PSYCHIATRIC SYMPTOMS AS PATHOGENS

Marcel van den Hout

Abstract

Disorders are typically seen as the causes of their symptoms. This makes sense in many fields of medicine, but not in psychiatry where symptoms constitute disorders: the notion that mental disorders cause symptoms is a tautology. Biological psychiatry tries to circumvent this logical fallacy by trying to identify pathophysiological parameters that are specific to given disorders. Unfortunately, research has not resulted in biological markers that reliably discriminate patients who suffer from a disorder from those that do not. A different approach is to regard psychiatric symptoms not as 'output' from underlying, yet to be identified (pathophysiological) dysregulation, but to consider symptoms as "input" that causally contributes to other symptoms. Fresh insights, mathematical methods and empirical data come from network analyses, derived from physics. These network approaches, treating "symptoms as input" converge with work in Cognitive Behavior Therapy and in Experimental Psychopathology. This convergence is illustrated with experimental work on Obsessive Compulsive Disorder. It is argued that data and concepts from network theory provide a sound conceptual rationale for treating symptoms as input and that network theory, Cognitive Behavior Therapy and Experimental Psychopathology are intellectual allies that reinforce each other.

Key words: experimental psychopathology, psychiatric symptoms, pathogen, cognitive behaviour therapy, obsessive-compulsive disorder

Declaration of interest: none

Marcel van den Hout
Utrecht University - The Netherlands
E-mail: m.vandenhout@uu.nl

1) Symptoms and disorders

Early 2003, in Belgium, a fifty-five year old male tourist was overrun by a car. To exclude skull or brain damage, scans were made. Incidentally the neurologist discovered a brain tumor. Though the patient showed no neurological symptoms, the tumor was evident and the doctor urged the patient to consult a neurologist at home. Suppose a psychologist or psychiatrist examines an individual, finds no psychiatric signs or symptoms, and tells the individual that he suffers from a mental disorder: "You may not have hallucinations, delusions and the like, but you *are s*uffering from schizophrenia". This would be absurd. The very fact that a sound neurological diagnosis can be made in the absence of symptoms while this would be ridiculous in the case of mental disorders, points to an important feature of psychiatric diagnosis. It has implications for our understanding of mental disorders and for the nature of research in psychopathology. These implications are discussed in the remainder of this paper. We will focus on:

- The logic of explanation in general and in psychiatry.
- How DSM inspires to tautological (pseudo) explanations.
- Ways to prevent the latter and introduce "network theory" as a fresh approach
- The common emphasis of network theory, Cognitive Behavior Therapy (CBT) and Experimental Psychopathology on the *effects* of psychiatric symptoms on other symptoms
- Research on Obsessive Compulsive Disorder (OCD) that illustrates how the causal nature of symptoms can be fruitfully studied.

To prevent misunderstanding from the outset, we do not question the existence of (relatively) distinct mental disorders, or the utility of diagnostic systems like the DSM or ICD. What we do question is that, in psychopathology, "diseases" or "disorders" explain symptoms or that symptoms are causally inert 'output' from deeper problems. Arguments like the latter easily become tautological and we will argue that, perhaps surprisingly, symptoms can be validly explained by other symptoms.

2) The logic of explanation: independence of explanans and explanandum

When we try to explain a phenomenon, the phenomenon to be explained is traditionally called the "explanandum" while the explanation itself is called the "explanans". When we want to explain why person X is rich and we learn that he won the lotto, the richness is the explanandum and winning the lotto is the explanans. Note that the explanans and explanandum need to be defined independently. If we explain X's richness by the fact that he owns a lot of money, the "explanation" fails because it is a tautology: richness is *defined* as owing much money, explanans and explanandum are not independent, and this 'explanation' boils down to the assertion that "X is rich because X is rich" (Nagel 1971). The Belgian neurologist, introduced at the beginning of this text, had a valid explanans: the brain tumor. It is defined independent from any symptoms and does allow for predicting that symptoms and signs (explanandum) will occur if the tumor (explanans) is left untreated. The situation in psychiatry is radically different. Yes,

Submitted October 2014, accepted December 2014

we have disorders, depression, OCD, addictions etc. but they are defined, entirely, by symptoms. This clarifies why e.g. claiming that someone has a phobia in the absence of phobic symptoms is absurd. There is no other way to establish a disorder than to assess symptoms, and the presence of a psychiatric disorder in the absence of symptoms is logically impossible.

3) DSM inspired pseudo-explanations

DSM, in its various editions since DSM III, was held by its authors to be a non-explanatory, descriptive system, used to label and categorize mental "*disorders"* by "*symptoms*". The very notion of 'symptoms', at least in everyday language and in biomedical medicine, suggests that they are the *outcome* of some underlying malfunctioning. In the same vein, the notion of "disorder" is, in common parlance, equivalent to 'disease' that serves to explain symptoms. And if we say, in terms of DSM, that e.g. hallucinations are a 'symptom' of a psychotic 'disorder', it is hard to resist the temptation to conclude that this psychosis somehow *caused* the symptoms. Perhaps this 'symptom/disorder' terminology is one of the reasons why, despite the integer intentions of its authors, the DSM is widely used to "explain" behavioral or emotional symptoms. (Hyman 2010). Why is Peter so sad? Because he suffers from depression". But how do we know he is depressed? Because of his sadness. Using a DSM disorder to casually "explain" symptoms is as nonsensical as claiming that Italy is the cause of its 20 regions. Yet the former reasoning is one of the most widespread explanatory fallacies in psychiatry and psychology. As an example, a famous introductory textbook of psychology writes:" it can be challenging to decide if a given behavior is c*aused* by psychopathology" (Gazzaniga et al. 2006)

Of course a clinician may feel it is is better for e.g. parents to attribute the hyperactivity of their son to "ADHD" instead of believing it represents morally unacceptable disobedience. The other way round, diagnoses may be used to discredit individuals: "this nonsense must be caused by a serious psychosis". But whether the motives for attributing symptoms to disorders are noble or malicious, the problem remains that such explanations are pseudo explanations. We cannot use depression as explanans to explain sadness, just like we cannot explain richness from the possession of abundant earthly goods. We need the equivalent of a lotto; an *independent* explanans.

In many sciences, including economics, physics and psychology, researchers are familiar with "latent variables", variables that cannot be directly observed, but can be assumed and calculated and that may serve to explain some explanandum. Intelligence cannot be observed like stripes on a zebra, but it can be inferred from IQ tests and may serve as a latent variable to explain and predict e.g. academic performance. A DSM defined mental disorder might be taken as a latent variable to explain symptoms. This, however, does not eliminate the tautology. The IQ test is independent from academic success. But claiming that a DSM category serves as latent variable to explain a symptom is like claiming that academic success is a latent variable that explains academic success.

4) How to prevent tautological 'explanations' with descriptive diagnosis

Understandably, researchers were and are unhappy with the fact that descriptive psychiatric disorders, (Cf. DSM) do not explain symptoms and have sought ways to liberate psychiatry from tautological explanations. Some of the efforts are described below.

4.1) Treat the disorder as something to be explained, not as explanation

If a disorder does not explain, but merely summarizes the presence of symptoms, this renders the disorder itself in need of explanation. It should not be treated as explanans but as explanandum. Given the impressive success of modern biomedical sciences, the most promising road to follow may be to try and uncover pathophysiological processes that underlie the various psychopathological conditions. And even if, for the moment, no sound understanding of biological *mechanisms* can be achieved, at least biological *markers* should be identified: genetic profiles, physiological tests, results from structural or functional brain imaging *et cetera* that are present in individuals with a specific disorder, but absent in others. Such markers would provide fruitful heuristics for research in suggesting where to search for pathophysiology and pathogenesis. However, despite thousands of dissertations and a multitude of biological psychiatric publications, the net-result is disappointing. Yes, there are genetic influences on mental disorders (Kendler 2005). But the insights come mainly from population-genetics and the genetic influences relate to rather broad vulnerability factors, like Neuroticism or a predisposition to develop schizophrenia or addictions. There are no genes or combination thereof that comes close to the brain tumor example given earlier (Stefanis 2008). And, on a group level, sometimes patient-control differences in biological functioning are sometimes reported (Borsboom and Cramer 2013), but they fall short of being serving as independent predictor, let alone explanans, of the explanandum.

Of course, this does not imply that biological markers cannot or will not be found. Who knows? It does seem however that the optimism and promise of biological approaches, widespread in the eighties and nineties of the last century, did not pay off in terms of clear cut pathophysiological insights or biological markers that are useful for explanatory diagnosis of individual patients.

4.2) Forget about descriptive disorders, explain symptoms

The DSM classifies various clusters of symptoms in discrete categories. Does DSM cut nature at its joints? We can be pretty sure about the nature and occurrence of a wide range of psychopathological symptoms. But how do we know if these clusters really reflect some underlying disorder-specific pathogenesis? One reason to be worried in this respect is that co-morbidity is high and is the rule rather than the exception (Caspi et al. 2014). Note that; "Comorbidity rates in psychiatry conform roughly to the rule of 50%: Half of individuals who meet diagnostic criteria for one disorder meet diagnostic criteria for a second disorder at the same time, half of individuals with two disorders meet criteria for a third disorder, and so forth (Newman et al. 1998). If the various categories had distinct pathogenetic profiles, why would they co-occur so often? And if we study e.g. the pathophysiology of depression in individuals with a co-morbid anxiety disorder, are the physiological

features observed responsible for depression, anxiety or both? Possibly, one might argue, looking for 'the pathophysiology' of any specific *disorder* is misguided. Perhaps one may more fruitfully concentrate on discrete *symptoms* and forget about the clusters in which they are grouped by DSM. This suggests that, other than with studying disorders, studying symptoms will result in pathophysiological explanations, genetic profiles, biological markers and the like. Whether this is true is an empirical issue, but settling it is likely to take another few decades of massive investments with real risks of new disappointments.

There is another problem with shifting the research focus from disorders to symptoms. Yes, co-morbidity frequently occurs, but some co-morbidities are far more prevalent than others and, perhaps more important, the DSM categories typically represent robust combinations of symptoms: panic disorder is often associated with agoraphobia, but not with compulsive hand washing while the latter often co-occurs with checking rituals but panic disorder does not. Freud's clinical descriptions of e.g. "anxiety neurosis" or "compulsive disorder" are easily identified as Panic Disorder and OCD and letting go of common *combination* of symptoms may be throwing away the child with the bathwater.

4.3) Symptoms as causes of other symptoms: network theory

Psychopathology is in need of causal explanations. These explanations should, at least, cover the fact that a) mental disorders consist of reasonably consistent clusters of symptoms and that b) co-occurrence of clusters, i.e. "co-morbidity", is widespread while c) 'underlying disease/latent variable' approaches have not yielded the biological or neuro-cognitive markers markers that may have been expected. In fact, a fresh and novel approach meets these requirements. The following is strongly indebted to the work by Borsboom et al. on network theory (Borsboom et al. 2011, Borsboom and Cramer 2013) and may be introduced in the following way. Symptoms, psychiatric or otherwise, are typically seen as the reflection, or *output* of an underlying disease, while the symptom itself is causally inert. Fever is a symptom of influenza, but the former does not contribute to the latter or its other symptoms. Network theory crucially proposes that matters are different in psychopathology. Symptoms are held not to be causally inert, but to causally contribute to other symptoms. Symptom a) may give rise to symptom b) that may reinforce symptom a) or contribute to symptom c) et cetera. The clearest example may be Specific Phobia. Its clarity may be taken as triviality but other examples to be discussed are non-trivial and even counter-intuitive. Symptoms of Specific Phobia include a) fear of specific objects and b) avoidance of those objects. It would be far-fetched to try and find a common pathogenic process (latent variable) that explains fear and avoidance. Rather, it suffices to postulate that phobic fear motivates to avoidance and that the former explains the latter. Depressed mood, self-reproach, insomnia, fatigue and concentration problems are symptoms of Major Depression (MD). Explaining the symptoms by "MD" is tautological. Explaining them by a common yet unknown cause may not be logically impossible, but Borsboom and Cramer (2013) point to a parsimonious alternative. Suppose an enduring environmental stressor X induces a depressed mood. Then consider this cascade: depressed mood→ self-reproach→ insomnia→ fatigue→ concentration problems. Each of the 4 transitions make perfectly sense and the explanation is certainly better than the tautology that MD causes the symptoms by which it is defined, or the explanation than the symptoms are caused by a common factor that, alas, is not yet known. ´The heart of this approach lies precisely in what separates medical conditions from mental disorders: the general idea that causal, meaningful relations between symptoms not only exist and should be acknowledged, but in fact are the very stuff of which mental disorders are made" (Borsboom and Cramer 2013).

At the beginning of this paragraph we argued that in the present context, an explanatory model should explain, first, that symptoms of mental disorders do not cluster randomly but come in reliable combinations, that, second, co-morbidity is widespread and that, third, there are no biological markers for specific disorders. Network theory suggests that reliable clustering occurs because a specific symptom (e.g. sleeplessness) is more likely to induce a symptom like fatigue than e.g. agoraphobia. A phenomenon like unpredictable panics is more likely to promote agoraphobic avoidance than sleeplessness. The second issue that needs to be covered by a credible model is co-morbidity. Take MD and Generalized Anxiety Disorders (GAD). Among the defining symptoms of both, one finds insomnia, concentration problems and fatigue. Such overlapping complaints are demonstrated to serve as "bridge symptoms". They may fuel other symptoms of e.g. MD and of GAD and, by fuelling both, the bridge symptoms explain co-morbidity. Finally, the fact that no robust biological markers for DSM disorders were found is explained by the simple hypothesis that there *are* no such markers and that their existence does not have to be assumed to begin with. Obviously there are general, constitutional and/or environmental, vulnerability factors and they may explain why in particular individuals, some isolated symptoms are more likely to emerge. How such symptoms cascade into full blown disorders however is held to be caused by symptoms acting as causes for other symptoms.

In the examples given above, the transition between from one symptom to another (phobic fear → phobic avoidance; sleeplessness→ fatigue etc.) was self-evident. In other cases explaining symptom→symptom transitions may transcend common sense. Note that the idea that psychiatric symptoms promote other symptoms is not new. It was assumed by clinicians and researchers in related traditions: Cognitive Behavioral Therapy (CBT) and Experimental PsychoPathology (EPP). This is not to argue that network-theory provides old wine in new bottles. On the contrary: network theory and the traditions of CBT/EPP arrived at the same "symptom→symptom" assumption from very different perspectives and they may fruitfully inform one another. We will discuss some CBT issues and EPP research on symptom→symptom effects, concentrating on OCD research.

5) Network theory, CBT, EPP and OCD research

CBT refers to psychological treatments that are typically not focusing on hypothetical distal origins or underlying causes of mental problems, but on processes that are held to *maintain* the problems. CBT has, certainly compared to other psychological treatments, a strong backing in (experimental) research that may, arguably and conveniently, be referred to by the term Experimental Psychopathology (EPP). Like biological

psychiatry, EPP covers the continuum between applied and fundamental research. Applied studies may e.g. compare the relative efficacy of treatments in randomized controlled trials, largely identical to pharmacological effect-studies. More fundamental studies try to unravel how psychopathological conditions persist and what constitute their "maintaining mechanisms". The idea that psychopathological symptoms are not caused by a disorder, but that *are* the disorder was formulated by H.J. Eysenck, one of the founding fathers of CBT, famously saying that if you take away the symptoms you have cured neurosis (Eysenck 1960). Eysenck was building on the seminal work on phobias by Mowrer who theorized that not only phobic fear motivates to avoidance of phobic objects but that phobic avoidance is more than 'output' (Mowrer 1960) It was held to produce immediate relief from the aversive state of anxiety and this immediate, avoidance-induced, relief was held to reinforce avoidance and thereby the phobia. Most behavior researchers will now believe Mowrer was mistaken. But, in time, all hypotheses will prove incomplete and what matters here is that Mowrer used a symptom as explanans rather than explanandum. An important breakthrough in the eighties was the development of a cognitive theory and therapy of Panic Disorder (PD) (Clark 1986). A hallmark of PD is the occurrence of panic attacks, the latter being defined as a combination of 1) bodily sensations and 2) intense fears about e.g. dying. Clark argued that 1) and 2) are not due to some underlying disorder, but that symptoms 1 and 2 are mutually reinforcing: symptoms were held to serve as input. In passing it may be noted that the work on phobia's and PD resulted in therapies that rank among the most effective psychological treatments (Hofman and Smits 2008).

Compared to phobias and PD, the symptoms of OCD are relatively heterogeneous although there is some system in the disorder. A first group of symptoms is mental and primarily includes the obsessions: involuntary thoughts, images or impulses that typically relate to doing unacceptable or horrifying things (e.g. killing ones children) or not preventing such catastrophes. Patients suffer from exaggerated uncertainty (did I really turn off the gas stove?) and responsibility (I should take away broken glass from the public road). In a clinically convincing effort to formulate the 'cognitive nucleus' of OCD, Mancini suggested that a common denominator of patients is a pre-occupation a "fear of being guilty for having acted in an irresponsible way" (D'Olimpio and Mancini 2014). In response to such pre-occupations, patients feel urged to, and carry out compulsions: repetitive acts often consisting of checking or cleaning/washing. Importantly, compulsions are *perseverative*: though the actions are goal directed (e.g. checking whether the alarm is set right) they are carried out repetitively, beyond the point where repetition has any use.

Responsibility and compulsions are associated but does responsibility *drive* compulsions? (Lopatka and Rachman 1995) reasoned that if so, manipulating responsibility in OCD patients should immediately affect the urge to engage in compulsions: *"responsibility down→ compulsions down*" and "*responsibility up → compulsions up"* . Thirty OCD patients were asked to refrain from compulsive behavior on three occasions. On one occasion responsibility was low, in another other it was high and these experimental conditions were compared with a control condition in which responsibility was not manipulated. The instruction to patients in the condition of 'low responsibility/do not carry out compulsions' read: *"I want you to know that I (the experimenter) will take complete responsibility if anything bad happens or anything is not perfect. You are not responsible for anything that happens or is not perfect. I will take on complete responsibility. I will be to blame if anything bad happens or is not perfect. Your name will not be mentioned. I will also take responsibility for any damage that may occur and will pay back or undo any damage or harm that may occur"*. In the 'high responsibility/do *not* engage in compulsions' condition the instruction was: *"I want you to know that you will have to take complete responsibility if anything bad happens or anything is not perfect. You are responsible for anything that happens or anything that is not perfect as a result of not checking. You will be asked to take on complete responsibility. You will be to blame if anything bad happens or if anything is not perfect. Your name will be mentioned. You will also take responsibility for any damage that may occur and will be asked to pay back or undo any damage or harm that may occur."*. The urge to engage in compulsions was dramatically lower in the low responsibility condition as compared to the neutral condition. In the high responsibility condition the urge was much higher. This shows, then, that the inflated responsibility is more than a descriptive feature of OCD but that it *causally affects* the urge to engage in compulsions. But no actual behavior was tested, only self-reported *urges* to act. Does perceived responsibility affect actual (motor) behavior? And would this be specific for OCD patients, or would the same occur in non-patients, or in patients with other anxiety disorders?

Arntz et al. (2007) tested the *"responsibility up→ compulsions up"* hypothesis comparing the performance of OCD patients, non-OCD anxiety patients and healthy controls. Participants were asked to select colored pills either with no information about possible harm due to mistakes (low responsibility) or high risk of harm (high responsibility). In the latter condition individuals were, cleverly, led to believe that accurate performance on the pill sorting task was crucial to the pills being admitted to third world countries and that failures on the task may postpone admittance with possible lethal consequences. Objective checking behavior (videotaped hand movements during the pill selection) and time to complete the task, increased in the high responsibility condition but mostly so in the OCD sample. The findings corroborate the notion that responsibility, in OCD patients, causally contributes to the occurrence of new compulsive compulsive acts.

D'Olimpio and Mancini (2014) reasoned that compulsions like checking or washing are not due to responsibility as such, but to a feeling of "deontological" guilt that is related, but not identical to responsibility. Deontological guilt refers to feelings after violating a general moral rule and has to be differentiated from "altruistic" guilt that relates to feelings after for having, willfully or not, inflicted suffering on others. The hypothesis tested was: "*deontological guilt → compulsions"*. In two experiments, healthy participants listened to stories that primed feelings of a) deontological guilt, b) altruistic guilt or c) no guilt. They then performed the pill sorting task also used by Arntz et al. (2007) (see above) in experiment 1 and a cleaning task in experiment 2. Compared to the other conditions, participants in the deontological guilt conditions reported more distress during the tasks and, importantly, engaged in more compulsive-like motor behavior.

These experiments on guilt/responsibility and compulsions demonstrate important symptom→symptom transitions of the type suggested by network theory: de-

ontological guilt and responsibility are not merely causally inert end-products of an underlying neuro-cognitive process. Guilt and responsibility *fuel* compulsions.

Other "symptom→symptom" EPP studies in OCD relate to association between the two hall-marks of the disorder: obsessions and compulsions. Obsessive concerns of patients do not entail the idea that some catastrophe will occur, or is likely to occur. Rather, patients are plagued by a crippling *uncertainty* that something horrible *might* occur. Indeed, the French used to reefer to OCD as the "folie de doute". Typically it is held that obsessions motivate to compulsions like repeated checking, the most frequent form that compulsions take. Indeed, most patients say that it is the uncertainty that drives them to carry out the compulsions. There is little reason to doubt that patients recollections hold true, but various authors claimed that the symptom-to-symptom effect may work the other way as well: "*perseveration → uncertainty*". In a first series of experiments testing this assumption, van den Hout and Kindt (2003 a, b) asked healthy volunteers to carry out compulsive-like perseveration by repeatedly checking a virtual gas stove or virtual light bulbs. At pre-test and at a posttest, all participants checked the gas stove: memory accuracy for that check was assessed as well as self-reported confidence in memory. In between the pre-test and post-test, participants either checked the same gas stove that was used at pre-test and at post-test 20 times ("relevant checking") or they checked virtual light bulbs (irrelevant checking) 20 times. While memory accuracy remained unaltered in both conditions, relevant checking induced sharp drops in vividness, detail and, crucially, in the confidence participants had for their memory. No such effects were observed in the control group of 'irrelevant checking'. Apparently, repeated checking items like a gas stove may induce uncertainty about ones checking behavior for that very item. The "*perseveration → uncertainty*" effect proved robust and replicable. That is, the effects occur far earlier than after 20 checks (Coles et al. 2006) they are present not only after checking virtual stimuli on a screen but also after checking real gas stoves (Radomsky et al. 2006), after checking abstract, threat irrelevant stimuli (Dek et al. 2010), after mental checking instead of physical checking (Radomsky and Alcolado 2010) and they also induce uncertainty about future mishaps. Two studies examined the ironic effects of repeated checking in OCD patients. Boschen and Vuksanovic (2007) reported that patients had, overall, less memory confidence than healthy controls but the checking induced *drop* in memory confidence was identical. Radomsky et al. (2014) likewise found that OCD patients and healthy controls displayed the same decrease in memory confidence after checking.

Van den Hout and Kindt (2003a) proposed an explanation of the "perseveration→ uncertainty" phenomenon. Repeated checking increases familiarity with the checked events; this may render the behavior relatively automatic with a decreased processing of perceptual details. The implication is that the "*perseveration → uncertainty"* effect can be blocked or reduced if, at the end of a checking bout, the perceptual features of the to be checked item is changed. Indeed (Dek et. al. 2014 submitted) found that, again, repeated checking induces uncertainty about memory, but when, at the last checking trial, the perceptual features of the checked item were changed, the drop in confidence was reduced by 50%.

Thus, the "*perseveration up → uncertainty up"* survived critical replications and it is likely that repetition-induced automation is involved. But is this symptom-to-symptom association reciprocal? Would OCD patients be inclined, perhaps more than others, to respond to mild uncertainty with perseveration, even when the uncertainty is unrelated to their obsessional concerns? To experimentally test this *"uncertainty up→ perseveration"* hypothesis, researches used a visual search task in which eye movements were recorded, yielding an objective measure of (visual) perseveration. The task contained 50 search displays, in which participants indicated whether a target was "present" or "absent". Target-present trials were straight-forward, but target-absent trials were ambiguous, because participants had to rely on not having overlooked the target (Toffolo et al. 2013, Toffolo et al. 2014). In a first study, participants low and high on OCD tendencies (but without a clinical diagnosis of OCD) were tested. Both groups were equally fast in deciding when a target was present. The target absent trials that induce uncertainty ("I may say there is no target, but I may have overlooked it") led, in both groups to a substantially longer decision time. Crucially however, in this ambiguous condition the high OC individuals were significantly slower than the participants with low OC tendencies (Toffolo et al. 2013). The experiment was replicated with similar individuals, producing identical results (Toffolo et al. 2014). In a third study, (Toffolo et al. 2014) patients with clinical OCD were compared to matched controls. Again, in the non-ambiguous "target-present" trials, patients and controls were equally fast. In the (ambiguous) target present trials patients engaged in far more visual checking as compared to the controls, the group differences being even stronger than in the studies with sub-clinical OC participants (Toffolo et al. 2013, Toffolo et al. 2014).

An intriguing interpretation of the "uncertainty→perseveration" cascade was given by Dar and coworkers. It was hypothesized that the common denominator of uncertainty in OCD is that it relates to internal states that may be cognitive (e.g. do memory or sense organs serve me well?), affective (e.g. do I really love my husband?) or bodily (do my bodily feelings correspond with my physical state?). This uncertainty about internal states is held to serve as motive for finding external "proxies": external information that serves as prostheses that compensates the uncertainty about internal states. Compulsive rituals are seen as such external proxies. Note that this proposal can be seen as a specification of the "uncertainty→perseveration" hypothesis. In a long series of experiments Lazarov et al. (Lazarov et al. 2010, 2012a, 2012b) instructed individuals with or without sub-clinical OCD to produce a certain level of muscle tension with or without biofeedback. Later they were asked to reproduce the same level of tension, while in one condition they were given biofeedback that was false, whereas in other conditions, extra bio-feedback was given upon request. Interestingly, the high OC individuals were less accurate without bio-feedback, requested more external feedback and were more affected by false bio feedback. The results were recently replicated in OCD patients who displayed the same pattern, while patients suffering from other anxiety disorders did not differ from healthy controls (Lazarov et al. 2014).

The selection of studies discussed above is not exhaustive. They were chosen to illustrate that EPP research on OCD has a strong focus on causal relationships between OCD symptoms. Causality is tested by experimental manipulation of one of the symptoms and it is tested whether other symptoms emerge. Clinical CBT research demonstrated that behavioral interventions (motivating patients to

stop carrying out compulsive rituals: 'exposure and response prevention') and cognitive approaches (targeting inflated responsibility and guilt) are effective therapeutic strategies. (ref) The EPP studies mentioned above provide a strong and coherent rationale for the intervention. Obsessions and compulsions are not merely inert symptoms of an underlying disorder, but they serve to mutually reinforce on another: Obsessions ←→ Compulsions.

6) Concluding remarks

Psychopathology comes in clusters of complaints. We have come to call the complaints "symptoms" and call the clusters "disorders". This may foster the idea that somehow, the disorders explain the symptoms. They do not. Efforts to avoid tautology by explaining the various disorders by specific underlying pathophysiologies have not yielded biological markers that differentiate patients with different disorders. Network theory provides a fresh perspective on these issues. Clusters of symptoms do exist and this is explained by symptom-to-symptom causality that may or may not be reciprocal. Co-morbidity is high in psychopathology and network theory explains this and specifies that "bridge symptoms" are responsible for co-morbidity. Biological markers have not been identified because they may not exist to begin with and there is no need to assume their existence. Network theory uses powerful and advanced mathematical techniques and it opens new vistas on the phenomenology and explanation of psychopathology. It has the potential to create a Kuhnian paradigm shift in the field.

The notion that symptoms affect other symptoms is not new. It is part and parcel of particular traditions in the treatment and study of mental disorders: CBT and EPP. Examples of EPP studies on OCD research were given above. What, then, has network theory to offer to EPP? First, network theory provides a solid conceptual rationale for experimental dissection of *symptom→ symptom* processes. Second, it gives powerful and empirically derived clues about what *symptom→symptom* associations are central and likely to be involved in the maintenance of specific disorders. What has experimental psychopathology has to offer to network theory? First, network theory suggests causality, but the royal road to testing and establishing causality is experimental research. This is what EPP does. Second, the examples of symptom→ symptom effects, giving in the emerging network literature, are explained by referring to common sense: yes, sleeplessness is likely to result in fatigue and yes, fatigue can safely be assumed to create concentration problems. However, many *symptom→symptom* effects are counterintuitive and need more than common sense to be understood. The studies on OCD, discussed above illustrate this. It is one thing to suggest that, e.g. compulsive perseveration reinforces obsessive uncertainty, but the question ensues *how* this takes place. EPP answers precisely such questions. Finally, the emerging network theory concentrates on *symptom→ symptom* associations where symptoms are derived from diagnostic nomenclatures like DSM. Clinical experience and systematic descriptive phenomenology may enrich and refine DSM like nomenclatures by identifying descriptive features that are not included in the Diagnostic System, like, in the case of OCD, (de-ontological guilt, uncertainty about internal states et cetera). Here, CBT, with its tradition on objective assessment of symptom-patterns has a role to play. It seems, in conclusion, that network theory and CBT/EPP start from comparable premises, use different methods and may mutually reinforce one another, much like psychiatric symptoms do.

References

Arntz A, Voncken M, Goosen AC (2007). Responsibility and obsessive–compulsive disorder: An experimental test. *Behaviour Research and Therapy* 45, 3, 425-435.

Borsboom, D, Cramer AO (2013). Network analysis: an integrative approach to the structure of psychopathology. *Annual Review of Clinical Psychology* 9, 91-121.

Borsboom D, Cramer AOJ, Schmittmann VD, Epskamp S, Waldorp LJ (2011). The Small World of Psychopathology. *PLoS ONE* 6, 11, e27407. doi:10.1371/journal.pone.0027407.

Boschen MJ, Vuksanovic D (2007). Deteriorating memory confidence, responsibility perceptions and repeated checking: Comparisons in OCD and control samples. *Behaviour Research and Therapy* 45, 2098-2109.

Caspi A, Houts RM, Belsky DW, Goldman-Mellor SJ, Harrington H, Israel S, Moffitt TE (2014). The p Factor One General Psychopathology Factor in the Structure of Psychiatric Disorders? *Clinical Psychological Science* 2, 2, 119–137. doi:10.1177/2167702613497473.

Clark DM (1986). A cognitive approach to panic. *Behaviour Research and Therapy* 24, 4, 461-470. doi:10.1016/0005-7967(86)90011-2.

Coles ME, Radomsky AS, Horng B (2006). Exploring the boundaries of memory distrust from repeated checking: Increasing external validity and examining thresholds. *Behaviour Research and Therapy* 44, 995-1006.

Coles ME, Radomsky AS, Horng B (2006). Exploring the boundaries of memory distrust from repeated checking: Increasing external validity and examining thresholds. *Behaviour Research and Therapy* 44, 995-1006.

Dek ECP, van den Hout MA, Giele CL, Engelhard IM (2014). Automatization and Familiarity in Repeated Checking: A Replication. *Submitted.*

Dek ECP, van den Hout MA, Giele CL, Engelhard IM (2010). Repeated checking causes distrust in memory but not in attention and perception. *Behaviour Research and Therapy* 48, 580-587.

D'Olimpio F, Mancini F (2014). Role of Deontological Guilt in Obsessive-Compulsive Disorder–Like Checking and Washing Behaviors. *Clinical Psychological Science* 2, 6, 727-739.

Eysenck HJ (1960). *Behavior therapy and the neuroses*. Pergamon Press, New York.

Hout MA van den, Kindt M (2003a). Repeated checking causes memory distrust. *Behaviour Research and Therapy* 41, 301-316.

Hout MA van den, Kindt M (2003b). Phenomenological validity of an OCD-memory model and the remember/know distinction. *Behaviour Research and Therapy* 41, 369-378.

Gazzaniga MS, Heatherton TF, Halpern DF, Heine SJ (2006). *Psychological science*. WW Norton, New York.

Hofmann SG, Smits JA (2008). Cognitive-behavioral therapy for adult anxiety disorders: a meta-analysis of randomized placebo-controlled trials. *The Journal of clinical psychiatry* 69, 4, 621.

Hyman SE (2010). The diagnosis of mental disorders: the problem of reification. *Annual Review of Clinical Psychology* 6, 155-179.

Kendler KS (2005). "A gene for…": the nature of gene action in psychiatric disorders. *American Journal of Psychiatry* 162, 7, 1243-1252.

Lazarov A, Dar R, Oded Y, Liberman N (2010). Are obsessive-

compulsive tendencies related to reliance on external proxies for internal states? Evidence from biofeedback-aided relaxation studies. *Behaviour Research and Therapy* 48, 516-523.

Lazarov A, Dar R, Liberman N, Oded Y (2012a). Obsessive-compulsive tendencies and undermined confidence are related to reliance on proxies for internal states in a false feedback paradigm. *Journal of Behavior Therapy and Experimental Psychiatry* 43, 556-564.

Lazarov A, Dar R, Liberman N, Oded Y (2012b). Obsessive-compulsive tendencies may be associated with attenuated access to internal states: Evidence from a biofeedback-aided muscle tensing task. *Consciousness and Cognition* 21, 1401-1409.

Lazarov A, Liberman N, Hermesh H, Dar R (2014). Seeking Proxies for Internal States in Obsessive-Compulsive Disorder. *Journal of Abnormal Psychology* 4, 695-704.

Lopatka C, Rachman S (1995). Perceived responsibility and compulsive checking: An experimental analysis. *Behaviour Research and Therapy* 33, 6, 673-684. doi:10.1016/0005-7967(94)00089-3

Mowrer O (1960). Learning theory and behavior. Retrieved from http://psycnet.apa.org/psycinfo/2005-06665-000

Nagel E (1971). *The Structure of Science: Problems in the Logic Gf Scientific Expla-nation*. Routledge & Kegan Paul.

Newman DL, Moffitt TE, Caspi A, Silva PA (1998). Comorbid Mental Disorders: Implications for Treatment and Sample Selection. *Journal of Abnormal Psychology* 107, 2, 305-311.

Radomsky AS, Alcolado GM (2010). Don't even think about checking: Mental checking causes memory distrust. *Journal of Behavior Therapy and Experimental Psychiatry* 41, 4, 345-351. doi:10.1016/j.jbtep.2010.03.005

Radomsky AS, Dugas MJ, Alcolado GM, Lavoie SL (2014). When more is less: Doubt, repetition, memory, metamemory, and compulsive checking in OCD. *Behaviour Research and Therapy* 59, 30-39.

Radomsky AS, Gilchrist PT, Dussault D (2006). Repeated checking does cause memory distrust. *Behaviour Research and Therapy* 44, 305-316.

Stefanis N (2008). Genes do not read DSM-IV: implications for psychosis classification. *Annals of General Psychiatry* 7, Suppl 1, S68.

Toffolo MBJ, Hout van den MA, Engelhard IM, Hooge ITC, Cath DC (2014). Uncertainty, checking, and intolerance of uncertainty in subclinical obsessive compulsive disorder: An extended replication. *Journal of Obsessive Compulsive and Related Disorders* 3, 338-344. doi: 10.1016/j.jocrd.2014.08.004

Toffolo MBJ, Hout van den MA, Hooge ITC, Engelhard IM, Cath DC (2013). Mild uncertainty promotes checking behavior in subclinical obsessive-compulsive disorder. *Clinical Psychological Science* 1, 103-109. doi: 10.1177/2167702612472487