experiences in a profound way. Outcome-primes (operationalized as sufficient amount of input to automatically process action-outcome information but not to form a goal to produce the outcome) do not engage attentional control processes. Hence, when this primed information matches the outcome of an action it has a smaller impact on experienced self-agency.

To examine these ideas, we first replicated earlier research while employing a novel task that allow for a test of goal-based and prime-based self-agency inferences under equal circumstances of duration and timing of pre-activation of outcome information in the sequence of action performance and observing outcomes. The results of Experiment 3.1 indeed revealed a larger effect of matching for goals than for primes. The present study therefore provides a better test for the investigation of the unfolding of prime-based versus goal-based inferences.

Secondly, we used a working memory manipulation to test whether goal-based inferences used more attentional control than prime-based inferences. Although the observed effects are somewhat small and weak, the general gist of our findings is that with increased working memory load agency inferences were attenuated in the goal-based condition but not in the prime-based condition, supporting the notion that goal-based (vs. prime-based) agency inferences rely more heavily on attentional control processes. These findings partly replicate earlier findings (Hon et al., 2013), also showing that high working memory load decreased self-agency experiences. However, although these previous findings are an important first step, they only allowed the general conclusion that self-agency processing is dependent on cognitive resources. The present study extends these findings by ruling out the involvement of motor prediction effects (i.e., actions did not predict outcomes), and by varying the exposure to outcome information. Importantly, although our findings show that working memory reduces but does not cease goal-based agency inferences, self-agency processing was only modulated when inferences are based on goals, while self-agency processing was rather unaffected when the inference is based on primes.

The finding that working memory load reduces goal-based agency inferences lends credence to the notion that goal-based agency inferences make more use of higher order cognitive processes than prime-based agency inferences. This notion is substantiated by recent neuroscientific research, suggesting the involvement of a specific cortical network dedicated to goal-based self-agency inferences. Specifically, in a neuroimaging study, participants who inferred that they caused an outcome to occur when the outcome matched their goal displayed increased activity in frontal and parietal regions such as the medial prefrontal cortex, bilateral superior frontal cortex and inferior parietal lobule (Renes, van Haren, Aarts, & Vink, 2015c). These findings are corroborated in an electroencephalography study to measure connectivity of brain areas (Dogge, Hofman, Boersma, Dijkerman, & Aarts, 2014). This study used a similar agency inference task to the one used in the present study, and showed strong connectivity between frontoparietal regions during goal-based agency inferences. Interestingly, this study also assessed prime-based agency inferences, and showed considerably weaker and more diffuse connectivity between frontoparietal regions during self-agency inferences as compared to when these inferences were goal-based. Although different in strength of connectivity, connectivity patterns analysis further showed directional flow from parietal to frontal regions in both goal-based and prime-based inferences, indicating that parietal regions communicate with frontal regions to arrive at the experience of agency (see also Nahab et al., 2011; for an account of the involvement of leading and lagging cortical networks for the translation of an observed outcome into higher order processing of agency).

Although our findings suggest that taxing attentional control does not compromise prime-based agency inferences, this does not mean to say that these inferences cannot be reduced or impaired. As argued before, because primed-based agency inferences rely on a well-communicated match between a primed outcome and an actual outcome, processes that hamper this communication might also reduce prime-based inferences. In line with this notion, recent research suggests that when people focus too much on the execution of motor movements (e.g., pushing a button), rather than on the occurrence of outcomes of their actions (e.g., produce a color-word), the effects of outcome priming on experienced self-agency over matching outcomes diminish (Belayachi & van der Linden, 2010; Dannenberg, Förster, & Jostmann, 2012; van der Weiden, Aarts, & Ruys, 2010). This suggests that when attention is not directed to the outcomes of one's own actions, agency inferences are less likely to follow from a match between primed and actual action-outcomes.

In addition to the importance of attending to outcomes of actions, neurobiological impairments that disturb communication within the neural network implicated in primed-based agency inferences may also reduce the establishment of prime-based agency inferences. Due to the inherent diffuse connectivity in the frontoparietal regions associated with prime-based self-agency inferences, the integrity of the frontoparietal fibers that broadcast the required outcome-information is probably vital, as primed information generally does not recruit cortical structures (Baars, 1988; Dehaene & Naccache, 2001). If these fibers are only subtly compromised, prime-based self-agency inferences might be compromised as well. In patients with schizophrenia –who as a part of their illness often exhibit difficulties in distinguishing one's own actions and outcomes from those of others– these vital frontoparietal regions are not properly connected (Ellison-Wright & Bullmore, 2009; Voineskos et al., 2010; Whitford, Kubicki, & Shenton, 2011). Consistent with this suggestion, a recent study indeed showed impairment in prime-based agency inferences in a group of patients with schizophrenia, but not in a healthy control group (Renes et al., 2013).

In conclusion, we observed that under conditions in which motor prediction signals cannot inform people about their sense of agency, goal-based self-agency inferences involve attentional control, whereas this is less the case when these inferences are prime-based. This observation may have implications for situations wherein we operate in a goal-directed fashion. For instance, in the context of law, moral judgments and human behavior, the experience of agency and responsibility are often thought to be intertwined (Frith, 2014; Greene et al., 2009; Haggard & Tsakiris, 2009); people are held responsible for actions that are commonly believed to be accompanied by agency. Accordingly, potential discrepancies between personal experiences and social norms and rules about agency and responsibility might occur when attentional resources are temporary usurped by other processes (e.g., distractions, mind wandering), thereby hampering the establishment of self-agency in goal-directed behavior. Whereas our findings do not directly address the relationship between the experience of agency and responsibility, it might be interesting for future research to study whether and how goal-based and primed-based agency inferences shape the experience of responsibility as a function of taxing attentional control. The present study might offer a test and starting point to examine this important and intriguing issue.

Chapter 4

An Exploratory fMRI Study Into Inferences of Self-Agency

Based on: Renes, R. A., van Haren, N. E. M., Aarts, H., & Vink, M. (2015c). An exploratory fMRI study into inferences of self-agency. *Social Cognitive Affective Neuroscience, 10*, 708–712.

Abstract

Building on the recent findings that the experience of self-agency over actions and corresponding outcomes can also rely on cognitive inferential processes, rather than motor prediction processes, this study aims to investigate the brain areas involved in agency inference processing in a setting where action and outcome are independent. Twenty-three right handed subjects were scanned using functional MRI while performing an agency-inference task, in which action-outcomes matched or mismatched goals. The experience of self-agency was associated with increased activation in the inferior parietal lobule as well as bilateral (medial) superior frontal cortex and medial prefrontal cortex. These findings provide new and exciting insights in the processing of inferential self-agency, providing a first look at the neural correlates of self-agency processing independent of motor-prediction processes.

Introduction

Considering yourself as the cause of your behavior is fundamental to self-awareness and social interaction. For instance, when you press a key on a piano and the intended sound is produced, you experience yourself as the author of this effect. This sense of agency over operant action – i.e., when an action is followed by a specific and anticipated consequence – has primarily been explained by comparator processes described in models on motor control (Blakemore et al., 2002; Farrer et al., 2003; Frith et al., 2000; Wolpert & Flanagan, 2001). These models often rely on paradigms in which visual, tactile or auditory feedback of an individual movement is manipulated (e.g., Sperduti et al., 2011; David, 2012). The volitional or goal-directed execution of the action is accompanied by the prediction of sensory action-outcomes based on internal copies of movement-predicting signals (i.e., efference copies) generated by the motor system. Because these internal motor predictions are generally very reliable, sensory outcomes are readily perceived as self-produced until this prediction no longer corresponds with the actual outcomes following one's action (Wolpert et al., 1995). This misprediction of motor processes in a self-agency context has been found to be associated with brain activity in various areas, including the superior temporal gyrus, the inferior parietal lobe, as well as motor regions such as the pre-supplementary motor area and the cerebellum (for an overview, see Sperduti et al., 2011).

While one's sense of agency is decreased when efference copies do not predict sensory outcomes, there is research to suggest that this does not necessarily always occur. People can experience self-agency even when moving involuntarily (Dogge et al., 2012; Moore et al., 2009), when there is no clear causal relationship between an action and a following event (Moore & Haggard 2008), or when actions have multiple causes and outcomes (van der Weiden et al., 2013b; Wegner, 2002). For instance, when two persons press a separate light switch and one light bulb turns on, they cannot exclusively rely on motor predictions to generate the sense of agency over the event. This recent work points to the existence of an additional – cognitive – route to agency experiences that may result from non-motor prediction cues. Specifically, it has been proposed that agency experiences can also arise from the inferred correspondence between actual action-effects and pre-activated knowledge of these outcomes, even though action and outcome are independent (Moore & Haggard, 2008; Wegner, 2002). In contrast to motor predictions, research on the neural components of cognitive inferences as agentive cues has received little attention. The present study aims to offer an initial test to fill this void.

According to the inference model, people quickly and fluently infer whether or not a perceived event results from their behavior. Experienced self-agency emerges when the perception of an outcome corresponds with the outcome that one consciously intends to attain by performing an action, while a mismatch is generally ascribed to other causes (Wegner, 2002; Synofzik et al., 2013).

In a test of this idea (Aarts et al., 2005; Renes et al., 2013), participants moved a single gray square in a counterclockwise direction on a computer screen while the computer moved another gray square in the opposite (clockwise) direction. Participants were instructed to stop their square with a key-press at one of eight possible locations. When they pressed a key, they saw one of the two squares stopped at a specific location. Thus, the participants or the computer could have caused the observed stop, and the observed stop could not be predicted by the key-press. Participants indicated whether they or the computer had caused the square to stop at that position. In actuality, the computer always determined where the square stopped, so action and outcome were independent and participants had no control. Enhanced self-agency was reported when their intended outcome matched the actual outcome as compared to when it did not. Since the experimental set-up did not allow the motor prediction process to produce reliable input for establishing a sense of agency, the agency experiences have likely resulted from inference processes based on the congruency between the intended outcome and the actual outcomes (Synofzik et al., 2013).

Whereas research on neural processes of self-agency inferences in action- outcome independent settings is lacking, there is some prior research on other types of inferences that provides clues about these processes. A recent meta-analysis on the neural substrates involved in the observation of other people’s behavior suggests that the mirror system, consisting of the anterior intraparietal sulcus and the premotor cortex, is engaged when one perceives the motions of body parts of another person (van Overwalle & Baetens, 2009). Furthermore, the mentalizing system, consisting of the medial prefrontal cortex and the temporo-parietal junction, seems to be implicated when the observation of another person’s behavior allows the observer to make inferences about goals and beliefs that might underlie the other agent’s behavior. Interestingly, unexpected motions of body parts (e.g., movements that do not fit with the predicted action-effects) seem to activate both the mirror and mentalizing system, suggesting that if the mirror system is unable to deal with the unexpected motion on inconsistency, the mentalizing system is activated to understand the occurrence of the error (van Overwalle & Baetens, 2009).

The present study aims to explore brain activation related to agency inferences of an individual’s own behavior in a context where action and outcomes are independent and thus motor processes do not relate to or predict outcomes. Thus, we address the experience of self-agency as they occur when intended action-outcomes or goals match or mismatch with the actual outcomes. In line with research on the neural foundations of mentalizing, there is research to suggest that the medial prefrontal cortex is also implicated in self-referential processing (Amodio & Frith, 2006; Mason et al., 2007; Northhoff et al., 2006; van Buuren et al., 2010). Accordingly, as agency experiences over one's own behavior are self-referential, it is likely that the medial prefrontal cortex is also involved in self-agency inferences. Furthermore, as these inferences are likely to follow from a comparison of intended outcomes and actual outcomes, specific brain areas in the parietal cortex (such as the inferior parietal lobule) that are associated with such comparisons (Farrer & Frith, 2002; Spence, 2002; O'Connor et al., 2010) may also be involved in the neural base of self-agency experiences.

Based on this earlier work, the present study thus aims to explore whether medial prefrontal and parietal areas are recruited to infer self-agency over the consequences of action that either match or mismatch with a person's goal to produce the outcome. For this purpose we used the agency inference task in an operant action performance context as described above. Simultaneously, brain activation related to the observation of the outcome is measured by using fMRI.

Methods

Participants

Twenty-three right-handed subjects (11 women; mean age = 21.7±2.6 SD) participated in the study. Participants were recruited from the University of Utrecht and received monetary compensation for participation. The study was performed at the University Medical Center Utrecht. Participants were excluded from participation in case of alcohol and drug abuse/dependence during the last six months, the presence of a psychiatric disorder in the participant or a first-degree relative of the participant, and in case of a serious medical condition. After detailed explanation of the study design and any potential risks, all subjects gave their written informed consent. The ethics committee of the University Medical Center Utrecht approved this study.

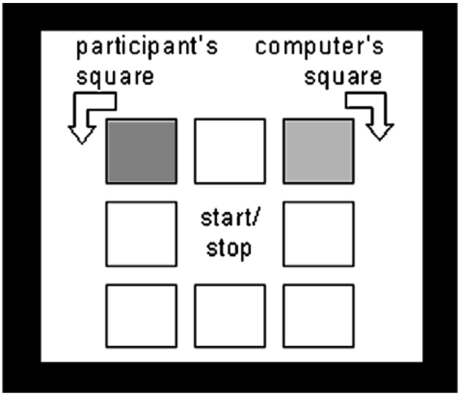

Figure 4.1. Illustration of the experimental task showing how the squares move in opposite direction. Start and stop commands are presented in the middle of the square. After the stop command, the participant pressed a key, thereby stopping the movement of the squares. This action turned one of the eight white tiles black.

Agency inference task and procedure

The agency inference task (Figure 4.1) was adapted from Aarts et al. (2005). Eight white tiles were presented on the screen. At the beginning of each trial, one of these eight tiles turned black, indicating this specific location as the outcome goal of this trial. Next, participants pressed a button on an MRI-compatible fiber-optic response box to cause a square to move along those white tiles in a counter-clockwise direction. The computer independently moved another square at the same speed, but in the opposite direction. When the stop cue appeared on the screen, participants had to press the button, thereby stopping the movement of the squares. However, as soon as the stop cue appeared, the squares disappeared. Participants were told that they continued to rotate invisibly until they pressed the button. Next, one of the eight white tiles turned black. This square represented either the participant's square or the computer's square thereby creating two potential causes of the outcome. Importantly, in half of the trials this outcome location corresponded with the location that was presented at the beginning of the trial (i.e., outcome goal), and in the other half of the trials it did not (i.e., the square stopped four locations farther away). Participants were asked to rate their level of self-agency experience on a nine-point horizontal visual analogue scale (not me (1) – me (9), see Figure 4.2), reflecting the extent to which they felt they had caused the displayed square to stop on that particular position.

Prior to the fMRI session, participants practiced the task both outside and inside the scanner. The total task consisted of 64 trials: 32 trials in which the outcome matched the participant's goal, 32 in which the outcome did not match the goal. For all participants, trials were presented in a single pseudo-random counterbalanced order. The four task blocks of 16 trials – each with 8 matching and 8 mismatching trials – were interleaved with 30s rest periods.

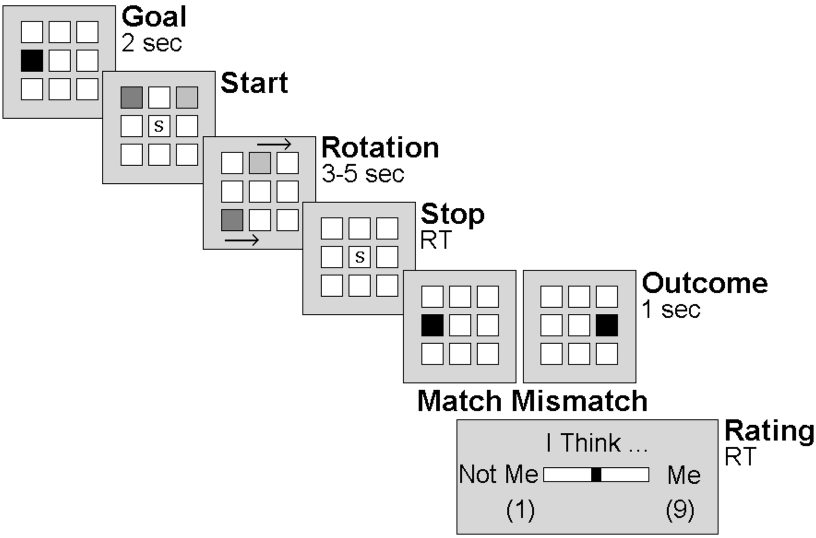

Figure 4.2. Outline of the agency inference task.

Image acquisition

The experiment was performed on a 3.0 T Philips Achieva MRI scanner (Philips Medical Systems, Best, the Netherlands) at the University Medical Center Utrecht. Head motion was restricted using a vacuum cushion and foam wedges. Images were acquired using an eight-channel sensitivity-encoding (SENSE) parallel-imaging head coil. Whole-brain T2*-weighted echo planar images (EPI) with blood-oxygen level-dependent (BOLD) contrast (625 volumes per task; 30 slices per volume; interleaved acquisition; repetition time, 1600 ms; echo time, 23.5 ms; field of view: 256×208 mm; flip angle = 72.5°; 64×51 matrix; 4×4 mm in-plane resolution; 4 mm slice thickness; SENSE-factor, 2.4 (anterior-posterior)) oriented in a transverse plane tilted 20° over the left-right axis were acquired in a single run. The first six images were dummy scans to allow for T1 equilibration effects. A whole-brain three-dimensional fast field echo T1-weighted scan (150 slices; repetition time =8.4 ms; echo time =3.8 ms; flip angle = 8°; field of view, 288×252×185 mm; voxel size: 1 mm isotropic) was acquired for within-subject registration purposes.

Imaging data pre-processing

Image preprocessing and analyses were carried out with SPM 5 (http://www.fil.ion.ucl.ac.uk/spm/). After realignment, the structural scan was co-registered to the mean functional scan. Next, using unified segmentation, the structural scan was segmented and normalization parameters were estimated. Subsequently, all scans were registered to a MNI T1-standard brain using these normalization parameters and a 3D Gaussian filter (8-mm full width at half maximum) was applied to all functional images.

Data analysis

For each subject, a model was generated describing event-related changes time-locked to the start of the trial (rotation of squares), the stop cue, the actual outcome, and the self-agency rating (self-agency experience[2]: rating > 5, no self-agency experience: rating < 5). Self-agency related activation was modeled as activation during the presentation of the actual outcome, based on the self-agency experience. This resulted in four conditions: outcome match and self-agency experience, outcome match and no self-agency experience, outcome mismatch and self-agency experience, outcome mismatch and no self-agency experience. To correct for head motion, the

[2] The middle of the 9-point scale is ambiguous as to the sense of agency. We therefore deemed it appropriate to not include these middle ratings in the fMRI analyses in order to create a clear contrast between self-agency experience and no self-agency experience.

six realignment parameters were included in the design matrix as regressors of no interest. Two participants were excluded from further analysis due to excessive head movement (> 4mm) during the acquisition of fMRI scans (van Dijk et al., 2012). To correct for drifts in the signal, a high-pass filter (discrete cosine transform basis functions) was applied to the data with a cut-off frequency of 0.0039 Hz. For each individual subject, brain activation related to self-agency was calculated by contrasting match-agency trials with mismatch-no-agency trials (henceforth referred to as the Agency > No-Agency contrast). The resulting individual statistical maps were used to perform a group-wise whole-brain analysis. Maps resulting from this analysis were tested for significance using cluster-level inference (cluster-defining threshold, $p < 0.001$; critical cluster size: 27 voxels, cluster probability of $p < 0.05$, family-wise error corrected for multiple comparisons). These parameters were determined using SPM and a script (CorrClusTh.m, http://www2.warwick.ac.uk/fac/sci/statistics/staff/academic-research/nichols/scripts/spm), which uses estimated smoothness (estimated Full Width at Half Maximum (FWHM): 3.56x3.65x3.46 voxels) and Random Field Theory to find these corrected thresholds. We were unable to perform a full-factorial analysis as the factors match-no-agency and mismatch-agency contained almost no trials (see Figure 4.3).

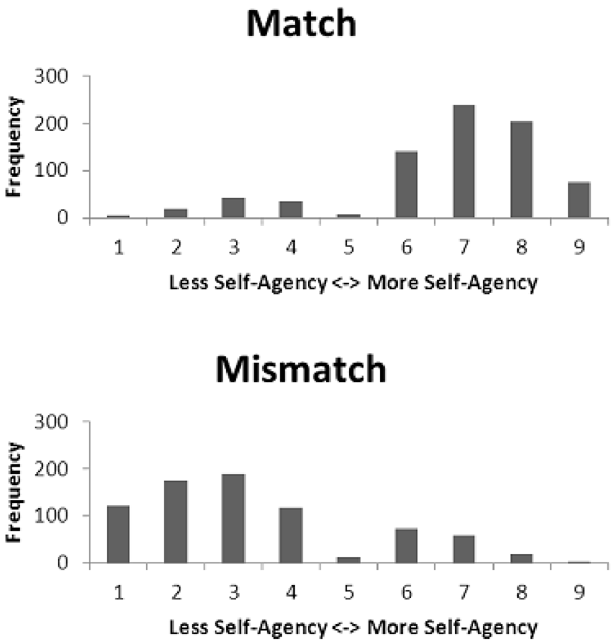

Figure 4.3. Frequency histograms of the self-agency ratings, separated by Matching condition.

Results

Behavioral self-agency experiences

Self-agency ratings are presented in Figure 4.3. A repeated-measures ANOVA yielded a significant main effect of matching ($F(1,22) = 71.50$, $p < 0.001$, $\eta_p^2 = .765$), indicating that participants experienced more self-agency when the actual outcome matched the outcome goal presented at the start of the trial (M = 6.75, SD = 0.99) as opposed to when it did not (M = 3.31, SD = 1.19).

Reaction times to the stop-cue

In order to check whether response time might influence the self-agency inference effects, we compared reaction times for the stop-cues in the match and mismatch condition (see Figure 4.2). A paired-samples t-test revealed no difference ($t(22) = 0.896$, $p = .380$) between matching trials ($M = 411$, $SD = 149$) and mismatching trials ($M = 402$, $SD = 119$). Accordingly, participants did not react differently on matching trials as compared to mismatching trials.

fMRI

Due to the nature of self-agency inferences, we analyzed brain activations during the presentation of the outcome. Self-agency related activation (as calculated with the Agency > No-Agency contrast) was found in the parietal cortex (inferior parietal lobule), and in three clusters in the frontal cortex: the left (medial) superior frontal cortex, right (medial) superior frontal, and medial prefrontal cortex (see Figure 4.4 and Table 4.1). No regions were associated with the opposite contrast (No-Agency > Agency).

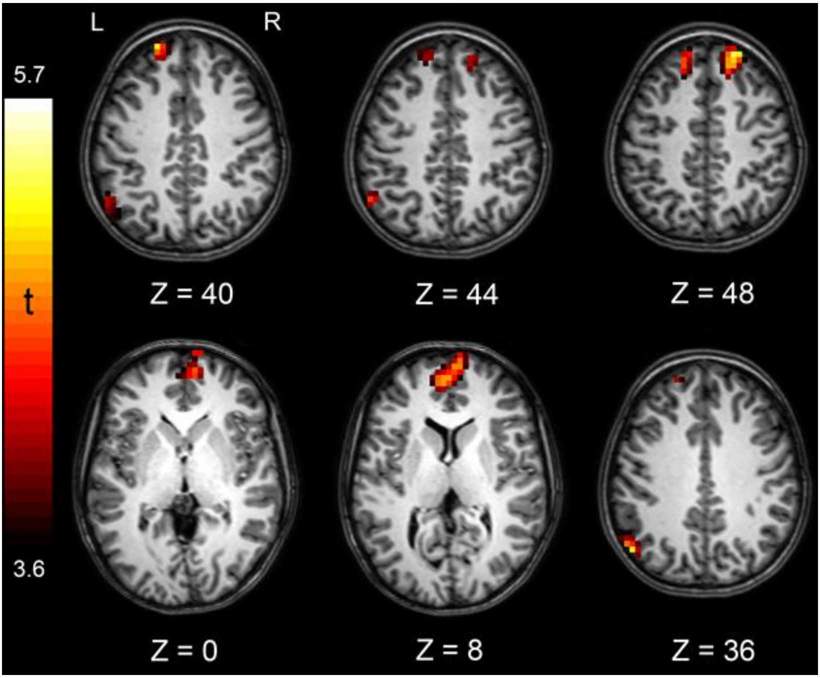

Figure 4.4. Brain areas activated in the Agency > No-Agency contrast. Cluster defining threshold of p < 0.001 with a p < 0.05 FWE-corrected cluster size of 27 voxels.

Table 4.1

Peak voxel, number of voxels and T-value of the brain areas activated in the Agency > No-Agency contrast, all at threshold p <.001 (p < 0.05 FWE-corrected cluster size of 27 voxels).

	MNI coordinates				
Brain region	*x*	*y*	*z*	*Voxels*	*T value*
Left Inferior Parietal Lobule	-52	-68	32	37	5.08*
Left (Medial) Superior Frontal Gyrus	-20	52	40	35	5.13*
Right (Medial) Superior Frontal Gyrus	20	36	52	43	5.67*
Medial Prefrontal Cortex	8	64	4	104	4.88*

* $p < .001$

Discussion

The present study used fMRI to reveal brain areas involved in self-agency inferences, i.e., when self-agency is retrospectively established in a situation where motor processes do not predict the outcomes. Our main finding is that self-agency inferences were associated with activation in the medial prefrontal cortex, bilateral (medial) superior frontal gyrus and the left inferior parietal lobule. Interestingly, these findings followed from the contrast test between Agency > No Agency, indicating that self-agency inferences are associated with the activation of these brain areas when the actual outcome matches the predicted outcome.

In contrast to findings in motor-prediction self-agency research, the present study shows bilateral (medial) superior frontal gyrus and medial prefrontal cortex activation while experiencing self-agency. These medial frontal regions have been found to be associated with thinking about self-agency judgments (Miele et al., 2011), self-referential processing (van Buuren et al., 2010) and broader inferential processing, such as trait inferences (Ma et al., 2011) and social inferences (van Overwalle & Baetens, 2009). Moreover, lateral areas in the cortex have been related to higher-order processing of the self, such as awareness of the self (Northoff et al., 2006). Furthermore, the left inferior parietal lobule has been associated with the integration of sensory information (Joseph, 1982; Seghier, 2013), lending credence to the idea that it can compare expected and actual outcomes. Interestingly, in the context of motor-prediction activation of the inferior parietal lobule has often been associated with a *mismatch* between the expected outcome and the actual outcome based on motor-sensory information (for a review, see Sperduti et al., 2011). However, in the present study the inferior parietal lobule showed more activation when the outcome *matched* participants' goals. This implies a reliance on either a different network or a different process in the same network, based on the signaling of a cognitive *match* between the participant's outcome goal and the actual outcome, without involvement of motor-sensory processes. This notion of cognitive matching is consistent with literature describing the involvement of this region in signaling a match between cognitive expectations of a specific outcome and subsequent memory retrieval experiences when this outcome occurs – a process similar to self-agency inferences (e.g., O'Connor et al., 2010).

An important question following from these observations is how the identified regions communicate to allow self-agency experiences in different contexts. Both motor prediction and inference processes rely on a comparison between predicted outcomes and actual outcomes that has to be translated into a conscious experience (cf., Dehaene & Naccache, 2001). Depending on the context (i.e., depending on the predictability of action-effects), the parietal region seems to inform conscious agency experiences in a different way. To date, only a few studies on the neural basis of agency have considered interactions between brain regions (David, 2012). In one study investigating motor predictions, incongruent visual feedback was associated with a leading network, consisting primarily of the left anterior inferior parietal lobe, the right supramarginal gyrus, the right temporo-parietal junction and the anterior insula, which was sending information to a lagging network consisting mainly of the cingulate, posterior inferior parietal lobe and the pre-frontal lobe (Nahab et al., 2011). The authors speculated that the leading network is likely to be involved in mismatch detection between motor predictions and sensory action effects, whereas the lagging network translates the outcome of this comparison into a conscious agency experience.

A recent study also explored cortical interaction in an agency inference context similar to the present study (Dogge et al., 2014). Here, electroencephalography recordings assessed phase synchronization of neural oscillations (Sauseng & Klimesh, 2008), which has been proposed as the mechanism underlying neural communication (Buszáki & Draghun, 2004; Fries, 2005; Sauseng & Klimesh, 2008; Valera et al., 2001). In line with the present study, they showed that agency inferences involve fronto-parietal regions, and that the inferences depend heavily on the connectivity between these regions. Furthermore, the connectivity patterns analysis in the Dogge et al., study showed directional flow from parietal to frontal regions, indicating that indeed the parietal regions inform frontal regions leading to self-agency experiences.

To conclude, the present study provides new and exciting insights in the processing of inferential self-agency, providing a first look at the neural correlates of self-agency processing independent of motor-prediction processes. The insights may help develop an initial brain model of inferential self-agency experiences, a process that is most likely relevant for efficient and high-quality social interactions.

Chapter 5

Abnormalities in the establishment of feeling of self-agency in schizophrenia

Based on: Renes, R. A., Vermeulen, L., Kahn, R. S., Aarts, H., & van Haren, N. E. M. (2013). Abnormalities in the establishment of feeling of agency in schizophrenia. *Schizophrenia Research, 143*, 50–54.

Abstract

People usually feel they cause their own actions and the consequences of these actions, i.e., they attribute behavior to the proper agent. Research suggests that there are two routes to the experience of self-agency: 1) an explicit route, where one has the intention to obtain a goal (if it occurs, I must have done it) and 2) an implicit route, where information about the goal is unconsciously available and increases the feeling of self-agency.

Schizophrenia patients typically experience no behavioral control and exhibit difficulties in distinguishing one's own actions from those of others. The present study investigates differences in both routes to self-agency experiences between schizophrenia patients and controls. Twenty-three schizophrenia patients and 23 controls performed a task where they performed an action (button press) and subsequently indicated whether or not they were the agent of the consequence of this action (the outcome) on a 9-point scale. The task can be manipulated to measure both the explicit and implicit route (by using priming) to the experience of self-agency. In the explicit condition (participants intended to produce a specific outcome, and this outcome matched their goal), both groups experienced enhanced self-agency. In the implicit condition (the outcome matched the primed outcome), healthy controls showed increased self-agency over the outcome, while patients did not. Potential differences in task motivation and attention did not explain these findings. These findings provide new evidence for the idea that implicit processes leading to feelings of self-agency may be disturbed in schizophrenia.

Introduction

I hold my hand up and a taxi stops for a ride. I make a joke, people start laughing. Whether engaging in simple motor movements or social interactions, we feel we cause our own actions and their consequences. This feeling is usually referred to as self-agency and is essential for human self-perception and social communication.

Common sense suggests that the feeling of self-agency results from the conscious intention to engage in behavior and attain specific outcomes. That is, if I had the explicit goal of doing it and then it occurred, I must have done it. However, in everyday social life humans regularly behave without much conscious thought, and their behavior produces outcomes over which they can nevertheless experience self-agency. In other words, information in our environment that we are not consciously aware of can influence our behavior and our feelings of self-causation (Wegner, 2002).

We are not all blessed with a well-operating sense of self-agency. Schizophrenia patients often exhibit difficulties in distinguishing one's own actions and outcomes from those of others. They hear voices or feel their limbs being controlled by external sources. As a consequence patients' autonomy and their professional and personal achievements are reduced and they experience problems in social interactions and relationships with family and peers (Walker et al., 2004).

Previous research has led to the notion that disturbed experiences of self-agency in schizophrenia may derive from disturbances in the sensory-motor system that controls voluntary action (Daprati et al., 1997; Franck et al., 2001; Haggard et al., 2003; Morrison and Haddock, 1997; Voss et al., 2010). When performing a voluntary motor action, the sensory-motor system compares the predicted and actual sensory consequences that follow from that action. To enable people to differentiate between self- and other-produced sensory signals, the sensory signals of self-generated movements are attenuated. This generates a feeling of self- agency when matching the actual sensory consequences with the predicted consequences (Blakemore & Frith, 2003; Wolpert, 1997). However, patients with schizophrenia fail to differentiate between the perception of self-produced and externally produced sensory signals. Consequently, schizophrenia patients' self-produced tactile stimulation feels as tickly, as other-produced tickling because it is not perceptually attenuated as is the case in controls (Blakemore et al., 2000; Shergill et al., 2005).

Interestingly, recent work shows that people can also experience self-agency over outcomes in situations where the motor prediction processes may not inform self-agency, i.e., outside of the context of volitional behavior (Aarts et al., 2005; Dogge et al., 2012; Moore et al., 2009). In these cases, the experience of causation between our actions and the resulting effects is an *inference* because one cannot directly observe causal connections between them. These cognitive inferences occur fluently and perfunctorily after action performance and, in principle, this process can operate outside of conscious awareness.

To infer that one was the agent of an action and its consequences is always retrospective. Recent research suggests two routes that model the inferential nature of authorship processing (Aarts et al., 2005; Wegner, 2002). An explicit one, in which people infer agency when an actual outcome of an action is in agreement with their intentions to produce the specific action-outcome (I do something, it happens so I must have done it); and an implicit one, in which agency inferences are based on matches between actual outcomes of action and subtly pre-activated information about the action outcome. By using short presentation times (often referred to as priming) one can decrease the likelihood of conscious processing of information that yet activates the representation of action outcomes before performing the action. Subsequently observing the actual outcomes can thus enhance the experience of self-agency.

Both routes can contribute to inferences of agency in that people use sensory evidence to establish agency in retrospect. Aarts et al. (2005) showed that both intention to cause a specific outcome and priming of the action-outcome increased the sense of being the agent of the action outcome when that outcome actually occurred. These findings have been replicated across different tasks (Linser & Goschke, 2007; van der Weiden et al., 2010), and cultures (Sato, 2009).

Things may be different for patients with schizophrenia. That the explicit route to inference of self-agency may be intact in patients with schizophrenia is suggested by a study focusing on intentional binding. This is the phenomenon that people perceive their own actions as occurring later in time when they are followed by an external effect, compared to actions not followed by such effects. As such, intentional binding is an indirect measure of self-agency and it can be predictively or retrospectively generated. A predictive sense of agency means that an action is predicted to produce a given effect, whereas retrospective sense of agency means that one infers retrospectively that one's action caused the effect. Voss et al. (2010) showed that patients are able to retrospectively infer a sense of agency over their actions using the intentional binding task within the context of voluntary action. The present study aims to conceptually replicate this finding by testing whether patients display enhanced experienced agency over behavior when the actual outcome of their action matches their explicit goal to produce the outcome in a context where motor prediction processes are ruled out.

The prediction is less clear-cut when considering the implicit route to inferences of self-agency in patients with schizophrenia. Therefore, we conducted an experiment to explore whether the implicit route to self-agency is impaired in patients. If it is impaired, then priming an outcome of an action before performing the action and observing the corresponding outcome may not alter their experiences of self-agency.

Methods

Participants

Twenty-three schizophrenia patients and 23 healthy controls participated in the study. Patients were recruited from the psychiatry department of the University Medical Centre Utrecht. The study was approved by the Humans Ethics Commission of University Medical Centre Utrecht. Participants gave written consent and were financially compensated for study participation.

Psychopathology levels were established by using the *Comprehensive Assessment of Symptoms and History* (CASH; Andreasen et al., 1992a). All patients met DSM-IV criteria for schizophrenia. Symptom levels were assessed with the *Positive and Negative Syndrome Scale* (PANSS; Kay et al., 1987) by trained raters. Patients were receiving atypical antipsychotics at time of testing, except for one who was on typical antipsychotic medication.

Comparison subjects had no psychiatric history, no first-degree relatives with a psychotic illness, and did not use chronic medication. A history of closed-head injury, neurological illness or endocrinological dysfunction were criteria for exclusion. Patients and controls did not differ significantly on demographic variables. See Table 5.1.

Table 5.1

Characteristics of patients with schizophrenia and control subjects (means ± s.d.).

	Schizophrenia patients (N = 23)	Normal controls (N = 23)
Age	32.7 ± 7.1	28.5 ± 8.6
Male / Female	20 / 3	19 / 4
Years of education	13.2 ± 2.0	14.1 ± 1.7
Parental years of education	13.9 ± 3.4	14.0 ± 2.5
Illness duration (years)[a]	13.8 ± 8.5	–
PANSS Positive score	14.7 ± 4.4	–
PANSS Negative score	16.5 ± 7.0	–
PANSS General score	32.2 ± 8.3	–
Medication dose[b]	7.3 ± 4.0	–

[a] Time between onset of psychotic symptoms and inclusion in the study

[b] Mean dose in mg/day haloperidol equivalents

Procedures and measures

Agency inference task and procedure

Participants learned that the study was designed to examine people's feelings of personal causation and how these feelings come and go. The agency inference task was taken from Aarts et al. (2005). See Figure 5.1. In this computer-task, participants pressed the S-key on the keyboard to cause a square to rapidly traverse a rectangular path, consisting of eight white squares, in a counter-clockwise direction. The computer independently moved another square along the path at the same speed, but in the opposite direction. When "stop" appeared in the center of the screen they had to press the "Enter" key immediately, thereby stopping the movement. This action turned one of the eight white tiles black, which represented the final position of either their own square, or the computer's. The computer always determined the stops and thus actual stops occurred independently of participants' action (i.e., key-press). After each stop, participants reported their sense of self-agency by indicating the extent to which they felt they had caused the displayed square to stop at that particular position [9-point scale: *not at all* (1)–*strongly* (9)].

After participants practiced and understood the task, the experiment proceeded with two conditions to examine the implicit and explicit routes to inferences of self-agency. Specifically, in the implicit condition an outcome location was subtly primed (i.e., the location flashed up for 17 ms) before participants pressed the stop-key and saw the outcome location. Priming refers to the very short (and often incidental) exposure to a stimulus that influences a response to a later stimulus, as the prime activates the representation of the outcome during ongoing action, without requiring a predetermined intention (Aarts et al., 2005). In the explicit condition they received the explicit goal (i.e., intention) to stop on a certain location before starting the trial.

Each condition comprises 32 trials that were divided in 2 blocks of 16 trials. In each block, the black square was used as a prime or as an explicit goal twice on each of the eight tiles of the path. Crucially, half of the trials matched the outcome information (being presented as a goal/intention or as a prime), and the other half mismatched this information. The trials were randomly presented within a block. To prevent instruction carryover effects, the session started with the implicit task and was followed by the explicit condition task. There was a short break (30 s) between the blocks within a condition, and a longer break (5 min) between the two conditions (see the online supplementary material for task details).

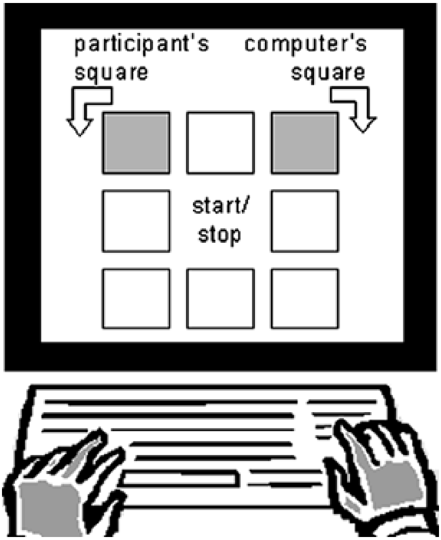

Figure 5.1. Illustration of the experimental task showing how the square of the subject and the square of the computer move in opposite directions before participants stop them. Participants are shown where one of them stopped (i.e., the location is the outcome of their action (or not)).

Task motivation and performance

Because schizophrenia is associated with decreases in motivation (Konstantakopoulos et al., 2011), we administered a self-report measure of task motivation for both conditions separately. Specifically, participants indicated the level of importance to perform well and how much they tried to focus their attention on the task [9-point scale: *not at all* (1)–*strongly* (9)].

Additionally, we assessed two measures to investigate attentional processes. First, participants indicated the extent to which they were able to follow their own rotating square in both tasks (9-point scale: *not at all* (1)–*strongly* (9)). This can be considered as a measure of visual attention maintenance. Second, response times to the stop cue were recorded and provide an objective measure of the ease of shifting attention from the rotating squares to the execution of the stopping behavior.

Statistical analyses

The averaged self-agency experiences on matching and mismatching trials were subjected to a repeated measures ANOVA with Group (patient/control) as a between-subjects measure and Type (implicit (prime)/explicit (intention)) and Matching (matching/mismatching outcome) as within-subjects measures.

To examine the role of task motivation and attention for both the implicit and explicit condition separately, ANOVAs were performed to test differences between groups, and ANCOVAs were used to control the main analyses for these measures.

Results

Self-agency experiences

A Group effect was found, implicating that patients experienced less self-agency compared to controls. Furthermore, main effects were found for Type and Matching. Agency experiences were lower in the implicit compared to the explicit condition, and agency experiences were stronger in matching relative to mismatching trials. In addition, the significant Type-by-Matching interaction indicated that the effect of matching was smaller in the implicit than in the explicit condition. Importantly, all these effects were qualified by a significant Type-by-Matching-by-Group interaction. The mean self-agency experiences of each cell in the design are displayed in Figure 5.2 and Table 5.2.

To gain insight in the nature of the 3-way interaction we used ANOVAs to test effects of Matching and Group in the explicit and implicit condition separately. In the explicit condition main effects of Group and Matching were found. Controls reported stronger self-agency experiences than patients. Furthermore, matches between the actual outcome and the intended outcome led to stronger experiences of self-agency than mismatches. Importantly, the Matching-by-Group interaction was not significant, indicating that the explicit route to the feeling of self-agency operated equally well in both groups.

In the implicit condition, a main effect of Matching indicated stronger self-agency experiences when actual outcomes matched with primed outcomes compared to mismatches. Furthermore, a significant Matching-by-Group interaction emerged. Simple main effects showed that the Matching effect was significant only in the control group, not in patients. This indicates that implicit (primed) pre-activation of outcome information did not increase self-agency experiences in patients only.

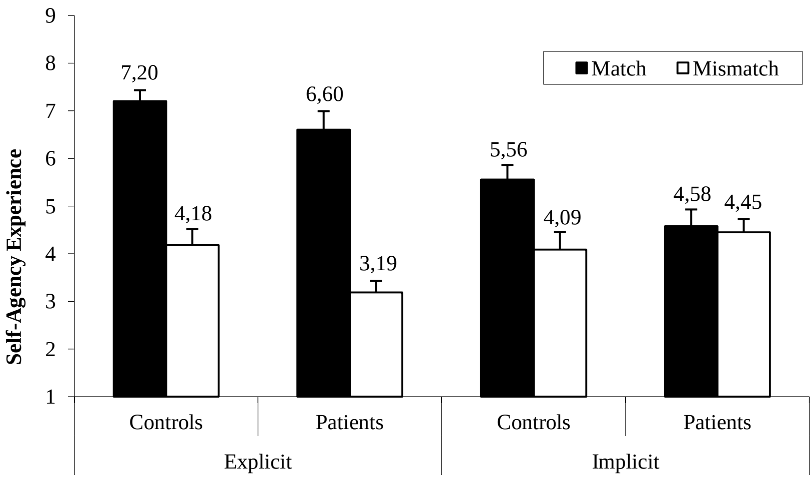

Figure 5.2. Self-agency experiences as a function of Group (patient/control), Type (explicit/implicit) and Matching (match/mismatch). Error bars represent standard errors of the mean.

Table 5.2

Statistical analyses for self-agency experiences

Main analyses (df = 44)				F	Sig.	η^2
Group				5.25	.03	.107
Type				6.04	.02	.121
Matching				79.2	< .001	.643
Type X Group				0.91	.345	.020
Matching X Group				1.08	.304	.024
Type X Matching				69.7	< .001	.613
Type X Matching X Group				9.00	< .01	.170
Follow-up Analyses (df = 44)	Explicit			Implicit		
	F	Sig.	η^2	F	Sig.	η^2
Group	5.72	.02	.115	0.71	.40	.016
Matching	145.8	< .001	.768	8.78	< .01	.166
Matching X Group	0.56	< .46	.013	6.15	< .01	.123
Simple main effects (df = 22)	Controls			Patients		
Explicit Matching	88.0	< .001	.800	64.7	< .001	.746
Implicit Matching	13.2	.001	.374	0.12	.72	.006

Task attention

No significant differences were found between the groups on the self-reported measure of task attention during both conditions (see supplementary tables 5.1 and 5.2), implicating that patients and controls were equally able to maintain visual attention to the rotating squares.

The response time to the stop-cue provides an index for speed of shifting attention from the rotating squares to the execution of the actual stopping behavior. As expected, there was a significant main effect of Type, indicating that participants took longer to respond to the stop-cue in the explicit than in the implicit task. This confirms that having an explicit goal to stop at a specific location takes more time to act than doing so without a conscious intention, as is typical for conscious processes (Kahneman, 2011). Importantly, there was no effect of Group nor Type-by-Group interaction, suggesting that groups performed equally well on switching attention from the rotating squares to the stopping behavior, and hence, potential differences in attention/motor execution performance do not seem to explain the pattern of findings on the self-agency experiences.

Task motivation

The two items were averaged to obtain a measure of task motivation for the implicit and explicit conditions. Correlations between this measure and the self-agency rating showed that subjective measures of motivation were relevant to the task (implicit: $r(46) = 0.37$, $p = .01$; explicit: $r(46) = 0.48$, $p = .001$). In the implicit condition no significant group difference was found, but in the explicit condition patients were significantly less motivated than controls (see supplementary tables 5.1, 5.2, 5.3**)**. A trend-level regression effect of the motivation measure on the matching effect was found, indicating that higher motivation was associated with a stronger matching effect. Importantly, controlling the implicit and explicit matching effects for the motivation measure produced the same pattern of results as the original findings.

Discussion

The present study explored the explicit and implicit routes to inferences of self-agency experiences in schizophrenia patients and healthy subjects. Our results demonstrate that the explicit route operates equally well in both groups, as both felt more self-agency when their intention to produce a specific action-outcome matched with the observed outcome compared to when the outcome did not match their intention. For patients, this finding is on par with other recent research suggesting that – in an explicit context – schizophrenia patients can use sensory evidence to form retrospective inferences of agency (Voss et al., 2010).

In line with previous research (Aarts et al., 2005), healthy subjects showed enhanced experiences of self-agency when an implicitly pre-activated outcome matched the observed outcome, suggesting that both explicit and implicit processing of action-outcome information augments agency experiences. However, patients did not show this effect, suggesting that their implicit processing route to self-agency experiences was impaired. Importantly, these group differences could not be attributed to differences in subjectively reported motivation or attention. Such disturbances are important to investigate as they might underlie poor everyday social interactions where behavior often starts and unfolds outside of conscious awareness (Waters & Badcock, 2008).

Unfortunately, no objective test was obtained to measure a potential covert attentional deficit in the patients, and therefore we cannot exclude the possibility that patients processed the primes in a different way as than controls. However, evidence suggests that patients show delayed conscious reporting of primes compared to controls, but –critical to the current study– are unimpaired in processing primes (Dehaene et al., 2003; Del Cul et al., 2006). Moreover, schizophrenia patients perform equal to healthy controls in spatial priming tasks, showing unimpaired processing of primed outcome-information even without fixating on this information (Spencer et al., 2011). It is important to note, though, that the duration of these primes was longer as compared to the primes in our task.

The observed differences in this study between patients and healthy controls raise questions about potential mechanisms that undermine the implicit (but not the explicit) nature of self-agency inferences in schizophrenia. One possible mechanism deals with the way the brain produces self-agency inferences. While the neurological basis is not yet fully delineated, it appears that experienced agency relies on frontal brain areas dealing with self-consciousness, and parietal regions representing primed goals or outcomes of movements (Frith, 1996; Jeannerod, 1999). Explicitly intended outcomes of behavior or goals are likely to enter the authorship process by gaining access to a widespread brain network broadcasting information to the frontal cortices (Baars, 1988; Dehaene & Naccache, 2001), and this process seems to effectively emerge in both health and schizophrenia. Once the outcome occurs, agency can be inferred by comparing the intention/goal and actual outcome, translating a match into experiences of self-agency. However, in implicit authorship processing (i.e., without global information broadcasting) the connection with the parietal area allows the frontal brain to establish a sense of agency by processing primed outcomes and actual outcomes. It might be that these regions are not properly connected in patients with schizophrenia (Burns et al., 2003; Honey et al., 2002). Indeed, evidence suggests disintegrated fiber integrity in the connection between frontal and temporo-parietal areas in schizophrenic patients (de Weijer et al., 2011). Thus, the fronto-parietal network appears essential in the authorship ascription process, and impaired neural connectivity in this network may render implicit processes underlying inferences of self-agency less likely to occur in schizophrenia.

In conclusion, we show that schizophrenia patients are disturbed in implicit information processes underlying inferences of experienced self-agency. These abnormalities might underlie poor social interactions that often unfold implicitly and outside of awareness.

Chapter 6

Abnormalities in the experience of self-agency in schizophrenia: A replication study

Based on: Renes, R. A., van der Weiden, A., Prikken, M., Kahn, R. S., Aarts, H., & van Haren, N. E. M. (2015a). Abnormalities in the experience of self-agency in schizophrenia: A replication study. *Schizophrenia Research*, *164*, 210–213.

Abstract

People usually experience agency over their actions and subsequent outcomes. These agency inferences over action-outcomes are essential to social interaction, and occur when an actual outcome corresponds with either a specific goal (goal-based), and matches with action-outcome information that is subtly pre-activated in the situation at hand (prime-based). Recent research showed that schizophrenia patients exhibit goal-based inferences, but not prime-based inferences. Intrigued by these findings, and underscoring their potential role in explaining poor social functioning, we replicate patients' deficit in prime-based agency inferences. Additionally, we exclude the account that patients are unable to visually process and attend to primed information.

Introduction

Problematic social interactions with family, friends and peers are only some of the debilitating consequences of schizophrenia (Walker et al., 2004). These problems may result from abnormalities in processes underlying the experience of self-agency –i.e., the feeling that one causes one's own actions and the consequences of those actions. Indeed, patients often experience difficulties in distinguishing their own actions and subsequent outcomes from those produced by others (Blakemore & Frith, 2003; Schneider, 1957).

Two processes have been proposed to shape the experience of self-agency (Moore & Fletcher, 2012; van der Weiden et al., 2013b). Motor prediction processes deal with comparing the sensory consequences of an action with internal copies of motor prediction signals (i.e., efference copies) generated by the motor system. Self-agency is experienced over action when the sensory consequences match these internal predictions (Wolpert et al., 1995). Non-motor prediction processes are particularly relevant when motor prediction signals are unreliable or ambiguous (as is often the case in social situations) and therefore cannot inform self-agency. Here, self-agency experiences are shaped by *retrospective inferences* via a goal-based (or explicit) and prime-based (or implicit) route (Aarts et al., 2005: Wegner, 2002). In the context of an explicitly set goal to obtain an outcome, people readily infer self-agency when the actual outcome matches this goal. When the goal is not explicitly set but subtly pre-activated in the situation at hand, self-agency might be inferred when the actual outcome matches the primed outcome information. Accordingly, observing outcomes that are primed in the mind during action performance provides the feeling that one caused the action-outcomes, and hence, priming action-outcome information can enhance the experience of self-agency. In healthy individuals both routes are suggested to support successful social interactions (Frith, 2013; van der Weiden et al., 2013a; Waters & Badcock, 2008).

Disturbances of agency processing in schizophrenia patients are mostly studied in terms of abnormal functioning of the sensorimotor system (Daprati et al., 1997; Franck et al., 2001; Haggard et al., 2003; Voss et al., 2010), suggesting that mismatches between motor-predictive signals and sensory feedback give rise to delusions of alien control, auditory verbal hallucinations, and other perturbations of self-agency (Frith et al., 2000; Frith, 1992; 2005a; 2005b; 2012). However, a recent study demonstrated that the inference process underlying experiences of self-agency might also be impaired in schizophrenia (Renes et al., 2013). Here, schizophrenia patients and healthy controls performed a task in which their action could produce several outcomes (i.e., pressing a key could cause a rotating square to stop on one of eight locations). The outcome could also be determined by another cause (the computer). In actuality, the computer always determined the outcome, and therefore, motor prediction processes could not contribute to the sense of agency. The outcome was either set as a goal or it was primed before performing the action and observing the outcome. While both groups experienced enhanced self-agency in the goal-based inference condition, only healthy controls showed enhanced self-agency in the primed-based inference condition. These findings were not explained by differences in task motivation and attention.

Intrigued by these recent findings, the present study serves two goals. First, we aim to replicate the impairment of prime-based inferences in an independent sample of schizophrenia patients. Second, we aim to exclude the possibility that impaired prime-based agency inferences are attributable to patients' inability to visually process and attend to the primes in the context of the experimental procedure.

Methods

Subjects

Based on the effect size (Cohen's d_s = 0.73) of the group-by-matching interaction effect within the prime-based condition observed in Renes et al. (2013), and a power of 80% (α = 0.05), we needed 62 participants to replicate the effect. Accordingly, 31 schizophrenia patients and 31 healthy controls participated. Patients were recruited from the psychiatry departments of the University Medical Centre Utrecht (UMCU) and Amsterdam Medical Centre. The UMCU's Humans Ethics Commission approved the study. See Table 6.1 for participant characteristics.

Table 6.1

Characteristics of patients with schizophrenia and control subjects (standard deviations in parentheses).

	Schizophrenia Patients (N = 31)	Healthy Controls (N = 31)
Age	29.4 (7.1)	31.3 (6.5)
Male / Female	28 / 3	28 / 3
Years of education[a]	13.1 (1.8)	13.2 (3.9)
Parental years of education	14.1 (3.1)	14.7 (2.6)
Premorbid intelligence[b]	102.1 (8.0)	107.7 (6.7)
Illness duration (years)[c]	9.2 (7.9)	–
PANSS Positive score	10.1 (2.7)	–
PANSS Negative score	11.8 (4.2)	–
PANSS General score	21.7 (3.4)	–
Typical / Atypical medication	3 / 25	–

Patients and controls did not statistically differ on any of the characteristics, except for premorbid intelligence ($t(60) = 3.04$, $p = .004$).

[a] Education information was estimated as part of the *Comprehensive Assessment of Symptoms and History* (CASH; Andreasen et al., 1992a).

[b] Premorbid intelligence was estimated with the Dutch Adult Reading Test (Schmand et al., 1992).

[c] Time between onset of psychotic symptoms and inclusion in the study.

Procedures and measures

Agency inference task

The agency inference task (Figure 6.1) was identical to the prime-based inference condition used in Renes et al. (2013). The general idea behind this task is that both the participant and computer can stop the rapid movement of a square traversing across 8 white tiles on a computer screen. Participants then indicate the extent to which they feel they caused the displayed square to stop at the position when pressing the key in response to a stop cue [not at all (1) – strongly (9)]. Just before pressing the stop-key, one of the tiles is briefly highlighted, representing the so-called prime (17 ms). The outcome location either matches or mismatches the primed tile (see online Supplementary materials for task details). There were 32 trials; 16 (2x8) match trials and 16 (2x8) mismatch trials.

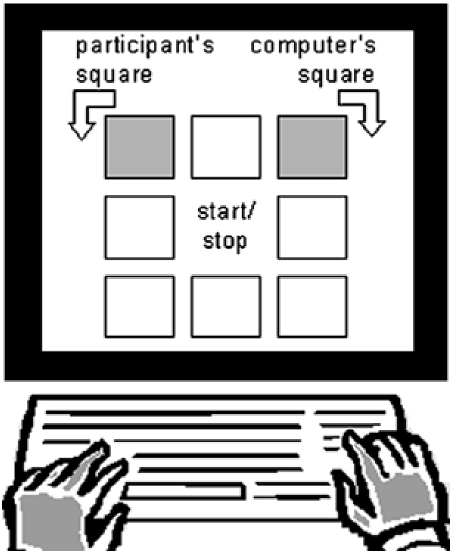

Figure 6.1. Illustration of the experimental task showing how the square of the subject and the square of the computer move in opposite directions.

Prime detection task

After the agency task participants performed a prime detection task, measuring the accuracy in detecting the primed location (one of the eight locations) used in the agency task. Note that participants usually are unaware of these primes in the agency task (Aarts et al., 2005; Belayachi & van der Linden, 2010; Dannenberg et al., 2012; van der Weiden et al., 2010). In contrast, in the detection task participants intentionally and fully attend to the primed location. Therefore, we expect prime detection performance to be above chance. To ensure contextual compatibility between the agency task and the prime detection task, the procedure was identical with one exception: instead of seeing the stopped location, the eight locations were numbered. Participants reported which number they thought corresponded to the briefly presented location. Furthermore, participants indicated their confidence in reporting the correct answer [unsure (1)–sure (9)]. There were 32 trials, presenting each of the eight locations four times.

Results

Self-agency experiences

Mean self-agency experiences were subjected to an ANOVA with Group (patient/control) as a between-subject variable and Matching (match/mismatch) as a within-subjects variable (see Figure 6.2 for means, Table 6.2 for statistics). A main effect for matching was found, indicating that participants experienced more self-agency when outcomes matched rather than mismatched the primed outcome information. Importantly, this effect was solely driven by healthy controls, as patients did not show an effect of matching. Although the group-by-matching interaction did not reach statistical significance, the effect size is moderate (Cohen's $d_s = 0.36$; CI: -0.15–0.86), and the 95% confidence interval largely overlaps with the interval of the Renes et al. (2013) study (Cohen's $d_s = 0.73$; CI: 0.12–1.31). Furthermore, examining the difference in effect size between the two studies yielded a Cohen's $d_s = 0.37$ (CI: -0.41–1.15), indicating that the effect sizes do not differ.

Task attention and motivation did not explain the pattern of findings (see Supplementary results 6.1).

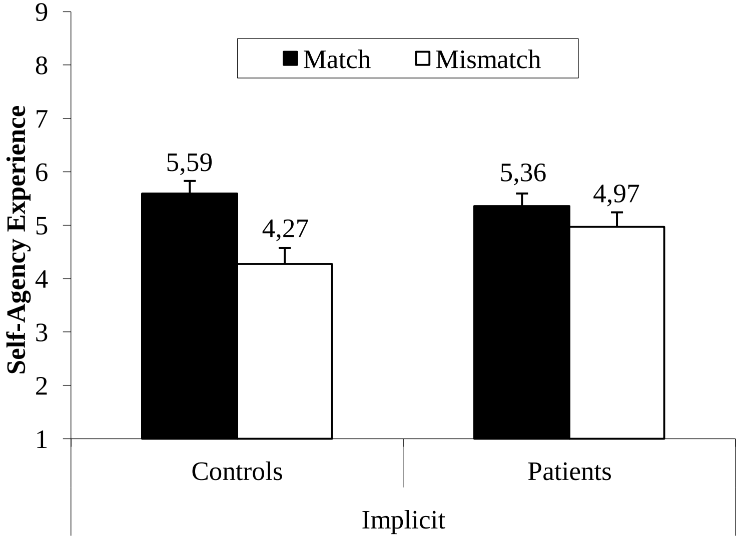

Figure 6.2. Self-agency experiences as a function of Group (patient/control) and Matching between the primed outcome and actual outcome (match/mismatch).

Table 6.2.

Statistical analyses for self-agency experiences

Main analyses (df = 60)	F	Sig.	η_p^2
Group	1.68	.200	.027
Matching	6.78	.012	.101
Matching X Group	2.01	.162	.032
Planned simple main effects (df = 60)			
Matching Controls	8.08	.006	.119
Matching Patients	0.70	.405	.012

Prime detection task

Patients' and controls' accuracy was similar and well above chance level (chance: 12.5% [1 out of 8], patients: 87.4% (SD=8.7); controls: 89.7% (9.2)), $F(1,60) = 1.36$, $p = .313$, $\eta_p^2 = .017$. Furthermore, both patients and controls reported equal confidence in their assessment of the prime location (patients: 7.34 (0.98); controls[3]: 7.63 (1.19)), $F(1,58) = 1.04$, $p = .313$, $\eta_p^2 = .018$. This suggests that both groups were able to visually process the primes and act upon them accordingly.

Discussion

The present study replicates previous findings (Renes et al., 2013), showing that schizophrenia patients (compared to healthy controls) display disturbances in prime-based inferences of agency. This suggests that patients are not able to use implicitly available information about the outcome of an action that would normally lead to a sense of self-agency. Importantly, we ruled out that these disturbances are due to impaired visual processing of the primed outcome in schizophrenia. Whereas some research suggests impaired visual prime processes in schizophrenia (e.g., Cadenhead et al., 1998), the observation that schizophrenia patients and controls were equally able to detect the briefly presented location primes (17 ms) concurs with other recent findings showing intact response-, semantic-, and spatial priming in schizophrenia (Del Cul et al., 2006; Kiefer et al., 2009; Spencer et al., 2011).

Whereas the exact nature of disturbances of primed-based agency inferences in schizophrenia requires further delineation, recent neuroimaging and electroencephalography studies might offer some clues

[3] Due to technical issues, confidence data of the first 3 control participants were lost.

(Dogge et al., 2014; Renes et al., 2015c). Specifically, this research points to a frontoparietal network dedicated to agency inferences. Interestingly, whereas strong connectivity between frontal and parietal regions is displayed during goal-based agency inferences, similar but weaker and more diffuse connectivity occurs in prime-based agency inferences. Crucially, as these latter inferences do not seem to engage attentional control processes (Renes et al., 2015b), they may primarily rely on frontoparietal white matter fibers to broadcast agency-relevant information. Impairments in these fibers in schizophrenia have been well-established (de Weijer et al., 2011; Ellison-Wright & Bullmore, 2009; Whitford et al., 2011). Although the evidence is indirect, the impairment of this vital fronto-parietal network may underlie patients' abnormalities in primed-based agency.

In conclusion, we replicated schizophrenia patients' disturbance in the processing of primed-based agency-relevant information. These abnormalities might underlie poor social interactions that often unfold implicitly and outside of awareness, posing a daily struggle for patients with schizophrenia.

Chapter 7

Impaired frontal processing during agency inferences in schizophrenia

Based on: Renes, R. A., Vink, M., van der Weiden, A., Prikken, M., Koevoets, M. G. J. C., Kahn, R. S., Aarts, H., & van Haren, N. E. M. (2016). Impaired frontal processing during agency inferences in schizophrenia. *Psychiatry Research: Neuroimaging, 248*, 134–141.

Abstract

People generally experience themselves as the cause of outcomes following from their own actions. Such agency inferences occur fluently and are essential to social interaction. However, schizophrenia patients often experience difficulties in distinguishing their own actions from those of others. Building on recent research into the neural substrates underlying agency inferences in healthy individuals, the present study investigates how these inferences are represented on a neural level in patients with schizophrenia. Thirty-one schizophrenia patients and 31 healthy controls performed an agency inference task while functional magnetic resonance images were obtained. Participants were presented with a task wherein the relationship between their actions and the subsequent outcomes was ambiguous. They received instructions to cause specific outcomes to occur by pressing a key, but the task was designed to match or mismatch the color outcome with the participants' goal. Both groups experienced stronger agency when their goal matched (vs. mismatched) the outcome. However, region of interest analyses revealed that only controls showed the expected involvement of the medial prefrontal cortex and superior frontal gyrus, whereas in patients the agency experience was not related to brain activation. These findings are discussed in light of a hypofrontality model of schizophrenia.

Introduction

The feeling that we are in control of our actions and their consequences is central to self-awareness and social interaction. Whether one makes someone smile with a funny remark, or raises one's hand to stop a bus, we generally experience ourselves as the author of the consequences of these actions. Whereas the experience of agency appears quite natural to many individuals, these experiences are impaired in psychiatric illnesses such as schizophrenia. Patients with schizophrenia often exhibit difficulties in experiencing or establishing agency, which may lead to delusions of control, ideas of reference, or hallucination as well as maladaptive social interactions (Blakemore & Frith, 2003; Schneider, 1957).

People experience agency when there is a match between their intended goal and the outcome. Often, these experiences derive from motor cue processes that involve internally-generated (efference) copies that fully predict outcome sensations of one's action (Frith, Blakemore, & Wolpert, 2000; Wolpert & Flanagan, 2001). However, there are many situations in which the relationship between actions and outcomes is less clear, such that individuals cannot easily rely on motor cue processes. The experience of agency, then, relies on non-motor predictions and may result from a cognitive inference process. Such agency inferences are prevalent and may occur when one's own action can produce multiple outcomes or when there are multiple agents who are potentially responsible for an outcome (Dogge et al., 2012; Moore et al., 2009; van der Weiden et al., 2013a; Wegner, 2002). The present study focuses on the neural underpinnings of such agency inferences.

A previous study showed that inferring agency over intended outcomes recruits frontal and parietal regions, specifically the medial prefrontal cortex, bilateral superior frontal gyrus and inferior parietal lobule

(Renes et al., 2015c). These frontal regions may be part of a broader inferential network that enables us to make inferences about goals and beliefs that underlie another agent's behavior (Van Overwalle & Baetens, 2009), and allows processing of self-relevant information (Amodio & Frith, 2006; Northoff et al., 2006; Mason et al., 2007; van Buuren et al., 2010). Furthermore, the parietal region has often been implicated in multisensory integration of information, and is a likely candidate for comparing goals with related action outcomes (O'Connor et al., 2010; Seghier, 2013).

To date, little is known about the mechanisms underlying (abnormal) agency inferences in schizophrenia. In one study, it was shown that in the context of high predictability of an action outcome, patients were not able to use this information to establish agency. However, when the task allowed them to compensate this by using retrospective inference to establish a sense of agency over outcomes, they were able to do so (Voss et al., 2010). This finding suggests that patients' inherent self-awareness difficulties might be overcome by a cognitive mechanism. Indeed, a study specifically testing agency inferences showed that although patients showed a generally lower sense of agency during an agency inference task, they displayed an increased experience of agency when action outcomes matched their intended outcomes – thereby showing a similar pattern as healthy individuals (Renes et al., 2013). The present study aims to investigate whether the same neural substrates are underlying these agency experiences in patients with schizophrenia as compared with controls, i.e., medial prefrontal cortex, bilateral superior frontal gyrus and inferior parietal lobule.

For this purpose, we used an agency inference task that showed robust and reliable effects in previous research in healthy individuals (Dogge et al., 2014; Renes et al., 2015b). In this task, participants are presented with two rapidly alternating color words (blue and red) in the middle of a computer screen. They are instructed to cause either one of the two colors to stop by pressing a key at a specific moment in time, and hence, the act of pressing a key is followed by the color word red or blue presented on the computer screen Thus, participants received the goal to produce a specific outcome by performing an action. The outcome either matched or mismatched the goal that was given to them before the action was performed. The actual color word presented on the screen is determined by the computer, and accordingly, the task is ambiguous in terms of the relation between the participants' action and the resultant outcome.

We have shown robust behavioral effects for this task in that experienced agency was significantly more pronounced when the goal matched rather than mismatched the outcome (Dogge et al., 2014; Renes et al., 2015b), and a recent electroencephalography (EEG) study using this paradigm showed fronto-parietal connectivity related to agency experiences (Dogge et al., 2014). Accordingly, based on the EEG data and our previous fMRI study (Renes et al., 2015c), we expect to conceptually replicate the involvement of fronto-parietal regions in agency experiences in healthy controls. For patients with schizophrenia, our expectations are less clear-cut. Because patients, like healthy controls, have shown increased agency experiences over matches (vs. mismatches) between goal and outcome, one might expect similar brain activation as in healthy controls. However, since accumulating evidence suggests that self-awareness processes in schizophrenia are disturbed at the neural level in the medial prefrontal cortex (e.g., Lee et al., 2006; Vinogradov et al., 2008), and because our task does not measure performance but self-awareness experiences pertaining to agency, it might be possible that the underlying process and the accompanying neural substrates leading to these experiences are different from those in healthy controls. The present study will test these competing possibilities.

Methods

Participants

Thirty-one patients with schizophrenia and 31 healthy controls participated in the study. The sample reported here engaged in a larger study with different tasks (see Renes et al., 2015a). Symptom levels were assessed with the *Positive and Negative Syndrome Scale* (PANSS; Kay et al., 1987) by trained raters, and their diagnosis was confirmed by the *Comprehensive Assessment of Symptoms and History* (CASH; Andreasen et al., 1992a). Participants did not have any drug abuse/dependence during the last six months prior to inclusion. Furthermore, neither controls nor their first-degree relatives had a psychiatric disorder. Patients were recruited from the psychiatry departments of the University Medical Centre Utrecht (UMCU) and Amsterdam Medical Centre. The UMCU's Humans Ethics Commission approved the study. See Table 7.1 for participant characteristics.

Table 7.1

Characteristics of patients with schizophrenia and control subjects (standard deviations in parentheses).

	Schizophrenia Patients (N = 31)	Healthy Controls (N = 31)
Age	29.4 (7.1)	31.3 (6.5)
Male / Female	28 / 3	28 / 3
Years of education[a]	13.1 (1.8)	13.2 (3.9)
Parental years of education	14.1 (3.1)	14.7 (2.6)
Premorbid intelligence[b]	102.1 (8.0)	107.7 (6.7)
Illness duration (years)[c]	9.2 (7.9)	–
PANSS Positive score	10.1 (2.7)	–
PANSS Negative score	11.8 (4.2)	–
PANSS General score	21.7 (3.4)	–
Typical / Atypical medication	3 / 25	–

Patients and controls did not statistically differ on any of the characteristics, except for premorbid intelligence ($t(60) = 3.04$, $p = .004$).

[a] Education information was estimated as part of the *Comprehensive Assessment of Symptoms and History* (CASH; Andreasen et al., 1992a).

[b] Premorbid intelligence was estimated with the Dutch Adult Reading Test (Schmand et al., 1992).

[c] Time between onset of psychotic symptoms and inclusion in the study.

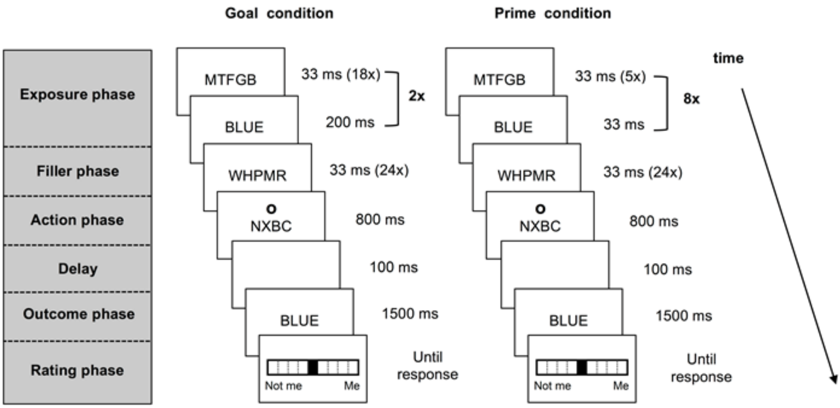

Figure 7.1. Schematic presentation of a match trial in the agency inference task for the goal condition and the prime condition. Presentation times are rounded based on a 60 Hz monitor (e.g., 33ms equals 2 cycles).

Agency inference task and procedure

The agency inference task (Figure 7.1) was taken from previous studies designed to gain high experimental control of timing and presentation parameters (Dogge et al., 2014; Renes et al., 2015b). Participants completed two versions of the task; first, they did a prime-based agency inference task which will be discussed in section 2.3; the goal-based task, which participants completed after the prime-based task, is the focus of this study and shall therefore be presented first. Before starting the experiment, participants were told that the task was designed to assess how experiences of agency come and go, and were asked to indicate how these experiences vary during the task. Similar to playing a slot machine, this task required participants to stop a sequence of rapidly presented information to produce a particular outcome (i.e., the color word red or blue[4]) on the computer screen. Specifically, participants pressed a button on an MRI-compatible fiber-optic response box in response to a cue while viewing alternating letter strings. Upon pressing this button, the stream of letter strings stopped and the color word ‘red’ or ‘blue’ was presented. This outcome could either match or mismatch with prior knowledge regarding the action-effect (i.e., goals). In addition, participants learned that the computer could have caused the presented outcome as well. In other words, the cause of the observed effect was ambiguous. After viewing the effect following their button press, participants reported their feelings of agency over causing the outcome.

Each trial consisted of five different phases: an exposure phase, a filler phase, an action phase, an outcome phase and a rating phase (see Figure 7.1). Each trial started with the exposure phase, where participants were exposed to a series of 18 letter strings followed by a color word that was clearly presented on the screen for 200 milliseconds. This sequence was repeated twice, such that participants were exposed twice to the goal within a 1600 milliseconds period. Participants were instructed to produce the color word that appeared within the series of letter strings (goal setting). During the filler phase, participants attended to rapidly alternating letter strings consisting of 4 or 5 random consonants. This interval served as a delay between exposure to pre-activated information (goal) and the action. Such a delay was also present in previous work on agency inferences (e.g., van der Weiden et al., 2013b). In the action phase, participants responded to a circle (the action-cue) that was presented above or below the letter strings throughout the action phase by pressing a key on the response box with their right thumb. The response could be given within an 800 millisecond

[4] Note that throughout the task, text was presented in a white font color with a dark gray background.

interval. The strings continued to alternate until the end of the response interval, regardless of when participants pressed the button. In case they pressed too late, an error message occurred and the trial was processed as missing (6.7% of the trials for controls, 7.2% for patients).

Following the action phase, the color word ‘red’ or ‘blue’ (counterbalanced between trials) was shown for 1500 milliseconds. A 100 milliseconds delay was added between the action and outcome phase to make these two phases more distinguishable. To ensure that participants maintained looking at the letter strings, participants were told that pressing the key during the presentation of a string containing the letter R (e.g., MTFR) would cause the word ‘red’ to appear, whereas a key press during the presentation of a string containing the letter ‘B’ (e.g., NXBCZ) was followed by the word ‘blue’. Letter strings were presented for 2 cycles on a 60 Hz MRI compatible LCD screen (thus, presentation time was ±33 ms). Importantly, no letter strings containing both B and R were present. Furthermore, this proposed mechanism did not actually cause these colors to occur. In reality, the computer always randomly determined the outcomes, and participants did not have actual control. Thus action and outcome were independent, ruling out the potential contribution of motor-prediction cues.

After each trial, experienced agency was assessed during a rating phase by asking participants to what extent they felt their key press caused the presented color word to occur. They could respond by moving a square on an 8-point analogue scale ranging from ‘*not me*’ (1) to ‘*me*’ (8). The square was positioned in the middle of the scale and participants had to provide their response by moving the square to the left (not me) or the right (me) of the scale. Before starting the next trial, a small white square was shown, functioning as a fixation point during the intertrial interval, which lasted for three seconds minus the response time to the rating phase.

Prior to the fMRI session, participants practiced the task both outside and inside the scanner. The goal trials consisted of 64 trials in a single pseudo-random counterbalanced order. In half of the trials, pre-activated color words corresponded with the actual outcome, whereas in the other half of the trials they did not correspond with this outcome. The ratio of the color words red and blue was always 50/50. Furthermore, the goal trials were divided into 4 parts of 16 trials – each with eight matching and eight mismatching trials – interleaved with 30s rest periods.

Prime-based agency inferences

The agency task described above assesses the individual's ability to experience agency as a result of goal-based inferences, that is, agency experiences over outcomes that ensue from the explicit goal to produce the outcomes by performing an action. However, building on the role of implicit processes in agency inferences, previous research showed that agency experiences are also enhanced when the mere activation (or priming) of outcome information matches (vs. mismatches) with inferences on the actual outcome, and these effects do not seem to mediated by explicit goal-based processes (Renes et al., 2015b). Thus, agency experiences can result from goal-based and primed-based inferences that can be empirically isolated in agency inferences tasks. Accordingly, the present fMRI study also included an agency task to examine the neural substrates of prime-based inferences in healthy controls and patients with schizophrenia. This prime-based inference task was presented to all participants prior to the goal-based inference task described above[5].

In the prime-based agency inference task (also consisting of 64 trials), participants were presented with subtle presentations (i.e., primes) of a color-word, which subsequently matched or mismatched with the actual outcome. Specifically, participants were exposed to a series of 5 letter strings followed by a briefly presented color word (±33 ms). This sequence of events was repeated eight times, resulting in a total of eight primes within a 1600 milliseconds period (see Figure 7.1). Note that the duration of the exposure phase was identical for both types of pre-activation (i.e., goals and primes). Importantly, participants were not instructed to formulate a goal in the prime trials, but were asked to simply respond to the action cue, after which they should trust their feeling to ascertain self-causation. As in the goal-based inference task, key-presses outside the time-window of 800 milliseconds were rare (5.1% of all trials). Crucially, previous studies indicate that patients with schizophrenia are able to process pre-activated information about the outcome of an action but, unlike healthy controls, they do not show the higher levels of experienced agency in the presence of a match relative to a mismatch (Renes et al., 2013; 2015a).

Image acquisition

The experiment was performed on a 3.0 T Philips Achieva MRI scanner (Philips Medical Systems, Best, the Netherlands) at the University Medical Center Utrecht. Head motion was restricted using a vacuum cushion and foam wedges. Images were acquired using an eight-channel sensitivity-

[5] Order effects do not play a statistically significant role in this agency inference task, an observation that has also been reported in a previous publication of this task (Renes et al., 2015a).

encoding (SENSE) parallel-imaging head coil. Whole-brain T2*-weighted echo planar images (EPI) with blood-oxygen level dependent (BOLD) contrast (410 volumes per task; 30 slices per volume; interleaved acquisition; repetition time, 1600 ms; echo time, 23.5 ms; field of view: 256×208 mm; flip angle = 72.5°; 64×51 matrix; 4×4 mm in-plane resolution; 4 mm slice thickness; SENSE-factor, 2.4 (anterior-posterior)) oriented in a transverse plane tilted
20° over the left-right axis were acquired in a single run. The sequence started with six dummy scans to allow for T1 equilibration effects. A whole-brain three-dimensional fast field echo T1-weighted scan (150 slices; repetition time = 8.4 ms; echo time = 3.8 ms; flip angle = 8°; field of view, 288×252×185 mm; voxel size: 1 mm isotropic) was acquired for within-subject registration purposes.

Imaging data pre-processing

Image preprocessing and analyses were carried out with SPM 5 (http://www.fil.ion.ucl.ac.uk/spm/). After realignment, the structural scan was co-registered to the mean functional scan. Next, using unified segmentation, the structural scan was segmented and normalization parameters were estimated. Subsequently, all scans were registered to an MNI T1-standard brain using these normalization parameters, and a 3D Gaussian filter (8 mm full width at half maximum) was applied to all functional images.

Data analysis

For each subject, a model was generated describing event-related changes time-locked to the start of the trial (the exposure, filler, and action phase), the outcome phase and the rating phase (no self-agency experience: ratings

1-4; self-agency experience: ratings 5-8). Agency experience-related activation was modeled as activation during the presentation of the actual outcome, based on whether this outcome matched or mismatched the pre-activated information and the subsequent agency experience. This resulted in four conditions: outcome match and agency experience, outcome match and no agency experience, outcome mismatch and agency experience, outcome mismatch and no agency experience.

To correct for head motion, the six realignment parameters were included in the design matrix as regressors of no interest. Two participants were excluded from further analysis due to excessive head movement (>4 mm) during the acquisition of fMRI scans (van Dijk et al., 2012). To correct for drifts in the signal, a high-pass filter (discrete cosine transform basis functions) was applied to the data with a cutoff frequency of 0.0039 Hz. For each individual subject, brain activation related to agency experience was calculated by contrasting match-agency trials with mismatch-no-agency trials (henceforth referred to as the Agency > No-Self-agency contrast). The resulting individual statistical maps were subjected to a region of interest (ROI) analysis. For this analysis, a mask (see Figure 7.2) was created from the results of the previous study (Renes et al., 2015c). This mask contains four regions: left superior medial frontal gyrus (lSFG), right superior medial frontal gyrus (rSFG), medial prefrontal cortex (mPFC) and left inferior parietal lobule (IPL).

Furthermore, to examine further brain activations outside of the mask, group-wise whole-brain analyses were performed. Maps resulting from this analysis were tested for significance using cluster-level inference (cluster-defining threshold, $p < 0.001$; critical cluster size: 21 voxels, cluster probability of $p < 0.05$, family-wise error corrected for multiple comparisons). These parameters were determined using SPM and a script

(CorrClusTh.m, http://www2.warwick.ac.uk/fac/sci/statistics/staff/academic-research/nichols/scripts/spm), which uses estimated smoothness (estimated full width at half maximum: 3.56 x 3.65 x 3.46 voxels) and random field theory to find these corrected thresholds.

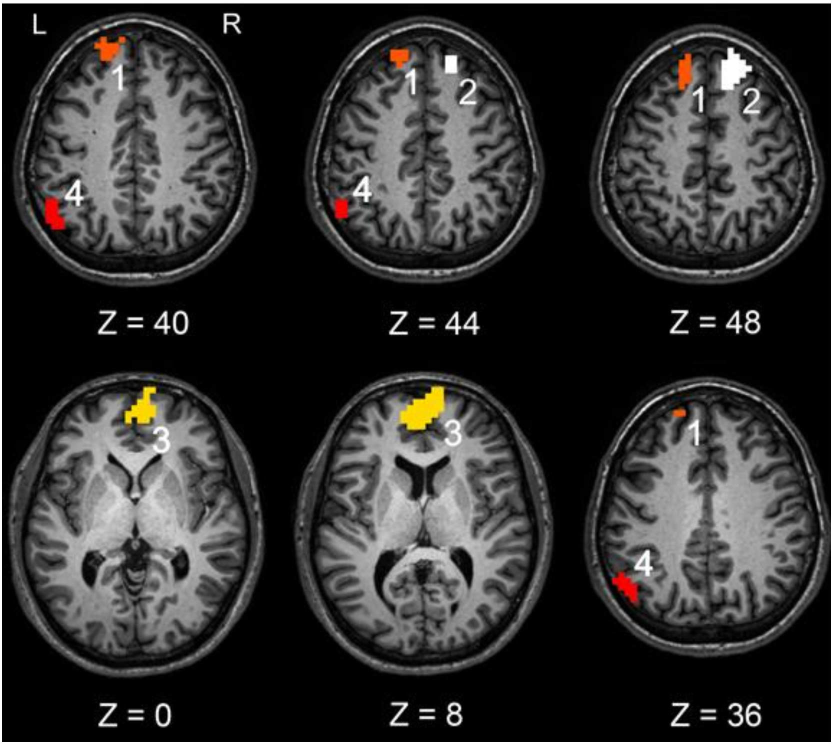

Figure 7.2. Mask of areas related to inferences of self-agency based on Renes et al. (2015c). Legend: 1 = left Superior Frontal Gyrus (lSFG); 2 = right Superior Frontal Gyrus (rSFG); 3 = medial PreFrontal Cortex (mPFC); 4 = Inferior Parietal Lobule (IPL).

Results

Behavioral data:

Agency ratings

Mean agency experiences were calculated for matches and mismatches (see Figure 7.3). A Group (2 levels: Schizophrenia vs. Control) by Matching (2 levels: match vs. mismatch) repeated-measures ANOVA yielded a main effect for Matching ($F(1,60) = 18.8$, $p < .001$, $n_p^2 = .24$), indicating that when a goal matched the actual outcome, more agency was experienced than when it mismatched the actual outcome. No effect of Group was found for mean agency experiences ($F(1,60) = 0.06$, $p = .803$, $n_p^2 < .01$), nor was there an interaction of Group by Matching ($F(1,60) = 0.02$, $p = .900$, $n_p^2 < .01$), indicating that goal-driven agency inferences operated equally well in both groups. Follow-up analyses confirmed this, as both controls ($F(1,30) = 7.14$, $p = .012$, $n_p^2 = .19$) and patients with schizophrenia ($F(1,30) = 13.1$, $p = .001$, $n_p^2 = .31$) showed a significant effect of Matching.

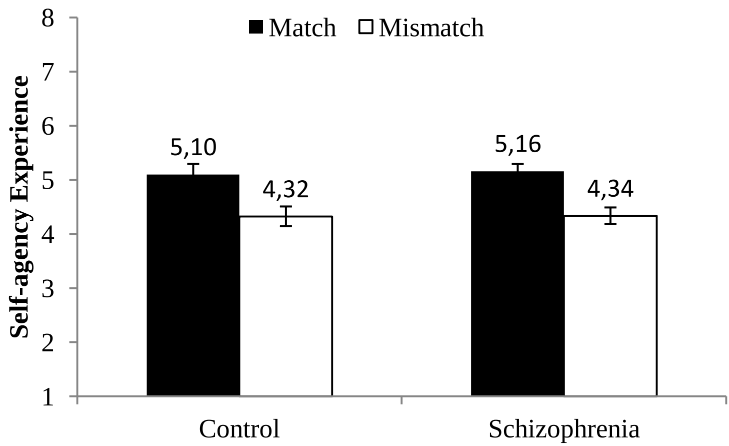

Figure 7.3. Goal based self-agency experiences as a function of Group (control/schizophrenia) and Matching (match/mismatch). Error bars represent standard errors of the mean.

Response times to the action-cue

To check whether response time might influence the agency inference effects, we compared response times for the action cues in the match and mismatch condition as a function of group. Importantly, no main effect of Group was found ($F(1,60) = 0.28$, $p = .595$, $\eta_p^2 < .01$), as both groups were equally able to respond to the action cue (controls: M = 351 ms, SD = 67 ms; patients: M = 359 ms, SD = 56 ms). Furthermore, neither the effect of Matching ($F(1,60) = 0.40$, $p = .528$, $\eta_p^2 < .01$), nor its interaction with Group was significant ($F(1,60) = 1.00$, $p = .321$, $\eta_p^2 = .02$).

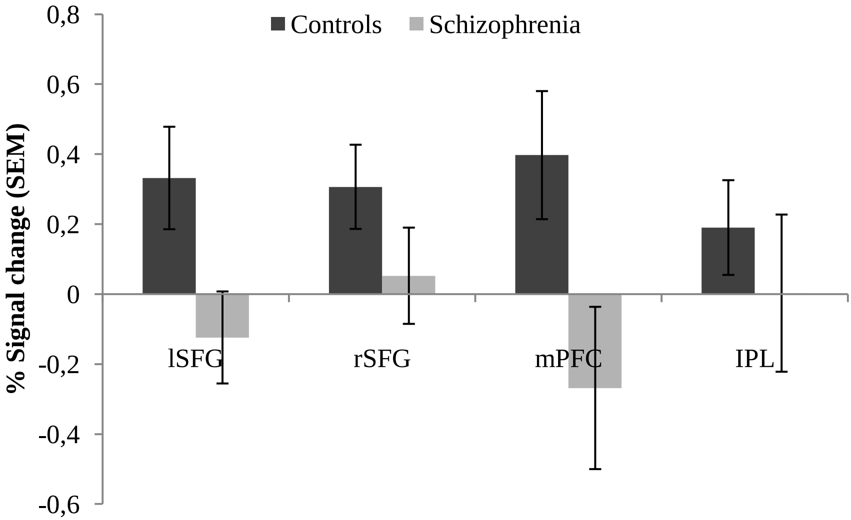

Figure 7.4. Level of activation in predefined regions of interest in patients and controls. lSFG = left Superior Medial Frontal Gyrus, rSFG = right Superior Medial Frontal Gyrus, mPFC = medial PreFrontal Cortex, IPL = Inferior Parietal Lobule.

fMRI

After excluding 4 outliers per group, i.e., participants with activation levels ± 2 SD from the mean activation per ROI, we performed a Group (2 levels: Schizophrenia vs. Control) by ROI (4 levels: lSFG vs. rSFG vs. mPFC vs. IPL) repeated measures ANOVA on the resulting activations in the Agency > No self-agency contrast (Figure 7.4; for sample characteristics, see Supplemental Table 7.1). There was a main effect of Group, $F(1,52) = 4.30$, $p = .043$, $n_p^2 = .08$, showing more brain activation in controls than in patients. No main effect of ROI was found, $F(3,156) = 0.33$, $p = .804$, $n_p^2 = .01$, nor was there an interaction effect between Group and ROI, $F(3,156) = 1.62$, $p = .187$, $n_p^2 = .03$. Follow-up analyses with t-tests (see Table 7.2) showed that for controls, all ROI's except the IPL were activated, whereas for patients no significant activations were found in the ROIs. The two-sample t-tests revealed that there was a significant difference between the groups for the lSFG and the mPFC, showing more activation in controls than in patients. Note that none of the findings of the t-tests would survive stringent bonferroni correction.

Whole brain analyses were performed to check for any activations outside of these regions of interest, both within each group and comparing group differences. However, no significant activations were found in the Agency > No self-agency contrast, nor in the reverse No self-agency > Agency contrast. Removing extend thresholds did not reveal any exploratory differences in these contrasts.

Table 7.2.

Analyses and statistics for the regions of interest.

	One sample t-tests (df=26)				Two sample t-tests (df=52)	
	Control		Schizophrenia			
Region of interest	t	Sig.	t	Sig.	t	Sig.
lSFG	2.27	.032	-0.94	.355	2.32	.025
rSFG	2.55	.017	0.38	.706	1.39	.170
mPFC	2.17	.039	-1.16	.258	2.25	.029
IPL	1.41	.172	0.01	.991	0.72	.478

lSFG = left Superior Medial Frontal Gyrus, rSFG = right Superior Medial Frontal Gyrus, mPFC = medial PreFrontal Cortex, IPL = Inferior Parietal Lobule.

Prime-based agency inferences

For the prime-based agency inference task, there were no significant findings. Matching failed to show a significant behavioral effect, $F(1,60) = 2.86$, $p = .096$, $n_p^2 = .05$, yielding no stronger agency experiences when primes matched the actual outcome as compared to when they mismatched it. Furthermore, no effect of Group was found, $F(1,60) = 1.10$, $p = .299$, $n_p^2 = .02$, nor an interaction of Group and matching, $F(1,60) = 1.39$, $p = .243$, $n_p^2 = .02$, indicating that there was no difference in the effect of Matching between the groups. Follow-up analyses confirmed this. Whereas the means are in the expected direction, for the controls there was no significant matching effect (M = 4.86, SD = 0.69 for match trials; M = 4.59, SD = 0.75 for mismatch trials; $F(1,30) = 2.35$, $p = .136$, $n_p^2 = .07$). For patients with schizophrenia the matching effect was completely absent (M = 4.90, SD = 0.66 for match trials; M = 4.85, SD = 0.59 for mismatch trials; $F(1,30) = 0.53$, $p = .473$, $n_p^2 = .02$). As a result, we did not perform fMRI analyses on prime-based agency inferences.

Discussion

The present study investigated the neural basis of agency inferences in patients with schizophrenia and healthy controls. We obtained functional MRI brain activation measures from brain regions previously found to be associated with agency processing in healthy individuals (Renes et al., 2015c). Both groups reported stronger experiences of agency when action outcomes matched intended goals, replicating earlier work (Renes et al., 2013). Healthy controls activated regions previously associated with agency inferences, being bilateral superior frontal gyrus and the medial prefrontal cortex, although this would not reach significance after correction for multiple comparisons. In contrast, our findings constitute suggestive evidence that the left superior frontal gyrus and the medial prefrontal cortex were not engaged in agency inferences within patients.

Our findings suggest that goal-based agency inferences are associated with reduced frontal activation in schizophrenia patients, implicating inadequate neural processing underlying these agency inferences. As both groups exhibited similar behavioral effects on agency ratings, our findings are not confounded by poor task performance. These findings add to a broader understanding of agency processes and perturbed frontal processing in schizophrenia. Our finding of reduced frontal activations during agency inferences is consistent with the general observation of frontal dysfunction in schizophrenia (Andreasen et al., 1992b; Buchsbaum et al., 1992; Karlsgodt et al., 2007; Ragland et al., 1998; van Veelen et al., 2010; 2011; Weinberger et al., 1992; Yurgelun-Todd et al., 1996), specifically that of hypoactivation in the superior frontal gyrus and medial prefrontal cortex (Bedford et al., 2012; Holt et al., 2011; Koch et al., 2008; Vinogradov et al., 2008).

These results suggest that the neural process underlying agency inferences is impaired in schizophrenia. Impairments in the regions involved in this process may be related to broader self-disturbances in schizophrenia. Indeed, hypoactivations in these frontal regions are associated with deficits in self-awareness (Lee et al., 2006), theory of mind (e.g., Brunet et al., 2003; Russel et al., 2000; Walter et al., 2009), and self-referential processing (Holt et al., 2011; van Buuren et al., 2012; Vinogradov et al., 2008). Despite these widespread deficiencies, patients still display the ability to process agency inferences in the context of our task. Interestingly, we did not detect group differences outside the regions of interest. One would expect to find such differences, as it is not unlikely that patients utilized a compensatory mechanism to overcome their frontal abnormalities.

A potential explanation is that the task, although well-validated, may have been relatively easy. Indeed, when patients with schizophrenia are faced with a more difficult agency inference task where outcome information is implicitly pre-activated (i.e., primed) instead of presented as an explicit goal, patients are no longer able to experience more agency when this pre-activated information is matched by the actual outcome (Renes et al., 2013; 2015b). This suggests that, despite abnormal frontal activation, patients might apply a compensatory mechanism enabling them to report agency in an easy context where the experience is informed by explicit goal-directed behavior. It might be that hypofrontality makes them vulnerable for misjudgments of agency in more complex (real-life) situations, where patients often experience difficulties in social functioning and communication.

For healthy controls, our finding of increased bilateral superior frontal gyrus and medial prefrontal cortex activation during agency inferences is consistent with previous findings testing a different type of agency inference task (Renes et al., 2015c). The medial prefrontal regions have also been associated with thinking about agency judgments (Miele et al., 2011), self-referential processing (Kelley et al., 2002; van Buuren et al., 2010), making trait or social inferences (Ma et al., 2011; van Overwalle & Baetens, 2009), whereas the more lateral regions are related to self-referential processing and other higher-order processing of self-awareness (Northoff et al., 2006).

In contrast to our hypothesis and earlier findings (Renes et al., 2015c), we did not find significant inferior parietal lobule activation during agency experiences in healthy controls. This discrepancy could be due to the difference between the tasks. In the previous study, subjects had to follow rotating squares across a rectangular field, and were instructed to stop them at a specific location by a button press (i.e., goal-directed processing; Aarts et al., 2005; Renes et al., 2015c). In contrast, the present task used semantic information which was centrally presented on the screen to prevent biases related to eye movement deficiencies typically observed in patients (e.g., Raemaekers et al., 2006).

Yet, the absence of involvement of the inferior parietal lobule was not expected, given recent findings of parietal lobe involvement during a similar semantic version of the task using EEG (Dogge et al., 2014). Also, a recent review describing the functions of this region suggested that the angular gyrus (a subregion of the IPL) is involved in both spatial attention and semantic processing, among many other functions (Seghier, 2013). Specifically, this area plays a major role in the integration of multisensory information and interpretation of the sensory information at a conceptual level. Therefore, it is not unlikely that the IPL is indeed involved in both tasks, as both semantic and special information is processed and integrated here. Hence, the absence of the expected inferior parietal lobe activation in the current study might be due to low statistical power.

In line with previous studies (Renes et al., 2013; 2015a), patients did not rely on pre-activated information about the outcome (i.e., primes) to guide experiences of agency. However, in contrast to earlier findings (Aarts et al., 2005; Linser & Goschke, 2007; Sato, 2009), no prime-based agency inferences were found in healthy controls either. Whereas we currently do not know the cause of the absence of the primed-based inferences in healthy controls, one possibility might be that the task environment (administering the prime-based agency inference task in the MRI scanner) increased stress and distraction in our participants (e.g., Tessner et al., 2006), such that the otherwise subtle effects of primed-based agency inferences vanished. Whatever the exact reason for the absence of a clear primed-based agency inference effect in healthy controls, we deemed further interpretation of the primed-based agency inference data uninformative.

We wish to stress that the present findings need to be interpreted in light of a few limitations. First, there is the potentially confounding factor of antipsychotic medication. Future studies could eliminate this factor by testing medication-naïve patients with schizophrenia. However, it is unlikely that medication actually confounds these findings, as hypoactivation in the frontal cortex has also been shown in medication-naive patients (e.g., Lee et al., 2006; Snitz et al., 2005; van Veelen et al., 2010; 2011). Additionally, it is important to note that the patients in the current study are relatively high functioning; they have mild symptoms, and education levels are similar to controls. Finally, the present study aimed to capture the strength of conscious experiences of agency, which may be more difficult to assess than, for example, simple motor performance, due to the inherent noisiness and complexity of measuring individual differences in, and reporting of conscious experiences (Frith et al., 1999; Rees et al., 2002; Block, 2005). In the context of our task this means that the attribution of a self-agency experience over an outcome of patients may differ from that of the healthy controls. One of the disadvantages of measuring conscious experiences is that it remains unclear whether patients and controls interpret and apply the agency rating scale in the same way, i.e., whether the experience of agency is qualitatively the same for healthy controls and schizophrenia patients.

Summary and conclusion

The present study employed an agency inference task to investigate the neural correlates of agency inference processing in patients with schizophrenia. This is the first study showing that agency inferences are associated with frontal hypofunction in patients with schizophrenia, contributing to a rapidly growing body of research showing disturbances in self-processing in schizophrenia. Future studies might investigate how agency deficiencies develop over time in a high-risk population to help understand how such experiences develop during transition to psychosis and how they relate to agency related symptoms and social functioning.

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Supplementary Materials

Supplementary Table 5.1

Visual attention scores (mean(SD)) and statistics.

To what extent were you able to follow your own rotating square on during the task?							
Implicit task				Explicit task			
Controls	Patients	F	Sig.	Controls	Patients	F	Sig.
7.83(1.47)	7.22(1.95)	1.43	.15	7.65(1.58)	7.39(1.85)	0.263	.61

Supplementary Table 5.2

Reaction times and statistics to the ‘stop’ cue as a function of Group and Priming type. All non-statistical values are in milliseconds.

	Explicit	Implicit
Controls	563(161)	393(169)
Patients	570(251)	450(167)
	F	Sig.
Group	0.43	.51
Type	24.1	< .001
Group X Type	0.703	.41

Supplementary Table 5.3

Subjective motivation scores (mean(SD)) and statistics as a function of Group and Type of task.

	Controls	Patients	F	Sig.
Implicit	8.30(.71)	8.11(.83)	0.74	.40
Explicit	8.07(.84)	8.57(.51)	5.94	.019
ANCOVAs covaried with corresponding motivation score				
Implicit Matching			4.38	.042
Explicit Matching			3.93	.054
Implicit Group X Matching			5.21	.028
Explicit Group X Matching			1.99	.17

Supplementary Results 6.1

Task motivation and attention

As we performed tests on three separate measures of attention and motivation, the bonferroni corrected alpha is .017 for the following tests.

The two items were averaged to obtain a measure of task motivation. The correlation between this measure and the effect of Matching showed that subjective measures of motivation were relevant to the task ($r(62) = 0.31$, $p = .016$). No difference between groups was found on this measure of task motivation, $F(1,60) = 0.83$, $p = .365$, $\eta\rho^2 = .014$; patients [M(SD) = 7.81(1.01)] vs. controls [M(SD) = 8.02(0.78)].

No statistical difference was found on the subjective measure of task attention, $F(1,60) = 4.91$, $p = .031$, $\eta\rho^2 = .076$; as controls reported similar ability in being able to maintain visual task attention [M(SD) = 7.90 (1.35)] as patients [M(SD) = 7.03 (1.72)]. Although approaching statistical significance, the previous study from Renes et al. (2013) also showed that no attentional differences between the group, lending credence to the idea that in these samples, no differences exist.

Finally, response times to the stop cues did not differ between patients [M(SD) = 527 (225) ms] and controls [M(SD) = 525 (303) ms], $F(1,60) = 0.001$, $p = .971$, $\eta\rho^2 < .001$. Accordingly, differences in motivation and attention did not explain the pattern of findings.

Effect sizes

Effect sizes were calculated with the help of the Center of Evaluation & Monitoring's website (http://www.cem.org/effect-size-calculator). The present study reports effect sizes of the previous study into prime-based self-agency inferences in schizophrenia (Renes et al., 2013), alongside with the effect size of the present study's findings:

Renes et al., 2013: Cohen's d_s*=0.73; CI: 0.12–1.31*

Present study: Cohen's d_s*=0.36; CI: -0.15–0.86*

Difference: Cohen's d_s*=0.37; CI: -0.41–1.15*

The calculated difference in effect sizes between these studies and the corresponding 95% CI expresses whether the effects found in studies differ (for an interesting discussion on the new statistics, see Cumming, 2014). The confidence interval is calculated by subtracting the two effect sizes, and pooling the standard error of these effect sizes:

$(X$

(see http://www.stat.wmich.edu/s216/book/node81.html)

Where *X* indicates the effect size, and *Se* indicates the standard error of the effect size.

For an indication of the effect size for future replications, the effects sizes of both studies can be pooled:

Pooled effect size: Cohen's d_s*=0.48; CI: 0.1–0.86*.

Supplementary Table 7.1

Characteristics of patients with schizophrenia and control subjects included in the region of interest fMRI analyses (standard deviations in parentheses).

	Schizophrenia Patients (N = 27)	Healthy Controls (N = 27)
Age	30.0 (7.3)	30.9 (6.6)
Male / Female	24 / 3	24 / 3
Years of education[a]	13.2 (1.8)	13.0 (4.0)
Parental years of education	14.0 (3.3)	14.8 (2.5)
Premorbid intelligence[b]	102.6 (8.0)	107.6 (6.6)
Illness duration (years)[c]	10.0 (8.0)	–
PANSS positive score	10.0 (2.7)	–
PANSS negative score	11.9 (4.5)	–
PANSS general score	21.7 (3.3)	–
Typical / Atypical medication	2 / 22	–

Patients and controls did not statistically differ on any of the characteristics, except for premorbid intelligence ($t(52) = 2.47$, $p = .017$).

[a] Education information was estimated as part of the *Comprehensive Assessment of Symptoms and History* (CASH; Andreasen et al., 1992a).

[b] Premorbid intelligence was estimated with the Dutch Adult Reading Test (Schmand et al., 1992).

[c] Time between onset of psychotic symptoms and inclusion in the study.

Contributions and funding

Contributions

<u>Chapter 1</u>

Solo-authored with helpful comments from Henk Aarts.

<u>Chapter 2</u>

Solo-authored with helpful comments from Henk Aarts.

<u>Chapter 3</u>

Author Renes aided in study design and data collection, conducted statistical analyses, interpreted results, and wrote the first draft of the manuscript. Author Aarts aided in designing the study, directed data collection, provided conceptualization and theory used to integrate the findings, interpreted results, and edited the manuscript. Author van Haren aided in study design, obtained grant funding, interpreted results, and edited the manuscript.

<u>Chapter 4</u>

Author Renes aided in study design and data collection, conducted statistical analyses, interpreted results, and wrote the first draft of the manuscript. Author van Haren aided in study design, obtained grant funding, interpreted results, and edited the manuscript. Author Aarts aided in designing the study, directed data collection, provided conceptualization and theory used to integrate the findings, interpreted results, and edited the manuscript. Author Vink conducted statistical analyses, interpreted results and edited the manuscript.

Chapter 5

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Chapter 6

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Chapter 7

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Nederlandse samenvatting

In dit proefschrift leg ik de loep op het gevoel van zelf-causatie, het gevoel dat je verantwoordelijk bent voor je eigen acties en de uitkomsten die deze acties teweegbrengen. Dit kan zo eenvoudig zijn als weten dat jij het licht aan hebt gedaan na het drukken op een lichtknop, maar we ervaren het ook in meer complexe situaties. Een mooi voorbeeld van dit laatste ervaren velen van ons regelmatig in het verkeer: we rijden haastig richting een rood verkeerslicht, en vlak voordat we moeten remmen verzoeken we met een gedachte dit verkeerslicht om op groen te springen – op het moment dat dit dan vrijwel meteen gebeurt hebben we kort het een gevoel van zelf-causatie, waarbij we denken dat onze gedachte ervoor zorgde dat het verkeerslicht op groen sprong. Natuurlijk realiseren we ons dat dit onmogelijk is, maar dit soort voorbeelden laten zien dat dit gevoel onze gedachten stuurt in onduidelijke situaties.

We ervaren zelf-causatie niet echter enkel alleen, maar het is ook een van de fundamenten van ons sociale leven. Doordat we weten en voelen dat we allemaal verantwoordelijk zijn voor onze acties, kunnen we elkaar verantwoordelijk houden voor ieders gedrag – we prijzen onszelf en anderen voor goed gedrag, maar straffen wanneer iemand zich misdraagt. Dit laatste doen we echter in mindere mate als we begrijpen dat iemand minder zelf-causatie ervaart over zijn gedrag, bijvoorbeeld bij kinderen of mensen met een psychische stoornis.

Voordat ik inga op het onderzoek in dit proefschrift, is het goed om kort toe te lichten waar dit gevoel van zelf-causatie vandaan komt. Al vanaf de eerste maanden van ons leven proberen we te ontdekken wat onze rol is in de wereld. In de wieg maken we dikwijls spontane bewegingen, en we merken steeds wat deze bewegingen tot stand brengen. Als een schop tegen een speeltje een leuk geluid voortbrengt, snappen we al snel dat we dit geluid kunnen herhalen door keer op keer tegen het speeltje te schoppen – er is namelijk een duidelijke relatie tussen onze actie (het bewegen van je been) en de uitkomst (een leuk geluid). In dit soort duidelijke situaties kan ons motorische systeem op den duur voorspellen welke uitkomst wordt veroorzaakt door elke actie, en dit zorgt ervoor dat we onderscheid kunnen maken tussen wat wij doen, en wat anderen doen – dit ligt ten grondslag aan het gevoel van 'zelf', wat zonder meer elke dag een onmisbare rol speelt in ons level.

Als we wat ouder worden leren we ook het verband te zien tussen onze doelen en uitkomsten, en kunnen daardoor zelf-causatie ervaren in situaties waarin we eigenlijk weinig controle hebben. Een mooi voorbeeld hiervan is toen ik als klein kind een SEGA controller pakte om vervolgens de acties van Calimero te besturen tijdens een TV-uitzending hiervan. Ondanks dat ik hier geen controle had over de bewegingen van Calimero, deed hij af en toe toevallig wat ik aangaf op mijn controller, waardoor ik toch controle ervoer. Dit illustreert dat we niet alleen met ons motorische systeem kunnen herleiden dat wij iets veroorzaken, maar ook dat het gevoel van zelf-causatie voort kan komen uit een *inferentie*, waarbij we zelf-causatie ervaren doordat we na het observeren van de uitkomst van een actie snel bedenken of wij dit veroorzaakt hebben.

Onderzoek naar zelf-causatie als een inferentie staat nog relatief in zijn kinderschoenen, pas in de laatste 15 jaar is daar steeds meer aandacht voor gekomen. Een belangrijk onderscheid dat gemaakt wordt in dit recente onderzoek is de bron van zo'n inferentie. Dit kan ofwel gebaseerd zijn op een doel, ofwel op een 'prime', hetgeen niet meer is dan een minuscule hoeveelheid informatie over de uitkomst, die vaak onbewust ons systeem binnen komt. Een van de bekendste voorbeelden van een prime komt uit de verkiezingscampagne van George W. Bush, die in het spotje het woord 'Democrats' liet volgen op het woord 'RATS', hetgeen maar een paar milliseconden in beeld was. Hier was het zijn bedoeling om bij kijkers een onbewuste associatie te maken tussen het woord 'ratten' en 'democraten. Hoewel het onbekend is of dit succesvol was in zijn campagne, heeft psychologisch onderzoek laten zien dat een prime daadwerkelijk informatie kan activeren in ons mentale apparaat. In het specifiek voor dit proefschrift, is reeds bekend dat het primen van een uitkomst voorafgaand aan een actie er voor kan zorgen dat we meer zelf-causatie ervaren als deze uitkomst later daadwerkelijk verschijnt. Dit is interessant, omdat mensen in het dagelijks leven veel informatie onbewust binnenkrijgen vanuit de omgeving, hetgeen ons gedrag vaak onbewust stuurt. Met het primen van informatie kunnen we dit simuleren terwijl de onderzoeker dan precies kan bepalen wat iemand te zien krijgt.

Verschillen tussen doelen en primes bij de totstandkoming van zelf-causatie

Zowel doelen als primes kunnen gezien worden als bron van informatie over de uitkomst bij inferenties van zelf-causatie. Eerder onderzoek heeft laten zien dat zolang deze informatie overeenkomt met de daadwerkelijke uitkomst, er een sterker gevoel van zelf-causatie ervaren wordt. Echter kan het ook zijn dat de uitkomst anders is dan verwacht op basis van deze informatie – hier werd gevonden dat – vergeleken bij een controlegroep – gevoelens van zelf-causatie minder worden bij informatie van doelen, maar niet van primes. In Hoofdstuk 3 zocht ik uit waarom dit verschil er was, en mijn uitgangspunt was dat het gebruik van het sturen van aandacht (*attentional control*) ervoor zorgde dat bij doelen minder zelf-causatie ervaren werd wanneer een uitkomst niet overeenkwam met het doel. Dit houdt in dat als we een doel hebben (bijvoorbeeld het veroorzaken van de kleur rood in een taakje), we dit actief houden in ons geheugen met behulp van aandacht. We herhalen 'rood' voor onszelf totdat we zien of we de gewenste uitkomt veroorzaken, en gebruiken deze informatie om ons gevoel van zelf-causatie te informeren. Bij primen zou dit niet moeten gebeuren, aangezien dit uitgaat van automatische processen die vaak buiten onze aandacht om gaan.

Dit heb ik getest door het vermogen van mensen om hun aandacht te richten op de bron van informatie (doelen of primes) te verminderen. Deelnemers moesten ofwel 2, ofwel 5 getallen onthouden tijdens het doen van een zelf-causatie taakje. Het bleek dat het inderdaad moeilijker was om 5 getallen te onthouden dan 2, en dit zorgde er daadwerkelijk voor dat mensen minder goed werden in het ervaren van zelf-causatie wanneer ze dit gevoel baseerden op doelen. Bij het gebruik van primes was er geen verschil in zelf-causatie ervaringen bij het onthouden van 2 of 5 getallen, waardoor dit onderzoek het idee ondersteund dat het doelgericht sturen van aandacht inderdaad er voor zorgt dat we in staat zijn om sterkere gevoelens van zelf-causatie te hebben over onze acties. Een belangrijke implicatie hiervan is dat als we op een doelgerichte manier handelen in het dagelijks leven en we veel aan ons hoofd hebben, we ons minder verantwoordelijk zullen voelen voor de uitkomsten – waardoor we mogelijk minder genieten van de fijne uitkomsten in het leven, maar ons ook minder aansprakelijk voelen voor onze fouten.

Zelf-causatie in onze hersenen

Om meer te weten te komen over hoe de ervaring van zelf-causatie tot stand komt, heb ik in meerdere studies gekeken naar de bron van dit gevoel: onze hersenen. Met behulp van moderne technieken heb ik hersenactiviteit gemeten bij deelnemers die tijdens het uitvoeren van een zelf-causatie taak in een MRI-scanner lagen (Magnetic Resonance Imaging). Deelnemers hadden tijdens de taak steeds een doel om een bepaalde uitkomst te veroorzaken, en dit was soms succesvol en soms niet. Deelnemers gaven na elke ronde aan in hoeverre zij het gevoel hadden de uitkomst te veroorzaken. Met behulp van deze aanduidingen heb ik gekeken wat voor hersenactiviteit gerelateerd was aan het gevoel van zelf-causatie. Halverwege Hoofdstuk 4 kun je een plaatje zien van de gebieden die hierbij betrokken zijn. Het belangrijkste gebied dat ik vond was de 'medial prefrontal cortex', een gebied aan de voorkant van onze hersenen die in andere onderzoeken ook is gerelateerd aan het maken van inferenties en het verwerken van zelfgerelateerde informatie. Een ander belangrijk gebied was de 'inferior parietal lobule', een gebied dat ongeveer boven ons linker oor zit. Dit gebied is betrokken van het verwerken van informatie van verschillende zintuigen, en is eerder gevonden in studies waarbij succesvol vergelijkingen gemaakt werden tussen eerdere informatie en nieuwe informatie. Deze bevindingen samen nodigen uit om tot een model te komen waarin de inferior parietal lobule analyseert of een doel bereikt is, en de uitkomst van deze vergelijking naar de medial prefrontal cortex doorstuurt en het daar tot een gevoel van zelf-causatie komt. Een vergelijkbaar onderzoek dat geen onderdeel is van dit proefschrift laat inderdaad zien dat tijdens het ervaren van zelf-causatie informatie in de hersenen in deze richting verstuurd wordt.

De ervaring van zelf-causatie in patiënten met schizofrenie

Tot nu toe heeft het onderzoek in dit proefschrift zich vooral gericht op mensen die gezegend zijn met een gezond brein, waarin zonder problemen onderscheid gemaakt kan worden tussen zelf en ander. Echter heeft niet iedereen deze luxe; patiënten met schizofrenie hebben vaak moeite met het onderscheid tussen zelf en ander, en hebben als onderdeel van hun ziekte vaak symptomen waarin zelf-causatie processen ernstig verstoord lijken. Sommige patiënten horen bijvoorbeeld stemmen in hun hoofd, en ervaren deze als komend van buitenaf – terwijl deze stemmen in werkelijkheid 'gewoon' door henzelf geproduceerd worden. Deze symptomen veroorzaken veel problemen voor deze patiënten, en zijn een duidelijk voorbeeld van hoe essentieel zelf-causatie processen zijn om goed te kunnen functioneren in onze complexe sociale maatschappij. Om meer te weten te komen over hoe zelf-causatie processen tot stand komen, en hoe patiënten met schizofrenie doelen en primes gebruiken om tot ervaringen van zelf-causatie te komen heb ik voor dit proefschrift meerdere onderzoeken gedaan om hier zoveel mogelijk over te weten te komen.

In Hoofdstuk 5 laat ik eerst zien dat patiënten met schizofrenie net zo goed in het infereren van zelf-causatie zijn als gezonde deelnemers wanneer men doelen gebruikt als bron van informatie. Echter ging dit niet zo voortvarend wanneer patiënten met schizofrenie alleen primes konden gebruiken – ze konden deze subtiele informatie niet goed gebruiken om te bepalen of zij een uitkomst wel of niet veroorzaakten. Om zeker te weten dat deze laatste observatie klopt, heb ik dit onderzoek in Hoofdstuk 6 nogmaals uitgevoerd. Hier kon weer dezelfde conclusie uit getrokken worden. Bovenop deze replicatie liet ik zien dat de zelf-causatie problemen niet ontstonden doordat patiënten met schizofrenie minder gemotiveerd waren, minder aandacht hadden, of de primes misschien niet konden verwerken. In dit alles waren de net zo capabel als gezonde deelnemers. Het lijkt er op dat er een specifiek probleem is met het omzetten van de subtiele primes naar het gevoel van zelf-causatie, een mechanisme dat kan verklaren waarom patiënten met schizofrenie soms moeite hebben met het onderhouden van sociale contacten, waarin we veel informatie subtiel en onbewust naar elkaar communiceren.

In het laatste hoofdstuk van dit proefschrift probeer ik uit te vinden hoe de ervaring van zelf-causatie tot stand komt in de hersenen van patiënten met schizofrenie. Het doel hiervan was om nogmaals de eerdere bevindingen uit Hoofdstuk 4 aan te tonen en eventuele kwetsbaarheden te ontdekken in de verwerking van zelf-causatie bij mensen met schizofrenie. In gezonde deelnemers vond ik inderdaad weer de betrokkenheid van de gebieden uit Hoofdstuk 4 bij het ervaren van zelf-causatie met behulp van doelen. Echter was er in deze gebieden geen activiteit gerelateerd aan zelf-causatie bij patiënten met schizofrenie – een opvallende bevinding, omdat de patiënten wel aangeven dat ze dit ervaren(!). Bij het napluizen van andere onderzoeken werd het duidelijk dat patiënten met schizofrenie vaak verminderde activiteit hebben in frontale hersengebieden, een observatie die waarschijnlijk ten grondslag ligt aan de bevindingen in mijn onderzoek. De implicatie hiervan is dat informatie met betrekking tot de 'zelf' op een minder efficiënte manier verwerkt wordt vergeleken bij gezonde mensen. Het kan dus goed zijn dat een ander hersengebied – eentje waar mijn analyse niet gevoelig voor was – de verwerking van de zelf-causatie inferentie op zich nam. Dit pakt goed uit omdat de taak relatief simpel was; deelnemers hadden immers enkel de opdracht om aan te geven of ze succesvol waren in het nastreven van een doel in een taak. Een andere verklaring is dat ze misschien wel *wisten* dat ze de uitkomst veroorzaakten, maar het niet *voelden* op dezelfde manier als dat gezonde deelnemers dat deden. Toekomstig onderzoek zou uit kunnen pluizen hoe de vork hier aan de steel zit. Voor nu is het echter wel goed voor te stellen dat deze inefficiënte manier van zelf-causatie verwerking voor problemen kan zorgen als de situatie ingewikkelder wordt – iets dat we ook terugzien in Hoofdstukken 5 en 6 waarin patiënten met schizofrenie inderdaad niet genoeg hebben aan subtiele primes om dit een gevoel van zelf-causatie te komen.

Al met al maakt het multidisciplinaire onderzoek in dit proefschrift belangrijke stappen in het onderzoek naar zelf-causatie. We begrijpen nu beter hoe dit gevoel tot stand komt via doelen en primes, er zijn eerste stappen gemaakt in het begrijpen van de onderliggende processen in de hersenen, en het onderzoek biedt aangrijpingspunten voor het begrijpen van verstoringen in zelf-causatie processen in mensen met schizofrenie.

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Zowel in het UMC als op de universiteit, van het begin tot het einde van mijn project kon ik altijd terecht bij Anouk. Qua onderwerp was je mijn voorganger, hetgeen ervoor gezorgd heeft dat ik je proefschrift grijs heb gelezen, daar bovenop heb ik je openheid, behulpzaamheid en humor ook altijd erg op prijs gesteld en wist je me altijd perspectief te geven met je adviezen over het PhD-student zijn. Ik ben blij dat de UU je terug heeft weten te halen en ik hoop dat ze zo wijs zijn om je nog lang te houden.

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Curriculum Vitae

Robert Alexander Renes was born October 19th, 1987 in Amersfoort, the Netherlands. After completing his secondary school at the *Nassau Veluwe College* in Harderwijk, he started his bachelor in psychology at Utrecht University in 2006. Here, he specialized in Social Psychology and graduated in 2009. This was swiftly followed by a research master's degree in Social and Health Psychology at Utrecht University in 2011, during which he also worked as a research assistant for Henk Aarts and Ruud Custers.

In 2011 he started working as a PhD-student under the supervision of Henk Aarts, René Kahn, Neeltje van Haren and Matthijs Vink, in a cooperative project between Utrecht University and the Psychiatry department of the University Medical Center Utrecht.

Currently he is working as a tutor/instructor at University College Utrecht, where he teaches multiple courses in the Psychology curriculum and acts as a tutor for 34 bachelor students. Furthermore, he is involved in the supervision of thesis students for the work and organizational psychology department at the University of Amsterdam.