Health complaints : testing a causal role of activated illness-memory in symptom reporting

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Esther E. Meerman

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Testing a Causal Role of Activated Illness-Memory in Symptom Reporting

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Co-promotoren:	dr. J.F. Brosschot
	dr. B. Verkuil
Overige leden:	Prof. dr. O. Van den Bergh (Katholieke Universiteit Leuven, België)
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"You know, I'm sick of following my dreams, man. I'm just going to ask where they're going and hook up with 'em later."

Mitch Hedberg, American comedian, (1968-2005).

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Chapter 1 |

General Introduction

INTRODUCTION

Medically unexplained (physical) symptoms (MUS, or MUPS) are symptoms that cannot be attributed to organic pathology and they represent a common category of complaints in health care (Brown, 2004). The most common unexplained symptoms in primary or ambulatory care are: back pain, feeling bloated, pain in limbs, dizziness, diarrhea, abdominal pain, chest pain, fatigue, headache, ear, nose and throat problems and nausea (Kirmayer, Groleau, Looper, & Dao, 2004; Kroenke & Mangelsdorff, 1989; Peveler, Kilkenny, & Kinmonth, 1997). MUS form a common problem in both primary care and specialist care. However, the symptoms mentioned above are also extremely common, albeit it in less severe form, in the healthy population, that is, in people that have not consulted a doctor for these symptoms. These medically undiagnosed minor symptoms are often also disabling and are frequently referred to as 'subjective health complaints' (SHC; Ursin, 1997).

Since decades there is an ongoing discussion of whether and how psychological factors play a role in health complaints, and in MUS in particular. Although it is clear that MUS are not "just between the ears" and MUS patients experience a lot of pain and suffer greatly from these complaints, several models of MUS include psychological factors and attribute a causal role to them. This thesis is focused on testing the most prevailing model, which proposes a causal role of illness-related cognitive schemata, or implicit memory, in the increased reporting of health complaints without a clear medical explanation. In this thesis, crucial assumptions of this model are tested which will provide more insight into the role of illness memory in the reporting of SHC, MUS, and in particular the most common complaint (pain).

In this chapter, I will first provide background information on MUS and SHC. Next, I will provide an overview of several previous and recent theoretical models that provide a link between cognitive processes such as memory and attention, and increased symptom reporting. In addition, I will present the current evidence for these theoretical models. Finally, I will provide the aim and outline of this thesis.

Prevalence

Subjective health complaints in the general population

In an often cited Norwegian survey in healthy people, 96% of the responding individuals reported to have experienced at least one health complaint in the last 30 days, with musculoskeletal pain, pseudoneurological and gastrointestinal problems as the most reported complaints (Ihlebaek, Eriksen, & Ursin, 2002). Despite this high prevalence, many of these complaints were not perceived as detrimental and most people had not sought medical help for them. Still, the proportion of these symptoms that actually lead to seeking medical help appears to be substantially enough to account for the most frequent reason for doctor visits (Eriksen, Svendsrød, Ursin, & Ursin, 1998; Eriksen & Ursin, 2004). Furthermore, these health complaints also do account for a

substantial part of long-term sickness compensation and permanent inability to work (Eriksen et al., 1998).

Prevalence and lifetime occurrence of MUS in primary care

When people eventually seek help and consult their general practitioner for their health complaints, at least one third of these complaints remains medically unexplained (60.6% in Fink, Sørensen, Engberg, Holm, & Munk-Jørgensen, 1999; 37% in Khan, Khan, Harezlak, Tu, & Kroenke, 2003; 32% in Marple, Kroenke, Lucey, Wilder, & Lucas, 1997; 35% in Peveler et al., 1997). One study found that the amount of somatic complaints without an organic cause ranged from 16% for back pain and 33% for fainting and menstrual problems (Kroenke et al., 1994). MUS are significantly more common in women than in men. About 18% of men in primary care had a lifetime occurrence of at least four unexplained symptoms whereas 25% of women in primary care had a lifetime occurrence of at least six unexplained symptoms (Escobar, Waitzkin, Silver, Gara, & Holman, 1998). A smaller number of patients (8.2%) have more than three unexplained symptoms for two years or longer, measured in a data set of 1000 patients of four primary care clinics (PRIME-MD Study; Kroenke et al., 1997).

Prevalence of MUS in specialist care

MUS are not only a common problem in primary care but also in specialist care. MUS are reported in a large group of internal medical outpatients (74% in Kroenke & Mangelsdorff, 1989; 30%-50% in van Hemert, Hengeveld, Bolk, Rooijmans, & Vandenbroucke, 1993). However, the percentage of MUS differs among the specializations. One study estimated the prevalence of MUS among seven specialties in two general hospitals (Nimnuan, Hotopf, & Wessely, 2001). They found that overall 52% of the patients fit the diagnosis of MUS, with the highest prevalence of 62% among the gynaecology department. The health care specializations have different names for the presented unexplained symptoms in their field. For example, physicians working in gastroenterology departments often classify MUS at their departments as irritable bowel syndrome (IBS) and rheumatologists classify MUS at their department as fibromyalgia (Wessely & Nimnuan, 1999). Table 1-1 provides an overview of these different classifications among the different medical specialties. There is still a debate going on whether these specific functional symptoms are manifestations of one and the same syndrome, with their different labels only depending on the medical specialty the patients initially presented their symptoms to (lumper view), or whether these symptoms are truly part of distinct syndromes (splitter view) (Wessely & Nimnuan, 1999; Wessely & White, 2004). It is likely that the truth lies somewhere in the middle. For example, one study found that a great amount of variance among the different labeled somatic syndromes in outpatients is accounted for by one underlying factor, while the rest of the variance is explained by the specific syndromes (Nimnuan, Rabe-Hesketh, Wessely, & Hotopf, 2001). Furthermore, a more recent study that used different statistical techniques found that among patients with MUS, different subgroups could

be best discriminated from each other based on their total symptom score (high versus low), which is in favor of a lumper view (Lacourt, Houtveen, & Van Doornen, 2013). On the other hand, when the symptoms were forced in to more than two groups, it was found that there were cluster-specific symptom patterns that defined the groups, which is evidence for the splitter view. Although, it was found that the model of the symptoms clustered in two groups only showed the best fit (Lacourt et al., 2013).

Medically unexplained symptoms do not only refer to somatic symptoms without a known medical cause but can also refer to symptoms in some people with medically

Table 1-1. Diagnostic labels for common functional symptoms used among medical specialties (modified from Hall, 2011)

Specialty	Diagnostic labels	Functional symptoms
Allergy/ toxicology	Multiple chemical sensitivity/ idiopathic environmental intolerance Chemical intolerance	Odor hypersensitivity to common chemical agents Headache
Cardiology	Non-cardiac chest pain/ atypical chest pain	Persistent chest pain often exacerbated by ingestion or exercise; heartburn; muscle and joint aches
Dentistry	Temporomandibular joint disorder	Pain, clicking, grating in the jaw joint; headache; restricted movement of the jaw
Gastroenterology	Irritable bowel syndrome Non-ulcer dyspepsia Interstitial cystitis	Abdominal bloating and pain lessened by defecation; constipation and /or diarrhea; change in frequency and/ or consistency of stools
Gynaecology	Chronic pelvic pain Interstitial cystitis/ painful bladder syndrome	Pain during sex; abdominal and pelvic pain; dysmenorrhea; detrusor instability; change in bladder capacity, frequency and urgency
Infectious disease	Chronic fatigue syndrome/ myalgic encephalomyelitis/ post-viral fatigue syndrome	Widespread muscle and joint pain; persistent fatigue; sleep disturbance; mental exhaustion; headaches
Military medicine	Gulf war syndrome	Fatigue, headaches, muscle pains, neurological symptoms, poor concentration
Neurology	Conversion disorder (formerly known as hysteria) Non-epileptic attack disorder	Loss or alteration of motor or sensory function; motor weakness and tremor, paralysis, impaired vision or hearing Seizures
Orthopedics	(Lower) back pain and other musculoskeletal pain symptoms	Muscle pains
Otolaryngology	Functional dysphonia	Hoarseness
Psychiatry	Somatization disorder/ Somatoform disorder (e.g., conversion disorder, pain disorder, undifferentiated somatoform disorder, or somatoform disorder not otherwise specified)	Depends on classification
Rheumatology	Fibromyalgia	Chronic widespread pain and tenderness; sleep disturbance

"explained" conditions, if the complaints are more severe than regarded as reasonable (Eriksen et al., 1998).

Somatoform Disorders

In mental health care, somatic health complaints are not uncommon. The psychiatric diagnosis of somatoform disorders are a specific subgroup within the broad defined medically unexplained symptoms (Creed, Barsky, & Leiknes, 2011). When people with MUS visit psychologists or psychiatrists, these professionals can classify the MUS as one of the somatoform disorders described in the Diagnostic and Statistic Manual of Mental Disorders fourth edition (DSM-IV). Yet, of patients that are already suffering from MUS only few patients with the syndromes mentioned in Table 1-1 are eventually diagnosed with a somatoform disorder. For example, one study demonstrated in 206 distressed, high-utilizing MUS patients that only 4.4% classified as any DSM-IV Somatoform Disorders (4.4%). However, 60.2% had non-somatoform ("psychiatric") diagnoses, which were primarily anxiety and depression (R. C. Smith et al., 2005). A systematic review found that the 12-month prevalence of somatoform disorders among 7 population-based studies with a total of 18.894 combined participants ranged from 1.1% to 11%, with the median of 6.3% (Wittchen & Jacobi, 2005).

In summary, patients that are diagnosed with a somatoform disorder seem to be only the "tip of the iceberg". One could see the somatoform disorder as the one end of a continuum, with the lowest prevalence. The different functional syndromes per specialization seem to belong in the middle of the continuum and subjective health complaints at the opposite side of the continuum with the highest prevalence (See Figure 1-1).

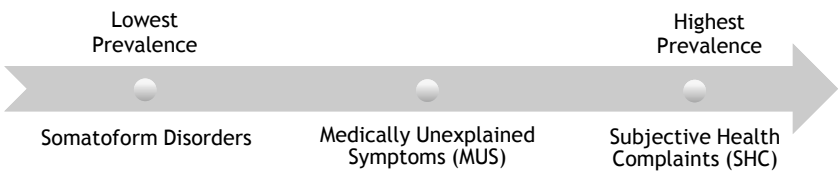

Figure 1-1. Continuum of prevalence among different diagnosis of somatic complaints

Costs and negative impact of SHC and MUS

Most health complaints disappear quickly, however still a considerable part persists over time and these symptoms cause long term distress and disability. For example, it has been found in a large sample of five hundred patients presenting to a medicine clinic with physical symptoms, that by 3 months, 37% of patients in primary care experienced complete symptom resolution, 43% were feeling better although the symptom remained, 12% were unchanged, and 8% were worse (Jackson & Passamonti, 2005). These outcomes were not influenced by whether the symptom was medically explained or not. Furthermore, of the patients without a medical explanation for their symptom, 28% of them reported that their symptom remained medically unexplained at 5 years follow up (Jackson & Passamonti, 2005). In extreme cases, symptoms can last many years. In a study among people suffering from DSM-IV diagnosed somatization disorder, it was found that the average symptom duration at the time of diagnosis was 29.8 years. Thus, symptoms can persist for a long time and the repeated consultations and examinations that are associated with such symptoms form a major burden on the health care system. For example, the patients suffering from somatization disorder had health care costs that were nine times the average (G. R. Smith, Monson, & Ray, 1986). One systematic review found that the excess health care costs of MUS patients in the US ranged from 432 to 5353 US dollars per person per year (Konnopka et al., 2012). In addition, one study looked at the impact of somatoform disorders (which is a smaller subgroup within MUS) on disease-related work disability (Hiller, Fichter, & Rief, 2003). Compared to the direct health-care costs, the number of workdays lost due to MUS is an indirect cost. In this study it was found that patients with a somatoform disorder had on average 121.3 sick days in the two previous years (SD = 158.3). Not only somatoform disorders impact our health-care costs and work-related disability, but SHC such as back pain as well. Recently, a Dutch cost of illness study examined back pain (Lambeek et al., 2011). The researchers found that the total costs of back pain decreased from €4.3 billion in 2002 to €3.5 billion in 2007. This corresponded to 0.9% of the gross national product (GNP) in 2002 and 0.6% of GNP in 2007. About 88% of the costs were due to indirect costs, such as governmental disability and sickness support and production losses (Lambeek et al., 2011). However, this study did not look at whether the back pain was due to a medical cause or not.

Not only do MUS impact society and our health care system, it of course impacts the quality of life of the patient as well. MUS cause decreased activities of daily living, social life, work and has an effect on mood (Nezu, Nezu, & Lombardo, 2001). One study examined a large random sample of patients in Dutch general practices and looked at differences in self-reported social isolation, and coping in patients with persistent MUS (meaning at least four consultations without a medical diagnosis) versus patients with a medical diagnosis and a group of remaining patients (i.e. who had less than four consultations for their MUS) (Dirkzwager & Verhaak, 2007). Patients with persistent MUS showed higher psychological distress, less quality of life, and more

social isolation compared to the other groups of patients. This difference was not caused by an unhealthy lifestyle, since the different patients groups did not differ in respect to this (Dirkzwager & Verhaak, 2007).

In conclusion, health complaints contribute considerably to sickness leave costs, health care costs and are associated with great personal suffering (Brown, 2004; Eriksen et al., 1998).

THEORETICAL MODELS PROVIDING POSSIBLE EXPLANATIONS FOR SYMPTOM REPORTING

Although health complaints, SHC and MUS, are a common problem, still not much is known about the factors causing people to report physical symptoms, especially not when there is no clear medical basis. Clearly, in order to reduce the burden associated with SHC and MUS, it is necessary to increase our understanding about the underlying causes of these complaints.

Historically, theoretical models on symptom reporting have focused on symptom reporting in its most severe form, i.e. MUS, and have attributed MUS to dissociation, conversion and somatization (Brown, 2004). A serious problem with these models so far is that there is no evidence for their major assumption that psychological distress, like anxiety or depression, is the cause of the unexplained symptoms (Brown, 2004). Although depression and anxiety are frequently found in MUS patients, it generally has turned out not to be the cause of their symptoms (as discussed in Brown, 2004).

Theories of symptom perception based on cognitive psychology principles

Instead of assuming that depression or anxiety is the cause for MUS, some have suggested that distorted cognitive processes, such as biases in memory and attention, can cause normal bodily signals to be perceived as symptoms of an illness (Brosschot, 2002; Brown, 2004; Pennebaker, 1982a). Normally, we remain unaware of most bodily processes and signals. However, sporadically some bodily signals and sensations are brought to our awareness due to changes in these cognitive processes (Deary, Chalder, & Sharpe, 2007; Pennebaker, 1982a). The next few paragraphs will present an overview of earlier theoretical models on cognitive processes such as memory and attention causing increased symptom reporting.

Increased attention to bodily signals causes increased symptom perception

Pennebaker's hypothesis of competing cues

Attention plays a role in shaping the contents of our conscious thought, and it controls our thought and action (Brown, 2004). The most important task of our attention system is to make a selection of potentially relevant information for further processing and to control our actions. One of the most influential models to examine the effect of attention on symptom perception is Pennebaker's 'hypothesis of competing cues' (1982b). This hypothesis states that with increasing external cues demanding atten-

tion, less attention resources are available for internal stimuli, or bodily signals. In this way, people will notice less bodily signals and thus report fewer symptoms. However, if people are in a deprived or boring environment with no external cues, people will notice more internal signals, and thus report more symptoms. Generally, when internal cues or bodily signals get more attention compared to external cues, people tend to report more symptoms. In the past decades, several studies have confirmed this effect of attention on symptom perception (Cioffi & Holloway, 1993; Cioffi, 1991; Kolk, Hanewald, Schagen, & Gijsbers van Wijk, 2002; L. C. Miller, Murphy, & Buss, 1981; Pennebaker, 1982a).

Research that tested this hypothesis of competing cues has often focused on people with high negative affect (NA) personality trait. People with a high NA personality trait are characterized as individuals that tend to experience more distressing negative emotions like anxiety and depression compared to people low on this trait. People with this trait, have been hypothesized to pay more attention to internal cues in general (Watson & Pennebaker, 1989) and also to have increased scanning of their body for symptoms. Watson and Pennebaker have indeed shown - in a cross-sectional study- that high NA is related to increased symptom reporting (Watson & Pennebaker, 1989). Other studies have also shown a positive correlation between NA and symptom reporting (Filipkowski et al., 2010; Vassend & Skrondal, 1999; P. G. Williams & Wiebe, 2000). In conclusion, NA seems to be an important factor in symptom reporting and should thus be taken into account when examining subjective health reports.

The somatosensory amplification model

Another influential model that examined the effect of attention on symptom perception is the somatosensory amplification model by Barsky & Wyshak (1990). Somatosensory amplification is the tendency to perceive normal somatic and visceral sensations as being relatively intense, disturbing and noxious. This model suggests that when people “amplify” benign somatic sensations, and misattribute those to a serious disease, they will, as a consequence, direct their attention to bodily sensations, and experience more somatic sensations, thus forming a vicious cycle. So, increased attention for bodily sensations, or hypervigilance, and misattribution are core elements of the model of somatosensory amplification (Barsky, Goodson, Lane, & Cleary, 1988). Other core elements of amplification are the tendency to focus on weak and infrequent bodily sensations and the tendency to react to bodily sensations with certain emotions or cognitions that intensify the sensations (Barsky et al., 1988). Somatosensory amplification, measured by a self-report questionnaire, in patients with upper-respiratory tract infections was a significant predictor of physical symptoms, while controlling for medical comorbidity (Barsky et al., 1988). Although this model was originally intended to explain hypochondria, it was later suggested that somatosensory amplification might play a more general role in symptom reporting (Barsky, Cleary, & Klerman, 1992). While several studies provided support for this hypothesis, other studies have shown that amplification does not correlate with one of the other

core elements of the model, i.e. hypervigilance which was measured as the ability to detect heart rate changes and other measures of interoceptive sensitivity (for a review see Duddu, Isaac, & Chaturvedi, 2006). It has been suggested that somatosensory amplification plays a partial role in symptom reporting, but other factors may also be important (Duddu et al., 2006). Since somatosensory amplification seems to be partial involved in symptom reporting, it is important to control for this tendency when exploring the subjective health reports.

Illness memory causing increased bodily attention

Some theoretical models have expanded on the role of attention in symptom reporting by adding the potential role of cognitive schema networks related to illness, or in short "illness memory", in guiding attention and misinterpretation of bodily signals. These models have been developed independently of each other, and they all have a slightly different focus. However, as will be shown below, all these models share the common idea that illness-related memory or schemata corresponding to increased accessibility of illness-related information, play an important causal role in symptom reporting by either directing attention towards bodily signals, guiding interpretation of these signals, or by influencing the process of information retrieval from memory during the reporting of somatic complaints. A few of these models will briefly be discussed, followed by empirical evidence for this common notion.

Cognitive activation model by Skelton & Strohmetz (1990)

One of the earliest models on the role of cognitive schemata in symptom reporting was the cognitive activation model by Skelton & Strohmetz (1990). They state that the mere cognitive activation of health related thoughts or memory may increase the subjects' awareness of physical symptoms, which results in reporting more symptoms. They also suggest that increased symptom reporting in an environment or setting that increases health related cognitions, such as hospitals or waiting rooms, is a normal reaction or response (Skelton & Strohmetz, 1990). Thus, the core of this model is that increased accessibility of memory related to illness can cause increased self-reports of somatic complaints.

Leventhal's common sense model

The common sense model (CSM) suggests that people create mental representations of their illness, and these representations help them (or not) to manage their illness (Leventhal, Diefenbach, & Leventhal, 1992; Leventhal, Leventhal, & Contrada, 1998). Individuals create a mental representation of their illness, based on different sources in a two-level process. Individuals make links between information stored at an abstract level - for example labels and diagnoses stored in memory- and information stored at a concrete level - for example the perception of a bodily signal. This information then causes a person to create a schematic representation of the illness, which stimulates a search for more concrete body symptoms related to the diagnosed condi-

tion. The core element of this model is that the interpretation of bodily information is decisive in whether someone acts upon it, and not the bodily information itself. Thus, this model incorporates the view that a higher cognitive schematic representation- or schemata- of illness first guides attention toward bodily signals and then influences the interpretation of these signals. This implies that our subjective awareness is not based on an objective reality but on the interpretation of the world (Brown, 2004). Thus, this model also suggests that cognitive schemata-related to illness play a role in signal interpretation, and therefore symptom reporting.

Symptom perception model by Brown (2004)

In a model that combines several of elements of the earlier models discussed above, Brown (2004) describes in great detail how chronic involuntarily (unconsciously) activated illness memory can lead to reporting of symptoms. It states that illness memory causes increased selective attention towards bodily signals, which - as described above - causes increased detection of these signals and increased interpretation and reporting of these signals as symptoms (Brown, 2004). The more trained and consolidated this memory network becomes, the easier and more frequently it will be triggered by associated stimuli (Brown, 2004), and the more likely it becomes that bodily sensations are misinterpreted as signs of illness, resulting in an increasingly reflexive and subjectively convincing symptom experience (Brown, 2004). I will describe this model in more detail, since it is one of the basic models that the studies of this dissertation are testing.

Interaction of memory and attention. Before our attentional system makes a selection of potentially relevant new information for further cognitive processing, a spread of activation in associative memory networks occurs, which is triggered by input from our sensory system. This spread of activation in both perception and memory systems analyzing information of previous experiences then generates several perceptual hypotheses to interpret this new information (Brown, 2004; Norman & Shallice, 1986).

Brown (2004) describes two different attentional systems that guide or control our behavior in general: the primary attentional system (PAS; which is similar to the contention scheduling of the model of Norman & Shallice, 1986) and secondary attentional system (SAS; which is similar to the “supervisory attentional system” of Norman & Shallice, 1986). The PAS selects the most strongly activated perceptual hypothesis to organize the sensory information into primary representations (Brown, 2004). The primary representations are then used to guide our behavior, by activating thought and motor schemata. This can be divided into two basic routes. Procedural representations or schemata control routine behaviors (for example, driving a car), specifying the attentional, cognitive and motoric responses involved in these routine behaviors (Norman & Shallice, 1986). The activation of these schemata is automatic and unconscious which causes rapid, efficient control of cognition and action, and uses few processing resources. If there are no appropriate schemata based on previous experiences, then novel actions are controlled by a secondary, or supervisory, attentional

system. This secondary attentional system (SAS) controls action indirectly by changing the activation levels of schemata in the PAS. The processes controlled by the SAS are cognitively demanding, conscious and need self-awareness (see Brown, 2004).

This PAS/SAS model has several important implications: 1) control of behavior is mostly unconscious, 2) subjective awareness is not based on an objective reality but on the interpretation of the world (similar view of Leventhal; Brown, 2004). Examples of comparable perceptual or sensory experiences that are determined by prior information or memory are; hallucinations, misperceptions, hypnotic and placebo effects (see Brown, 2004). The result with respect to MUS is a misinterpretation of the sensory world that causes subjectively "real" symptoms (Brown, 2004).

Brown used the term "rogue representations" to describe the inappropriate hypotheses selected by the PAS (Brown, 2004). Brown provides a couple of examples of these hypotheses in relation to somatoform disorders: "For example, in the case of unexplained sensory loss, an inappropriate hypothesis would be one instructing the PAS to inhibit attention either to a particular sensory modality (as in blindness or deafness), a part of the body (as in focal sensory loss), or an aspect of the external phenomenal world (as in tunnel vision)" (as cited in Brown, 2004). Another example could be that a trigger of the memory of a specific episode of fatigue (perhaps someone who previously had an infection of mononucleosis) which would lead to the inappropriate hypothesis of feeling exhaustion, could cause someone to actually feel the fatigue associated with this previous episode, which could be an explanation for chronic fatigue syndrome. These rogue representations can be acquired by lots of different experiences and sources, many of which were recognized already by the earlier models (Leventhal et al., 1992; Pennebaker, 1982b), such as physical states of oneself (i.e. history of physical illness, symptoms that occur in response to traumatic events) but also of others (observing illnesses in others), sociocultural information about health (general health information transmitted through the media and society) and verbal suggestions (hypnotism) (Brown, 2004). Everybody possesses information or material that could feed rogue representations (Brown, 2004). However, not everyone develops MUS or a somatoform condition. Symptoms become chronic when the SAS directs high-level attention towards the symptoms, which also boosts the rogue representations and lowers the selection threshold by the PAS (Brown, 2004). Thus, it is a self-perpetuating process, which is facilitated by the attention focus of the SAS on health related information that is relevant to the individual (cognitive bias). This is also what Deary et al. (2007) describe as a "self-producing" process, which is an important aspect in MUS. Every time the memory networks are triggered, the further the networks are strengthened (see also Brosschot, 2002, below). Or alternatively, by classical conditioning, some emotions could get coupled with certain physiological states like pain (Brosschot, 2002). The same model could be applied to less severe symptom reporting (SHC) in the non-clinical population and in a magnified form in the clinical population.

As I will argue below, crucial aspects of this recent model have not been tested, such as the assumption that the activation of thought or motor schemata by the PAS based on inappropriate hypotheses (rogue representations) can cause people to experience subjective real symptoms, while no somatic explanation exists for these symptoms.

Cognitive bias and sensitization

The theoretical models discussed previously all share the common notion that symptom reporting is influenced by cognitive processes such as attention, memory and interpretation. The models suggest that MUS patients show an attentional bias toward bodily signals and an interpretation bias by interpreting those signals as symptoms of an illness, and finally a memory bias for these interpretations, together called cognitive biases. Whereas the models discussed above solely focus on cognitive biases, Brosschot (2002) proposed that these biases are not the sole factor explaining symptoms, but that these biases interact with alterations in neural activity that are observed in patients with MUS. That is, these patients show signs of "physiological sensitization", together with sensitization at the cognitive level (i.e. cognitive biases). Sensitization or physiological sensitization is a process that causes sensations resulting of normal physiological processes, to become intolerable (Eriksen & Ursin, 2004). A previous experience of certain stimuli can cause a heightened response to those stimuli or even far less potent stimuli later on. This is referred to as sensitization, and has been linked to MUS (Brosschot, 2002; Eriksen & Ursin, 2004). At the cognitive level, sensitization is manifested as selective processing of information that is of high relevance, such as feared situations, including illness and pain, and is called cognitive sensitization. It is also known as cognitive bias, especially in the field of experimental psychopathology (Brosschot, 2002). Potentially, cognitive biases, such as having increased attention towards bodily sensations, could then result in increased symptom reporting (Brosschot, 2002). Brosschot suggests that sensitisation at one level can cause sensitization at another level. I will first describe physiological sensitization, before I describe the evidence of cognitive sensitization, i.e. cognitive bias, in symptom reporting (see section below).

One very basic sensitization mechanism is called long term potentiation (LTP), which can be induced in the neural pain pathways (see Deary et al., 2007). Long-term potentiation is the enhancement of the signal strength between two synapses, caused by the simultaneous signaling. Prior pain experiences can cause this sensitization in the pain pathway, which results in lower pain thresholds for later pain experiences. Certain cognitive or emotional factors, such as anxiety, attention, and stress may lower the pain threshold even further (see Rygh et al., 2005). The result is that normal, non-painful bodily sensation could be experienced as pain, which in turn leads to increased attention and further sensitization. It has been suggested that pain in muscles, like in fibromyalgia patients, starts with sensitization of peripheral nociceptors and then leads to sensitization of the central nociceptive systems (see Eriksen &

Ursin, 2004). This form of sensitization has not only been suggested to play a role in fibromyalgia, but also in other MUS, such as IBS, functional dyspepsia, and chemical intolerance. For example, patients with IBS and functional dyspepsia have a lower tolerance for sensations for the gut (see Eriksen & Ursin, 2004). Furthermore, 'higher up' in the nervous system, kindling or sensitization of limbic brain structures may also play a role. It has been suggested to be a shared underlying etiological factor in medically unexplained pain and certain psychiatric disorders like major depression, panic disorder and anxiety (see Eriksen & Ursin, 2004). For example, Rome & Rome (2000) proposed the limbically augmented pain syndrome (LAPS) in which they suggest that depression and other affective disorder can cause the corticolimbic system to become sensitized for noxious stimuli, such as pain. It also has been found that spinal cord sensitization is influenced by cognitive factors (Matre, Casey, & Knardahl, 2006). Finally, at the highest level cognitive sensitization can occur, which is similar to cognitive bias, which includes the enhanced attention for health information, interpretation of ambiguous signals as symptoms and above all, activated illness memory which guides attention and interpretation.

In conclusion, cognitive biases, such as increased attention towards illness-related information and increased memory for symptom-related information, are possibly a causal factor in MUS. Furthermore, these cognitive biases might be related to physical sensitization, for example to pain, which may be a perpetuating factor in MUS. Now that the theory of illness memory in MUS has been laid out, I will turn to examining available evidence for the common overlapping notion of these models, namely that illness-related memory or schemata might play a causal role in the reporting of MUS.

SUPPORTING EVIDENCE SO FAR FOR THE CAUSAL ROLE OF COGNITIVE PROCESSES IN SYMPTOM PERCEPTION

Thus, several symptom-perception models suggest that symptoms become represented in memory. Later experiences that share similarities to this memory representation, can automatically and unconsciously re-activate and strengthen this memory, negatively influencing the interpretation and perception of the actual bodily experience in a feed forward, vicious circle-like manner. Despite the high number of studies on the link between symptom reports and selective attention towards illness and innocuous bodily information, few studies have yet tested the crucial notion of the cognitive theory of MUS that activation of illness or pain memory causes symptoms. Next, I will give an overview of the cross-sectional evidence for this idea and then I will discuss the experimental evidence found so far.

Supporting cross-sectional evidence

Several studies have examined whether patients with MUS indeed show selective attention towards health related information as is suggested by the theoretical models discussed above. Many of these studies have used a so-called' modified Stroop task' or 'visual-probe task' to measure attention towards health-related stimuli, typically

comparing a patient group with MUS to a control group of healthy participants or participants with another (mental) health problem such as depression. Many studies found evidence for attentional biases in somatoform patients and chronic pain patients (Asmundson, Kuperos, & Norton, 1997; Crombez, Hermans, & Adriaensen, 2000; Pearce & Morley, 1989; Snider, Asmundson, & Wiese, 2000). Although some studies did not find evidence for an attentional bias (Pincus, Fraser, & Pearce, 1998). One study of Idiopathic Environmental Intolerance (IEI) and Somatoform Disorder patient groups found that in a modified Stroop task, attention was biased toward symptom words such as 'dizziness' and 'nausea' but not toward IEI-trigger words such as 'radioactivity' and 'paint smell' (Witthöft, Gerlach, & Bailer, 2006). A recent meta-analysis found that individuals with chronic pain, compared to controls, showed a significantly greater attentional bias towards pain-related information on a visual-probe task (Schoth, Delgado Nunes, & Liossi, 2012). Furthermore, patients with irritable bowel syndrome have been found to show selective attention towards gastrointestinal symptom-related words compared to neutral words, but only when the words were presented subliminally and not when they were presented supraliminally (Afzal, Potokar, Probert, & Munafò, 2006).

Other studies have focused on memory bias and examined whether patients with MUS have increased implicit memory for illness or health. Better memory for pain-related words was found in chronic pain patients (Pincus, Pearce, McClelland, & Isenberg, 1995). Pain patients remember more pain-related words than neutral words, but only before surgery. Six months after surgery, neutral words were remembered better instead (L. C. Edwards, Pearce, & Beard, 1995). One study found that patients with somatoform disorders showed decreased explicit but increased preconscious or implicit memory (as measured with the lexical decision task) for health-related stimuli compared to depressive patients (Dohrenbusch, Scholz, & Ott, 2006). A study by Martin, Buech, Schwenk & Rief also found that a participant group with somatoform disorders showed an implicit memory bias for illness-related stimuli (measured with a word-stem completion task), but did not show an explicit memory bias (2007). This implicit memory bias was not found in a control group of depressed patients, which suggests that this effect could not be explained by comorbid depression. In contrast, another study found that somatoform patients did not show an implicit memory bias measured by a tachistoscopic word identification, but an explicit memory bias for physical threat words on a free recall task (Lim & Kim, 2005). Similarly, a study found that patients with irritable bowel syndrome recalled words related to gastrointestinal sensations better than other categories in a free recall task (Gibbs-Gallagher et al., 2001). Cognitive biases have not only been found in patients with MUS, but also in people with SHC. One study has found that healthy female participants with higher severity of SHC in the previous month had a bigger or stronger memory bias for health-related words compared to females with less severe SHC (Verkuil, Brosschot, & Thayer, 2007).

Although many studies have found a cross-sectional link between attentional bias and different patient groups with MUS, the cross-sectional evidence of these memory biases remains questionable due to differences in study findings. Furthermore, the above mentioned studies all have the limitation of being a cross-sectional study, which makes it unclear whether increased attention or implicit memory for illness-related information is the cause or the effect of having MUS. Prospective and experimental studies are warranted to address the causality in the relationship between cognitive biases and symptom reporting.

Worry and catastrophizing

There is some indirect evidence of illness memory causing increased symptom reporting, since illness worry or catastrophizing have been thought to increase illness memory and are found to be related to increased symptom reporting. This will be further explained by using an example specifically related to pain. Pain catastrophizing is a concept specific to pain, that has been thought to increase the accessibility of pain related thoughts or pain schema (Sullivan, Rouse, Bishop, & Johnston, 1997; Sullivan, Stanish, Waite, Sullivan, & Tripp, 1998). Catastrophizers are hypothesized to have pain schemata that contain excessive negative information (Sullivan et al., 2001; Sullivan, Bishop, & Pivik, 1995; Turk & Rudy, 1992). If these pain schemata become activated they may cause an abnormality in cognitive functioning that could lead to an enhanced pain experience (Sullivan et al., 2001). Several studies have shown that pain catastrophizing is associated with a greater pain experience (Sullivan et al., 1995, 1998). However, the relation between pain catastrophizing and pain is not completely clear in cross-sectional research; do people have more pain or distress because they have catastrophic thoughts about their pain or do people have more catastrophic thoughts because they have more pain? Prospective studies, however, did find a relation between catastrophizing and pain. In a longitudinal study, a predictive effect of catastrophizing on pain intensity ratings after controlling for initial scores on the dependent variables, demographic variables -like age, sex, socioeconomic status-, duration of pain, and disability support status was found (Keefe, Brown, Wallston, & Caldwell, 1989). A similar study found that catastrophizing predicted pain during dental hygiene treatment, even when controlling for gender and oral hygiene status (Sullivan & Neish, 1998). Kabat-Zinn (1982) suggests that mindfulness applied by chronic pain patients could lead to a desensitization process because of the absence of catastrophic thoughts during exposure to pain.

In conclusion, studies focused on pain catastrophizing show additional support for the idea that illness-schemata could play a causal factor in symptom reporting. However, again more prospective studies are necessary. Furthermore, the assumption that pain catastrophizers have increased accessibility of pain-related schemata needs to be addressed, and future studies should examine whether this increased accessibility is the cause of increased pain reporting in high pain catastrophizers.

(Experimental) manipulations of illness memory

It is unclear from the above mentioned evidence resulting from cross-sectional studies whether activated illness memory –or schemata- can lead to increased symptom reporting, or whether actually experiencing symptoms causes increased accessibility of illness memory - which admitted, is not unlikely. Therefore, studies in which the activation of memory is manipulated to examine its effect on symptom reporting are needed to answer this question. Several such studies have been reported, that used different types of experimental manipulations of cognitive schemata or memory, and these studies will be discussed next.

Experimental priming studies with words or pictures

Several studies have investigated the effect of increased cognitive accessibility of illness memory on reporting of symptoms by priming participants with illness or pain-related information. Priming is the effect in which exposure to a stimulus influences a subsequent response and is an implicit memory process. Priming causes the increased cognitive accessibility or activation of the memory network and is believed to be due to a mechanism called 'spreading-of-activation'. That is, knowledge is stored in a network of interconnected semantic and associative concepts, with more closely related concepts located closer together within the network (Collins & Loftus, 1975). Proof for the principle underlying priming comes from studies showing that priming of a word increases the recognition speed of a semantically related word. For example, the response latencies are faster when the words "nurse" and "doctor" are both displayed on the screen compared to "nurse" and "butter" (Meyer & Schvaneveldt, 1971).

One study showed that participants showed lower pain tolerance by keeping their hand less long in ice cold water while watching pictures of painful events compared to patients who watched pictures of other negative events. The pictures of painful events presumably activate a memory network related to pain- compared to other negative pictures- and thus is supportive for the notion that pain or illness-related memory networks causes increased symptom reporting (De Wied & Verbaten, 2001). However, many of these pain-related pictures were disgusting, thus it is unclear whether the lower pain tolerance is actually due to activation of pain-related memory networks or due to disgust-related memory networks. Another study showed that pain intensity reports significantly increased when painful stimuli were simultaneous administered with images showing human pain, while pictures with identical emotional values but no somatic content did not increase pain intensity (Godinho, Magnin, Frot, Perchet, & Garcia-Larrea, 2006).

In MUS patients there is experimental evidence of pain-related pictures on pain symptom reporting as well. A study by Arnold et al. (2008) examined the effect of pain-related pictures on pressure pain intensity ratings in different MUS-groups: fibromyalgia patients, back pain patients, and somatoform patients, compared to

healthy individuals as control groups. Overall, it was found that pain intensity ratings were higher during the viewing of the pain-related pictures compared to negative pictures. Although there was no interaction effect of complaint-specific picture content and patient group, the fibromyalgia patients and the somatoform patients rated the pain-related pictures as more negative in valence and arousal compared to other negative pictures (Arnold et al., 2008). This makes it unclear whether the effect of the pain-related pictures is due to their content or due to their valence.

Another study found that not only symptom-related pictures but also generally negative pictures, compared to positive pictures, increased symptom reporting (enhanced breathlessness/dyspnea) in (non-clinical) high but not in low symptom reporters (Bogaerts, Janssens, De Peuter, Van Diest, & Van den Bergh, 2010). This is clearly not in line with the hypothesis that illness memory-activation causes increased symptom reporting. However, since the participants were told that physiological (i.e. respiratory) measures would be taken while viewing pictures, it might have occurred to the participants that the experimenters were looking for increased symptom reports viewing negative pictures, whether symptom related or not. In addition, it cannot be excluded that the extensive and rather invasive respiratory recordings (in which a participant's mouth was covered by a respiratory measuring device) acted as a clearly health related context, that could easily have primed illness memory, which means that all negative pictures, not only the illness-related ones, could have acquired an illness-related meaning.

Several studies used words as stimuli instead of pictures. One study found that pain-related words that were shown to pain patients caused higher brain potentials in areas that may corresponded to higher implicit memory and selective attention for pain, and also increased pain perception (Flor, Knost, & Birbaumer, 1997). Another study also examined the effect of pain-related stimuli on pain intensity ratings. They used words of three semantic categories, namely somatosensory pain-related, affective pain-related and neutral words in combination with a pain-inducing heat stimulus (Dillmann, Miltner, & Weiss, 2000b). Although they did not find any difference in pain intensity ratings between the different prime groups, they did find an increase in brain activity during pain caused by laser stimulation while reading the pain somatosensory or affective words compared to neutral words. The authors suggest that pain words might pre-activate neural networks that are responsible for pain memory and processing (Dillmann, Miltner, & Weiss, 2000a; Dillmann et al., 2000b). Still, this activation was not sufficient to actually increase the pain reports.

In conclusion, most of the above mentioned studies provide support for the cognitive model of symptom reporting by showing that pain or illness-related stimuli (which presumably activate the associated memory networks) decrease pain tolerance or increase pain intensity. However, the studies show several important limitations, which makes the support for the model inconclusive.

Other priming methods

The previously described studies all used words or pictures as priming stimuli. However, other priming methods exist which will be described next. For example, one study (Wooley, Blackwell, & Winget, 1978) measured tolerance of pain produced by immersion of the hand in ice water under two experimental conditions. In one condition, the experimenter wore a white coat and gave verbal comments to the participants at 15 second intervals. This 'medical' condition presumably activates pain memory, which presumably makes participants expecting feeling pain. In the other condition, the experimenter was wearing normal street clothes and remained silent. The participants indeed showed lower pain tolerance if the experimenter wore a white coat.

One study had participants either run in place for 2 min or walk for 2 min. A few minutes later they were brought to another room and asked to fill in a symptom checklist. To half of the participants the experimenter added that it was of the flu season that they wanted them to fill in the symptom checklist (as discussed in Pennebaker, 1982b). Participants reported the greatest amount of symptoms if they had been running and if they had received the comment of the flu.

Research has demonstrated that when people are simply asked to fill in a self-report mood questionnaire, it can prime mood-related cognitive contents and information-processing strategies (as discussed in Skelton & Strohmetz, 1990). One study showed that participants indeed report more somatic symptoms on a questionnaire after they had performed a task in which they had to make comparative judgments about the meaning of health related words. This result was controlled for individual's symptom-reporting dispositions, mood, arousal and task-related pressure (Skelton & Strohmetz, 1990).

In conclusion, the above mentioned studies also show support for the cognitive model of symptom reporting, however, it is not conclusive evidence since the participants might have been aware of the goal of the experiment.

Supraliminal versus subliminal priming

The previously described studies all have used health-related stimuli that were presented in a supraliminal manner to the participants, meaning that the participants were consciously aware of seeing these stimuli. A limitation of presenting stimuli supraliminally is that participants might figure out the underlying goal of the experiment and behave in a socially desirable manner. A way to circumvent this problem, is by showing the stimuli under the awareness threshold of the participants, which is referred to as subliminal priming. With this technique words or pictures are shown for a very short time duration, so that the participant remains unaware of seeing anything. While several studies testing symptom reporting effects of health memory used supraliminal priming technique, as discussed above, no studies thus far have used the subliminal priming technique.

Indirect priming of previous symptoms

Implicit memory or associations can be created by classical conditioning, and classical conditioning has been used to examine symptom reporting. It has been hypothesized that cues of previous illness ('conditioned cues' or cues that people have learned to associate with illness) can also prime the individual to express the symptoms of the illness. This type of priming is based on associations and is thus indirect priming memory of illness or pain, compared to directly priming of illness or pain memory described in the previous paragraphs. Indeed, a series of symptom conditioning studies by van den Bergh and colleagues has shown that it is possible by showing associative cues to indirectly prime memory of previous symptoms that cause increases in current symptom reporting (Van den Bergh, Winters, Devriese, & Van Diest, 2002). Presentation of cues that were previously associated with experimentally induced symptom episodes of breathlessness triggered increased reports of breathlessness while there was no physiological cause. It was found that only stimuli with negative valence (foul smelling cue compared to neutral or positive smelling cue) could cause conditioning of symptoms, furthermore, symptom learning is more likely to occur in participants with high NA, and/or high levels of symptom reporting in daily life, in psychosomatic patients (Bogaerts et al., 2010; Van den Bergh et al., 2002). Although these studies do show support for the idea that the indirect priming of illness memory of a specific symptom previously experienced by presenting associative cues, can cause increased symptom reporting, it does not support the idea or hypothesis that priming illness memory directly can cause increased symptom reporting.

AIM AND OUTLINE OF THESIS

In summary, several studies have found that increased accessibility of illness memory seems to be related to increased symptom reporting. However, a large part of these studies show only cross-sectional evidence for this evidence and thus do not address the causality aspect. Most studies that did use experimental manipulations to investigate the causal effect of illness memory, used techniques to manipulate the accessibility of memory that might have been noticeable to the participants, which may have caused them to behave unnaturally during the experiments because they may have guessed the experiment's purpose. Thus, the crucial assumption of the cognitive model of SHC and MUS, that activated illness memory causes symptom reporting has not been rigorously tested. The aim of the current thesis is therefore to test whether the activation of illness memory networks causes increased symptom reporting.

To circumvent the problem of the participants possibly behaving in a socially desirable way, we used stimuli that participants were not consciously aware of. Furthermore, previous experimental studies examining the effect of illness memory have not always controlled for important factors that influence symptom reporting as well, such as negative affect. In addition, several studies used methods that seem to indirectly prime illness memory (such as classical conditioning of symptom reports) but only few

studies have used the standard procedure to manipulate illness memory, which is priming. In the present thesis, we have addressed these limitations of previous studies. In the first part, we have used manipulation techniques that allow testing of the hypothesis whether increased cognitive accessibility illness memory causes increased symptom reporting while the participants remain unaware of the study's aim. Furthermore, we tried to manipulate illness memory more directly by using priming methods in the laboratory while controlling for several moderators. In addition, we conducted the first study that examines the effect of illness memory on symptom reporting prospectively. The dissertation is organized in two parts. Part I examines whether unconsciously manipulated illness-related memory causes increased symptom reporting. Part II examines the prospective association between illness-related memory and symptom reporting using consciously perceived techniques. In the first part of this thesis, the hypothesized effect of implicit illness-related memory on symptom reporting was examined in the laboratory. The implicit illness memory networks were manipulated by using subliminal priming techniques. With this technique stimuli ("primes") are presented under the awareness threshold, and are believed to activate the implicit memory of the category that fits with the used stimuli. We then tested whether activated illness memory would indeed cause more symptom reporting. Importantly, we controlled for possible confounders of illness priming, such as negative valence of illness information and the sensory aspect of illness information by comparing the result of illness priming to control groups with either neutral words, negative words or sensory words. In this case we used low pain tolerance as a measure of symptom reporting since pain is the most common MUS. In addition, we examined the effects of self-focused attention, self-priming, negative affect, health worry on symptom reporting. The first part of this thesis consists of four studies. In **Chapter 2**, we examined whether we could manipulate illness memory unconsciously, and whether this caused an increase in symptom reporting, as measured with a pain task. We also explored whether negative affectivity (NA), health worry, and common HCs interacted with the hypothesized effect of illness-related memory on symptom reporting (Kolk et al., 2002; Petrie et al., 2005; Verkuil et al., 2007; Watson & Pennebaker, 1989). In **Chapter 3**, we replicated the previous study by making slight modifications to the research design, in order to measure the effect of unconsciously manipulated illness memory on symptom reporting even better. Illness-related memory is more likely to influence reporting of complaints when its activation is enmeshed with that of self-related memory. Therefore, in **Chapter 4**, the relationship between unconscious illness-related memory and self-schemata were experimentally manipulated to be stronger associated with each other. We then examined the effect of this manipulation on symptom reporting. In addition, we examined the effect of self-priming on symptom reporting and whether self-focused attention (SFA) acted as a moderator of this effect. Although subliminal priming is an often used procedure to activate concepts in memory, its effectiveness is seldom tested. Therefore, in the final chapter of Part I (**Chapter 5**), we examined the subliminal priming techniques that were used, where indeed increasing the cognitive

accessibility of illness memory. Because evidence from these studies remained inconsistent for the hypothesized role of illness memory in causing an increase in symptom reporting, we concluded that this could mean two things: 1) the hypothesized effect of illness memory on symptom reporting does not exist, or 2) the methods used in Part I were not adequate in manipulating illness memory in the way that we wanted to. **Chapter 5** present the results of the study in which we looked at whether the subliminal priming technique in the first two studies actually did increase the accessibility of illness memory.

Part II consists of two studies. These studies addressed the problem of inadequacy in manipulating illness memory by using different priming techniques that do not use unconscious stimuli (**Chapter 6**) and measuring the association between symptom reporting and illness-related memory prospectively without trying to manipulate it (**Chapter 7**). In **Chapter 6**, the effects of a randomized controlled trial using an online intervention focused on activating positive health memory was examined on symptom reporting in healthy students. Again we examined the effect of important possible moderators, such as negative affect and somatosensory amplification. **Chapter 7** presents the results of a study that examined the relation in time between implicit illness-related memory and symptom reporting among patients with fibromyalgia, irritable bowel syndrome and chronic fatigue syndrome in comparison with healthy controls. This is the first study that we know of that examined the activation of illness memory repeatedly over time in MUS patients and examines the effect on symptom reporting prospectively. **Chapter 8** provides a summary of the main findings, methodological considerations, clinical implications and future directions in this field of research.

Part I. The Unconscious Manipulation of Illness-Related Schemata in an Experimental Setting

Chapter 2 |

Decreasing Pain Tolerance Outside of Awareness

Meerman, E. E., Verkuil, B., & Brosschot, J. F. (2011). Decreasing pain tolerance outside of awareness. *Journal of Psychosomatic Research, 70*(3), 250–257.

ABSTRACT

Objective Medically unexplained symptoms (MUSs) are a humanitarian and economic burden. Among them, pain complaints without organic pathology are the most prevalent. Theoretically, activated illness-related memory may cause reporting of symptoms by changing perception and interpretation of bodily signals to the extent that they are not tolerated and become complaints. We tested whether activating illness-related memory without conscious awareness leads to decreased pain tolerance (PT).

Methods Activation of illness-related memory without conscious awareness was manipulated by a subliminal priming technique. Eighty participants were randomly assigned to four conditions, with prime words describing either (a) health complaints (HCs), to activate an illness-related memory, or three control categories: (b) neutral content, (c) general bodily sensations, and (d) negative valence. The latter two conditions were added to test the alternative hypotheses that reduced PT could be observed with the semantic activation of these two components of HCs. We measured PT using a cold pressor task.

Results Participants who were subliminally primed with HC words reported lower PT compared with participants who were primed with neutral words. Priming with the other words did not lead to significantly different effects relative to priming with neutral words.

Conclusions The findings suggest that PT can be involuntarily decreased by activating illness-related memory. This implies partial evidence for a crucial element of a cognitive model of medically unexplained symptoms, which holds that chronically activated illness-related memory causes the development of somatic complaints without observable bodily pathology.

INTRODUCTION

Approximately one-third of health complaints (HCs) presented to primary care professionals cannot be attributed to organic pathology and are called medically unexplained symptoms (MUSs) (Khan et al., 2003; Kroenke & Mangelsdorff, 1989; Peveler et al., 1997). Most MUSs involve pain, and they form a major burden on the health care system (Brown, 2004; Khan et al., 2003). How can innocuous bodily signals become intolerable and turn into HCs? It is assumed that there is no one-to-one correspondence between physiological changes and the perception of physical symptoms but that the latter is modulated by cognitive top-down processes (Pennebaker, 1982b). Recent additions to this symptom perception model state that a chronic involuntarily (unconsciously) activated memory network of illness can lead to increased selective attention toward innocuous bodily signals, which causes increased detection of these signals and increased interpretation and reporting of these signals as symptoms (Brosschot, 2002; Brown, 2004; Rief & Barsky, 2005). Brown (2004) hypothesized that activation of such an illness- or pain-related memory network produces a vicious cycle by increasing attention toward bodily sensations (SEN) and increasing the inappropriate perception of these signals as symptoms, which in turn reactivates this memory network. The more trained and consolidated this memory becomes, the easier and more frequently it will be triggered by associated stimuli (Brown, 2004; Pincus & Morley, 2001) and the more likely it becomes that SEN are misinterpreted as signs of illness, resulting in a reflexive and subjectively convincing symptom experience (Brown, 2004).

There is evidence that people with MUSs more easily report symptoms during painful stimulation. For instance, reporting of more pain is found in a variety of MUSs, such as irritable bowel syndrome, and in common HCs, such as headache (Rodrigues, Verne, Schmidt, & Mauderli, 2005; Verkuil et al., 2007). In addition, a large number of studies found that patients with MUSs and people suffering from common HCs also show increased selective attention for external information related to their HCs, including pain (Afzal et al., 2006; Karademas, Sideridis, & Kafetsios, 2008; Pincus & Morley, 2001). Likewise, several studies have linked symptom reporting with increased attention to SEN (Barsky et al., 1988; Kolk et al., 2002; L. C. Miller et al., 1981; Pennebaker & Lightner, 1980).

Despite the high number of studies on the link between symptom reports and selective attention toward illness information and innocuous bodily information, few studies have yet tested the crucial notion of the cognitive theory of MUSs that activation of an illness- or pain-related network in memory causes symptoms (Brown, 2004). In the present study, we aimed to test whether activating illness memories results in enhanced reporting of symptoms. We specifically focused on the reporting of pain, which is the most frequently reported MUS (Khan et al., 2003). Everyone experiences pain from time to time, but not everyone develops pain complaints. In general, pain becomes a symptom when a pain signal becomes intolerable and people start reporting

about it. For these reasons, we used pain tolerance (PT) during a cold pressor task (CPT) as a measure of symptom reporting.

To unambiguously test the hypothesis that involuntarily (i.e. unconsciously) activated illness-related memory can cause participants to report lower PT, we used a subliminal priming technique. This technique of presenting stimuli ("primes") under the awareness threshold activates, or primes, the semantic category of a word in memory while participants remain unaware of it. We used words describing common HCs to activate the illness-related memory and we compared the reported PT of participants primed with these HC words with those of participants who were shown neutral (NEU) words. In an explorative manner, we also tested two alternative hypotheses, namely that lower PT would already be observed with the semantic activation of SEN or negativity in general. To test this, we added two groups that were shown either words describing SEN or negative valence (NEG) words.

Two earlier studies showed that pictures illustrating physical suffering, which activate pain or illness memory, cause people to report lower PT (De Wied & Verbaten, 2001) and pain intensity (Godinho et al., 2006). While this is in line with the hypothesized role of illness memory, the researchers' use of consciously perceived pictures to activate memory makes their findings difficult to interpret and possibly even confounded. First, the findings are silent about whether memory is activated involuntarily. Second, the participants may have guessed the experiment's purpose and may not have responded spontaneously. In the current study, this problem was circumvented by using subliminal priming. Moreover, in these studies, the pictures illustrating physical suffering were presented at the same time as the pain stimuli. This procedure cannot exclude the possibility that the pictures simply interfered with attempt to tolerate pain. In the present study, we presented the primes first and administered the pain stimulus immediately afterwards.

Negative affectivity (NA), health worry, and common HCs have all been linked with increased reporting of more symptoms. Therefore, we measured these traits and symptoms and explored whether they interacted with our hypothesized main effect (Kolk et al., 2002; Petrie et al., 2005; Verkuil et al., 2007; Watson & Pennebaker, 1989).

In sum, our main hypothesis was that activating illness-related memory, by subliminally priming with HC words, would cause enhanced pain complaints, operationalized as a lower tolerance for induced pain.

METHODS

Subjects

Eighty students from Leiden University participated in the present study. Participants received either course credits or 8 Euros for participating. This study was approved by the ethics committee of the Leiden University Institute of Psychological Research. Prior to participating, subjects were screened for any medical disease, feelings of

anxiety or depression, and native language. Participants were required to refrain from taking pain killers 4 h prior to the experiment.

Materials

Questionnaires

Subjective health

Subjective health was measured in specific and general ways. Specific subjective HCs (SHCs) were measured with the SHC Questionnaire (Eriksen, Ihlebaek, & Ursin, 1999). The SHC Questionnaire is a 29-item self-report questionnaire that reliably measures the number and severity of SHCs experienced during the last month. It has five areas of complaints as subscales: musculoskeletal pain, pseudoneurology, gastrointestinal problems, allergy, and flu. Severity of each complaint is rated on a four-point scale. Total number of complaints and a total severity score were used. The SHC does not measure whether or not the 29 items are caused by a medical disease. However, we used "being diagnosed with a medical disease" as an exclusion criterion. The internal consistency of the SHC Questionnaire has been proven to be sufficient (Eriksen et al., 1999). The internal consistency of the total SHC scale (Severity × Days) was sufficient, α = .75.

In addition, we also measured general self-rated health (SRH) (Idler & Benyamini, 1997). Participants were asked to rate their health in comparison with that of people of the same age. They could respond with "worse, " "the same, " or "better."

Health worry

Complaint-specific worry was assessed by asking the extent to which participants had been worrying about a complaint for each of the 29 complaints on the SHC Questionnaire. The participants could indicate on a four-point scale how much they had worried about that specific complaint during the last month. The total score of worry on the SHC Questionnaire was used as a measure of health worry. The internal consistency of this added scale to the SHC was high, α = .81.

Positive and Negative Affect Schedule (PANAS)

The Dutch trait version of the PANAS consists of 10 positive [positive affectivity (PA)] and 10 (NA) adjectives. Participants indicate on a five-point scale the extent to which the items apply to how they generally feel in normal daily life. The reliability and construct validity of the PANAS have been documented (Engelen, De Peuter, Victoir, Van Diest, & Van Den Bergh, 2006; Watson, Clark, & Tellegen, 1988). The internal consistencies of the NA and PA scales in our sample were high, α = .79 and α = .75, respectively.

Priming task

Prime words

To activate general illness memory, we used words related to somatic complaints. Participants were randomly assigned to four conditions, with prime words describing either (a) HCs, to activate an illness-related schema, or the three control categories: (b) NEU words, (c) words describing SEN and (d) NEG words (Appendix). The NEU prime words consisted of animals, and the NEG words consisted of negative personality traits that were rated on their valence in earlier research by Hermans and de Houwer (1994). We generated the list of words describing SEN and HCs, with each word rated on the representativity of the semantic category, along with three colleagues. Only words rated high (at least 4 on a six-point scale) on representativity were chosen for primes. All categories contained 10 words and did not differ in number of syllables, length, and frequency in the Dutch language [Kruskal–Wallis: $H_{(3)} = 1.50$, $p = ns$; $H_{(3)} = 1.10$, $p = ns$; and $H_{(3)} = 3.65$, $p = ns$]. In every prime condition, the 10 prime words were shown randomly 10 times, thus giving a total of 100 trials.

Priming task

In order to rule out any effects on pain of distraction by the computer task, we performed the computer task (with primes) immediately before the pain task. Several studies have shown that subliminal priming effects can last for at least a couple of minutes (Bargh & Chartrand, 2000; Levy, Hausdorff, Hencke, & Wei, 2000; Lowery, Eisenberger, Hardin, & Sinclair, 2007). The priming manipulation was a variation of a common paradigm in which participants judge as quickly and accurately as possible whether briefly flashed letter strings appear on the right or left side of a computer monitor (Lowery et al., 2007). Because we wanted to ensure that the priming effect would last during the CPT, we decided to use a prime stimulus duration that would resemble the prime duration closest that in a previous study was found to have long-lasting subliminal priming effects (Lowery et al., 2007). That study used 34 ms; however, because of computer-related technical restrictions, we used 33 ms. Many other studies used the same prime duration of 33 ms (for example, Refs. Kiefer, 2002; Levy, 1996; Pierce & Lydon, 1998). The present subliminal priming task consisted of a simple computer task presented to the participants as a reaction time task. For each trial of the task, a fixation cross with a random duration of 500–1000 ms appeared in the center of the screen. Students were then exposed to the prime word (33 ms) and immediately after a string of XXX's that served as a backward mask for the prime word. The prime word and mask appeared on either the right side or the left side of the screen in the parafoveal region (at a 2-deg visual angle (Bargh & Chartrand, 2000). Participants indicated with the arrow keys what the position of the XXX's was. Each trial was separated by a 500-ms interval in which the screen was blank. The mean total duration of the priming task was 2.62 min (SD = 0.34).

Awareness checks

In order to see whether the primes were indeed shown under the awareness threshold, we checked after the pain task whether the participants could detect the primes. We used a subjective threshold in which conscious awareness is indexed by participants' self-reports with a funneled debriefing questionnaire that consisted of increasingly specific questions that were designed to probe for any suspicions regarding the priming task and its purpose (Bargh & Chartrand, 2000). We also used an objective threshold in which conscious awareness is indexed by the d' measure, a measure of the participants' discriminative abilities based on signal detection theory (Macmillan, 2005). We calculated the d' measure and its 95% confidence intervals from the proportion of true hits and correct rejections that the participants made on 30 discrimination trials. The corrections of 1/(2N) and 1−1/(2N) were used for perfect accuracy scores with n = 15, the number of trials on which the proportion is based. If the 95% confidence intervals of the d' measure included zero, then these participants were assumed to have not been able to discriminate between the prime words (Macmillan, 2005). Only six participants could discriminate between the words after they were told that it involved a subliminal priming task. Although a non-zero d' measure does not have to imply awareness, it could still be a result of an unconscious process; we thus excluded these participants to use the most stringent criterion of awareness.

Pain Tolerance (PT)

For pain stimulation, we used a CPT. During a CPT, participants are asked to keep their non-dominant hand in a basin filled with ice-cold water for as long as they can. The basin is, on the surface of the water, divided into two sections. One is filled with ice and the other is kept free of ice to allow a hand to be immersed in the water without direct ice contact. A pump kept the water flowing continuously to prevent buildup of warmer water around the hand. The mean water temperature was 1.64°C (SD = 0.81). PT was defined as time elapsed (in seconds) between immersion and withdrawal (De Wied & Verbaten, 2001). Unbeknown to the participants, the maximum duration of hand immersion was limited to 4 min. For exploratory reasons, pain intensity and pain unpleasantness ratings were also rated on a scale of 0–10, from "not at all intense" or "not at all unpleasant" to "extremely intense" or "extremely unpleasant". To prevent interference with PT, we took these measures immediately after the participants withdrew their hand from the water.

Procedure

Information about the experiment was posted on the Internet, making clear that it consisted of filling in questionnaires, with a special focus on study skills (which served as a cover story), reaction time tasks on the computer, and a pain task. Participants were tested individually by one male experimenter. The experimenter was kept blind about the random assignment of the participants. When the participants arrived at the

laboratory, they were screened as to whether they fulfilled the requirements. The participants were asked to provide demographic information (age and gender), and the computer task was started. The experimenter moved to an adjacent room, where he followed the procedure. After questionnaires regarding health and mood, participants filled in questionnaires about study skills for 10 min to mask the goal of the experiment. Thereafter, the priming task started, immediately followed by the CPT. After they took their hand out of the water, participants were asked to rate pain unpleasantness and pain intensity. Awareness of the priming procedure was assessed with the funneled debriefing questionnaire and with the forced-choice word identification task. Finally, participants rated the negative versus positive valence of all prime words on a seven-point scale, and they performed the same priming task but with positive health words to counteract any potential longer-lasting effects of the previous priming that might have a negative effect on PT. At last, the participants were fully debriefed and received money or course credits.

Data analyses

We used an analysis of variance with PT as dependent variable and the four groups as independent variables, producing three pairwise planned comparisons. Stepwise backward regression analysis with a high *p* value criterion of .55 was used to select an optimal set of covariates among the baseline and experimental factors (Steyerberg & Harrell, 2003). The critical F values for the planned comparisons are reported (Tabachnick & Fidell, 2007). Because of our specific hypotheses, we used one-tailed tests, but we also report the two-tailed *p* values.

RESULTS

Data of participants who afterwards indicated on the funneled debriefing questionnaire that they thought the task involved priming (n = 3), participants who could discriminate between the primes according to their d' measure (see forced-choice test above) (n = 6), participants who had a diagnosed minor medical disease (n = 3), and participants with missing data due to computer failure (n = 2) were excluded.

Prior to analysis, the variables were examined separately for the four conditions on accuracy of data entry: missing values, linearity, homogeneity of variance and regression, and normality (Tabachnick & Fidell, 2007). Variables were transformed if necessary.

Descriptives

The mean age of the participants was 21.57 years (SD = 3.45), and 84.8% were female. Participants in the four conditions did not differ at baseline in factors that might influence PT, including (a) demographic features, such as age and gender; (b) psychosocial factors, such as SRH and NA; and (c) experimental factors, such as water temperature of the CPT (see Table 2-1).

Table 2-1. Sample baseline characteristics among the four experimental groups
(mean of untransformed data ± SD)

Characteristics	NEU group (*n* = 17)	SEN group (*n* = 17)	NEG group (*n* = 17)	HC group (*n* = 15)	Test statistic	*p*	Post hoc
Gender, female [n (%)][a]	13 (76.5)	14 (82.4)	16 (94.1)	13 (86.7)	2.20	.58	n.s.
Age (reciprocal)[b]	21.23 ± 2.47	21.75 ± 3.23	21.99 ± 4.40	21.32 ± 3.72	0.13	.94	n.s.
PA[b]	32.29 ± 4.95	34.59 ± 4.03	34.47 ± 5.59	34.13 ± 5.28	0.78	.51	n.s.
NA[b]	17.18 ± 4.22	17.47 ± 5.91	17.47 ± 4.69	16.40 ± 6.79	0.13	.94	n.s.
SRH[b]	1.29 ± 0.59	1.12 ± 0.49	1.18 ± 0.53	1.13 ± 0.52	0.38	.77	n.s.
SHC (Number × Severity)[b]	8.94 ± 5.07	10.24 ± 5.64	13.94 ± 8.17	12.33 ± 7.35	1.87	.14	n.s.
SHC worry (log)[b]	4.88 ± 4.00	4.41 ± 4.42	9.18 ± 8.28	4.93 ± 5.68	2.42	.08	n.s.
SHC musculoskeletal pain subscale[b]	2.94 ± 2.49	3.00 ± 2.21	4.06 ± 3.34	3.67 ± 3.22	0.61	.61	n.s.
SHC worry about musculoskeletal pain (log) subscale[b]	1.53 ± 1.87	0.76 ± 1.20	1.94 ± 2.93	1.33 ± 1.59	0.81	.49	n.s.
Water temperature at start[b]	1.71 ± 1.08	1.67 ± 0.70	1.51 ± 0.92	1.66 ± 0.44	0.19	.90	n.s.
Water temperature at end of CPT[b]	1.92 ± 1.02	1.82 ± 0.75	1.71 ± 0.96	1.83 ± 0.49	0.17	.91	n.s.
Difference in water temperature before and after the CPT[b]	0.21 ± 0.15	0.15 ± 0.15	0.21 ± 0.15	0.17 ± 0.14	0.71	.55	n.s.
Time of day experiment[b]	14:14 ± 1:57	13:25 ± 1:54	13:54 ± 2:10	13:58 ± 2:09	0.46	.71	n.s.
d' measure[b, c]	0.19 ± 0.49	0.21 ± 0.54	0.28 ± 0.46	0.28 ± 0.41	0.14	.94	n.s.
Valence rating of prime words per group[d]	43.41 ± 6.87	31.88 ± 5.69	17.76 ± 4.97	22.53 ± 6.07	50.94	< .001	3 < 4 < 2 < 1

SHC, total severity of SHCs experienced in prior month; SHC worry, total severity of worry about SHCs in prior month. [a] Percentages may not equal 100% due to rounding. Fisher's exact test statistic, $p \leq .05$; post hoc repeated 2 × 2 Fisher's exact test statistic, $p \leq .05$. [b] Analysis of variance F statistic, $p \leq .05$; Scheffé' s post hoc test, $p \leq .05$.[c] One missing value. [d] Kruskal–Wallis test statistic, $p \leq .05$; post hoc Mann–Whitney tests, $p \leq .05$.

Priming effect on PT

Stepwise regression revealed that water temperature at the beginning of the CPT task and the difference in water temperature between the start and finish were significant predictors of PT (log). Higher starting temperature of the water and bigger increases in temperature were associated with significantly higher PT: $F_{(1, 60)} = 6.36$, $p < .05$, and $F_{(1, 60)} = 27.22$, $p < .001$, respectively (see Table 2-2). Because significance did not differ much after adjusting for these variables as covariates and since there were no

Table 2-2. Tests of between-subjects effects

Source	df	F	Sig.	μ_p^2
Model 1				
Corrected model[a]	3	1.345	.268	.061
Group[b]				
HC	1	3.853	.027[c]*	.059
NEG	1	.738	.197[c]	.012
SEN	1	.338	.282[c]	.005
Error	62			
Model 2				
Corrected model[d]	11	3.844	.000	.439
Water temperature at end of CPT	1	4.586	.037*	.078
Difference in water temperature	1	16.297	.000***	.232
Gender	1	1.013	.319	.018
SRH	1	.646	.425	.012
NA	1	.756	.388	.014
SHC worry (log)	1	.835	.365	.015
SHC musculoskeletal pain subscale	1	.559	.458	.010
SHC worry about musculoskeletal pain (log) subscale	1	.380	.540	.007
Group[b]				
HC	1	3.494	.033[c]*	.061
NEG	1	.179	.337[c]	.003
SEN	1	.019	.446[c]	.000
Error	54			

[a] R^2 = .061 (adjusted R^2 = .016). [b] Pairwise comparisons with the NEU group. [c] One-tailed. [d]R^2 = .439 (adjusted R^2 = .325). *One-tailed significance, p< .05. **Two-tailed significance, p< .05. ***Two-tailed significance, p< .001.

differences between the experimental groups on these variables, the unadjusted effects of priming on PT are given (see Table 2-2).

The planned comparisons showed that participants primed with HC words (M = 77.87 s, SD = 79.71) reported less PT compared with participants primed with NEU words (M = 127.18 s, SD = 92.52): $F_{(1, 62)}$ = 3.85, p < .05 (one-tailed), p = .054 (two-tailed), d = 0.72 (medium effect). The means of PT are shown in Figure 2-1. On average, participants primed with HC words kept their hand in the water for 49.31 s less than participants primed with NEU words. Participants primed with either SEN words (M = 95.94 s, SD = 75.33) or NEG words (M = 95.35 s, SD = 77.84) did not significantly differ in PT from participants primed with NEU words—$F_{(1, 62)}$ = 0.34, p = *ns* (one-tailed), d = 0.21 (small effect), and $F_{(1, 62)}$ = 0.74, p = *ns* (one-tailed), d = 0.30 (small effect), respectively, although these conditions both showed a tendency to reduce PT,

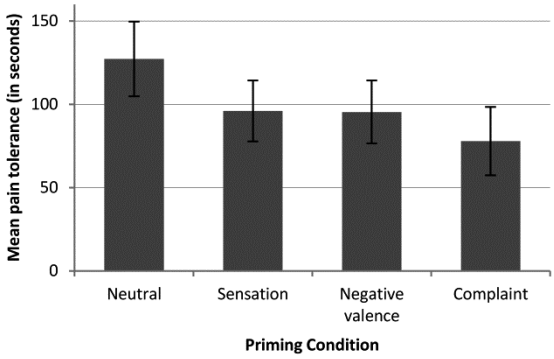

Figure 2-1. Effect of subliminal priming task on PT. Bars indicate PT scores, defined as the duration of hand immersion, for each priming condition (± S.E.M.)

which is in the same direction as the HC condition. Exploratory post hoc comparisons of the unadjusted means did not reveal any other significant differences between the groups on PT.

Secondary pain outcomes: intensity and unpleasantness

The effect of priming on pain intensity and pain unpleasantness (both inverse log) was examined exploratorily (Fig. 2). Stepwise backward regression analysis revealed no significant covariates for pain intensity (M = 6.68, SD = 1.84). There was no overall effect of priming condition on the ratings of intensity: $F_{(3,\ 56)} = .369$, $p = ns$. The variables worry about HCs on the SHC (log) and age (reciprocal) were used as covariates for pain unpleasantness (M = 7.21, SD = 2.19). Pain unpleasantness was related to worry about HCs (higher worry, higher pain unpleasantness: $F_{(1,\ 52)} = 5.62$, $p < .05$) and age (older participants' higher pain unpleasantness: $F_{(1,\ 52)} = 4.37$, $p < .05$). No effect of priming was found on pain unpleasantness: $F_{(3,\ 52)} = 0.67$, $p = ns$. Again, it is important to note here that these pain ratings were taken just after withdrawal from the water and thus at each participant's moment of "highest intolerance."

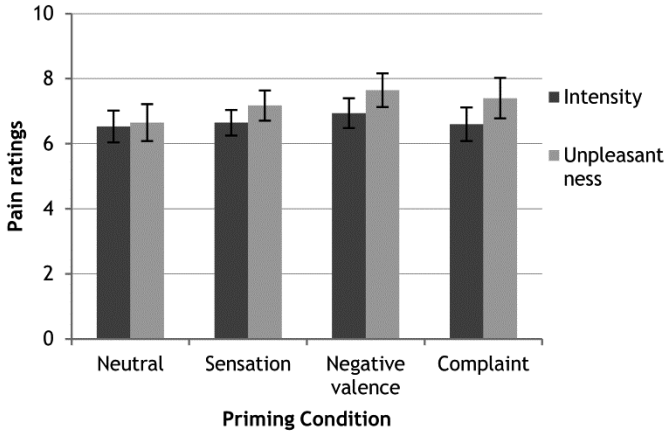

Figure 2-2. Effect of subliminal priming task on pain ratings. Bars indicate pain rating scores on a scale ranging from 0 to 10 for each priming condition (± S.E.M.). A higher score means greater pain intensity and pain unpleasantness

Valence ratings

The analyses of the valence rating per semantic category of all the participants showed that there was a significance difference among the semantic categories: $\chi^2_{(3)}$ = 180.38, p < .001. If we inspected only the valence ratings that the participants made for the words that were actually shown as prime words to the subjects (neutral valence ratings of the participants in the neutral condition and so forth), they also differed for each condition: $\chi^2_{(3)}$ = 50.94, p < .001. The outcome of the post hoc analyses for the latter analyses is shown in Table 2-1. The NEG words were rated as the most negative in valence compared with the words of the other groups. Thus, the finding that PT in the HC group was reduced compared with the NEU group, whereas this was not the case in the NEG group, could not be explained by increased negative values of the words, since the NEG prime words were rated as more negative than the HC words: U = 70, p < .05 (two-tailed).

Moderator effects

Potential moderating effects of NA, SRH, SHC (Number × Severity), health worry (log), SHC musculoskeletal pain subscale, and SHC worry about musculoskeletal pain (log) subscale were also analyzed exploratorily with regression analyses. First, the scores of the potential moderators were centered, and then this was used to calculate the product with the dummy variables of the priming condition to create interaction terms

(West, Aiken, & Krull, 1996). After adjustments were made for the same covariates used in Table 2-2 for PT (log), no moderator effects of NA, SHC, SHC worry (log), and SRH, nor the SHC subscales on musculoskeletal pain and worry about musculoskeletal pain (log), were found: respectively, $F_{(3, 51)} = 2.51$, $p = .07$; $F_{(3, 50)} = 0.62$, $p = ns$; $F_{(3, 51)} = 0.04$, $p = ns$; $F_{(3, 51)} = 1.64$, $p = ns$; $F_{(3, 51)} = 0.34$, $p = ns$; and $F_{(3, 51)} = 0.07$, $p = ns$. Moderator analyses without adjusting for the covariates did not change the results.

DISCUSSION

The results suggest that showing healthy subjects subliminal words (i.e., below the awareness threshold) related to illness causes them to retract their hands from ice-cold water considerably earlier than people who were shown NEU words. In other words, unconsciously perceived illness-related information lowered PT. This finding is likely due to the activation of illness memory by these illness-related words. The fact that our subjects were unaware of the manipulation means that the effects were involuntary and excludes that they were influenced by conscious thoughts (e.g., about the experiment's purpose). We also demonstrated that prime words related to sensations or negative emotion alone did not influence PT significantly, ruling out the possibility that the effect was due to these subcomponents of somatic complaining. The insignificant results that we found of sensation and NEG words on PT do not mean that they do not have any effect on PT. They merely mean that there is a possibility that they had a small effect that we were unable to detect due to the rather small sample sizes of the conditions. Despite the sample sizes, the effect size found of the main hypothesis, namely whether priming participants with HC words causes reduced PT compared with priming participants with NEU words, was clearly sufficiently large to obtain a statistically significant result.

The finding that priming healthy subjects with HCs without awareness reduced PT supports recent cognitive theories about MUSs (Brown, 2004), which propose that activated illness memory on itself is sufficient to cause symptom reports. Importantly, the effect that we found in this study after a short (2 min) priming task, although already substantial (earlier withdrawal from the water of 49 s), might be even much larger in daily life, in which we are very frequently and much more intensively exposed to illness information, in the media, and in our private lives.

The results yield some findings that require more discussion though. Several variables that could have a potential effect on PT, such as NA, health worry, and number and severity of HCs experienced in the prior month, were not found to be moderators. It is possible that fear of pain and pain catastrophizing, which are also variables that have been associated with increased reporting of pain (Crombez, Vlaeyen, Heuts, & Lysens, 1999; R. R. Edwards, Smith, Stonerock, & Haythornthwaite, 2006; Vlaeyen & Crombez, 1999), could have moderated the effect. However, these variables overlap considerably with NA, and NA did not explain or moderate the effects of the priming task in this study. Still, it is possible that activating illness-related memory causes

increased fear of pain or pain catastrophizing during a CPT, leading to reduced tolerance of pain.

Furthermore, the subliminal priming procedure did not show an effect on our secondary outcomes of pain intensity and pain unpleasantness. However, these ratings were taken just after withdrawal from the water. This is a different moment for each individual participant and at the moment in which the pain became unbearable for each participant (except for those who kept their hand in until the end). It is also likely to be influenced by feelings of numbness in the hand, which were reported by some of the participants. Measuring earlier or continuously would have been possible, but as we stated before, this would probably have interfered with the pain task itself; however, the PT measurement still inherently results in different pain exposure periods. As argued in the Introduction, we chose PT because pain experiences only become a symptom or complaint when the experience becomes intolerable and people decide to report them and even seek medical help. In addition, rating intensity and unpleasantness is behavior initiated by others (in this case, the experimenter), while reduced PT is self-initiated behavior and more closely resembles people's decision to report symptoms in daily life.

A limitation of this study is that we assumed that activation of illness-related memory causes an increased selective attention toward bodily symptoms and leads to a bias in their interpretation. We did not measure these mechanisms directly; however, it was difficult in the current design to add a selective attention test without disturbing the delicate effects of priming.

In addition, we did not take menstruation cycle of the female subjects into account, which also influences pain measures (Riley, Robinson, Wise, & Price, 1999). Because we used an experimental approach, it is likely that menstruation cycle, trait fear of pain, and trait pain catastrophizing have been randomized among the four groups. Another limitation is that we have examined the effect of illness memory on symptom perception in a healthy sample. Although the study's aim was to find proof for a purely psychological cause of symptoms, which may play a role in the development of MUSs (and excess complaints in medically explained conditions), we realize that the situation for chronic MUS patients may be quite different. Future research should examine whether this priming effect plays a role in an MUS sample.

The results of the current study and the two related studies (De Wied & Verbaten, 2001; Godinho et al., 2006) seem to urge replications in patients and using other bodily symptoms. Other research had already shown that MUS patients show selective attention toward information that is related to their symptoms (Afzal et al., 2006; Karademas et al., 2008) and that symptom reporting is related to increased attention to SEN (Barsky et al., 1988; Kolk et al., 2002; L. C. Miller et al., 1981; Pennebaker & Lightner, 1980). The results of this study should therefore be tested in these populations as well to provide a broader insight into the cognitive aspects of symptom reporting. If effects such as those we found here would hold in other studies, it would suggest that future interventions might do well to focus on reducing the effects of an

overactive illness memory network—for example, by pairing negative illness memories with positive stimuli (evaluative conditioning) or by reducing the attention toward bodily signals with an attentional retraining task (Dijksterhuis, 2004; MacLeod, Rutherford, Campbell, Ebsworthy, & Holker, 2002). Future studies could also focus on the potential mechanisms by which illness-related memory causes reporting of lower PT. For instance, a recent study found that pain catastrophizing, in which increased attention to pain is a core element, is related to amplified proinflammatory immune system responses to noxious stimulation. This pathway may represent one important mechanism by which cognitive-attentional processes can influence the experience of pain (R. R. Edwards et al., 2008).

In conclusion, this study supports the view that activation of illness-related memory, and not other related concepts or components, can cause people to report less tolerance for experimentally induced pain. According to the symptom perception model, this is caused by activation of illness-related memory, which is thought to be chronically overactivated in MUS patients (Brown, 2004). In other words, MUS patients are continuously in the state in which the participants in the HC prime condition were only briefly in. This would explain why they have complaints without observable bodily pathology and thus without a medical explanation. This study shows that bodily complaints are not always simple products of physical characteristics of bodily signals ("bottom-up") but can be produced by mere activation of a relevant memory network ("top-down") (Brown, 2004) and (Brosschot, 2002). In more general terms, our results add to those of the several recent lines of research showing that our behavior can be easily influenced by very subtle information (e.g., Refs. Aarts, Custers, & Marien, 2008; L. E. Williams & Bargh, 2008), and our study is the first to show this in the context of health. Even when subtle illness-related information is only briefly shown for a couple of minutes, the behavioral effects are already substantial.

Appendix. Words used as prime words. English words are translated from Dutch prime words.

Neutral	Sensation	Negative Valence	Complaint
"bear"	"tight"	"mean"	"throw up"
"squirrel"	"stiff"	"cruel"	"wound"
"elephant"	"burning"	"hostile"	"fever"
"gorilla"	"itch"	"antisocial"	"diarrhea"
"rhino"	"ice cold"	"coward"	"allergy"
"giraffe"	"pounding"	"unfair"	"infection"
"gazelle"	"smarting"	"liar"	"flu"
"chimpanzee"	"scalding"	"evil"	"asthma"
"lynx"	"sweltering"	"hateful"	"invalid"
"jackal"	"tickling"	"heartless"	"headache"

Chapter 3 |

The Effect of Priming Illness Memory on Pain Tolerance: a Failed Replication

A version of this chapter appeared as:
Meerman, E. E., Brosschot, J. F., & Verkuil, B. (2012). The effect of priming illness memory on pain tolerance: a failed replication. *Journal of psychosomatic research*, *72*(5), 408–9.

ABSTRACT

Objective In our previous study (Meerman, Verkuil & Brosschot, 2011) we found that activating illness-related memory caused a lower pain tolerance during a pain task. This served as support for a model that uses cognitive psychology principles to explain medically unexplained symptoms. In the present study we tried to replicate and extend this previous study. We investigated whether reduced pain tolerance was due to specific prime words, and whether administering health-related questionnaires before priming with health-complaint words could account for the effect found, because it might have acted as an unintended prime.

Methods Activation of illness-related memory was manipulated by a priming technique using subliminally presented words. Eighty-one participants were randomly assigned to one of four priming conditions; (a) health-complaints, to activate an illness-related memory, or the three control categories: (b) neutral content, (c) general bodily sensations and (d) negative valence. We measured pain tolerance using a cold pressor task. Half of the participants completed a health-complaint questionnaire before the priming task, and half completed this questionnaire a week later.

Results Unlike the previous study, no significant differences were found between participants primed with health-complaint and neutral words. No interaction-effect was found between the timing of the health-related questionnaires and prime type.

Conclusions We could not replicate the priming effect of health words on pain tolerance, and therefore did not support the model that states that activated illness-related memory causes increased symptom reporting, suggesting that illness memory networks only affect symptom reporting if seriously threatening primes are used.

INTRODUCTION

Everyone experiences somatic complaints that are not caused by a medical disease. Between 80 and 90% of healthy adults experience one or more somatic complaints per week (Mayou, Bass, & Sharpe, 1995). At least one third of these symptoms remain unexplained (Kroenke & Price, 1993). It has been hypothesized that complaints without any medical origin are the result of illness-related memory networks, which cause increased selective attention towards innocuous bodily signals, and in turn cause increased detection, interpretation and reporting of these signals as complaints (Brosschot, 2002; Brown, 2004; Meerman, Verkuil, & Brosschot, 2011). The reporting of these signals as complaints, in turn, reactivates the memory network of illness, and thus produces a vicious cycle. With repeated triggering of illness memory, its activation by associated stimuli becomes more likely and therefore more frequent (Brown, 2004; Pincus & Morley, 2001), and bodily sensations are increasingly likely to be misinterpreted as signs of illness, resulting in a reflexive and subjectively convincing symptom experience (Brown, 2004).

Two earlier studies showed that consciously perceived pictures illustrating physical suffering, which activate pain or illness memory, cause people to report lower pain tolerance (De Wied & Verbaten, 2001) and pain intensity (Godinho et al., 2006). We argued (Meerman et al., 2011) before that conscious primes have the disadvantage that subjects may guess the experiment's goals and act accordingly, and that it is unclear whether illness memory is activated involuntarily, as the model predicts (Brown, 2004). Moreover, in these studies the effect on pain might have been caused by simple interference by the simultaneously presented conscious primes. Therefore, in a previous study (Meerman et al., 2011) we used subliminal priming with illness words to assess whether an activated illness memory network could influence pain tolerance, and presented these words before rather than during pain measures. The technique of presenting stimuli ('primes') under the awareness threshold activates the semantic category of a word in memory while participants remain unaware of it. We used words describing common health-complaints (HC) to activate illness-related memory and we compared the pain tolerance of participants primed with these HC words to participants that were shown neutral words (NEU). We indeed found that only participants primed with HC words showed lower pain tolerance compared to participants primed with NEU words: they held their hand in the ice water of the cold pressor nearly 50 seconds shorter. In that study, we also tested two alternative hypotheses, namely that lower pain tolerance would already be observed after the semantic activation of bodily sensations or negativity in general. To test this, we added two groups that were shown either words describing bodily sensations (SEN) or negative valence words (NEG). However, these two groups did not show any significant difference in pain tolerance compared to participants primed with NEU words.

In the current study, we attempted to replicate the findings of this previous study, while addressing some of its limitations. Firstly, in our previous study participants

were asked to fill in health-related questionnaires before the priming task. Although these questionnaires were followed by a distracter questionnaire about study skills that lasted for 10 minutes, the possibility remains that filling in the health-complaints questionnaire has acted as an additional priming intervention for all participants. The priming effect of HC words could actually be the result of an interaction between filling in the health related questionnaires and the HC words as primes later on. In addition, in our previous study we used some prime words that were not a perfect representation of the category, such as "invalid" for the health-complaint group, or words related to heat that could have interfered with the cold pressor task, like "burning" and "scalding" for the sensation group. Finally, we did not control for smoking or coffee intake on the day of participation and in daily life, which are known to influence pain tolerance (Jamner, Girdler, Shapiro, & Jarvik, 1998; Nastase, Ioan, Braga, Zagrean, & Moldovan, 2007). All of these above mentioned limitations were addressed in the current study, by (a) varying the timing of the health questionnaires, that is, before the priming procedure and a week after the experiment, (b) we replaced the words mentioned by more appropriate words and (c) by measuring and controlling for coffee intake and smoking.

Similar to our previous study we exploratory examined whether negative affect, health worry and common health-complaints were moderators of our hypothesized main effect (Kolk et al., 2002; Meerman et al., 2011; Petrie et al., 2005; Verkuil et al., 2007; Watson & Pennebaker, 1989).

Thus, our main hypothesis was that activating illness-related memory, by subliminally priming with health-complaint words, would cause a lower tolerance for induced pain.

METHODS

Subjects

Ninety-seven students from Leiden University participated in the present study. Participants received either course credits or eight Euros. This study was approved by the Ethics Committee of the Leiden University Institute of Psychological Research. Subjects were required to meet the following criteria: no medical disease, no anxiety or depression disorder, and Dutch native language. Participants were required to refrain from taking pain-killers. We also asked the participants not to drink caffeinated drinks on the day of the experiment and to smoke cigarettes up to one hour prior to the experiment, which was an addition compared to our previous study.

Materials

Questionnaires

Subjective health

Subjective health was measured in a specific and general way. Specific subjective health-complaints (SHCs) were measured with the SHC Questionnaire (Eriksen et al., 1999). The SHC is a 29-item self-report questionnaire that measures the number and severity of SHCs experienced in previous month on a 4-point scale, from "not at all" to "very much". Its subscales are; musculoskeletal pain, pseudoneurology, gastrointestinal problems, allergy, and flu. A total score was calculated by summing the severity of the health-complaints. The internal consistency of the SHC questionnaire has been proved sufficient (Eriksen et al., 1999).

In addition, we also measured general Self-Rated Health (SRH)(Idler & Benyamini, 1997). Participants were asked to rate their health in comparison with that of people of the same age. They could respond with "worse, " "the same, " or "better."

Health worry

Complaint-specific worry was assessed by asking to what extent participants had been worrying about a complaint for each of the 29 complaints on the SHC Questionnaire on a 4-point scale, from "not at all" to "very much". The total score of worry on the SHC questionnaire was used as a measure of health worry. The same subscales were used as the SHC subscales.

Positive and Negative Affect Schedule (PANAS)

The Dutch trait version of the PANAS consists of 10 positive (positive affectivity [PA]) and 10 negative adjectives (negative affectivity [NA]). Participants indicate on a 5-point scale the extent to which the items apply to how they generally feel in normal daily life. The reliability and construct validity of the PANAS have been found to be satisfactory (Engelen et al., 2006; Watson et al., 1988).

Demographics and biobehavioral variables

We asked the participants to report; gender, age, Body Mass Index (BMI), ethnicity, physical activities, usage of sleeping medication, pain killers or tranquilizers in the last 30 days, number of doctor visits in the last 6 months, and habits in smoking, coffee and alcohol drinking, drug use, medication use, illnesses, history of and current psychological problems.

Priming task

Prime words

Participants were randomly assigned to one of four conditions, with prime words describing either (a) Health-complaints (HC), or the three control categories: (b) neutral (NEU) words, (c) words describing bodily sensations (SEN) and (d) negative valence (NEG) words. With a few exceptions, the prime words in this study were similar to our previous study (Meerman et al., 2011). In the sensation group we replaced previous prime words that were describing sensations that were related to heat by the words "trembling", "throbbing" and "tingling", and for the HC group we replaced the word "invalid" (in the sense of a seriously disabled person) by "heartburn". The neutral prime words consisted of animals and the negative valence words consisted of negative personality traits that were rated on their valence in earlier research by Hermans and de Houwer (1994). In order to keep the word frequency, length and syllables the same among the four categories, we also had to change the word "evil" into "fake" for the NEG group. The Appendix shows the prime words that were used in the current study. All categories contained 10 words and did not differ in number of syllables, length and frequency in the Dutch language [respectively Kruskal-Wallis $H_{(3)} = 1.19$, $p = .76$, $H_{(3)} = 0.44$, $p = .93$ & $H_{(3)} = 4.90$, $p = .18$]. In every prime condition the 10 prime words were shown randomly 10 times, leading to a total of 100 trials.

Priming task

The present subliminal priming task consisted of a simple computer task presented to the participants as a reaction time task and was exactly the same as in our previous study (Meerman et al., 2011). We used a prime stimulus duration (33 ms) approximate to that of studies that found long-lasting subliminal priming effects (Kiefer, 2002; Levy, 1996; Lowery et al., 2007; Pierce & Lydon, 1998). The priming manipulation was a variation of a common paradigm in which participants judge as quickly and accurately as possible whether briefly flashed letter strings appear on the right or left side of a computer monitor (Lowery et al., 2007). Each trial started with a fixation cross of a random duration between 500 and 1000 ms in the center of the screen. Students were then exposed to the prime word (33 ms), followed by a string of XXX's that served as a backward mask for the prime word. The prime word and mask appeared on either the right or left side of the screen, in the parafoveal region [at a ˚2 degree visual angle (Bargh & Chartrand, 2000)]. Participants indicated with the arrow keys what the position was of the mask. Each trial was separated by a 500 ms interval in which the screen was blank.

Awareness checks

In order to examine whether the primes were indeed shown under the awareness threshold, we checked after the pain task whether the participants could detect the primes. We used both a subjective threshold, in which conscious awareness is indexed

by participants' self-reports with a funneled debriefing questionnaire and an objective threshold, in which conscious awareness is indexed by the d' measure, a measure of the participants' discriminative abilities based on signal detection theory in a forced choice test (Bargh & Chartrand, 2000; Macmillan, 2005).

Pain tolerance and threshold

Similar to our previous study, we used a cold pressor task (CPT) for pain stimulation (Meerman et al., 2011). During a CPT, participants are asked to keep their non-dominant hand in a basin filled with ice-cold water for as long as they can. The basin is, on the surface of the water, divided into two sections. One is filled with ice and another kept free of ice to allow a hand to be immersed in the water without direct ice contact. A pump kept the water flowing continuously to prevent buildup of warmer water around the hand. The mean water temperature at the start was 2.64°C (SD = 1.25). To control for differences in increases in water temperature during the CPT, we also measured the water temperature at the end of the CPT and we used the difference in water temperature as a possible covariate. Pain tolerance was defined as time elapsed (in seconds) between immersion and withdrawal (De Wied & Verbaten, 2001). Pain threshold was defined as time elapsed between immersion and start of pain (Kállai, Barke, & Voss, 2004). Unbeknown to the participants, maximum duration of hand immersion was limited to four minutes. For exploratory reasons, pain intensity and pain unpleasantness ratings were also rated on a Visual Analogue Scale of 0-100, from not at all intense or unpleasant to extremely intense or unpleasant.

Procedure

Contrary to the previous study the study had two versions: in version A (similar to previous study) participants were required to fill in the questionnaires before the priming task, while in version B participants started out with reading magazines for 6 minutes, then they performed the priming task and a week later they came back for the questionnaires. Information about the experiment was posted on the internet, making clear that it consisted of filling in questionnaires, with a special focus on study skills (which served as a cover story), reaction time tasks on the computer and a pain task. Participants were tested individually by one male and one female experimenter. The experimenters were kept blind about the random assignment of the participants. When the participant arrived at the laboratory, they were screened whether they fulfilled the requirements. The participants were asked to provide demographic information (age and gender) and the computer task was started. The experimenter left to an adjacent room, where he followed the procedure. After the study skills questionnaire that served as a distraction, the priming task started, immediately followed by the CPT. In order to rule out any effects on pain of distraction by the computer task, the computer task (with primes) was performed immediately before the pain task instead of simultaneously. After participants took their hand out of the water, they were asked to rate pain unpleasantness and intensity. Awareness of the

priming procedure was assessed with a funneled debriefing questionnaire and with a forced-choice word identification task. Finally, participants rated the negative versus positive valence and arousal of all prime words on a 7-point scale, and they performed the same priming task but with positive health words to counteract any potential longer lasting effects of the previous priming that might have a negative effect on pain tolerance. At last, the participants were fully debriefed and received money or course credits.

Data analyses

We used a 2 by 4 analysis of (co)variance with Version (A or B) and priming condition (neutral, sensation, negative and illness) as the independent variables and the pain measures as dependent variables. Stepwise regression analysis was used to select an optimal set of covariates amongst the baseline and experimental factors (Steyerberg & Harrell, 2003). We first report the analysis without covariates (based on unadjusted means) and then the analyses with covariates (based on adjusted means)(Simmons, Nelson, & Simonsohn, 2011). For the planned comparisons, we compared each priming group with the neutral group, producing three pairwise comparisons, the critical F values for these are reported (Tabachnick & Fidell, 2007). Because of our specific planned comparisons, we used one-tailed tests but we also report the two-tailed *p* value. For the exploratory analyses, we report the two-tailed *p* value and for post hoc comparisons we used Bonferroni adjustments for the three pairwise comparisons ($p < .0167$). Prior to analysis, the variables were examined separately for the eight conditions on accuracy of data entry, missing values, linearity, homogeneity of variance and regression, and normality (Tabachnick & Fidell, 2007). Variables were transformed if necessary.

RESULTS

As in the previous study, data was excluded of participants that afterwards indicated on the funneled debriefing questionnaire that they thought the task involved priming ($n = 2$), participants that could discriminate between the primes according to their d' measure (see forced-choice test above) ($n = 6$), if they had a diagnosed minor medical disease ($n = 4$), who did not participate in the second part of version B ($n = 3$), who still reported to have used coffee on the day of the experiment ($n = 8$), and if they afterwards indicated to have participated in an experiment related to the current study ($n = 3$).

Descriptives

A total of 73 participants remained with 18 participants in the health-complaint priming group (HC), 18 participants in the negative priming group (NEG), 20 participants in the sensation group (SEN) and 17 participants in the neutral group (NEU). The factor Experiment Version had 39 participants in version A and 34 participants in

version B. The mean age of the participants was 21.07 years (SD = 4.52) and 68.5% was female.

We checked whether the participants in the eight groups differed in factors measured at baseline that might influence pain tolerance, including; (a) demographic features, such as age and gender, (b) psychosocial factors, such as self-rated health and NA, (c) experimental factors, such as water temperature of the CPT. The number of participants that normally drink coffee differed among the groups, Fisher's Exact Test = 15.46, p = .03. The SEN group of version A did not have any coffee drinkers, while the others groups did. The groups also differed in positive affect (PA) [$F_{(7, 65)}$ = 2.26, p = .04] and the total score of SHC [$F_{(7, 65)}$ = 3.41, p = .00]. Post hoc pairwise comparisons among the experimental groups with Bonferroni adjustments showed that the NEG group of version A had significantly lower SHC total scores compared to the SEN group of version A and B. Post hoc tests did not show any significant differences in PA.

Priming effect on pain tolerance

Experiment Version had no main effect on pain tolerance (PT) and the effect of Priming did not differ across the Experiment Versions A and B (see Table 3-1). The planned comparisons showed that participants primed with HC words (M = 116.78 s, SD = 91.67) or with the NEG words (M = 107.50 s, SD = 99.70) did not differ in PT compared to participants primed with NEU words (M = 94.24 s, SD = 87.42). However, participants primed with SEN words (M = 148.00 s, SD = 104.69) had marginally significant higher PT compared to participants primed with NEU words. Additional exploratory comparisons of the unadjusted means did not reveal any other significant differences between the groups on PT.

Several covariates were found to have an effect on pain tolerance: lower pain tolerance was found for female participants, right-handed participants, coffee consumers, and for participants with a decrease in water temperature during the CPT (see Table 3-2). After adjusting for the covariates, no significant effects were found on PT.

Table 3-1. ANOVA results for dependent variables based on unadjusted means

Dependent Variable	Source		df	*F*	*p*	μ_p^2
Pain tolerance	Experiment Version		1	.235	.629	.004
	Priming	HC vs NEU[a]	1	.494	.485	.008
		SEN vs NEU[a]	1	2.815	.098[†]	.042
		NEG vs NEU[a]	1	.180	.672	.003
	Experiment Version × Priming		1	.062	.980	.003
	Error		65			
Pain threshold (log)	Experiment Version		1	.579	.449	.009
	Priming	HC vs NEU[a]	1	.009	.923	.000
		SEN vs NEU[a]	1	2.676	.107	.040
		NEG vs NEU[a]	1	.975	.327	.015
	Experiment Version × Priming		1	.330	.803	.015
	Error		65			
Pain intensity	Experiment Version		1	.047	.829	.001
	Priming		3	2.443	.072[†]	.101
	Experiment Version × Priming		1	.159	.923	.007
	Error		65			
Pain unpleasantness	Experiment Version		1	.105	.747	.002
	Priming		3	.153	.927	.007
	Experiment Version × Priming		1	.161	.922	.007
	Error		65			

[a] Planned pairwise comparisons. [†]$p < .05$ (one-tailed), *$p < .05$ (two-tailed), **$p < .01$ (two-tailed), ***$p < .001$ (two-tailed). HC, Health-complaint group; NEU, Neutral group; SEN, Sensation group; NEG, Negative group

Since a large group of participants could leave their hand in the water for the maximum of four minutes (35.6% versus 16.7% in our previous study), we explored whether we might find a priming effect on pain threshold instead. The unadjusted means of the three pairwise comparisons showed a marginal difference between the sensation (*M* threshold = 67.70 s, SD = 91.02) and neutral group (*M* threshold = 21.41 s, SD = 10.87) (Table 3-1). No difference was found between the HC (*M* threshold = 24.89 s, SD = 17.00) and NEG (*M* threshold = 19.06 s, SD = 19.69) group compared to the neutral. Several covariates were found to have an effect on pain threshold. Lower pain threshold was found for participants with a decrease in water temperature during the CPT, with lower temperature at the start of the CPT, with more general health worry, and, surprisingly, for participants with less worry about musculoskeletal pain (see Table 3-2). After including the covariates, the difference between the sensation and neutral group seemed to be different for the two Experiment Versions and on the increase in

Table 3-2. ANOVA effects for the pain measures including covariates

Dependent variable	Source		df	*F*	*p*	μ_p^2
Pain tolerance	Gender		1	6.695	.012*	.102
	Handedness		1	8.532	.005**	.126
	Coffee drinkers		1	2.925	.092†	.047
	Alcohol drinker		1	1.830	.181	.030
	Difference in water temperature start to finish		1	4.676	.035*	.073
	Age (reciprocal)		1	2.270	.137	.037
	Experiment Version		1	.087	.769	.001
	Priming	HC vs NEU[a]	1	.041	.840	.001
		SEN vs NEU[a]	1	.591	.445	.010
		NEG vs NEU[a]	1	.005	.945	.000
	Experiment Version × Priming		3	.248	.863	.012
	Error		59			
Pain threshold (log)	Difference in water temperature start to finish		1	12.569	.001**	.198
	Water temperature at start		1	6.162	.016*	.108
	SHC Worry		1	4.331	.042*	.078
	SHC Worry subscale Musculoskeletal pain (log)		1	3.581	.064†	.066
	SHC subscale Musculoskeletal pain (log)		1	1.213	.276	.023
	Alcohol drinker		1	1.210	.277	.023
	Coffee drinkers		1	2.449	.124	.046
	Experiment Version		1	.026	.872	.001
	Priming	HC vs NEU[a]	1	1.459	.233	.028
		SEN vs NEU[a]	1	1.448	.234	.028
		NEG vs NEU[a]	1	1.784	.188	.034
	Experiment Version × Priming		3	.551	.650	.031
	Experiment × Diff. water temperature		1	.503	.482	.010
	Priming × Diff. in water temperature		3	1.264	.297	.069
	Experiment × Priming × Diff. in water temperature		3	2.959	.041*	.148
	Error		51			

Table 3-2. ANOVA effects for the pain measures including covariates (continued)

Dependent variable	Source	df	*F*	*p*	μ_p^2
Pain intensity	Gender	1	8.716	.004**	.127
	Handedness	1	3.734	.058†	.059
	Experiment leader	1	2.764	.102	.044
	Difference in water temperature start to finish	1	9.765	.003**	.140
	Age (reciprocal)	1	6.470	.014*	.097
	Experiment Version	1	.278	.600	.005
	Priming	3	2.803	.047*	.123
	Experiment Version × Priming	3	.989	.404	.047
	Error	60			
Pain unpleasant-ness	Handedness	1	9.563	.003**	.136
	Difference in water temperature start to finish	1	13.413	.001**	.180
	SHC Worry subscale Musculoskeletal pain (log)	1	7.000	.010*	.103
	SHC subscale Musculoskeletal pain (log)	1	8.852	.004**	.127
	Experiment Version	1	.014	.906	.000
	Priming	3	.313	.816	.015
	Experiment Version × Priming	3	.644	.590	.031
	Error	61			

[a] Planned pairwise comparisons. †p < .05(one-tailed), *p < .05(two-tailed), **p < .01 (two-tailed), ***p < .001 (two-tailed). HC, Health-complaint group; NEU, Neutral group; SEN, Sensation group; NEG, Negative group; SHC, Subjective Health-complaints.

water temperature during the CPT. However, these effects did not survive the Bonferroni correction, which suggests that they probably occurred by chance.

Secondary Pain Outcomes: Intensity and Unpleasantness

We exploratory examined the priming effect on pain intensity (PI) and pain unpleasantness (PU). As before, Experiment Version had no effect on PI and PU and the priming effect on these variables did not differ across the Experiment Versions A and B. No priming effect was found on PU (Table 3-1, *M* neutral = 66.12, SD = 23.91; *M* HC = 64.56, SD = 24.66; *M* NEG = 61.22, SD = 26.61; *M* SEN = 60.95, SD = 32.43). However, we found a marginal significant effect on PI, which became more significant, after adjusting for the covariates (see Table 3-2, *M* neutral = 68.53, SD = 21.59; *M* HC = 67.22, SD = 24.77; *M* NEG = 55.56, SD = 33.24; *M* SEN = 45.50, SD = 31.45). Higher PI was found for females, right-handed participants, participants with a decrease in water temperature during the CPT, and older participants (see Table 3-2). Pairwise

comparisons, however, did not survive Bonferroni corrections. Higher PU ratings were found for right-handed participants, participants with a decrease in water temperature during the CPT, lower worry about musculoskeletal pain but higher actual experienced musculoskeletal pain (Table 3-2). After adjusting for covariates of PU (Table 3-2), no priming effect was found.

Moderator effects

Just like in our previous study, we examined potential moderating effects, by adding the interaction term of the potential moderator with Priming, Experiment Version and Version × Priming. No significant unadjusted moderating effects were found of SRH, health worry, SHC (log), SHC subscale musculoskeletal pain (log) and SHC subscale worry about musculoskeletal pain (log). However, we did find a significant moderating effect of NA on the priming effect on the unadjusted means of pain threshold (log), $F_{(3, 57)} = 2.91$, $p = .04$. Simple effect tests showed that only for the low NA subgroup (-1SD) a significant main priming effect was found, $F_{(3, 57)} = 4.44$, $p = .01$. Tests with Bonferroni adjustments within the low NA subjects did not show any significant differences of the three priming conditions with the neutral control group, but showed that the sensation group had a significantly higher threshold compared to the negative and health-complaint group, respectively $p = .012$ and $p = .022$. This moderating effect of NA on pain threshold disappeared after adjusting for the covariates.

After we adjusted for the covariates, we did find a significant moderation effect of SHC subscale worry about musculoskeletal pain on the priming effect of group on PT, $F_{(3, 51)} = 3.41$, $p = .02$. The simple effect of priming was not significant for the low worry musculoskeletal subgroup (-1SD), but it was marginal significant at the high subgroup (+1SD), $F_{(3, 51)} = 2.58$, $p = .06$. Pairwise comparisons with the neutral group and with Bonferroni adjustments did not show any significant differences, which means that this finding was likely due to chance.

For PU, we found a significant moderating effect of SHC on the priming effect, F(3, 53) = 3.11, $p = .03$, but only after adjusting for the covariates. Only the low subgroup (-1SD) of SHC showed a marginal significant priming effect, $F_{(3, 53)} = 2.49$, $p = .07$. Again, however, Bonferroni adjusted pairwise comparisons did not show a significant difference between the groups. No moderating effects were found on PI.

Comparison of samples

We compared the participant samples of this experiment to our previous experiment on the measures of demographics, personality traits and experimental variables. The current sample had: more negative valence ratings of the health-complaints words, *Mann-Whitney U* = 1483, $p = .00$, more positive valence ratings of the Sensation words, $U = 1674$, $p = .00$, higher Positive Affect, $U = 1863.5$, $p = .02$, less SHC worry, $U = 1955.5$, $p = .05$, a higher Water temperature at the start ($M = 2.65$ degrees, SD = 1.31 versus $M = 1.64$, SD = 0.81), $U = 1228.5$, $p = .00$, more men, $\chi^2 = 5.12$, $p = .03$ and more

participants that could reach the maximum of four minutes at the CPT, $\chi^2 = 6.37$, $p = .01$.

DISCUSSION

The present study could not replicate the finding of our previous study that subliminal priming with illness words causes lower pain tolerance (Meerman et al., 2011). The only effect found was a small increasing effect of priming with sensation words on pain tolerance that disappeared when the analyses included the covariates, suggesting that it was most likely due to the difference of coffee drinkers among the groups. No priming effects were found on pain unpleasantness and pain intensity scores. Furthermore, the current study showed that administering a health-related questionnaire before a subliminal priming task using health-complaint words does not influence pain tolerance. This suggests that the results of our previous study were not caused by an interaction between the questionnaire and the health-complaint prime words.

It is possible that since the effects are relatively subtle, either the previous or the current result is due to chance. Another possibility is that the priming method used does not consistently activate illness memory. In neither the current nor the previous study we checked whether the subliminal priming task was actually successful in activating illness-related memory. On the other hand, this priming method is broadly used and standard (see for example Ref. Lowery et al., 2007). Provided that the methods are sound, another possible cause for the failed replication that is still consistent with the hypothesis is the removal of the prime word "invalid", which seems the most 'intense' ill health word. Is it possible that the lower pain tolerance in our previous study was the result of mainly priming with "invalid", perhaps in interaction with 'surrounding' health-related words? Although this might seem unlikely, the prime "invalid" reflects a condition that is likely to be more threatening for the bodily integrity than words like "wound", or "headache" or "heartburn". The possibility that illness memory networks – and with that symptom reporting – are only affected by primes that seriously threaten bodily integrity, such as "invalid" is further supported by a study (De Wied & Verbaten, 2001) showing that pain tolerance was successfully lowered by other really intrusive stimuli, namely pictures depicting blood and serious wounds (though consciously presented), that also do not necessarily refer to common daily health experiences (De Wied, personal communication). This clearly suggests a path for future studies. In sum, our current study with methodological improvements could not confirm the evidence found in the previous study and therefore does not yield support for the theory that an activated illness memory network causes increased symptom reporting (Brown, 2004; Meerman et al., 2011). However, it is possible that support would be obtained with more intensely physically threatening primes, since we removed one such prime in the current study. Future experiments using more intense stimuli might help to elucidate this. Importantly, such studies should include a test of actual memory activation, like the lexical decision task. However, the current results suggest that the result of our previous study is either due to chance or due to the

threatening content of the prime "invalid". Though, in case of the latter, the dependence of the effects on one single subliminally presented word makes one question the validity of the method and merits using different techniques in the future. The non-trivial prevalence and humanitarian and economic costs of medically unexplained health complaints in our society warrants further investigation.

Appendix. Prime words used in current study. Prime words in italics differ from previous study. English prime words were translated from Dutch.

Neutral	Sensation	Negative Valence	Health Complaints
"bear"	"*throbbing*"	"fake"	"allergy"
"*butterfly*"	"*tingling*"	"hostile"	"asthma"
"*seal*"	"*trembling*"	"hateful"	"throw up"
"giraffe"	"pounding"	"coward"	"diarrhea"
"gorilla"	"tickling"	"liar"	"flu"
"rhino"	"smarting"	"heartless"	"headache"
"*panda*"	"tight"	"antisocial"	"fever"
"*turtle*"	"stiff"	"unfair"	"*heartburn*"
"chimpanzee"	"ice cold"	"mean"	"infection"
"squirrel"	"itch"	"cruel"	"wound"

Chapter 4 |

The Effect of Subliminal Evaluative Conditioning of Cognitive Self-Schema and Illness Schema on Pain Tolerance

Meerman, E. E., Brosschot, J. F., van der Togt, S. A. M., & Verkuil, B. (2013). The effect of subliminal evaluative conditioning of cognitive self- schema and illness schema on pain tolerance. *International Journal of Behavioral Medicine*, *20*(4), 627-635.

ABSTRACT

Background Cognitive models explaining medically unexplained complaints propose that activating illness-related memory causes increased complaints such as pain. However, our previous studies showed conflicting support for this theory.

Purpose Illness-related memory is more likely to influence reporting of complaints when its activation is enmeshed with that of self-related memory. We therefore investigated whether inducing this association would cause a stronger decrease in pain tolerance. In addition, we examined whether self-focused attention (SFA) acted as a moderator of this effect.

Methods We used subliminal evaluative conditioning (SEC) to induce an association between activated self-related and illness-related memory. Seventy-six participants were randomly assigned to four combinations of two priming factors: (1) the self-referent word "I" versus the nonself-referent "X" to manipulate activated self-related memory; (2) health complaint (HC) words versus neutral words, to manipulate activated illness-related memory. Pain tolerance was assessed using a cold pressor task (CPT).

Results Participants primed with the self-referent "I" and HC words did not demonstrate the expected lower pain tolerance. However, SFA acted as a moderator of the main effect of the self prime: priming with "I" resulted in increased pain tolerance in participants with low SFA.

Conclusions The current study did not support the hypothesis that associations between activated self-related memory and illness-related memory cause increased reporting of complaints. Instead, activating self-related memory increased pain tolerance in participants with low SFA. This seems to indicate that the self-prime might cause an increase in SFA, and suggests possible new ways to promote adaptive coping with pain.

INTRODUCTION

Somatic complaints with no apparent medical explanation are a common phenomenon in the general population (Eriksen & Ursin, 2004). Most of these complaints disappear quickly and only few people with these complaints will visit a doctor. Nevertheless, at least one-third of all health complaints (HCs) presented to primary care professionals lack an adequate organic explanation (Peveler et al., 1997). Such complaints are referred to in the literature as medical unexplained symptoms (MUS), functional somatic syndromes or somatoform disorders (Henningsen, Zipfel, & Herzog, 2007; Page & Wessely, 2003). Although past research has uncovered several predisposing and precipitating factors of MUS, still little information exists that can explain how these complaints are produced and maintained (Page & Wessely, 2003). Recently, it has been hypothesized that these complaints can be explained by individual differences in neural sensitization of certain parts of the central nervous system, such as limbic system or peripheral and central parts of the pain pathway (Eriksen & Ursin, 2004; Henningsen, Zimmermann, & Sattel, 2003; Henningsen et al., 2007). This sensitization might in turn be enhanced or even caused by cognitive processes such as selective attention to and enhanced memory of illness-related information, such as bodily signals (Brosschot, 2002; Brown, 2004).

Early research on these cognitive processes involved in the production of HCs has focused on the role of attention on the perception of bodily signals, showing that a lack of distraction of external cues causes people to focus their attention on internal signals, thereby perceiving more bodily signals compared to when external distraction is present (Pennebaker, 1982b; Watson & Pennebaker, 1989). Several studies have found that dispositional measures of increased self-focused attention (SFA) were related to increased complaint reports (for more studies see Cioffi, 1991; Fenigstein, Scheier, & Buss, 1975; Watson & Pennebaker, 1989; P. G. Williams, Wasserman, & Lotto, 2003), although one study found the opposite: people with high SFA had less HCs compared to people with less SFA when facing stress. This finding was explained as followed: people with high SFA might be more aware of the effects of stress and, therefore, might deal with the stress using better coping strategies (Suls & Fletcher, 1985). Thus, the association between SFA and HCs is still ambiguous.

More recently, it has been suggested that this increased bodily focused attention is actually the result of activation of implicit illness memory networks. Brown's model suggests that when illness memory networks are activated, they guide automatic attentional processes to select innocuous body signals for further processing (Brown, 2004; Skelton & Strohmetz, 1990). Thus, Brown's model provides a link between perceptual processes and cognitive processes, such as attention and memory. A concept related to illness memory networks is expectancy. Expectations can have a big influence on pain perception, such as the placebo effect and also on reporting of flu symptoms (Pennebaker, 1982b). It has been hypothesized that MUS patients might have high expectations of experiencing somatic complaints. In turn, these expectations

can prime subsequent bodily sensations. However, expectancy of somatic complaints also interacts with illness memory networks. If a memory bias causes people to memorize more painful events, then more somatic complaints will be expected in the future (Rief & Broadbent, 2007). Another model suggests that normally, a filtering system, which consists of cognitive processes such as attention, filters out irrelevant bodily signals. However, when this filtering systems becomes distorted, for example, by increased attention to bodily signals, then more irrelevant bodily signals will become noticeable (Rief & Broadbent, 2007). Although some studies have shown that illness-related cues, which presumably activate illness memory networks, cause increased reporting of complaints, including lower pain tolerance, it still remains a largely unrevealed research area (De Wied & Verbaten, 2001; Godinho et al., 2006; Skelton & Strohmetz, 1990). A previous study by our group found that unconsciously processed illness-related cues resulted in lower pain tolerance during a cold pressor task (CPT) (Meerman et al., 2011). However, a follow-up study could not reproduce this effect (Meerman, Brosschot, & Verkuil, 2012).

The strength with which activated illness memory can guide attention and reporting of complaints is likely to depend on the specific associations that are simultaneously activated in this memory. For example, in the context of chronic pain, it has been proposed that biases in information processing are the result of a co-activation between three cognitive schemata, namely, those related to pain, illness, and self (Pincus & Morley, 2001). Pain schema represents sensory intensity, spatial, and temporal features of a pain experience, whereas illness schema represents affective and behavioral consequences of illnesses. The self-schema is a cognitive representation of the self and organizes knowledge about the self and guides the processing of self-relevant information. Repeated simultaneous activation of the content of these three different schemas may result in “enmeshment”, which causes an increased implicit association of the self with illness or pain. The extent of the enmeshment and the main content of the schema determine the strength of the cognitive bias (Pincus & Morley, 2001) and ultimately reporting of complaints. However, this hypothesis has not yet been tested. Importantly, studies have shown that the association of the self with another concept can be experimentally induced, or in other words, that enmeshment between schemata can be created. For example, implicit self-esteem can be enhanced as well as reduced by pairing the self-related schema with a positive schema, which was done by presenting a self referent word (“I”) with a word of positive or negative valence (Dijksterhuis, 2004; Riketta & Dauenheimer, 2003). This procedure is called evaluative conditioning and is theoretically based on the classical conditioning paradigm.

Since our two previous priming studies yielded inconsistent results, the purpose of the current study was again to examine whether activation of implicit illness memory networks would increase reporting of complaints during a pain task. However, this time, we changed the experimental paradigm into an evaluative conditioning paradigm in order to increase the possibility of finding support for the implicit illness memory

networks model as an explanation for MUS (Brown, 2004; Meerman et al., 2011). More precisely, in the current study, we aimed to investigate whether pain reporting would be more strongly affected when enmeshment of the self schema and illness schema was created, compared to activation of the implicit illness schema alone. We, therefore, hypothesized that priming of HC words in combination with the self-referring "I" would lead to a lower pain tolerance compared to priming of HC words in combination with the nonself-referring word "X". Similar to our previous study, we also hypothesized that priming with HC words would lead to lower pain tolerance compared to priming with neutral words.

In addition, we investigated whether dispositional SFA was related to pain tolerance. We did not have an explicit directional hypothesis regarding dispositional SFA as studies, thus far, have yielded opposing results (see above). In addition, we examined whether dispositional SFA moderated priming effects as previous studies found that priming is more effective for participants high on this 'trait' (i.e. private self-consciousness [PSC], see Hull, Slone, Meteyer, & Matthews, 2002).

Negative affect, health worry, and common HCs have all been linked with increased reporting of somatic complaints (Brown, 2004; Fenigstein et al., 1975; Verkuil et al., 2007; Watson & Pennebaker, 1989). It is possible that these traits make people more sensitive to activation of illness memory or SFA. Therefore, we measured these traits and complaints and checked whether the experimental conditions differed on them.

We used subliminal techniques for presentation of the stimuli to prevent the participants from becoming aware of the goal of the experiment and to act with socially desirable responses.

METHODS

Subjects

Eighty-seven students from Leiden University participated, and received course credits or 8 Euros for their effort. This study was approved by the Ethics Committee of the Leiden University Institute of Psychology. Subjects were required to meet the following criteria: no medical disease, no anxiety or depression, and Dutch as a native language. Participants were required to refrain from taking pain killers and to drink caffeinated drinks or alcohol on the day of the experiment and smoking cigarettes up to 1 h prior to the experiment.

Materials

Questionnaires

Self-focused Attention

To measure dispositional SFA, we used the private subscale of the self-consciousness scale (SCS) (Fenigstein et al., 1975; Vleeming & Engelse, 1981, Dutch translation). The private SCS consists of ten items that are rated on a five-point Likert-type scale, of 0 ('not at all characteristic) to 4 ('very characteristic'). *Cronbach's a* for the subscale PSC was .68.

Demographics and Biobehavioral Variables

We measured gender; age; body mass index (BMI); ethnicity; physical activities; usage of sleeping medication, pain killers or tranquilizers in the last 30 days; number of doctor visits in the last 6 months; and habits in smoking, coffee and alcohol drinking; drug use; medication use; illnesses; history of and current psychological problems; negative affect; number of HCs; and self-rated health.

Subliminal Evaluative Conditioning Priming Task

Prime Words

The forward conditioning method was used, which is the most common in evaluative conditioning research (Dijksterhuis, 2004). In this method, a cognitive schema is temporarily 'charged' with affective meaning by pairing a stimulus activating the schema with one from an affective schema. In our study, participants were repeatedly presented, on a computer screen, with either the self-referring word "I" (the Dutch word "ik"), to activate a self-schema, or the non self-referring word "X" as a control manipulation. Immediately after each presentation of "I" or "X", another prime followed that was either a word describing HC, to activate an illness-related schema, or neutral (NEU) words for the control group. The neutral prime words described animals. The Appendix shows the prime words that were used in the current study. The HC and neutral categories contained ten words and did not differ in number of syllables, length, and frequency in the Dutch language (respectively, $t_{(18)} = .61$, $p = .55$, $t_{(18)} = .59$, $p = .56$, and $t_{(18)} = .01$, $p = .99$). In every prime condition, the ten prime word pairings were shown randomly ten times, thus a total of 100 trials.

Priming Task

The present subliminal priming task consisted of a simple computer task presented to the participants as a reaction time task. For each trial of the task, a row of Xs, with a random duration of 500 ms, appeared in the center of the screen. Students were then exposed to either the self-referring "I" or neutral "X" prime words, followed by the health or neutral prime. Most prime words (82 %) were shown for 33 ms, as we did in

our previous study (Meerman et al., 2011) and as is quite common for this kind of studies (Kiefer, 2002; Levy, 1996; Pierce & Lydon, 1998), but due to a slight programming error, some primes (18 %) were shown for 17 ms, which is, however, also quite common (Kawakami, Dovidio, & Dijksterhuis, 2003; Spalding & Hardin, 1999) and successful subliminal evaluative conditioning (SEC) has also been accomplished with priming durations of 17 ms (Dijksterhuis, 2004). The prime duration was on average 31.62 ms. It was somewhat longer for the self-referent primes ("I" and "X"; *M* = 32.89 ms, SD = 0.180) than for the health and neutral primes (*M* = 30.33 ms, SD = 1.803, $t_{(86)}$ = 14.644, $p < .01$). A string of random letters served as a backward mask for the prime words. The backward masks were presented to the participants as target words, and the participants were asked to decide as quickly as possible whether the letter string started with a vowel or consonant. The trials were presented in random order. The prime words and masks appeared in black in the center of the white screen. Each trial was separated by a 1000 ms interval in which the screen was blank.

Awareness Checks

In order to check whether the primes were indeed shown under the awareness threshold, we tested after the pain task whether the participants could detect the primes. We used both a subjective threshold, in which conscious awareness is indexed by participants' self reports with a funneled debriefing questionnaire and an objective threshold in which conscious awareness is indexed by the d' measure on a forced-choice word identification task. The d' is a measure of the participants' discriminative abilities based on signal detection theory (Bargh & Chartrand, 2000; Macmillan, 2005).

Pain Tolerance

Similar to our previous study, we used a CPT for pain stimulation (Meerman et al., 2011). During a CPT, participants were asked to keep their nondominant hand in a basin filled with ice-cold water for as long as they can. The basin is, on the surface of the water, divided into two sections. One is filled with ice and another kept free of ice to allow a hand to be immersed in the water without direct ice contact. A pump kept the water flowing continuously to prevent buildup of warmer water around the hand. The mean water temperature at the start was 0.88 °C (SD = 0.72). Pain tolerance was defined as the total duration between the immersion and the withdrawal of the hand (De Wied & Verbaten, 2001; Meerman et al., 2011). Unbeknown to the participants, maximum duration of hand immersion was limited to 4 min. For exploratory reasons, pain intensity (PI) and pain unpleasantness (PU) ratings were also rated on a Visual Analogue Scale, ranging from not at all intense or unpleasant to extremely intense or unpleasant (Price, McGrath, Rafii, & Buckingham, 1983). To prevent interference with pain tolerance, these measures were taken immediately after the participant withdrew their hand from the water.

Procedure

Information about the experiment was posted on the internet, making clear that it consisted of filling in questionnaires, with a special focus on study skills (which served as a cover story), reaction time tasks on the computer, and a pain task. Participants were tested individually by one female experimenter. The experimenter was kept blind about the random assignment of the participants. When the participant arrived at the laboratory and gave their (partial) informed consent, they were asked to provide demographic information (age and gender) and the questionnaires started. The experimenter left to an adjacent room, where she followed the procedure. After the study skills questionnaire, which served as a distraction, the SEC task started. In order to rule out any effects on pain of distraction by the computer task, the computer task (with primes) was performed immediately before the pain task. Several studies have shown that subliminal priming effects can last for at least a couple of minutes (Bargh & Chartrand, 2000; Levy et al., 2000; Lowery et al., 2007). After participants took their hand out of the water, they were asked to rate PU and PI. Awareness of the priming procedure was assessed with the funneled debriefing questionnaire and with the forced-choice word identification task. Finally, participants rated the negative versus positive valence and arousal of all prime words on a seven-point scale, and they performed the same SEC task but with positive health words (such as "vital", "healthy" and "fit") to counteract any potential longer lasting effects of the previous priming that might have a negative effect on pain tolerance. At last, the participants were fully debriefed, asked again for permission to use their data, and then they received money or course credits.

Data Analyses

We used a 2-by-2 analysis of (co)variance with the self-referent prime word ("I" or "X") and priming condition (NEU, neutral, and, HC) as the independent variables and the pain measures as dependent variables. A stepwise regression analysis was used to select an optimal set of covariates among the baseline and experimental factors with a high p-criterion of .20 (Steyerberg & Harrell, 2003). The critical F values for the planned comparisons are reported (Tabachnick & Fidell, 2007). Because of our specific planned comparisons, we used one-tailed tests but we also report the two-tailed *p* value. For the exploratory analyses, we report the two-tailed *p* value. We first report the unadjusted effects and then the adjusted effects of priming (Simmons et al., 2011). Prior to analysis, the variables were examined separately for the four conditions on accuracy of data entry, missing values, linearity, homogeneity of variance and regression, and normality (Tabachnick & Fidell, 2007). Variables were transformed if necessary.

RESULTS

Data of participants was excluded if they: afterwards indicated on the funneled debriefing questionnaire that they thought the task involved priming (*n* = 4), could discriminate between the primes according to their d' measure (see forced-choice test above) (*n* = 2), had a diagnosed minor medical disease (*n* = 3), still reported to have used coffee on the day of the experiment (*n* = 1), were currently being treated for anxiety (*n* = 1), listed special medication use (*n* = 2) and participated in a previous experiment similar to the current study (*n* = 1).

Descriptives

A total of 76 participants remained with 19 participants in the "I"-HC priming group, 18 participants in the "X"-HC priming group, 20 participants in the "I"-NEU group and 19 participants in the "X"-NEU group. The mean age of the participants was 22.21 years (SD = 10.87) and 88.2 % were female. Participants had on average 8.12 HCs in the last month (SD = 3.01) and rated on average their own health as similar to people of the same age (*M* Self-Rated Health [SRH] = 1.14, SD = .48).

We checked whether the participants in the four groups differed in factors measured at baseline that might influence pain tolerance including: (1) demographic features, such as age and gender; (2) psychosocial factors, such as self-rated health and NA; and (3) experimental factors, such as water temperature of the CPT and the average duration of the prime presentation. The four experimental groups significantly differed only in self-rated health, $F_{(3, 75)} = 3.02$, $p = .04$, and marginally on the use of painkillers, $F_{(3, 75)} = 2.50$, $p = .07$. Post hoc tests with Bonferroni correction showed that the X-NEU group had a significantly higher self-rated health compared to the I-HC group, but similar tests for painkillers did not show any significant differences between the conditions. However, while SRH was not related to any outcome measures in the stepwise regression analyses used to assess potential covariates, use of painkillers was related to pain tolerance, and was thus used as a covariate. The other variables, including the mean prime durations, did not differ among the groups. However, as the stepwise regression analyses showed that besides painkillers, water temperature of the pain task, coffee consumers, physical activity, BMI, doctor visits in the past month, SHC musculoskeletal pain (rec), gender and cigarette consumption were also related to one or more of the pain measures, they were used as covariates to remove noise variance in these dependent variables (G. A. Miller & Chapman, 2001).

Priming Effect on Pain Tolerance

Contrary to our hypotheses, neither self-referent priming ("X" versus "I") nor HC priming (HC versus neutral words) had a main effect on pain tolerance, nor did these priming factors interact (Table 4-1). These results remained the same after adjusting for the covariates (Table 4-2).

Secondary Pain Outcomes: Intensity and Unpleasantness

The effect of priming on PI and PU was examined for exploratory purposes. Neither self-referent priming nor priming with HC words had a main effect on PI and PU (Table 4-1), nor did these priming factors interact. These results remained the same after adjusting for the covariates (Table 4-2).

Self-focused Attention

No significant correlation of SFA was found on any of the pain measures. However, we also tested whether SFA acted as a moderator of the experimental manipulations. The expected Self-referent × HC × SFA interaction was not significant. However, we found that SFA acted as a moderator of the effect of self-referent priming (see Table 4-1). Simple effect tests of the unadjusted means showed that participants with low SFA (< *M* -1SD) had significantly higher pain tolerance when primed with "I" compared to "X", $F_{(1, 68)} = 4.70$, $p = .03$, $\mu_p^2 = .07$, while no significant difference was found for participants with high PSC (>*M* +1SD), $F_{(1, 68)} = .83$, $p = .37$, $\mu_p^2 = .01$ (see Fig. 4-1). Analyses with adjusted means showed the same pattern (see Table 4-2).

Table 4-1. ANOVA results for dependent variables based on unadjusted means

		Main effects of priming				Main effects of priming plus self- focused attention			
Source	**Dependent variable**	***df***	***F***	***p***	μ_p^2	***df***	***F***	***p***	μ_p^2
Self-referent priming	Pain tolerance[a]	1[c]	.974	.327	.013	1[f]	5.205	.026*	.071
	Intensity rating	1[d]	.000	.999	.000	1[g]	.000	.986	.000
	Unpleasantness rating[b]	1[e]	.109	.742	.002	1[h]	.664	.418	.010
Health com-plaint priming	Pain tolerance[a]	1	.326	.570	.005	1	.943	.335	.014
	Intensity rating	1	.123	.727	.002	1	.195	.660	.003
	Unpleasantness rating[b]	1	.147	.703	.002	1	.071	.790	.001
Self-referent × health com-plaint priming	Pain tolerance[a]	1	2.049	.157	.028	1	.529	.470	.008
	Intensity rating	1	.371	.544	.005	1	.567	.454	.008
	Unpleasantness rating[b]	1	1.336	.251	.018	1	.285	.595	.004
Self-focused attention	Pain tolerance[a]					1	.099	.754	.001
	Intensity rating					1	1.394	.242	.020
	Unpleasantness rating[b]					1	.970	.328	.014
Self-referent × self-focused attention	Pain tolerance[a]					1	4.588	.036*	.063
	Intensity rating					1	.000	.992	.000
	Unpleasantness rating[b]					1	.639	.427	.009
Health com-plaint × self-focused attention	Pain tolerance[a]					1	.852	.359	.012
	Intensity rating					1	.151	.699	.002
	Unpleasantness rating[b]					1	.019	.892	.000
Self-referent × health com-plaint × self-focused attention	Pain tolerance[a]					1	.162	.689	.002
	Intensity rating					1	.757	.387	.011
	Unpleasantness rating[b]					1	.668	.417	.010
Error	Pain tolerance[a]	72				68			
	Intensity rating	72				68			
	Unpleasantness rating[b]	72				68			

[a] Log transformed; [b] Inverse square root transformed; [c] R^2 = .046 (Adjusted R^2 = .006); [d] R^2 = .007 (Adjusted R^2 = -.034); [e] R^2 = .022 (Adjusted R^2 = -.019); [f] R^2 = .118 (Adjusted R^2 = .027); [g] R^2 = .038 (Adjusted R^2 = -.061); [h] R^2 = .057 (Adjusted R^2 = -.040).*p < .05

Table 4-2. ANOVA results for dependent variables based on adjusted means

		Main effects of priming					Main effects of priming plus SFA				
Dep.var.	**Source**	***B***	***df***	***F***	***p***	μ_p^2	***B***	***df***	***F***	***p***	μ_p^2
Pain tolerance (log)	Water temp.	.160	1[a]	12.184	.001**	.154	.148	1[d]	10.603	.002**	.144
	Painkiller usage	-.065	1	7.447	.008**	.100	-.078	1	10.663	.002**	.145
	Coffee drinkers	-.177	1	5.937	.017*	.081	-.173	1	5.780	.019*	.084
	Physical activity	-.060	1	2.835	.097†	.041	-.071	1	4.227	.044*	.063
	BMI (rec)	9.838	1	3.656	.060†	.052	8.775	1	2.942	.091†	.045
	HC		1	.307	.582	.005		1	.772	.383	.012
	Self		1	2.446	.123	.035		1	8.660	.005**	.121
	Self × HC		1	1.085	.301	.016		1	.150	.700	.002
	SFA						-.015	1	.598	.442	.009
	SFA × self							1	7.058	.010*	.101
	SFA × HC							1	1.155	.287	.018
	SFA × self × HC							1	.024	.877	.000
	Error		67					63			
Pain Intensity	Doctor	6.006	1[b]	5.476	.022*	.077	5.756	1[e]	4.438	.039*	.067
	BMI (rec)	-814.030	1	6.863	.011*	.094	-883.019	1	7.846	.007**	.112
	SHC musc. (rec)	22.672	1	7.162	.009**	.098	24.675	1	7.280	.009**	.105
	Physical activity	5.149	1	5.606	.021*	.078	5.382	1	5.888	.018*	.087
	Gender	-19.627	1	8.262	.005**	.111	-19.726	1	7.994	.006**	.114
	Smokers	-16.695	1	4.350	.041*	.062	-19.091	1	5.537	.022*	.082
	HC		1	.323	.572	.005		1	2.402	.126	.037
	Self		1	.018	.892	.000		1	.004	.952	.000
	Self × HC		1	.794	.376	.012		1	1.610	.209	.025
	SFA						.472	1	1.207	.276	.019
	SFA × self							1	.002	.961	.000
	SFA × HC							1	2.176	.145	.034
	SFA × self × HC							1	2.188	.144	.034
	Error		66					62			

Table 4-2. ANOVA results for dependent variables based on adjusted means (continued)

		Main effects of priming					Main effects of priming plus SFA				
Dep.var.	**Source**	***B***	***df***	***F***	***p***	μ_p^2	***B***	***df***	***F***	***p***	μ_p^2
Pain unpleas-antness (inverse square root)	Doctor	-.643	1[c]	7.252	.009**	.096	-.659	1[f]	6.555	.013*	.093
	Smokers	1.125	1	2.584	.113	.037	-.452	1	2.108	.151	.032
	BMI (rec)	64.017	1	4.782	.032*	.066	74.147	1	6.065	.016*	.087
	Physical activity	-.485	1	5.668	.020*	.077	1.043	1	4.677	.034*	.068
	HC		1	.616	.435	.009		1	.043	.837	.001
	Self		1	.048	.828	.001		1	.048	.827	.001
	Self × HC		1	.435	.512	.006		1	1.047	.310	.016
	SFA						.004	1	1.189	.280	.018
	SFA × self							1	.046	.831	.001
	SFA × HC							1	.190	.664	.003
	SFA × self × HC							1	1.528	.221	.023
	Error		68					64			

[a] R^2 = .314 (Adjusted R^2 = .233); [b] R^2 = .358 (Adjusted R^2 = .271); [c] R^2 = .241 (Adjusted R^2 = .162); [d] R^2 = .398 (Adjusted R^2 = .284); [e] R^2 = .407 (Adjusted R^2 = .283); [f] R^2 = .277 (Adjusted R^2 = .153). Rec = reciprocal transformed, log = log transformed, SFA = Self-Focused Attention, HC = Health Complaint Priming, Self = Self-Referent Priming, Water temp = Water temperature at the end of task, Doctor = Doctor visits in past month, SHC Musc. = SHC musculoskeletal pain. †p < .05(one-tailed), *p < .05, **p < .01

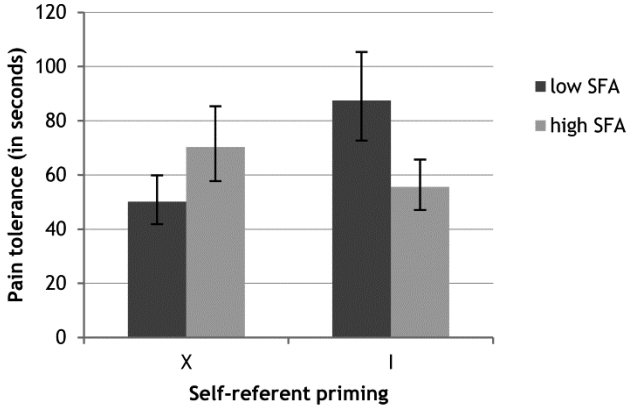

Figure 4-1. The estimated means for pain tolerance per self-referent priming condition and self-focused attention (SFA)(values have been transformed back to represent original scale, error bars represent 1 standard error of the mean).

DISCUSSION

The present study was conducted to replicate and extend our previous studies, in which we tested an explanatory model for HCs without a medical explanation, based on principles from cognitive psychology (Meerman et al., 2011). Our previous study found that the activation of an illness-related cognitive schema, using subliminal priming, seemed to cause lower pain tolerance (Meerman et al., 2011). However, a follow-up study that used slightly different prime words could not reproduce this effect (Meerman et al., 2012). Therefore, we decided to replicate the previous study but this time using SEC to cause a temporary stronger association between the self and illness, which presumably would have a stronger effect on pain tolerance compared to activation of illness-related cognitive schemata alone (Pincus & Morley, 2001). Again, contrary to our first study (Meerman et al., 2011), and studies by others using supraliminal primes (De Wied & Verbaten, 2001; Godinho et al., 2006), we did not find that activating an illness-related cognitive schema caused a lower pain tolerance. We also did not find support for the hypothesis that an increased association between the self-schema and illness-schema would cause lower pain tolerance compared to activating an illness-related cognitive schema alone. Yet, priming with a self-referent word ("I") seemed to enhance pain tolerance, but only in participants with low SFA.

There are several factors that could account for the failure to replicate our previous study. Previously, we used subliminal priming to activate an illness-related cognitive schema (Meerman et al., 2011) while in the current study we used SEC techniques based on other studies that were able to improve self-esteem by pairing a self-referent word to a positive word (Dijksterhuis, 2004; Riketta & Dauenheimer, 2003). One could argue that the duration of part (18%) of the primes (17 ms) in the current study was too short to have any effect. Yet, successful SEC has been accomplished with priming durations as low as 17 ms (Dijksterhuis, 2004).

Another difference between the current study and the former study in which we did find that the HC words lowered pain tolerance (Meerman et al., 2011) is that we removed the prime word "invalid" (in the sense of 'severely disabled person') in the present study, which we also did in the follow-up study that could not replicate the finding of our first study as well (Meerman et al., 2012). These results seem to indicate that the lower pain tolerance found due to illness priming in our previous study was the result of priming with the word "invalid", perhaps in interaction with the other health-related words used. It is possible that illness memory networks are only, or most easily, affected by seriously threatening primes such as "invalid", or really intrusive pictures such as the blood- and wound-containing primes as used in other previous studies (De Wied & Verbaten, 2001), which would then result in more reporting of complaints. This clearly suggests a path for future studies.

Another possible explanation for not finding the expected interaction between self- and illness primes might be that activating self- and illness schema only influences pain tolerance in people that already have strongly enmeshed schemata, for example,

chronic pain patients. It has indeed been suggested that only vulnerable chronic pain patients who have enmeshed schemas of pain and the self will show a tendency to preferentially process pain stimuli in reference to themselves in contrast with healthy people who will preferentially process positive and neutral information that is congruent with their self-schema (Pincus & Morley, 2001).

With respect to the expected effects of priming of the self-schema and dispositional SFA on pain tolerance, the literature up to now gives rise to contrary hypotheses: a higher pain tolerance could have been expected, caused by an increase in implicit positive affect resulting from 'self priming' that was found recently by Quirin et al. (Quirin, Bode, & Kuhl, 2011) or caused by increased effective coping with stress in people with high SFA, as found by Suls and Fletcher (1985) or the opposite: lower pain tolerance instead as a result of enhanced SFA or internal focus, which has been linked to increased reporting of complaints (Cioffi, 1991; Fenigstein et al., 1975; Watson & Pennebaker, 1989; P. G. Williams et al., 2003). In fact, we found support for the first hypothesis: participants primed with the self-referent word "I" showed increased pain tolerance compared to participants primed with the non self-referent word "X", but only for participants with lack in SFA. It might be speculated that 'boosting' the activation of the self-schema stimulates a strategy to cope with pain. Since this seems solely the case in people who seem to lack in SFA, it might be that this effect is mediated by enhanced SFA. Still, this would suggest that high self-focused participants would have shown a higher pain tolerance which was not evident, at least not statistically confirmed. The finding that only participants with low SFA showed an effect of self-referring priming also seems to be inconsistent with an earlier study that found that priming was only effective in participants with high SFA and not low SFA (Hull et al., 2002). The reliability of the scale used however was relatively low; therefore, we have to interpret these results with caution.

In conclusion, we could not replicate our previous study in which we found support for the theory that activation of cognitive schemata related to health can cause increased reporting of complaints and thereby provide evidence for an explanatory model for medically unexplained symptoms. However, due to our sample size, we were only able to detect large effect sizes and not smaller. The possibility remains that the hypothesized effect does exist but only with a medium or smaller effect size. We did find, however, that activating a self-schema seems to increase pain tolerance, especially in people lacking in SFA. This suggests that increasing attention on the self, implicitly as well as explicitly may offer a clue to improve prevention or treatment of these complaints, despite theories that predict the opposite (Cioffi, 1991; Fenigstein et al., 1975; Watson & Pennebaker, 1989; P. G. Williams et al., 2003). However, one major limitation of our study is the fact that we could not perform a manipulation check. Although the manipulation we employed is broadly used, with success, we cannot be sure whether our experimental manipulation of activating illness memory networks and/or self-related memory networks actually worked. The reason that such a manipulation check is seldom used, is perhaps that it is difficult to implement it

without seriously impairing the design. For example, a lexical decision task immediately after the priming, that is typically used to measure priming effects, would create an unwanted supraliminal priming effect. It might also be rare because most results that are published are positive (i.e., due to publication bias) and although there remains comparable ambiguity about the mechanism in these studies, such a test is not commonly required. Thus, the results of this study need to be carefully interpreted. Future studies should try to replicate the effect found for the effect of increased self-attention causing less perception of pain while also administering experimental manipulation checks to rule out the possibility of a "fluke" finding. Perhaps supraliminal evaluative conditioning techniques might give a different result compared to the subliminal techniques used in this study, as earlier research has shown that supraliminal techniques have stronger effects than subliminal ones (Hofmann, De Houwer, Perugini, Baeyens, & Crombez, 2010).

Appendix. Prime words used for the complaint versus neutral prime factor. English words are translated from Dutch prime words.

Complaint	Neutral
"Allergy"	"Bear"
"Asthma"	"Chimpanzee"
"Vomiting"	"Squirrel"
"Diarrhea"	"Giraffe"
"Flu"	"Gorilla"
"Headache"	"Rhino"
"Fever"	"Panda"
"Heartburn"	"Turtle"
"Inflammation"	"Butterfly"
"Wound"	"Seal"

Chapter 5 |

Can Illness Memory be Activated by Subliminal Stimulation? Two Validation Studies of Subliminal Priming and Subliminal Evaluative Conditioning

Meerman, E.E., Brosschot, J.F., & Verkuil, B. (*Manuscript in Preparation*). Can illness memory be activated by subliminal stimulation? Two validation studies of subliminal priming and subliminal evaluative conditioning.

ABSTRACT

Objective We attempted to validate whether the paradigm for subliminal priming and subliminal evaluative conditioning that we used in our previous studies and that is commonly used to prime behavior in social psychological studies, was actually effective in activating semantic memory networks for at least several minutes.

Methods In the first study we subliminally primed participants with either neutral or illness words. We then measured with a lexical decision task whether participants primed with illness words had quicker response latencies for illness words. In the second study, participants were subliminally exposed to either a self-referring word "I" or a nonself-referring word "X" paired with illness words using subliminally evaluative conditioning. We then measured whether participants exposed to "I" and illness words showed stronger associations of the self with illness on an implicit associations task.

Results The priming or subliminal evaluative conditioning did not cause differences in response latencies on subsequent tasks.

Conclusions In both studies, we did not find that the priming techniques were effective in activating semantic memory networks. This study shows that it is important for future studies to include a manipulation check of subliminal priming to see whether it is effective in manipulating implicit memory. In addition, future studies should examine ways in which to make priming techniques more reliable.

INTRODUCTION

In previous studies (Meerman, Brosschot, Van der Togt, & Verkuil, 2013; Meerman, Brosschot, & Verkuil, 2012; Meerman, Verkuil, & Brosschot, 2011) we tested a model of symptom reporting that holds that medically unexplained symptoms (MUS) are at least partly caused by chronically activated illness-related memory networks- or schemata of illness (Brosschot, 2002; Brown, 2004; Rief & Barsky, 2005). The basic rationale is that activated illness memory would lead to increased selective attention towards bodily signals, which in turn causes increased detection of these signals and increased reporting of these signals as symptoms. We have experimentally tested this cognitive model of symptom perception by priming healthy participants subliminally with illness-related words to (temporarily) increase activation of illness-related cognitive memory networks and afterwards examined whether this caused a lower pain tolerance (Meerman et al., 2011). The results of these studies have, however, been inconsistent. In one study we indeed found that pain tolerance was involuntarily decreased by activating illness-related memory, but we could not confirm this finding in a subsequent replication study (Meerman et al., 2012). The question rose whether our methods were sufficiently adequate to draw strong conclusions concerning the tenability of the illness activation model. We started to suspect that our priming method was suboptimal, in that its effects did not last long enough or that the prime stimulus duration itself was inadequate. As to the first possibility, several studies have shown that behavioral effects of subliminal priming can last for at least the duration of a subsequent task, usually several minutes (for example Bargh, Chen, & Burrows, 1996; Levy et al., 2000), and thus long enough for our purpose. With respect to the second possibility, i.e. prime stimulus duration, we used a duration (33 ms) that successfully produced effects before (for example, Kiefer, 2002; Levy, 1996; Pierce & Lydon, 1998; Lowery et al., 2007) amongst which long-lasting subliminal priming effects of up to four days (Lowery et al., 2007). Thus, prime duration is unlikely to have caused the negative findings.

It is theoretically possible that priming does have no prolonged memory effects, despite is prolonged behavioral effects. However, several studies have found that priming leads to increased memory accessibility of the primed construct (Aarts, Custers, & Holland, 2007; see for example Aarts & Dijksterhuis, 2003). Our current study set out to test whether our subliminal priming task used in our previous studies was indeed successful in activating illness memory. If illness-related subliminal primes would turn out not to induce prolonged memory effects this could explain our inconsistent findings mentioned above, because the priming effects, if any, might be too brief to have substantial effect on symptom reports.

Since our two previous priming studies (Meerman et al., 2012, 2011) yielded inconsistent results, we conducted a third study using another paradigm, namely an evaluative conditioning paradigm, in which illness memory (illness schema) and self-schema was simultaneously activated. With this paradigm we aimed to investigate whether

symptom reporting would be more strongly affected when illness schema was repeatedly coactivated or 'enmeshed' with the self-schema (as suggested by Pincus & Morley, 2001). However, we did not find that such a simultaneous subliminal priming by self- and illness-stimuli increased symptom reporting. The question that remained was whether we actually succeeded in temporarily associating self with illness information. However, several other studies were successful in increasing the association of the self with another concept (e.g. Dijksterhuis, 2004; Riketta & Dauenheimer, 2003). Dijksterhuis (2004) verified the strengthened association between self and positive trait terms (thus temporarily increasing 'self esteem') by use of the Implicit Association Test (IAT, see below). In the current study we aimed to do the same for the association between self and illness.

In conclusion, two out of our three priming studies using either subliminal priming or subliminal evaluative conditioning, did not show support for the hypothesis that illness-schemata cause increases in symptom reporting. However, it is unclear whether this is due to a faulty model or due to the subliminal priming techniques being unreliable in temporarily activating the illness-related schemata. In the current studies, we first attempted to validate whether the paradigm for subliminal priming that we used in our previous studies and that is commonly used to prime behavior in social psychological studies, was actually effective in activating semantic memory networks for at least several minutes. This was done using a lexical decision task, which is a standard test to measure spreading of activation of across specified memory content. In the second part of the study we attempted to validate whether the subliminal evaluative conditioning was effective in creating an increased association between the self and another concept. We examined the effectiveness of the procedure by administering an IAT, which is designed for examining the strength of implicit associations. Our first hypothesis was that subliminal priming with illness words causes a significant quicker reaction time for illness words on a subsequent lexical decision task due to an activated illness memory network (study 1). Our second hypothesis was that subliminal evaluative conditioning of illness with the self-schema causes quicker reaction times of words related to illness and self on a subsequent implicit association task (Greenwald & Farnham, 2000; Greenwald, McGhee, & Schwartz, 1998), indicating a stronger association between the self and illness (study 2).

STUDY 1

Methods

Subjects

Forty-two students from Leiden University participated in the present study. Participants received either course credits or five Euros for participating. This study was approved by the Ethics Committee of the Leiden University Institute of Psychological Research. Subjects were required to meet the following criteria: no medical disease,

no chronic pain, no feelings of anxiety or depression, Dutch native language and no dyslexia.

Materials

Questionnaires

Demographics and bio-behavioral variables. We measured only gender, age, Body Mass Index (BMI), ethnicity, physical activities, usage of sleeping medication, pain killers or tranquilizers in the last 30 days, number of doctor visits in the last 6 months, and habits in smoking, coffee and alcohol drinking, drug use, medication use, illnesses, history of and current psychological problems.

Experimental manipulation: subliminal priming task

Prime words. Participants were randomly assigned to two different conditions, with prime words describing either (a) Health Complaints (HC), to activate an illness-related schema, or a control category: (b) neutral (NEU) words. Appendix A shows the prime words that were used in the current study. These words were also used in our previous study (Meerman et al., 2012). The categories contained 10 words and did not differ in number of syllables, length and frequency in the Dutch language In every prime condition the 10 prime words were shown randomly 10 times, thus a total of 100 trials.

Priming task. The priming task was exactly the same as in our previous study (Meerman et al., 2012). The priming task was performed immediately before the lexical decision task. The priming manipulation was a variation of a common paradigm in which participants judge as quickly and accurately as possible whether briefly flashed letter strings appear on the right or left side of a computer monitor (Lowery et al., 2007). The present subliminal priming task consisted of a simple computer task presented to the participants as a reaction time task. For each trial of the task, a fixation cross with a random duration of 500-1000 ms, appeared in the center of the screen. Students were then exposed to the prime word (33 ms), and immediately after a string of XXX's that served as a backward mask for the prime word. The prime word and mask appeared on either the right or left side of the screen, in the parafoveal region [at a ˚2 degree visual angle (Bargh & Chartrand, 2000)]. Participants indicated with the arrow keys what the position was of the XXX's. Each trial was separated by a 500 ms interval in which the screen was blank. Stimuli were presented on a personal computer using the E-Prime 2.0 software (Psychology Software Tools, Pittsburgh, PA).

Lexical decision task (LDT)

The LDT (Meyer & Schvaneveldt, 1971) took place after participants were exposed to all the subliminal primes. Participants were told to identify, as quickly as possible, whether or not each character string is an actual Dutch word by pressing the arrow keys. Prior to the task, participants had ten practice trials (five words and five

non-words), in which all word stimuli were neutral. Subsequently, 28 different words and 28 non-words were randomly shown. The non-words were neutral words of which several letters were mixed up. The words consisted of seven illness words (e.g. 'infection', 'coughing'), seven negative valence words ('coward', 'vulgar') and 14 neutral words (e.g. 'art', 'child'). The words were matched on syllable, length and frequency. The onset of each trial was marked by a cross (+), which served as a fixation point. After 500 ms latency, the fixation point was replaced by a character string. The stimulus item disappeared after the participant responds.

Neutralizing priming task

For ethical reasons, the last task of the experiment contains a subliminal priming task with originally neutral prime words. This priming was done to avoid a long-term impact of the subliminal priming task with illness related words.

Awareness checks

To see if participants during the experiment were aware of the fact that they were subliminally primed, two different methods were used to check whether participants were able to detect prime words. After participants were primed and had done the LDT, they had to fill in a questionnaire with increasingly specific questions about the research purpose and suspicions. The questionnaire contained the following questions: '*What do you think what the purpose was of this study?' 'Have you noticed something special in the computer tasks?' 'Do you think something has influenced your performance on the computer tasks?*' When the answers of the participants do not contain information about subliminal priming it can be assumed that the participants were not aware of the fact that they were subliminally primed. After this questionnaire the participant is explained that he/she is subliminally primed and that in the next computer task the same is going to happen. The participant is told that words are being represented and that he/she must try to guess what they are. If the participant is not able to guess any of the words, it is safe to say that the subliminal presentation has been achieved (Bargh & Chartrand, 2000).

Procedure

Participants were recruited personally by the researcher (E.E.M) at the Leiden University. Before they actually participated in the study they were informed that the experiment consisted of different computer tasks, but they were not informed about the subliminal priming. After the introduction and screening, participants signed an informed consent. This informed the student that the purpose of the study is to get information about study skills (which served as a cover story) and reaction times. Participants were tested by an experimenter who was kept blind about the random assignment of the participants.

The participants completed four different computer tasks. The first computer task consisted of different questionnaires. The second computer task consisted of a ques-

tionnaire about study skills (cover story), followed by the subliminal priming task. The third computer task consisted of the LDT were participants had to decide as quickly as possible if it was an existing word or a nonsense word. The participants then completed the awareness checks, followed by the neutralizing priming task. After the experiment, participants were informed about the subliminal priming tasks and the true purpose of the study and received money or credits for participating in the experiment.

Data analyses

We used a repeated measures ANOVA with priming condition as the between-subjects factors (neutral, and illness) as the independent variables. The LDT reaction time measures for the illness words and for the negative control words were the dependent variables. We report the two-tailed *p* value.

Results

Participants that were excluded were: with disease (*n* = 3), medication use (*n* = 3), used alcohol on day of experiment (*n* =1). A total of 36 participants remained for the analyses. Reaction times of correct answers to the illness words and negative control words were analyzed. Data was checked for outliers (also within subject), homogeneity of variance and normality.

Participants reacted in general quicker on the illness related words (*M* RT = 606.00, *SE* = 15.06) compared to the other negative control words (*M* RT = 694.16, *SE* = 22.81), $F_{(1,33)} = 21.951$, $p = .000$, $\mu_p^2 = .399$ (see Figure 5-1). However, participants in the illness priming condition did not significantly react quicker to the illness words (*M* RT = 592.86, *SE* = 21.61) compared to the negative control words (*M* RT = 619.13, *SE* = 21.00), $F_{(1,33)} = .151$, $p = .701$, $\mu_p^2 = .005$. In addition, the illness priming did not influence the reaction times in general, $F_{(1,33)} = .989$, $p = .327$, $\mu_p^2 = .029$.

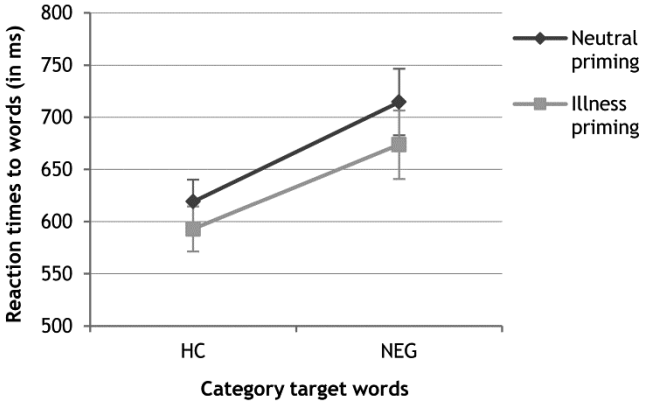

Figure 5-1. Average reaction time per word category and priming group

Several of the demographic variables were associated with reaction times (RTs) in the LDT. However, even adjusting for these covariates, still no effect of priming was found on the RT's, $F_{(1,31)} = .489$, $p = .489$, $\mu_p^2 = .016$.

Discussion

The result of this part of our study do not yield support for our hypothesis that subliminal priming with illness words causes a significant quicker reaction time for illness words on a subsequent lexical decision task. This seems to indicate that the subliminal priming paradigm used in this and our previous studies was not effective in activating illness-related cognitive memory networks, at least not for the time frame used in this study (that is, several minutes) and our earlier studies.

STUDY 2

Methods

Subjects

Twenty-eight healthy students from the Leiden University participated in this study in return for either course credits or a small fee (five euros). Participants criteria were: be a student, at least 16 years old, native language Dutch, no medical illness, anxiety or depression. The following requirements were added to have the same conditions as to our previous study: no coffee or painkillers intake on the day of the experiment, and no smoking one hour before participation (Meerman et al.,2013).

Materials

Questionnaires

Demographics and bio-behavioral variables. The same variables were measured as in study 1.

Experimental manipulation: Subliminal evaluative conditioning (SEC) task

We used the exact same task as our previous SEC study (Meerman et al., 2013). In the present study the subliminal evaluative conditioning consists of a simple computer task during which words were shown for a short duration (33 ms), followed by a 'mask' to abolish any afterimage. For each trial of the task, a row of Xs, with a random duration of 500 ms, appeared in the center of the screen. Because in our previous study (Meerman et al., 2013) some of the primes were shown for 33 ms and some were shown for 17 ms, in this study we made sure that all primes were shown for 33 ms. Participants were subliminally exposed to either a self-referring word "I" or a nonself-referring word "X" paired with illness words. Illness words were similar to the words in Study 1 and our previous studies (Appendix A). A string of random letters served as a backward mask for the prime words, and the participants were asked to decide as quickly as possible whether the letter string started with a vowel or consonant. The trials were presented in random order, the ten prime word pairings were shown randomly ten times, thus a total of 100 trials. The prime words and masks appeared in black in the center of the white screen. Each trial was separated by a 1000 ms interval in which the screen was blank. Participants were randomly assigned over the two different conditions (I+illness or X+illness). Stimuli were presented on a personal computer using the E-Prime 2.0 software (Psychology Software Tools, Pittsburgh, PA).

Implicit Association task (IAT)

In the implicit association task the participants were asked to sort words according to their category. The categories were either self vs. others, or healthy vs. sick. The target labels were 'self' and 'other', and the attribute labels were "healthy" and "sick". Each category consisted of five stimuli (see Appendix B). Words appeared in random order in the middle of a computer screen and participants were instructed to sort them with a left response or right response key (Greenwald, Nosek, & Banaji, 2003; Nosek, Greenwald, & Banaji, 2005). In the instructions participants were told that the words only belonged to one category. Participants were also told they had to work as quickly and as accurately as possible and if they were too slow or made too many mistakes, it would result in non-interpretable scores. Participants were instructed to keep their fingers on the response keys, in order to react as quickly as possible. In addition, after each block they received feedback whether their average reaction speed was fast enough (below 5000 ms), or if they had to increase their speed. A fixation cross (+) appeared in the middle of the screen for 150 ms. The words were shown either in white or green, corresponding to the color that the associated label

was shown in. The stimulus word remained on the screen until a categorization had been made. If the participants made a wrong response a red X would appear, and the participants had to make the correct response in order to continue. Trials were separated by blank screens of 150 ms. The IAT procedure uses five blocks, and in each block the stimuli are shown in random order. First, participants discriminate between self (left) and other (right) with each item shown twice and in random order, thus in total twenty trials (block 1). Then participants were asked to discriminate between sick (left) and (health), also in twenty random trials (block 2). In blocks 3 and 4, participants were shown the combined two categories. Block 3 consisted of twenty practice trials and Block 4 consisted of forty critical trials. In block 5 participants were asked to discriminate again between health (left) and sick (right), but this time the categories switched sides (20 trials). In block 6 and 7, participants were shown the combined two categories again, with the self and health on the left, and other and sick on the right. Block 6 were 20 practice trials and block 7 were 40 critical trials. Category labels were displayed on the left and right sides of the window (and remained there during the complete block). Half of the participants followed the specified order described above (block 1 through block 7). The other half of the participants started with block 1, then block 5 through 7, followed by block 2 through 4. Thus, they first started with the self and healthy on the left side, and later switched to self and sick on the left side.

Positive evaluative conditioning task

This task was used, out of ethical considerations, at the end of the procedure to cancel out any possible negative effects of the first evaluative conditioning task, in which the self was paired with health complaints. In this task only the word “I” was paired with positive health words.

Procedure

Participants read the information sheet and began with the questionnaires, followed by a ten minute questionnaire about their study skills, to mask the goal of the experiment. Next, they moved on to the subliminal evaluative conditioning task. During the subliminal evaluative conditioning task, participants were asked to react as quickly as possible to the question whether a string of random letters starts with a vowel or not (the backward mask). The IAT began immediately after the conditioning task. The participants finished with the positive subliminal evaluative conditioning task where “I” was paired with good health words like vital, healthy and fit. In the end, the true nature of the experiment was revealed through a debriefing.

Results

Participants that were excluded were: with disease (n = 1), computer crashed during IAT (n = 1). A total of 26 participants remained for the analyses, with 14 participants in the “I”+illness group and 12 participants in the “X”+illness group. We used the im-

proved scoring algorithm of the D-measure as proposed by Greenwald et al., (2003) that uses the reaction times of the practice blocks 3 and 6 as well to analyze the IAT data. We used the D_1 measure in which trials with reaction times above 10,000 ms are discarded. This *D* measure also uses the reaction times of erroneous responses by adding the reaction time of the duration of correcting the response to the duration of the initial erroneous response (Greenwald et al., 2003; Nosek et al., 2005). The *D*-measure divides the difference between average reaction times between two blocks by the standard deviation of all the reaction times in the two test blocks and therefore adjusts for differences between means because of underlying variability (Greenwald et al., 2003). Data was checked for outliers (also within subject), homogeneity of variance and normality.

The average of the D_1-measure over the whole group was negative, which means that most participants seemed to have stronger associations of the self with healthy words compared to sickness related words (*M* =-.39, *SE* = .06). However, no significant difference was found between the "I" + illness group (*M* = -.43, *SE* = .08) and the "X" + illness group (*M* =-.35, *SE* = .09), $F_{(1,24)} = .52$, $p = .48$, $\mu_p^2 = .02$. As with study 1, we used stepwise regression analyses to select the two strongest predictors for the d'-measure to examine the difference of the adjusted means for the two groups. However, the adjusted means between the groups did not differ, $F_{(1,22)} = 1.11$, $p = .30$, $\mu_p^2 = .05$.

Discussion

The results of the second study did not support our second hypothesis that subliminal evaluative conditioning of illness with self-referent stimuli causes quicker reaction times of words related to illness and self on a subsequent implicit association task. This means that the subliminal evaluative conditioning technique used in our previous study did not create a stronger association between the self and illness.

GENERAL DISCUSSION

The current studies were carried out to test the validity of two priming methods to temporarily increase illness memory. These tests are important for at least two reasons. First, the outcome will help to determine whether our previous negative findings with these methods (Meerman et al., 2013) represent a true disconfirmation of the hypotheses that activated illness memory causes increased symptom reporting (Brosschot, 2002; Brown, 2004), or method failure instead. Second, the outcome can potentially have consequences for understanding prolonged behavioral effects of subliminal priming that have repeatedly been found in other areas, especially in social psychology (for example, Refs. Kiefer, 2002; Levy, 1996; Pierce & Lydon, 1998; Lowery et al., 2007). Thus, we examined whether subliminal priming with illness stimuli did indeed activate illness memory, using a lexical decision task (LDT). We also examined whether subliminal evaluative conditioning technique in which 'self' is associated with 'illness' actually showed the supposed manipulation effect, which is increased implicit

association between self-schema and illness-related schema using an implicit association task (IAT). The results of the first study showed that the subliminal priming technique did not result in significantly quicker responses on illness words on a LDT compared to neutral words. The second study showed that the subliminal evaluative conditioning technique did also not result in quicker reaction times for the word "I" in combination with illness related words in an IAT. Given that these tasks are standard tasks within psychological research to examine the cognitive phenomena in question; these findings lead us to conclude that these priming methods are unfit to increase illness memory or increase associations between the self and illness. This implies that our previous studies failed to find effects of these methods on symptom reporting (i.e. pain tolerance) do not falsify the hypothesis that activated illness memory can increase symptom reporting, since we it is unlikely that we have actually activated illness memory in the first place.

We set out using these widely used methods in our previous studies trusting that they would induce the supposed memory activation. That they do not do so is surprising given their broad use in psychology and the vast range of behavioral findings. This brings us to the second implication of our finding. Does the failure of these methods mean that the broadly published behavioral findings are not caused by activated memory? Is it possible that they lead to triggering behavioral programs on a lower, motoric level without having substantial effect on memory? It is perhaps too early to ask these questions. First, it is theoretically possible, though not likely, that the supposed memory effects may still be found for other content than illness related content. Second, it should be noted that this study was conducted in a small group sample. Nonetheless, these priming techniques should have a large and stable effect, and as mentioned, many studies have used the same techniques for manipulating various schemata and affect. Thus, again, the conclusion seems warranted that the use of the priming techniques as used in our studies as ell s these other studies was not, contrary to our expectations, manipulating illness-related schemata at all, at least not during the time frame in which the found behavioral effects are usually found.

In conclusion, our finding that subliminal priming and evaluative conditioning concerning illness information did not activate illness memory may reflect a more general failure to support priming as a basic phenomenon. We would like to stress that future studies using a priming technique, whether it is subliminal or supraliminal priming, should always include a manipulation check to ensure that the technique indeed resulted in the expected manipulation of memory.

Finally, and in a way sadly, the results of this current study imply that we have not yet adequately tested yet whether the hypothesis that illness-related cognitive memory network causes increased symptom reporting because the subliminal priming techniques did not temporarily activate the illness-related schemata. We derive some solace though from the fact that our studies contributes at least to a better understanding of the phenomena priming.

Appendix A. Prime words used in current study. English words are translated from Dutch prime words.

Neutral	Health Complaints
"bear"	"allergy"
"butterfly"	"asthma"
"seal"	"vomiting"
"giraffe"	"diarrhea"
"gorilla"	"flu"
"rhino"	"headache"
"panda"	"fever"
"turtle"	"heartburn"
"chimpanzee"	"inflammation"
"squirrel"	"wound"

Appendix B: Words used in the IAT

Self: eigen ("self"), ik ("I"), mezelf ("myself"), mijn ("mine"), zelf ("self").

Other: ander ("other"), hun ("them"), jullie ("you"), zij ("they"), zijzelf ("themselves").

Healthy: fit ("physically fit"), vitaal ("vigorous") , blakend ("healthy"), energiek ("energetic"), sterk ("strong").

Sick: onwel ("unwell"), beroerd ("nauseous"), kwaal ("ailment"), aandoening ("illness"), pijn ("pain").

Part II. The Explicit Measurement and Manipulation of Illness Schemata in Daily Life

Chapter 6 |

The Effects of a Positive Health Priming Intervention on Somatic Complaints

Meerman, E. E., Brosschot, J. F., & Verkuil, B. (2013). The effects of a positive health priming intervention on somatic complaints. *Psychology & health, 28*(2), 189-201.

ABSTRACT

Somatic complaints are common and form a major burden. Previous studies suggested that such complaints might be increased by 'illness-related memory', for example due to worries about health. In this ambulatory study we tested whether we could decrease somatic complaints through enhancing the activation of health-related memory by a 'positive health'-priming intervention. Forty-three students were randomly assigned to the 'positive health'-group or a control group. Using online measures, participants reported negative affect (NA) and somatic complaints for a period of six days, while each morning performing the priming task. The intervention caused a decrease in somatic complaints but only for participants with low trait NA or low somatosensory amplification.

These findings seem to suggest that priming or other interventions directed at activating positive health memory might reduce health complaints, but only in certain subgroups.

OBJECTIVE

Medically unexplained somatic complaints are complaints that cannot be attributed to organic pathology. They represent a common category of complaints in health care (Brown, 2004). At least one third of complaints in primary care are medically unexplained (e.g. 37% in Khan et al., 2003). In a survey from 2002, 96% of the individuals reported to have experienced at least one complaint in the last 30 days, with musculoskeletal pain, pseudo-neurological and gastrointestinal problems as the most reported complaints (Ihlebaek et al., 2002). Although many of these complaints are not serious and most people do not seek medical help for them, they are the most frequent reason for doctor visits and they account for a large number of long-term sickness compensation and permanent inability to work (Eriksen et al., 1998). Moreover, these somatic complaints and self-rated health (SRH) significantly predict mortality better compared to objective measurements of health (Idler & Benyamini, 1997; Sha et al., 2005). Importantly, MUS also occur in some people with medically 'explained' conditions, if the complaints are more severe than regarded as reasonable (Eriksen et al., 1998). In conclusion, it follows that if we could reduce the number of somatic complaints, it would not only benefit the individual's well-being, but it could also reduce our health care costs significantly because the number of unnecessary doctor visits would decrease.

Numerous theoretical models exist that try to explain the cause of somatic complaints without any organic pathology. Some have suggested that cognitive processes such as illness-related attention and illness-related memory networks can cause normal bodily signals to be perceived as a somatic complaint (Brosschot, 2002; Brown, 2004; Pennebaker, 1982b). Normally, people remain unaware of most bodily processes and signals. However, periodically some bodily signals and sensations are brought to our awareness due to changes in these cognitive processes (Pennebaker, 1982b).

With regard to attentional processes, several studies have linked reporting of somatic complaints to increased attention to bodily sensations or external cues related to illness (see, e.g. Barsky et al., 1988; Cioffi, 1991; Pennebaker, 1982b). Generally, people appear to report more somatic complaints when internal cues or bodily signals get more attention compared to external cues (Pennebaker, 1982b). Some people seem to report more complaints because they tend to amplify benign somatic sensations, and misattribute those to a serious illness (Somatosensory amplification theory, see Barsky et al., 1988). Attentional processes might on their turn be influenced by negative affect (NA). People with high NA tend to have more somatic complaints because they might focus more on internal physical sensations (Watson et al., 1988), possibly in conjunction with a heightened self-focus (the so called "joint impact hypothesis" see Gendolla, Abele, Andrei, Spurk, & Richter, 2005). This increased attention to bodily signals and illness information has been suggested to be caused by the (over-) activation of illness-related thoughts or (Brosschot, 2002; Brown, 2004; Rief & Barsky, 2005; Skelton & Strohmetz, 1990). Illness-related memory networks would

cause increased detection of and selective attention towards bodily signals, and increased interpretation and reporting of them as somatic complaints. The more trained and consolidated this memory network becomes, possibly because people keep on worrying about their health, the easier and more frequently it will be triggered by associated stimuli. In turn, it becomes more likely that bodily sensations are misinterpreted as signs of illness (Brosschot, 2002; Brown, 2004; Pincus & Morley, 2001).

While numerous studies have demonstrated an association of somatic complaints with selective attention (e.g. see studies in Kolk et al., 2002), only few studies have tested the association with illness related memory, or more specifically whether activation of an illness or pain related network in memory actually causes somatic complaints. A recent study found the expected association between severity of somatic complaints and SRH with a better memory for health-related information (Verkuil et al., 2007). In addition, a few studies that used a method called 'priming' to activate implicit memory networks, found indirect support for the theory that illness-related memory might cause participants to report more health complaints. Priming tasks are designed to investigate the influence of implicit (or unconscious) memory, without necessitating conscious retrieval processes as opposed to conventional memory measures (Crano & Brewer, 2002). Priming produces, for a certain amount of time, a level of activation or accessibility of a memory representation comparable to a chronic, long-term process (Bargh & Chartrand, 2000). For example, Skelton, and Strohmetz (1990) showed earlier that participants reported more (general) somatic complaints on a complaint checklist after they had performed a task in which they had to make comparative judgments about the meaning of health related words (Skelton & Strohmetz, 1990). This task presumably activated their illness memory. Others found that pictures illustrating physical suffering, which also presumably activate pain or illness memory, cause people to report lower pain tolerance and pain intensity (De Wied & Verbaten, 2001; Godinho et al., 2006). These effects could have been due to experimental demands created by a too evident presentation of illness information. However, in a recent study, this possibility was circumvented by presenting illness related words using subliminal priming, which is a common technique to activate cognitive memory networks without conscious awareness, by using stimuli that were not consciously perceived by the participants. This study found that subliminal priming with illness related words resulted in lower pain tolerance as well (Meerman et al., 2011).

Taken together, although most research has focused on increased attention and reporting of somatic complaints, it seems there is also evidence for activated illness memory being involved in the reporting of somatic complaints. As argued above, an activated illness memory might be crucial in the production of somatic complaints in that it determines attentional and interpretational processes. Two important questions arise: can an activated illness memory influence symptom complaints over the course of several days outside the laboratory? And can the effects of activated illness memories on health complaints be reversed by using a positive health priming intervention?

(In real life negatively influencing illness memory is unethical). In contrast to activated illness memory, activated positive health-related memory could hypothetically reduce complaints. Thus, our goal was to attempt to cause the positive health memory network to become more activated, which would result in less somatic complaints. We therefore, designed an intervention in which the memory networks of positive health were repeatedly primed during six days, and we tested whether it improved subjective health using a daily diary method. This study is thus an extension of the previous experimental study that found that subliminal illness-related words caused lower pain tolerance (Meerman et al., 2011), but the current study uses 'positive' priming instead, and real life measurements, to investigate the effect of changing illness-related memory networks on the reporting of somatic complaints. The intervention was delivered via internet. Our hypothesis was those participants who were primed with positive health words would report less, and less severe, somatic complaints and would have a higher SRH compared to participants that were primed with neutral words.

Because of the established role of negative affectivity, somatic amplification, and possibly health worry on the reporting of somatic complaints, we measured whether the intervention would be more effective in subgroups scoring high on these traits.

DESIGN

Participants

Students of Leiden University participated in this online study for either course credits or money (5 euro). The students could participate if they had a good internet connection at home, and if they were at least 16 years of age, native Dutch-speaking, and did not have any somatic illness, anxiety or depression. The ethics committee of the Psychology Department of Leiden University approved this study. The number of participants that agreed to participate in this study was 55. Participants who only filled in the baseline measures but did not complete at least one diary measure (n = 8) and participants that did not complete the baseline questionnaires (n = 4) were excluded from the analyses. So, a total of 43 participants remained for analyses.

Procedure

The study was registered over the internet. Participants were asked to read the informed consent and agree to participate. To mask the primary goal of the study (reducing somatic complaints via a priming task), we presented this study as having two different goals; the first goal was 'to examine the effect of sleep on certain cognitive tasks' (fake) and the second goal was 'to study the effect of worrying on health' (true). We did not explain the true primary goal of the experiment to prevent socially desirable responses. On the first day of the experiment, participants filled in the baseline measures and were randomly assigned to either the neutral or positive priming group. The next morning, just after waking up, the participants were requested to complete the morning measures (SRH see below) and they ended with the prim-

ing task. Then in the evening, before bedtime they filled in the first set of evening measures, which included our primary outcome measures (Somatic measures & PANAS, see below). After the evening measure on day 6, the participants received the link with an 'awareness questionnaire' (see below) and the debriefing. During the debriefing the actual goal of this study was explained and the participants were again asked for their permission to use their data.

Materials

Experimental manipulation: Positive health priming task

Positive versus neutral health priming was done in two ways: in the first four days by a scrambled sentence task, and in the last two days, another task was presented – reading newspaper stories – to prevent the subjects from getting weary or bored by the first task and to prevent the participants figuring out the purpose of the study. We presented the priming tasks to the participants as a cognitive task in order to prevent awareness of the priming.

Scrambled sentence task

A frequently used task to assess the influence of implicit memory processes is the scrambled sentence task. In this task, participants are fully aware of the priming stimuli, but they are unaware of the underlying concept that the experimenters are trying to investigate (which is also referred to as supraliminal priming). During the task, participants are told to make grammatically correct sentences out of a random string of words, and meanwhile they are being exposed to words related to the concept that the experimenter is trying to investigate. Afterwards, the effect of this implicit memory construct activated by the scrambled sentence task is assessed on a subsequent task (Crano & Brewer, 2002).

Our scrambled sentence task was an adapted version of a task used in a well-known study and has been used in many studies since (Srull & Wyer, 1979). The scrambled sentence task consisted of 15 sentences each, and each sentence consisted of five words in a scrambled order (Srull & Wyer, 1979). In the positive priming group, 10 out of the 15 sentences contained positive health words ('[physically] fit', 'healthy', 'in good health', 'lusty', 'energetic', 'still keen', 'strong', 'well', 'lively/ brisk', 'vigorous'). In the neutral priming group we used different words each day, for example 'computer', 'bicycle', 'important'. Every day a new version of the scrambled sentence task was given, however the 10 positive words remained the same across the different versions for the positive group. The participants were instructed to make a grammatically correct sentence with four of the five words.

News story task

During the last two days, participants were asked to read two stories that were used to prime them. For the positive health group, one of the two newspaper stories was

related to some positive health aspect (e.g. a new hotel focusing on health, or a story about wellness). The other newspaper stories were of a neutral content (such as finances). The participants were asked to read the newspaper stories and they were told that at the end of the study some questions would be asked about the stories. Stories have been used before in other studies to accomplish priming (see, e.g. Charash & McKay, 2002).

Awareness checks

In order to check whether the participants were indeed unaware of the priming procedure, we checked just before the debriefing whether the participants could accurately describe the goal of the experiment with a funneled debriefing questionnaire, which consisted of increasingly specific questions that were designed to probe for any suspicions regarding the scrambled sentence task and the newspaper stories and their purposes (Bargh & Chartrand, 2000).

Daily measures

Somatic health measures

Perceived health during our experiment was measured in two different ways; with a general question about perceived health and with a questionnaire about specific health complaints. Every evening the participants were asked to fill in the subjective health complaint (SHC) questionnaire (see below for a detailed description of the SHC questionnaire) concerning their complaints of that day (resulting in the variables: Number of SHC, SHC Severity). In addition, every morning and evening we measured general SRH at that moment (SRH morning/SRH evening) (Idler & Benyamini, 1997). Participants were asked to rate their current health with a number from 0–10, very poor to excellent.

State NA

We used both state and trait measures of NA. For the state daily measures, feelings 'of that day' were reported on the PANAS in the evening (see below for a description of the questionnaire).

Baseline measures

The following questionnaires were used to assess any imbalances in baseline characteristics across the two intervention groups.

Sociodemographics

We measured gender, age, body mass index, ethnicity, physical activities, usage of sleeping medication, pain killers or tranquilizers in the last 30 days, number of doctor visits in the last six months, smoking and drinking habits, drug use, medication use, illnesses, history of and current psychological problems.

Somatic health before the intervention

Specific SHCs were measured with the SHC Questionnaire (Eriksen et al., 1999). The SHC Questionnaire is a 29- item self-report questionnaire that reliably measures the number and severity of SHCs experienced in the normal population. Severity of each complaint is rated on a four-point scale (0–3). In this study, we used a slightly adapted version of the SHC that assessed complaints experienced during the last three days (baseline measure) or during the past day (daily measure) (Brosschot & Van der Doef, 2006). To create a baseline assessment of somatic complaints, we created the following variable: the sum of the number of health complaints experienced in the last three days (Number of SHC-3). The items about depression and anxiety were disregarded for our analyses, just like in our previous studies (Brosschot & Van der Doef, 2006; Verkuil, Brosschot, Meerman, & Thayer, 2012).

Health worry before the intervention

Complaint-specific worry was assessed by asking to what extent participants had been worrying about a complaint for each of the 29 complaints on the SHC Questionnaire. They indicated on four-point scale (0–3) how much they had worried about that specific complaint during the last three days. The sum of the number of complaints that participants had worried about (Number of SHC-3 Worries) was used as an index of the amount of health worry experienced before the intervention.

Trait NA

We assessed trait NA at baseline. The Dutch trait version of the Positive Affect and NA Schedule (PANAS) consists of 10 positive (positive affectivity) and 10 negative adjectives (NA). Participants indicate on a 5-point scale (1–5) the extent to which the items apply to how they generally feel in normal daily life. The reliability and construct validity of the PANAS have been documented (Engelen et al., 2006, Dutch translation; Watson et al., 1988). *Cronbach's a* in the present study for this entire questionnaire was 0.76, and for the subscales NA and PA it was 0.88 and 0.72, respectively.

Somatosensory Amplification

We used the Somatosensory Amplification Scale (SSAS) to measure the extent to which an individual is likely to report enhanced perception of physical signals (Barsky et al., 1988; Speckens, Spinhoven, Sloekers, Bolk, & Van Hemert, 1996). This scale comprises 10 items, yielding a total score range from 10 to 50. *Cronbach's a* for the present study was 0.79.

Data analysis

Data screening

Variables with skewed distributions were transformed, including the dependent variable Number of SHC, which was log transformed. If none of the transformations worked

to normalize the distributions of a variable, we used the transformed version, which were non-normal albeit, 'more normal' than the untransformed versions. Univariate outliers were identified as lower of higher than z-scores at the $p < 0.001$ value.

Data analyses

Baseline data were compared across the intervention and control group by using chisquare tests for binary data and simple t-tests for the continuous data. A two-level multilevel model using maximum likelihood technique assessed the effects of the intervention on somatic complaints, with the repeated measures nested within participants (the above described daily measures) as the first level and the between subject measures (the above described baseline measures) as the second level (Tabachnick & Fidell, 2007). The variable coding of the two experimental groups was considered a fixed predictor at the second level too rather than specifying it at an additional third level (Tabachnick & Fidell, 2007). The intra-class correlation (ICC) for Number of SHC was 0.61, showing that 61% of the variance was due to individual differences between participants, relative to differences within the participants, thereby providing evidence for a two-level hierarchical structure of the data. The ICC for the other dependent variables ranged from 0.26 to 0.71. We used a diagonal covariance structure for the repeated measures, since it resulted in the best fit. Next, we checked the random coefficients for the variable time of the following models: random intercept, random slope and random intercept and slope. We chose to work with the random intercept model, since this model showed the lowest Akaike Information Criterion (Tabachnick & Fidell, 2007). All independent variables were centered around their grand mean to make interpretation of the results easier. To test whether the positive priming intervention reduced health complaints, we looked at the intervention effects on both the number and severity of somatic complaints (Number of SHC and SHC Severity) and SRH. All analyses were performed with SPSS, version 17 (PASW). Two-tailed probability tests are reported with $\alpha = 0.05$.

Model building

The first step was to estimate fixed effects for the intervention groups on the measures of health (Hypothesis 1). We started with the model that included the terms for intervention group (2nd level), time (1st level) and group-by-time interaction. If the time effect or group-by-time interaction was significant, the response (linear trend) was more precisely examined by including the quadratic or cubic trend. If these were non-significant, they were removed again. The terms of interest were the main effect of intervention group and the group-by-time interaction. Because the factor type of priming (i.e. the embedded task in the first four days versus newspaper text in the last two days, see above) and the factor time highly correlated ($r = .81$), we decided to exclude priming type from the analyses to prevent multicollinearity (Tabachnick & Fidell, 2007).

RESULTS

Descriptives

The mean age of the participants was 22.27 years (SD = 5.66; range 18–50) and 88.8% was female. All baseline characteristics did not differ between the two groups, except for ethnicity. The intervention group had a significantly lower rate of Dutch ethnicity participants (80%) compared to the control group (100%) (Fisher's exact test, p =.031).

The diary method yielded 214 measurement occasions in the 43 participants. Participants experienced on average 2.82 complaints per day (SD = 2.77) with a mean of 1.03 (SD = 0.50) severity per complaint. The average health rating in the morning was 7.38 (SD = 1.32) and in the evening was 7.43 (SD = 1.26). The average level of experienced NA was 2.97 (SD = 4.01).

Awareness checks

None of the participants showed awareness of the priming procedure on the funneled awareness questionnaire.

Intervention effects on somatic complaints

The number of somatic complaints (Number of SHC) sharply decreased over the first three days and then slowly increased again (linear trend was significant originally, however became non significant after adding quadratic and cubic time trends; time quadratic trend, β = 0.138, p =.002, 95% CI: 0.053 to 0.222; time cubic trend, β = -0.261, p =.024, 95% CI: -0.487 to -0.035), but this was similar for both the intervention and the control group. Overall, the intervention group did not report less somatic complaints than the control group. The same results were found for SHC Severity. Controlling for the imbalance of ethnicity across the groups did not change these results. No significant changes over time or group differences were found for SRH in the evening.

Negative affectivity, somatic amplification and baseline complaints

We examined whether the intervention was effective for people scoring high on one of the following baseline variables; on SHC in the three days preceding the study (Number of SHC-3, M = 5.67, SD = 3.04), worries about these complaints (Number of SHC-3 Worries, M = 2.42, SD = 2.88), trait NA (M = 16.47, SD = 5.06) or on SSAS (M = 22.84, SD = 6.08). For simplicity, we checked for each of these factors one by one in different models by adding the main effect and interactions with group and time to the previously described models. These factors correlated only moderately (range of correlations 0.07–0.41), and were thus reasonably independent. As expected, the intervention effect on Number of SHC, but not SHC Severity or SRH, was affected by trait NA, SSAS and Number of SHC at baseline. More in detail, trait NA interacted significantly with intervention group ($F_{(1, 44.875)}$ = 5.832, p = .020), and it interacted significantly with the change over time per group (trait NA × time × group effect, $F_{(1, 102.236)}$ = 4.851, p =

.030). We used simple slope tests as illustration of the direction of this interaction. We found that for the participants with low trait NA scores ≤ 12 (n = 10) a difference started to show, with the intervention group having on average a lower number of health complaints compared to the control group (trait NA = 12, β = -0.063, p = .086, 95% CI: -0.136 to 0.009). This difference between intervention and control group got lower significance values with lower trait NA scores. For participants with high trait NA ≥ 21 (n = 5), the opposite effect started to show, with the intervention group showing more SHC compared to the control group (trait NA = 21, β = 0.066, p = .088, 95% CI: -0.010 to 0.141).

However, taking the factor time into account, we found differences for participants with a little less extreme trait NA scores (trait NA ≤ 13 and trait NA ≥ 19 versus the above mentioned trait NA ≤ 12 and trait NA ≥ 21). The interaction effect between NA and group was not found at the first couple of days, but started to first show at day 5. We found that at day 5 and day 6, the low trait NA group (trait NA ≤ 13, n = 14) showed (marginally) significantly less health complaints in the intervention versus control group (trait NA = 13, day 5, β = -0.065, p = .058, 95% CI: -0.002 to 0.132; day 6, β = -0.076, p = .039, 95% CI: 0.004 to 0.149). While the high trait NA group (trait NA ≥ 19, n = 14) started to show a marginal trend at the last day, which was the opposite: they showed marginally more health complaints in the intervention versus control group (trait NA = 19, day 6, β = 0.060, p = .091, 95% CI: -0.010 to 0.130). Figure 6-1 shows the intervention effect over days using a median split to create two groups based on NA (high and low). It should be noted that in this figure, using all participants, the differences seem to diminish at day 5. This was not the case for the simple slope analyses using the high and low scores.

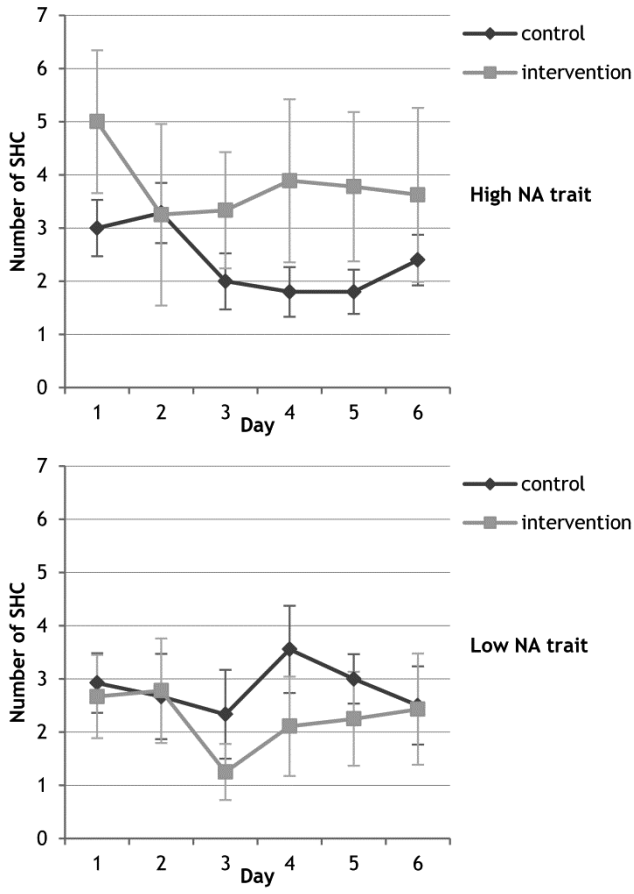

Figure 6-1. Group effects on the average daily number of subjective health complaints (SHC) for the lowest and highest 50% on trait negative affect (NA)
Error bars: +/- 1 SE

A similar interaction was also found between SSAS with group, albeit marginally significant ($F_{(1,\ 41.386)}$ = 3.769, p = .059). Although these interaction effects were significant with the continuous scale of SSAS over the whole group, we used simple slope tests with high and low values as illustration of the direction of this interaction. Further exploration revealed that the difference between the intervention and control group started to marginally show at SSAS ≤ 17 (n = 7) but this difference between intervention and control group got lower significance values with lower SSAS scores. Again contrary to the hypothesis – these participants with the lowest SSAS scores in the intervention group did show a marginal significant lower Number of SHC compared to the control group (β = -0.692, p = .092, 95% CI: -1.506 to 0.118). No difference in

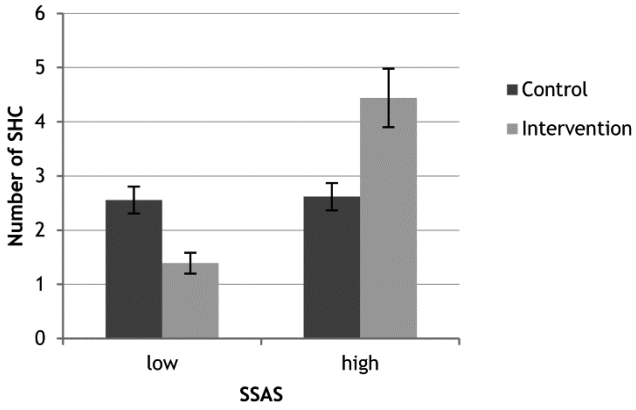

Figure 6-2. Group effects on the average daily number of subjective health complaints (SHC) per day for the lowest and highest 50% on the trait somatosensory amplification (SSAS) Error bars : +/- 1 SE

simple slopes between the intervention and control group were found for the participants with higher SSAS scores. Figure 6-2 shows the intervention effect over days using a median split to create two groups based on SSAS (high and low).

Finally, interactions were found between the variable Number of SHC-3 at baseline with group (marginally significant) and group × time (respectively, $F_{(1, 39.568)} = 4.005$, $p = .052$ and $F_{(1, 88.033)} = 5.978$, $p = .016$). Only in the intervention group, a significant effect of Number of SHC-3 at baseline on Number of SHC was found, starting at day 1: the higher Number of SHC-3 at baseline, the higher Number of SHC during the study ($\beta = 1.556$, $p = .000$, 95% CI: 0.816 to 2.296). The control group started to show the same effect of Number of SHC at day 3 ($\beta = 0.969$, $p = .014$, 95% CI: 0.198 to 1.741). This effect seemed to gradually become stronger.

Adjusting for the imbalance of ethnicity across the groups did not affect the above results with NA, SSAS and SHC-3.

Positive bias reporting or positive mood?

In order to determine whether the intervention effect found for the low trait NA group and low SSAS group was perhaps due to a general positive reporting bias or to positive mood induction, we also examined the effect of the intervention on the reported positive affect (PA) scores per day. No main effect of the intervention, or for the subgroups of SSAS were found on the PA scores. However, the intervention did show differences in the PA changes over time for the trait NA subgroups (group × time × trait NA, $F_{(1, 83.819)} = 4.107$, $p = .046$). Yet, further exploration of this interaction using

simple slope tests of the highest and lowest NA scores revealed no significant intervention effect for each day separately (thus the three-way interaction). Even if we used more the maximum and minimum NA scores, we could not find any significant differences, which suggest that this three-way interaction is likely due to chance.

CONCLUSION

In this study, we examined whether a positive health priming intervention has a beneficial effect on somatic complaints in daily life, supposedly by making positive health memory networks more active (Brown, 2004). We did not find an effect of the intervention on somatic complaints or SRH for the whole group, but analyses showed that participants with low negative affectivity had significantly less complaints over time in the intervention group compared to the control group. This effect appeared to diminish in the last two days of the study, during which the newspaper text task was used. The same effect seemed to appear for participants with low SSAS, although only marginally significant, but this effect was not significantly affected by time (or the second task). These results seem to suggest that for these 'less vulnerable' groups, the intervention – at least the embedded word type – might have had a beneficial effect. In participants high in trait NA, the intervention appeared to increase the number of complaints instead. No such difference was found for the high SSAS group, though. A possible explanation for this difference could be that high NA people associate any, even positive health-related primes with illness, because their illness memory network might be negatively biased. Thus, priming them with positive primes could, ironically, also activate negative memory instead, and even swing the balance in favour of the latter, or even prevent activation of a positive health memory network.

Another explanation for the increase in somatic complaints for the high NA people could be that repeatedly asking them about their somatic complaints actually served as a prime itself. As noted in the introduction, people with high NA generally report more somatic complaints and thus might have stronger illness-memory networks. Priming them with a health complaint questionnaire might make them more aware of symptoms, and therefore report more. This effect could have been more powerful than the positive health priming intervention. Taken together, the results seem to suggest that a 'positive health priming' intervention might work but only for people who do not automatically thwart the spread of activation of positive health information that is expected from the positive health primes, even when they are repeated during six morning sessions. Unfortunately, since low NA and low SASS have not generally been associated with increased somatic complaints, the beneficial intervention effect will be somewhat limited in practice. However, our study does show that with a simple priming intervention administered in daily life, we can influence how many somatic complaints people report, but only for people with low NA. A modified, more intense priming intervention might also work for the more vulnerable high NA and SASS-people.

On a critical note, our intervention study is based on the assumption that the priming task indeed caused an activation of positive health-related memory in the positive health group. However, we did not measure whether the priming task indeed showed such an effect on positive health-related memory. This priming method, which can be considered common practice in priming research, still leaves open the possibility that another mechanism was responsible for the decrease in somatic complaints. Future studies should therefore consider including (an ambulatory version of) a test of the activation of illness-related memory, such as a lexical decision task, although there is a danger that such a task may interfere with the priming itself.

A possible explanation for the reduction of health complaints found for the less vulnerable groups is that the positive priming might have caused a general positive reporting bias or an induction of positive mood, which caused the participants to report less somatic complaints. However, when we investigated whether these less vulnerable groups also showed higher positive mood ratings during the intervention, we could not find support for this alternative explanation.

In conclusion, this study found that an intervention based on enhancing the activation of health-related memory by a positive health priming task, did reduce somatic complaints but only in participants with low NA or with low SSAS. Although these findings generally correspond with the current theory concerning the role of activated illness memory, their practical use may still be somewhat limited since MUS is particularly prevalent among the very people for which the priming intervention does not seem to work (high NA and SSAS), and even has an reversed, unwanted effect for those high in NA. It seems important to address this problem before preventive and therapeutical practice can profit from positive priming techniques.

Chapter 7 |

The Role of Illness Memory in Symptom Reporting in Patients with Medically Unexplained Symptoms

Meerman, E. E., Brosschot, J. F., & Verkuil, B. (*Manuscript in Preparation*). The role of illness memory in symptom reporting in patients with medically unexplained symptoms.

ABSTRACT

Objective We investigated the role of illness-memory in symptom reporting in patients with medically unexplained symptoms (MUS). One hypothesis is that chronically activated memory networks of illness may lead to increased selective attention towards bodily signals, which causes increased detection and reporting of these signals as symptoms. We hypothesized that patients with MUS would show persistent (i.e. trait) activation of illness-related memory compared to healthy individuals. Moreover, we hypothesized that state illness-related memory predicts symptom reporting during the subsequent week.

Methods Seventy participants were included in this online unmatched case-control study. We administered a lexical decision task (LDT) to measure implicit illness-related memory bias over three non-consecutive days, during two weeks, in patients (n = 49) diagnosed with fibromyalgia, irritable bowel syndrome and/or chronic fatigue syndrome. We compared the results with a control group (n = 31).

Results We found that patients showed an implicit memory bias for illness stimuli compared to the healthy controls. However, this bias was not more stable in the patient group. We also did not find that illness-related memory was associated with the concurrent number of health complaints or health complaints in the next week.

Conclusions People with MUS have an implicit memory bias for illness stimuli, but we could not find support for the hypothesis that this memory bias is associated with heightened reporting of symptoms. Possibly, the trait variance of this bias will predict symptoms on the longer term. Implications of these findings for the cognitive model of symptom reporting are discussed.

INTRODUCTION

High levels of symptom reporting have been associated with sensitization, on the somatic perception level as well as the cognitive level. For example, there is evidence that people with fibromyalgia syndrome (FMS), irritable bowel syndrome (IBS) or chronic fatigue syndrome (CFS) report more symptoms during painful stimulation compared to healthy individuals. Several studies have found a lower pain tolerance in fibromyalgia (Diers et al., 2008; Staud et al., 2003), in IBS (Rodrigues et al., 2005) and in CFS after exercise (Whiteside, Hansen, & Chaudhuri, 2004). These findings have made some researchers to speculate that these pain reports in CFS, FMS and IBS might be the result of one common mechanism (Jackson, George, & Hinchey, 2009). In addition, lower pain tolerance has also been found in people with high numbers of common health complaints like headache (Verkuil et al., 2007), which might indicate that this is a common mechanism for the reporting of multiple health complaints in general.

Not only do patients with FMS, IBS or CFS report a lower pain tolerance, they also show increased cognitive processing of external information related to their health complaints, including pain (Afzal et al., 2006; González et al., 2010; Hou, Moss-Morris, Bradley, Peveler, & Mogg, 2008; Pincus & Morley, 2001). For example, several studies have linked the reporting of complaints in patients with MUS with increased cognitive processing of bodily sensations (Barsky et al., 1988; Cioffi, 1991; Kolk et al., 2002; L. C. Miller et al., 1981; Pennebaker & Lightner, 1980). Again, increased attention to illness-related stimuli and enhanced memory of such stimuli has not only been found in patients but also in healthy people with several common health complaints (Brown, 2004; Pincus & Morley, 2001; Verkuil et al., 2007).

In the past decade, a theoretical symptom perception model has been proposed that specifically describes how increased cognitive processing of illness-related information is related to enhanced symptom reporting (Brosschot, 2002; Brown, 2004). This model assumes that cognitive top-down processes change the relation between physiological bodily signals and the perception of physical symptoms. Chronic unconsciously activated memory networks of illness may lead to increased selective attention towards bodily signals, which causes increased detection of these signals and increased reporting of these signals as symptoms (Brosschot, 2002; Brown, 2004; Rief & Barsky, 2005). Brown (2004) has hypothesized that activation of such an illness-related memory network produces a vicious cycle, by increasing attention towards bodily sensations and increasing the perception of these signals as symptoms, which in turn reactivates this memory network. The more trained and consolidated this memory becomes the easier and more frequently it will be triggered by associated stimuli (Brown, 2004; Pincus & Morley, 2001). We (Meerman et al., 2011) have experimentally tested this cognitive model of symptom perception in healthy people and found that pain tolerance was involuntarily decreased by activating illness-related memory, but we could not confirm this finding in a subsequent replication study (Meerman et al.,

2012). Due to these inconsistent findings there is no evidence yet that illness memory increases symptom reporting, at least not in healthy people. There were, however, several limitations to these studies. First, the laboratory manipulation to activate illness-memory (subliminal semantic priming) might have been too subtle and not naturalistic enough. Second, the subjects in the studies were healthy, while it is possible that the expected memory effect is only manifested in people with excessive subjective health complaints. Therefore in the present study, instead of manipulating illness-memory, we measured it, using a standard technique, namely a lexical decision task (Meyer & Schvaneveldt, 1971), on three different days, with a week in between. Moreover, we tested people with excessive subjective heath complaints, and did so in their natural surroundings in daily life. We believe that by increasing the ecological validity of the study, and by using a high risk group as well repeated measurements with a standardized technique we provided a more stringent test of the hypothesis than in our laboratory studies.

Most studies assessing reaction times to measure a cognitive bias, such as interpretation bias, attention bias or -in the case of this study- a memory bias, use group means of single assessments to identify differences between groups. However, reaction times (RTs) are not highly reliable. That is, they may fluctuate over time, reflecting state variance as well as trait variance in responses. Single measurements therefore might not be sufficient to capture the stable (i.e. trait) performance that is thought to be characteristic of specific psychopathological patient groups (as discussed in: Kindt & Brosschot, 1998; Nosek & Banaji, 2005; Nosek, Greenwald, & Banaji, 2007; Stuss, Pogue, Buckle, & Bondar, 1994; Uhlmann et al., 2012). In order to be a risk factor for excessive health complaints, the implicit memory bias should be stable, i.e. trait-like, since the theory predicts that people suffering from MUS have a chronic activation of illness memory networks compared to the healthy people. Thus, although the activation of implicit memory networks for illness may fluctuate greatly over time, we tested whether this fluctuation is less for a MUS patient group, that is, whether they showed greater performance stability for the illness-LDT. At the same time, it is possible that the fluctuation in activated illness memory is associated with fluctuations in complaints and even predicts them, supporting the hypothesized notion of a causal relation.

Our main hypothesis was that CFS, IBS and FMS patients, who experience excessive symptoms in general, would show (a) higher activation of illness-related memory, manifested as faster reactions to categorizing illness words in a LDT, as compared to categorizing neutral control words. We also expected that (b) these patients would show high activation of illness memory with less fluctuation (i.e. more stable or chronic) compared to healthy individuals. This means that they were expected to show heightened activation of the illness-related memory network (or memory bias) at all three test days. In addition, we explored the following two hypotheses: namely, whether (c) in both groups the activation of illness-related memory network at a given day (i.e. short term activation), would be associated with increased reporting of

symptoms that same day. Finally, we expected that (d) an activated illness memory network could predict symptom reporting on subsequent days, one or two weeks later. Tests and questionnaires were administered through internet to enhance ecological validity.

METHODS

Subjects

Eighty subjects agreed to participate in this study. Participants for the patient group were diagnosed (self-reported) with either fibromyalgia (FMS), irritable bowel syndrome (IBS) and/or chronic fatigue syndrome (CFS). They were recruited via interest groups on social internet pages. The largest group consisted of patients with both FMS and IBS (*n* = 19), the next largest group consisted of patients only diagnosed with FMS (*n* = 16), then patients diagnosed with all three syndromes (*n* = 8), then patients with IBS and CFS (*n* = 3), then FMS and CFS (*n* = 2), then finally a patient diagnosed with IBS (*n* = 1). Participants for the control group had to be healthy and were recruited through student groups and their relatives. The participants did not receive money as a reward but we explained that with their participation, they would help us in understanding symptom reporting in FM, CFS and IBS. The medical ethics committee of the Leiden University Medical Centre (LUMC) approved this study.

Materials

Questionnaires

Health complaints

Specific subjective health complaints (SHCs) were measured with the SHC Questionnaire (Eriksen et al., 1999). The SHC Questionnaire is a 29-item self-report questionnaire that reliably measures the number and severity of SHCs experienced during the last 24 hours. It has five different areas of complaints as subscales; musculoskeletal pain, pseudoneurology, gastrointestinal problems, allergy, and flu. Severity of each complaint is rated on a 4-point scale (0-3). The total number of SHCs was used, abbreviated here SHC-1, -2 and -3 for the respective measurements. The internal consistency of the SHC questionnaire has been proved sufficient (Eriksen et al., 1999).

Memory task: Lexical decision task

A frequently used task to measure implicit memory is the Lexical Decision Task (LDT; Meyer & Schvaneveldt, 1971). This task is used to measure the implicit activation of cognitive schemata or memory networks (Aarts, Dijksterhuis, & Midden, 1999; Förster, Liberman, & Higgins, 2005; Koole, Smeets, van Knippenberg, & Dijksterhuis, 1999; Verkuil, Brosschot, de Beurs, & Thayer, 2009). The idea is that people are likely to recognize words belonging to a certain category faster if this category is more active in

memory compared to other categories. Participants were told that 80 words would appear on the screen, of which 40 words would be existing Dutch words and the other 40 would be nonsense words. For every word appearing on the screen they were asked to decide as fast and as accurately as possible whether the word was a meaningful word or a nonsense word. Responses were collected from the PC's keyboard. Participants were asked to press the key “q” for word and “p” for non-word. The participants were instructed to keep their fingers above the keys throughout the entire task to obtain maximum speed. The stimuli appeared at the same location on the screen, preceded by a row of asterisks for 200 ms, which served as a fixation point. The words remained on the screen until the participant had responded. Response latencies were measured in milliseconds from the onset of the word to until a button was pressed. The words were presented in random order, and were preceded by ten practice trials, so the participants could get used to the task.

We used 10 illness words related to CFS, IBS and FMS, 10 control words which are not related to illness, but also negatively charged (see Appendix) and 20 neutral words for distraction (e.g. eyes, art). The word categories did not differ in word frequency, word length and syllables. Faster reaction times (RTs) to illness words compared to negative control words were taken as evidence of higher activity of the memory network for illness.

The participants were instructed before every LDT to make sure nothing could distract them and to close any unnecessary computer programs, because that might influence the measurements of the reaction time tasks. The LDT was designed using the program called WebExp 2, version 1.1, which is a JAVA-based applet specifically designed by the University of Edinburgh to measure reaction times reliably over the internet (Keller, Gunasekharan, Mayo, & Corley, 2009).

The internal consistency of the average RTs (including all trials to calculate minimum reliability) to the illness words on the three individual LDTs was high, ranging from α = .833 to .927).

Distraction Task

The SHC was filled in after the LDT, to prevent priming participants’ illness memory by the reporting of symptoms. However, earlier research has showed that self-reports of physical symptom frequency also increased after making abstract decisions about health connotations of common words (Skelton & Strohmetz, 1990). This means that it was crucial in our study that we prevented any effects of the LDT on the symptom reports. Therefore we designed a distraction task, in which participants were shown fragments of number sequences, consisting of three to four numbers that were arranged in a logical order. Participants were asked to complete these fragments. This task kept the participants occupied and distracted them for several minutes, before they continued to fill in the symptom reports.

Procedure

Potential participants received an email with a link to the Informed consent form. After the participants agreed to the informed consent (online form with a checkbox), they could continue with the tasks and questionnaires. To ensure the privacy of the respondent, they were asked not to use their name but to use a personal code that they had to generate themselves, which was also used as a participant number. In this way, we remained unaware of the actual identity of the participants but we were still able to link the data of the various measurements with each other.

In order to see whether FMS, CFS, or IBS patients have a higher stable (i.e. trait) activity of their illness-related memory networks, we administered the LDT three times. To prevent any learning effects on this task, we employed a between test interval of seven days. Thus, the total study duration was two weeks. Every test day the participants completed the LDT, distraction task, the health complaint measures which were then followed by several trait and state questionnaires that were not used in the results of this paper. After the measurements on the last day, the participants were sent a debriefing and they were asked to answer some general questions about the study itself.

Data analyses

Data manipulation

Following previous LDT studies we removed the error latencies (Aarts et al., 1999; Förster et al., 2005; Koole et al., 1999). Error responses were minimal, with only 3.28% of the trials performed erroneously. We also excluded correct response latencies that were three standard deviations greater or less than the mean for each stimulus in each group (2.2%) (Förster et al., 2005). We used a log transformation for the RT's calculated within stimulus categories (illness vs control) as well as experimental groups (patients vs healthy controls). Homogeneity of variance was achieved. To transform the data back to its original scale for interpretation with it's appropriate confidence interval, we calculated the corresponding standard error for the untransformed data based on the standard error for the transformed data (Jørgensen & Pedersen, 1998). We also calculated an index for the difference in reaction time (LDTdiff) by subtracting the reaction times (RTs) of the negative control words from the illness words. Thus, the quicker the participants reacted to illness words (i.e lower RTs) in comparison to the control words (indexing higher illness-related memory activation), the more negative the LDTdiff. To correct for nonnormality this index was log transformed.

Hypotheses a, and b: To test the difference between the groups in activation of illness-related memory, we performed a multilevel analysis on the reaction times (RTs). Random intercepts were estimated for each subject and for the effects of word category (nested within-subjects) and measurement day (nested within-subjects). Restricted Maximum Likelihood (REML) estimation (which is the recommended type, especially for small data sets, when not testing pairs of nested models, see Tabachnick

& Fidell, 2007) and an unstructured covariance type were used. As recommended by Koole et al. (1999) we used both the RT for control words and the RT for illness words, in order to have a within-subject baseline to control for the great variability in speed of responding.

Hypotheses b, c and d: To examine the stability of illness-related memory and its temporal associations with SHC scores, we applied structural equation modeling (SEM). A cross-lagged panel design was employed based on the difference score between the RT for the control and illness words (LDTdiff). The SEM analyses were conducted with EQS 6.1 (Bentler & Wu, 2005). We used a cross-lagged analysis procedure which involved an iterative and subtractive procedure of model comparison (Martens & Haase, 2006; Tabachnick & Fidell, 2007).

First, a target model was specified that included (1) Autoregressive or stability paths (i.e., relations between repeated measures of the same variable at adjacent assessments, e.g., LDTdiff1→LDTdiff2. These paths provided information pertaining to the stability of illness memory; hypothesis b). The covariance between the error terms of the repeated measures of the same variable at adjacent assessments was not included otherwise the model would not converge. This target model also included (2) concurrent paths, specified as the covariance between the error terms of LDTdiff and SHC at the same assessment (e.g., LDTdiff2→SHC2; relevant for hypothesis c). The second step was to add the lagged or "antecedent-consequent" paths from LDTdiff at one assessment to SHC at the subsequent assessment (e.g., LDTdiff1→SHC2; hypothesis d) to examine whether this significantly improved the target model. The next step was to add the cross-lagged paths from SHC at one assessment to LDTdiff at the subsequent assessment (e.g.,SHC1→LDTdiff2) to the target model and examine whether this improved the model significantly. The final step was to add both lagged and cross-lagged paths and see whether this was a significant improvement compared to the previous model. Besides fitting an appropriate model for the effects of the previous measurements on its subsequent measurement, we also examined the second order effects of first wave measurements on the third wave measurements (e.g. LDT1→SHC3) to test whether illness memory predicted SHC after two weeks. To examine whether the groups differed with respect to the stability of illness-memory (hypothesis b), models were analyzed in a multigroup format, which allowed separate estimates of all paths in the patient and control group. After having determined the best-fitting model, we evaluated whether the groups differed on the stability paths with La Grange Multiplier constraints of group invariance.

Yuan Bentler chi-square tests were used to compare differences between the subsequent models (Bentler & Wu, 2005). In doing so, we used a scaling correction to calculate the differences between two scaled Yuan Bentler chi-square tests (Bentler & Wu, 2005; Tabachnick & Fidell, 2007). However, because the chi-square difference test has difficulty detecting differences when sample sizes are small, we selected the final model by also inspecting the Comparative Fit Index (CFI; cut-off >.95), the standardized root mean square residual (SRMR, cut-off< .08) and the root mean square

error of approximation (RMSEA; cut-off< .01). The parameters were estimated by full information maximum likelihood, which uses all of the observed data and is superior to traditional methods in handling missing data (Bentler & Wu, 2005) and we used robust estimation to deal with non-normal data because a Bonett-Woodward-Randall test indicated multivariate non-normality. Because of our explicit directional hypotheses we used one-tailed significance tests with an *a* of 5%.

RESULTS

Descriptives

Eighty subjects agreed to participate in this study, with 31 healthy subjects and 49 subjects diagnosed with either FM, and/or IBS and/or CFS (see methods). However, after we removed the participants that only filled in the baseline questionnaires, 78 participants remained for analyses, with 48 participants in the patient and 30 participants in the control group. The patient group scored significantly higher on the number of SHCs on day 1 (n = 48, M = 13.48, SD = 4.65) compared to the healthy control group (n = 30, M = 3.53, SD = 1.93, $t_{(68.00)}$ = 13.119, p < .001). The patient group also scored significantly higher on the number of SHCs on day 2 (n = 40, M = 12.05, SD = 5.33) compared to the healthy control group (n = 27, M = 2.81, SD = 2.83, $t_{(62.12)}$ = 9.205, p < .001). Finally, the patient group also scored significantly higher on the number of SHCs on day 3 (n = 37, M = 12.59, SD = 5.17) compared to the healthy control group (n = 26, M = 2.81, SD = 2.42, $t_{(54.33)}$ = 10.062, p < .001).

Difference in activated illness-memory between the patient and control group

There was significant variance in intercepts of RTs across participants and across different measurement days within participants (respectively, var(u_{0j}) = .003, Wald Z = 5.06, p < .001 & var(u_{0j}) = .001, Wald Z = 5.85, p < .001). There was no significant variance in RTs across the two different word categories within participants (var(u_{0j}) = .000, Wald Z = .395, p = *ns*.

Means and 95% confidence intervals of the RTs are presented in Fig. 1. Results of the MLA on these data showed that the participants' RTs decreased over time. The patient group (RT; *M* = 870.96, 95% CI = 836-907) was significantly slower compared to the healthy controls (*M* = 716.14, 95% CI = 681-753, see Table 7-1). Participants showed significantly faster reaction times for illness words (*M* = 772.68, 95% CI = 749-798) compared to the control words (*M* = 807.24, 95% CI = 782-833, see Table 7-1), and the interaction Word category × Group showed that this acceleration difference was larger for the patient group (*M* illness = 843,33, 95% CI = 810-862, *M* control = 897.43, 95% CI = 862-935, $t_{(75.224)}$ = 7.11, p < .001, r = .63) compared to the control group (*M* illness = 706.32, 95% CI = 672-742, *M* control = 724.44, 95% CI = 689-761, $t_{(74.544)}$=2.28, p = .03, r = .26, see Table 7-1; Figure 7-1). This is in congruence with our hypothesis a. In addition, we examined the average LDTdiff score per patient and control group using an independent t-test. This showed the same result: The patient group had a bigger LDTdiff score (*M* = -56.70, 95% CI = -39.10- -74.30) compared to the control group (*M* = -16.78, 95% CI = -2.70- -30.85, $t_{(78)}$ = -2.99, p = .004, r = .32).

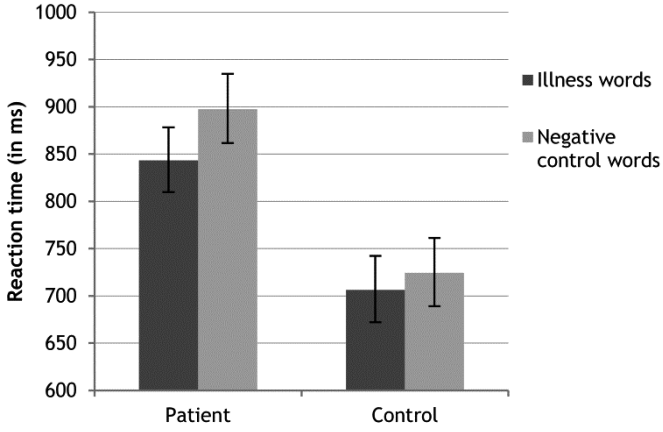

Figure 7-1. The estimated means of reaction times per group and per word category. (error bars display 95% confidence interval, data has been transformed back to original scale)

Table 7-1. Type III Tests of Fixed Effects of reaction times (log transformed)

Source	Num df	Den df	F	p	r
Intercept	1	79.826	178309.702	.000	
Day	2	132.408	9.750	.000***	
Word category	1	74.815	39.176	.000***	.586
Group	1	79.826	38.458	.000***	.570
Day × Group	2	132.408	.601	.550	
Day × Word category	2	141.351	.080	.923	
Word category × Group	1	74.815	7.438	.008**	.301
Day × Word category × Group	2	141.351	.062	.940	

***p < .001, **p < .01

Stability of illness memory bias and the prediction of the number of health complaints

A common way to examine stability of a test is to inspect the test-retest reliabilities. In this case the test-retest reliability of the mean response latencies to the illness category words (log transformed) was considerable, LDT1-LDT2, r = .62 & LDT2-LDT3, r = .79. However, test-retest reliability of the difference in mean latencies of the two word categories was low, LDTdiff1-LDTdiff2, r = -.05 & LDTdiff2-LDTdiff3, r = .20, even if we calculated the test-retest reliabilities separately for the patient group (LDTdiff1-LDTdiff2, r = .19 & LDTdiff2-LDTdiff3, r = -.24) and the health control group (LDTdiff1-LDTdiff2, r = .20 & LDTdiff2-LDTdiff3, r = .26). However, the low test-retest reliabilities are confounded with error, and the best way to look at stability is with a latent variable approach in which measurement error is separated from stability measurements as done below (as discussed in Cunningham, Preacher, & Banaji, 2001). To examine the stability of the memory bias for illness words in the patient and control group and its relationship between the number of health complaints we used structural equation modeling.

Model comparisons

Stability of the LDTdiff index, and its associations with the number of SHCs of the three days (square root transformed) were examined using cross-lagged panel analysis. The results of the model comparison tests are presented in Table 7-2.

The Y-Bχ^2 test of overall model fit was not significant for all models; however, as this test is highly influenced by sample size, preference is typically given to the CFI, RMSEA and SRMR in characterizing model fit (Tabachnick & Fidell, 2007). Using the previously described cut-off scores on these indices, we selected the fully cross lagged

model (model 4) as our final model to examine whether LTDdiff predicted SHCs one week later (e.g, LDT1→SHC2, or SHC2→LDT3). The RMSEA was not below .10 but this might be because the RMSEA has been found to have larger values in small samples (Tabachnick & Fidell, 2007). We then continued with examining the second order effects (i.e. whether LTDdiff predicted SHCs two week later; Table 7-2). Adding the predicting path of LDT1→SHC3 in model 5 seemed to change the values of our selection criteria, so that all three criteria were satisfied. The same applies to model 7. However, we chose model 5 to continue with our analysis, since this model was the more parsimonious compared to model 7 (higher number of degrees of freedom). Next, we examined whether the path parameters in the model were significantly different among the patient versus control group by setting constraints on the parameters. We tested these paths in five stages: (a) stability coefficients, (b) concurrent paths, (c) cross lagged path coefficients, (d) lagged paths, and (e) cross lagged second order path. At every stage, significant constraints were freed before proceeding to the next stage. Tests of the constraints are provided in Table 7-3. Figure 7-2 shows the final model, with the parameters that did not significantly differ among the two groups set to be similar.

Table 7-2. Summary of Cross-Lagged Panel Design Models

Model	Model Yuan Bentler χ^2	df	p	Robust RMSEA (<.10)	Robust CFI (>.95)	SRMR (<.08)	Δ Scaled Yuan Bentler χ^2	Δ df	p
First order models									
1. Autoregressive (LDT1→LDT2, and SHC1→SHC2 etc;	21.31	16	.167	.125	.921	.122	160.47	14	< .001
2. Cross-lagged (LDT→ SHC)	14.37	12	.278	.107	.957	.112	8.03	4	< .1
3. Lagged (SHC → LDT)	17.13	12	.145	.133	.933	.088	3.70	4	ns
4. Fully cross-lagged (LDT→SHC & SHC→LDT)	9.84	8	.277	.111	.969	.062	12.21	8	ns
Second order models									
5. Fully cross-lagged + second order crosslag (LDT1→ SHC3)	5.33	6	.502	.058	.994	.054	17.94	10	< .1
6. Fully cross-lagged + second order lag (SHC1 → LDT3)	7.99	6	.239	.121	.972	.059	13.32	10	ns
7. Fully cross-lagged second order	3.80	4	.433	.068	.994	.050	19.32	12	< .1
Model with added constraints (see table 7-3)									
8. Model 5 with constraints of path parameters equality between groups	11.78	14	.624	.014	.999	.113	25.57	2	< .001

SHC=Subjective health complaints; LDT=Lexical Decision Task; RMSEA= root mean square error of approximation; CFI= Comparative Fit Index; SMR= standardized root mean square residual

Table 7-3. LaGrange constraints and tests of group invariance.

Constraint	LaGrange χ^2 (*df*=1 for all)	*p*
1. Stability paths		
LDTdiff1→LDTdiff2	0.022	.881
LDTdiff2→LDTdiff3	12.102	.001***
SHC1→SHC2	1.798	.180[a]
SHC2→SHC3	0.083	.773[a]
2. Concurrent paths		
LDTdiff1←→SHC1	5.624	.018*
LDTdiff2←→SHC2	1.528	.216
LDTdiff3←→SHC3	0.424	.515
3. Cross-lagged paths		
LDTdiff1→SHC2	5.806	.016*[a]
LDTdiff2→SHC3	0.008	.927[a]
4. Lagged paths		
SHC1→LDTdiff2	8.710	.003**
SHC2→LDTdiff3	0.761	.383
5. Cross-lagged second order		
LDTdiff1→SHC3	2.683	.101[a]

[a]Based on non-robust La grange multiplier test, since robust test could not be computed due to numerical error. ***p* < .01, **p* < .05

Stability of memory bias

There was a moderately significant positive association between LDTdiff1 and LDTdiff2 in both the patient and control group. However, the association between LDTdiff2 and LDTdiff3 differed significantly between the patient and control group when controlling for all other variables in the model. The control group showed a moderately significant positive association between LDTdiff2 and LDTdiff3. On the other hand, the patient group showed a significantly negative association between LDTdiff2 and LDTdiff3. Overall, this seems to indicate that the patient group has less stability in the accessibility of illness-related memory networks compared to the healthy group, which is contrary to our hypothesis.

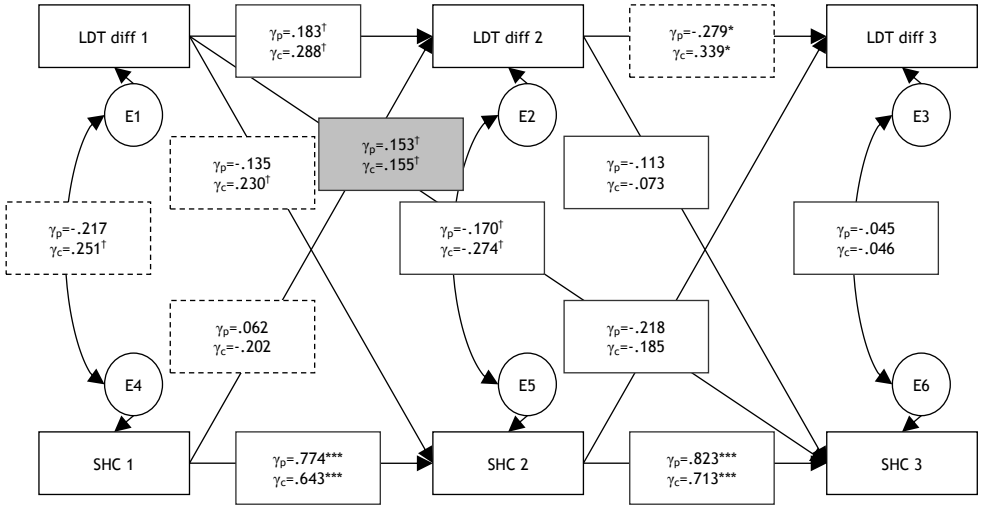

Figure 7-2. Model 8 with path parameters for each group (control versus patient) and non-significant parameters set to be similar among the two groups. The path parameters that are in a box with a dashed line are significantly differed between the patient and control group. †p < .05 (one-tailed), *p < .05(two-tailed), ***p < .001 (two-tailed). No change scores between the different days were used in the model, only the observed scores per day. γ_p=path parameter of patient group, γ_c=path parameter of control group. Shaded box is the path parameter from LDT diff 1 → SHC 3. LDTdiff was log transformed and SHC was square root transformed

Associations between illness-memory and somatic health complaints

We first examined the relations between LDTdiff and concurrent SHCs (hypothesis c). A marginal significant negative association was found between LDTdiff and SHC, but only during measurement 2. This association indicated that larger illness-memory bias was associated with more SHCs. Yet, this association was not apparent at the other two time points. What's more, the association between LDTdiff and SHCs differed between the groups at measurement 1 (see Table 7-3).The control group showed a marginal significant positive association between LDTdiff1 and SHC1, such that greater illness-related memory activation for illness words was related to less SHC at measurement 1.

Next, the temporal associations (hypothesis d) were explored. In both groups SHCs were most strongly predicted by SHCs at the previous assessment. A group difference was apparent for the association between LDTdiff1 and SHC2. Only in the control group there was a marginal positive association, which is in contrast with our hypothesis, i.e, greater illness-related memory activation for illness words was related to less SHC at measurement 2. Furthermore, a marginal significant positive association was found between the LDTdiff1 and SHC3 for both groups. Contrary to the hypothesis, a greater implicit memory bias for illness words on measurement 1 seemed to be related with less SHC at measurement 3.

DISCUSSION

The purpose of this study was to examine whether FM, IBS and CFS patients showed a high chronic activation of illness memory compared to healthy controls. In addition, we explored whether an implicit memory bias was predictive of the reporting of somatic symptoms.

We indeed found that patients showed a stronger implicit memory bias for illness stimuli compared to the healthy controls. This result complements studies that found enhanced attentional bias for illness information in these patients (Afzal et al., 2006; Hou et al., 2008; Pincus & Morley, 2001) and supports the idea that increased activity of illness memory networks underlies these findings. The healthy controls in our study also showed an implicit memory bias for illness stimuli, although this bias was less strong than in the patient group. Thus, this study is the first to find clear evidence of enhanced illness-related *memory* activation in patients suffering from medically unexplained syndromes. However, contrary to our expectations, we did not find that this memory bias was more stable in the patients when compared to the healthy control group. Although we found that the internal consistency and retest reliability of illness RT latencies was high on each assessment, the test-retest correlations between the successive assessments of the difference in LDT (LDTdiff) scores for the illness versus neutral words was low. Thus, although MUS patients – as a group - showed a larger illness-memory bias than controls on each of the measurement days, the patients still showed considerable individual variation in illness-memory from week to week. This seems to indicate that this measure of activation of illness memory might for a considerable part tap state variance rather than trait variance (as discussed in: Kindt & Brosschot, 1998; Nosek et al., 2005, 2007; Stuss et al., 1994; Uhlmann et al., 2012).

Interestingly, although the proposed cognitive factor of the theoretical model that was tested did not show much stability, the health complaints showed great stability. Using cross-lagged panel analysis we examined whether these health complaints were associated with the implicit memory bias for illness. However, we found no support for this hypothesis which forms a crucial aspect of the cognitive model of symptom reporting. Although the predicted concurrent relation between illness memory and SHC was found, this was only on the second day. Moreover, we only found evidence for predictive associations in the opposite direction. Thus, a greater implicit illness memory bias was related to less number of health complaints in the control group a week later, and even two weeks later in both groups. It is an interesting finding that only the first implicit memory measurement showed any significant predictions and not the second measurement. This might suggest that the first measurement of implicit memory is the most valid one, and later measurements might be more influenced by learning effects and thus less reliable. Although this seems questionable since we did find the predicted concurrent relation between SHC and LDT measurement on measurement 2. Another possibility is that we simply used an inadequate time window frame. Perhaps, an

implicit illness-related memory bias has a phasic (state) effect on symptom reporting that acts sooner than a one-week time frame. Future studies might more specifically examine the temporal association between illness-related memory and SHC using more measurements, for example every day, or multiple times per week, to see which time frame window is best suited. However, this has also more practical implications compared to the current study, such as much stronger learning effects. An alternative possibility is that the time frame is in fact too brief, and that the effects of overactivated illness memory take longer and act in a more tonic, trait-like fashion over many months, to produce medically unexplained symptoms.

There are some other limitations of the study. One is that there might have been a selection bias in the healthy controls since they were aware that we were investigating health complaints (although not the relation between the reaction time tasks and SHC). Furthermore, we relied on the self-reported illnesses of fibromyalgia, irritable bowel syndrome and chronic fatigue syndrome, which could be less reliable than if we have used official doctor's records. In addition, one obvious limitation of conducting this study online is that the circumstances under which the LDT was being administered were not standardized and this could have introduced noise in the data. For example, when doing the LDT participants have to remember which keys on the keyboard correspond to a yes ('word') answer and which key corresponds to a no ('non-word) answer. Although these key instructions were continuously presented on the screen, it still could have influenced the reaction times if participants had to look at these instructions every time they made a response. Although error rates were low, we might have gotten different results if we have used a simpler version of the lexical decision task, which is adapted after the go/no go task (pushing a button after words only). Preliminary work suggests that this version yields more reliable results compared to the version that we used (as discussed in Borkenau, Paelecke, & Yu, 2009).

In short, this study suggests that people with chronic health complaints, like fibromyalgia, chronic fatigue and irritable bowel symptoms, have a stronger implicit memory bias for illness-related information. This finding offers support for the notion of role of illness-memory networks in symptom reporting as proposed by cognitive models on symptom perception (Brosschot, 2002; Brown, 2004). However, we could not find support for the idea that single-moment measures of memory bias causes people to report more symptoms during the brief time period (3 weeks) of this study, or that MUS patients show a more chronic memory bias for illness. Therefore, the alternative explanation for the enhanced illness memory bias in MUS patients remains possible, namely that MUS-sufferers' illness memory is activated because they feel ill. Future studies should try to further explore the distinctions between the state and trait variance of implicit memory bias measures, since this might lead to important new insights into the temporal aspect of the possible effect of illness-related cognitive memory networks on the reporting of symptoms.

Appendix. Overview of words used per category for the lexical decision task. English words are translated from Dutch words.

Complaint words	Negative control group
"Exhausted"	"Repulsive"
"Tiredness"	"Mean"
"Diarrhea"	"Vulgar"
"Stomach pain"	"Coward"
"Cramp"	"Heartless"
"Nauseous"	"Fake"
"Muscle pain"	"Tactless"
"Stiff"	"Impertinent"
"Joint pain"	"Antisocial"
"Neck pain"	"Cruel"

Chapter 8 |

Summary and General Discussion

Medically unexplained symptoms (MUSs) are a humanitarian and economic burden. Among them, pain complaints without organic pathology are the most prevalent. For many years, researchers have tried to answer the question how it is possible that people can have somatic complaints without any medical explanation. Early theoretical models on dissociation, conversion and somatization have contributed to the understanding of MUS (Brown, 2004). But their assumption that psychological distress like anxiety or depression, is the cause of unexplained symptoms is often not true (Brown, 2004). Later theoretical models on MUS were influenced by principles of cognitive psychology. The earliest cognitive models on this topic focused on increased self-focused attention to bodily signals (Barsky & Wyshak, 1990; Cioffi & Holloway, 1993; Cioffi, 1991; Kolk et al., 2002; L. C. Miller et al., 1981; Pennebaker, 1982b), while later models focused more on activated illness-related cognitive networks that causes this increase in attention (Brown, 2004; Leventhal et al., 1992; Skelton & Strohmetz, 1990). Furthermore, it has been suggested that increased attention and memory bias towards bodily sensations and other illness information, could result in increased symptom reporting by causing normal bodily sensations to become intolerable (referred to as physiological sensitization) (Brosschot, 2002).

The main aim of this thesis was to examine the possible causal role of illness-related memory or schemata in increased symptom reporting. Several studies have found that increased accessibility of health-related cognitive networks are related to increased symptom reporting. However, only a few studies have examined this relationship experimentally to determine its causality. Of those studies, most used 'explicit' techniques to manipulate the accessibility of cognitive networks, that is, techniques in which the stimuli were salient and noticeable to the participants. This may have caused them to guess the goal of the study and caused them to behave in unintended ways, for example in a cooperative or otherwise socially desirable way, which may have biased the results, often in favor of the hypothesis that increased cognitive accessibility of illness-related networks causes increased symptom reporting. In this thesis, I have used different manipulation techniques to manipulate the cognitive schemata related to illness more directly by leaving the participants unaware of the study's aim, and thus allowing an unbiased way of testing of this hypothesis. In the following section, I will provide an overview of the findings and conclusions of our studies described in chapter 2 to chapter 7.

OVERVIEW OF FINDINGS

In the first part of this thesis, the hypothesized effect of implicit illness-related memory on symptom reporting was examined in the laboratory. We used subliminal priming techniques in which stimuli ("primes") are shown under the awareness threshold, and this assumingly activates the implicit memory of the associated category. We then looked at whether an activated implicit memory network of illness would indeed cause more symptom reporting. In the first three studies we used low pain tolerance as a measure of symptom reporting since pain complaints are the most common.

In **Chapter 2**, we found that participants who were subliminally primed with health complaint words reported lower pain tolerance compared to participants who were primed with neutral words. This implies evidence for our hypothesis that activated illness-related memory causes, at least partly, increased symptom reporting. In **Chapter 3**, we attempted to replicate these results with some improvements to the research design. More in detail, we left out specific prime words concerning serious medical conditions that were judged less than optimally representative of common illness. We also tested whether administering health-related questionnaires before priming with health-complaint words (as was done in the first study) could account for the effect found, because it might have acted as an unintended prime. No interaction-effect was found between the timing of the health-related questionnaires and prime type. In addition, we could not replicate the priming effect of health words on pain tolerance. Therefore the results either did not support the activated illness-related memory model or suggest that illness memory networks only affect symptom reporting if seriously threatening primes are used. Because we found two conflicting results in the first two studies, in the next study we tried a somewhat different approach in manipulating illness-related memory networks. In **Chapter 4**, the relationship between implicit illness-related memory and self-schemata was experimentally manipulated in order to induce a stronger association between the two (using subliminal evaluative conditioning), and then examined the effect of this manipulation on pain tolerance. The rationale was that illness-related memory would be more likely to influence reporting of complaints when its activation is enmeshed with that of self-related memory. In addition, we examined whether habitual self-focused attention (trait-SFA) acted as a moderator of this effect. However, participants primed with the self-referent "I" and health complaint words did not demonstrate the expected lower pain tolerance. Unexpectedly, trait-SFA acted as a moderator of the main effect of the self-prime: priming with "I" resulted in increased pain tolerance in participants with low trait-SFA. This study again did not support the hypothesis that associations between activated self-related memory and illness-related memory cause increased reporting of complaints. Instead, activating self-related memory increased pain tolerance in participants with low trait-SFA. One interesting possible interpretation was that the self-prime causes a temporal increase in *state*-SFA, or perhaps self-confidence, in those for whom trait-SFA was low, which in fact suggests possible new ways to promote adaptive coping with pain.

Because we could not find hard evidence for the hypothesized role of illness memory in causing an increase in symptom reporting, we concluded that this could mean two things: 1) the hypothesized effect of illness memory on symptom reporting does not exist, at least not in the laboratory, or 2) the methods used in part 1 were not effective in manipulating illness-related memory network in the way that we wanted to. To rule out the second alternative explanation, we conducted a study in which we investigated whether the priming methods were indeed sufficiently adequate in manipulating the illness memory networks. Because, if our methods were insuffi-

cient, this would mean that we were not able to draw strong conclusions about the tenability of the illness memory activation model. **Chapter 5** presents the results of this study in which we looked at whether the subliminal priming techniques in the first three studies actually did increase the accessibility of illness-related cognitive networks, that is, after priming with illness related words. This was done using a lexical decision task, which is a standard test to measure spreading of activation across specified memory content. We found that subliminal illness primes did not cause a significantly quicker reaction time for illness words on the subsequent lexical decision task. This seems to indicate that the subliminal priming paradigm used in this and our previous studies was not effective in activating illness-related cognitive memory networks, at least not for the time frame of several minutes used in this study and our earlier studies. In the second part of the study we attempted to validate whether the subliminal evaluative conditioning (used in chapter 4) was effective in creating an increased association between the self and another concept. The results of this part of the study were also negative and showed that the subliminal evaluative conditioning was not effective in creating stronger associations between illness and the self-schema. The overall result of this study shows that we did not effectively manipulate illness memory networks in the way we assumed we did in the first three studies, and thus not yet employed an appropriate test to examine the hypothesis that illness-related memory causes increased symptom reporting.

In the second part of the thesis, I took on a different approach in examining the association between illness memory and symptom reporting. First, because of our previous study that showed that the subliminal (unconscious) manipulations of illness-schemata were ineffective, we examined directly the association between the illness-related memory and symptom reporting in normal daily life, by manipulating and measuring illness-related memory in a conscious way instead of using subliminal priming techniques. In **Chapter 6**, the effects of a randomized controlled trial using an online intervention focused on activating a positive health memory network and determining its effect on symptom reporting was examined in healthy students. The intervention caused a decrease in somatic complaints but only for participants with low trait NA or low somatosensory amplification. These findings suggest that priming or other interventions directed at activating positive health memory might reduce health complaints, but only in certain subgroups. It lead us to speculate that participants with high NA or somatosensory amplification might perceive even positive health-related information in a negative way that fits their illness-related memory network, with the result that it did not decrease their health complaints.

Using yet another approach to test the illness memory activation hypothesis, **Chapter 7** presents the results of a study that examined the cross-sectional and temporal relationships between implicit illness-related memory and symptom reporting among patients with fibromyalgia, irritable bowel syndrome and/or chronic fatigue syndrome. The rationale was that if any population would show activated illness memory, and even persistently so, it would be patients with relatively severe medically unexplained

symptoms (MUS). We found that patients showed a stronger implicit memory bias for illness stimuli compared to the healthy controls, although the latter showed a similar memory bias. However, this bias was not more stable in the patient group. We also did not find that illness-related memory was associated with the concurrent number of health complaints or health complaints in the next week. Thus, people with MUS have an implicit memory bias for illness stimuli, but we could not find support for the hypothesis that this memory bias is temporally associated with heightened reporting of symptoms, at least not across a time span of one week. Possibly, the trait variance of this bias will predict symptoms on the longer term.

IMPLICATIONS OF FINDINGS

Theory of increased accessibility of illness memory causing increased symptom reporting

We found little evidence for the causal role of illness-related schemata in symptom reporting. Even though our laboratory-based priming studies, using pain tolerance as a model for symptom reporting, were not successful in examining the causality of an illness-schemata – symptom reporting association, our real life studies that used different methods and also tested cross-sectional relationships, found some modest but still partial support for the model. We found that MUS patients show a stronger implicit memory bias, but our findings – albeit limited to a one-week interval - did not provide any evidence for causality. Obviously, the result found in chapter 7 that patients showed a bigger or stronger implicit memory bias for illness stimuli compared to the healthy controls, could be the result of having more symptoms which increases the accessibility of illness-related information in cognitive schemata, which then causes them to detect illness-related words quicker compared to healthy controls. However, it is still possible that illness-related cognitive constructs might cause increased symptom reporting, which eventually leads to the development of MUS. This would be a possible effect on the long term, since we did not find any support of short term (i.e. one-week) increased accessibility preceding more symptom reporting. Another possibility is that this effect is only present on the short term, for example within several hours or a couple of days, instead of a week.

On the other hand, the results from our fourth study (chapter 6) seem to imply that it is possible that illness-related schemata might play a causal role in symptom reporting, since we found that a 'positive health priming' intervention reduced symptoms, but only for people with low trait negative affect or low somatosensory amplification, and thus perhaps for all people who might not automatically link the spread of activation of positive health information to negative health information. Although of potential interest, this finding is not yet of immediate clinical importance, since people that score low on these traits are not the ones showing the highest symptom reporting. It is possible that more intense positive priming may also decrease symptom reporting in

high NA and somatosensory amplification groups. First, however, replication studies are clearly needed to examine whether this effect holds strong in future studies.

On a side note, it is important to realize that both healthy controls and patients with MUS showed increased implicit memory for illness-related stimuli (although the MUS groups showed the largest effect). A recent meta-analysis found a similar result for attentional bias to pain-related information in chronic pain patients versus healthy volunteers. Interestingly, they found that overall both groups showed an attentional bias for pain-related information and the groups did not differ in the strength of this bias (Crombez, Van Ryckeghem, Eccleston, & Van Damme, 2013) This might be due to people showing an implicit memory bias to negative information in general. Humans give more priority to signals indicating danger, which is a results of our evolution in which, it was of great importance to be aware of immediate surrounding danger. This has resulted in a tendency to have a greater accessibility of possible threat in cognitive constructs. This could therefore serve as an explanation for why both healthy populations as MUS patients showed an implicit memory bias to illness-related information. An alternative explanation is that our study was focused on health, which involved multiple administering symptom inventory questionnaires, which on themselves could have made the illness-construct more accessible as well. Thus, future studies with a large number of participants should try to replicate our findings to see whether our result holds.

Implications for priming research in general

During carrying out the validation study testing the effectiveness of subliminal priming and evaluative conditioning, it became slowly clear - because of concurrent publications - that we were not the first to discredit the effects of subliminal priming. Recently, the journal *Nature* posted a letter of the psychologist and Nobel-prize winner Daniel Kahneman that he wrote to his colleagues in the field of psychology that have used priming in their studies (Yong, 2012). In this letter, he urges his colleagues to replicate classic priming studies in the social psychology. Although Kahneman is a 'strong believer' of the priming effect (he wrote a book about the importance of priming research in the study of associative memory), he started to seriously worry when it came out that well known researchers have simulated data (such as the Dutch ex-professor Diederik Stapel), and when failed attempts to replicate classic priming studies (Doyen, Klein, Pichon, & Cleeremans, 2012) and concerns about replicability in psychology in general started to be uttered in the literature.

Our finding that subliminal priming and evaluative conditioning concerning illness information did not activate illness memory may reflect a more general failure to support priming as a basic psychological technique to subliminally activate memory and influence behavior. We would like to stress that future studies using a priming technique, whether it is subliminal or supraliminal priming, should always include a manipulation check to ensure that the technique indeed resulted in the expected manipulation of memory.

Treatment of MUS

Cognitive-behavioral treatment (CBT) is the best established therapy for treating MUS, however, other kinds of therapies such as antidepressants and providing a psychiatric consultation letter to the primary care provider, have also shown to be beneficial (Deary et al., 2007; Kroenke, 2007). In addition, it is uncertain what the key working elements are in CBT. There are types of therapy that are based on the main concept of this dissertation, namely activated memory networks or schemata. For example, schema-focused therapy is a more recently developed type of cognitive therapy in which maladaptive cognitive schema's of the patient are being challenged (Young, Klosko, & Weishaar, 2003). This type of therapy is currently being used in personality disorders. However, if future studies do find evidence for a causal relationship between illness-related memory networks or schemata and symptom reporting, MUS-specific schema-focused therapy might be a possible effective therapy for reducing symptoms.

STRENGTHS OF THE STUDIES

One of the strengths of this thesis is that I have attempted, in several ways, to answer the cause-and-effect question of implicit illness memory and symptom reporting. Most of the studies that have examined this relationship have used correlational designs that cannot answer the causality. The theoretical models discussed in the introduction of this thesis all assume that it is either increased hypervigilance or attention for bodily signals or increased accessibility of health constructs in the mind that causes increased symptom reporting, both in populations with medically unexplained symptoms as well as in the relatively healthy populations with common subjective health complaints. For an obvious reason, these models easily invoke the classic chicken or the egg problem: it is possible that because these people have more symptoms, their illness and health cognitive constructs become more accessible; just as the opposite - the main tenet of these models - is possible (see also Skelton & Strohmetz, 1990). Two decades ago, Skelton and Strohmetz (1990) already suggested that to examine the causal role of illness-related schemata in symptom reporting, not only evidence for correlations between dispositional symptom reporting and individual measures of construct accessibility is needed, but also studies that vary the degree of accessibility of illness-related constructs or schemata and examine its influence on subsequent symptom reports (Skelton & Strohmetz, 1990). Indeed many studies have shown that MUS patients exhibit a cognitive bias, whether attentional or a memory bias. However, as said, this could simply be the result of having symptoms, and not a causal factor in the etiology of symptoms. Individuals for who a particular category is more accessible *because of their complaints* recognize category-congruent content more quickly (Higgins, King, & Mavin, 1982). Thus, people that report symptoms frequently may have better memory accessibility for health related constructs or prominent self-schema (for refs see Skelton & Strohmetz, 1990). Again, it is never clear whether

increased memory accessibility causes more symptom reporting, because increased symptom reporting can also increase the accessibility. This is why it is important to conduct studies that manipulate the core phenomenon, i.e. accessibility of illness-schemata, or studies that measure the relationship of illness-schemata and symptom reporting prospectively.

Another strength of this thesis is that we have attempted - even though we failed - to replicate our own study. As discussed above, studies in social priming have been under attack, and it has been suggested that replication studies are necessary and that researchers need to submit their manuscripts for publication with their non-findings as well, in order to reduce the file-drawer effect (Lieberman, 2012).

A third strength of the studies in this thesis, is that we examined the role of activated illness memory on symptom reporting while also controlling for two alternative hypotheses; namely that increased symptom reporting would already be observed with the semantic activation of sensations or negativity in general. We controlled for these alternative hypotheses because it has been hypothesized that people who experience more negative feelings (i.e. negative affect), pay more attention to internal cues in general (Watson & Pennebaker, 1989) and also to have increased scanning of their body for symptoms.

Finally, a fourth strength of the studies in this thesis is that we used several different techniques to examine the role of activated illness memory on symptom reporting. Not only did we examine the relationship between illness memory and symptom using experimental manipulations in the laboratory, we also examined this in real life. In addition, we used several different priming techniques to manipulate illness memory; from subliminal priming, and subliminal priming in combination with priming of self-related schema, and supraliminal priming. Furthermore, we examined this relationship in both healthy controls and patients with medically unexplained symptoms.

LIMITATIONS OF THE STUDIES

One obvious limitation is that we only learned in the end of a series of studies that the methods used to manipulate the subject of interest, activation of illness memory, turned out to be of questionable validity. However, this finding corresponds to other's recent negative findings of priming studies (as discussed above) and hopefully will ultimately lead to better methods to manipulate memory networks or schemata. Because our experimental manipulations turned out to be ineffective, the hypothesis that illness memory activation *causes* MUS remains untested, at least under rigorous laboratory conditions.

A related limitation is that we did not check whether our intervention study using supraliminal priming with positive health words, did actually increase activation of positive health memory networks. Just as we found out in the validation study of subliminal priming that it was ineffective in activating the illness memory, the same could apply to our supraliminal study. Therefore in order to truly know whether the effect of the positive health intervention was indeed reducing health complaints in

some subgroups by increasing positive health memory networks, a subsequent study should examine whether the intervention is effectively activating positive health memory networks.

A second limitation is that we only used two consecutive weeks for the study that examined whether the association between symptom reporting and implicit illness memory bias was prospective. We found that while MUS patients indeed showed the hypothesized implicit memory bias for illness words, we did not find that the strength of this implicit memory bias was associated with reporting of symptoms a week later or two weeks later. Perhaps if we had used a longer (or much shorter, for that matter) period of assessment, we could have found evidence for this prospective role. Future studies that measure implicit memory bias and symptom reporting over longer periods of time with shorter intervals between measurements could shed more light on the hypothesized association.

A third limitation of our research is that we only used semantic priming techniques using words in our studies: it is possible that if we would have used pictures or other objects, we might have found a different effect. For example, most of the few studies examining the effect of *explicit ('conscious')* priming with illness stimuli on pain tolerance, that were done before we started with the studies of this thesis, used pictures as stimuli and not words. Interestingly, recently a study has showed that a placebo effect (more or less the opposite of 'increasing symptoms') can be created merely by looking at a bottle of pain medication instead (Rutchick & Slepian, 2013). This study found that participants who were judging the design of a bottle of ibuprofen later on had higher pain tolerance compared to participants who judged the packaging of noodles (Rutchick & Slepian, 2013). However, it is unclear whether this placebo effect is due to decreased activation of illness memory networks or something else entirely. Future studies are necessary to examine which part of our cognition is responsible for this placebo effect.

POSSIBLE FUTURE STUDIES

In chapter 6 we found that priming participants with positive health information caused lower symptom reporting in certain subgroups. Because we did not examine whether positive health priming indeed activated positive health memory networks, or deactivated illness memory networks, it is plausible that this effect is perhaps not caused by illness memory networks but by some other construct. For example, it is possible that the participants in the positive health priming group, were having less negative affect (NA) and therefore reported less complaints. Although we found that these subgroups did not report higher positive affect because of the intervention, we did not examine whether they reported less NA because of the intervention. It could be that these two opposite constructs are not one-to-one related. Future studies examining the causal role of illness-memory networks in symptom reporting should account for the possible role of NA, as we did in our first two studies, unfortunately with ineffective manipulation techniques. Previous studies have found that partici-

pants with high NA indeed show a stronger attentional bias toward internal sensations (Stegen, Diest, Van De Woestijne, & De Bergh, 2001), and perhaps people with high NA also show increased activation of illness-memory activation. In conclusion, there is a possibility that NA is the underlying causal factor in increased symptom reporting and future studies should carefully examine its role within illness memory networks.

One recent study found that patients with somatoform disorders have implicit self-concepts that are significantly more associated with illness than the self-concepts of healthy individuals, which are more strongly associated with positive health (Riebel, Egloff, & Witthöft, 2013). Similar to our view, they suggest for future studies to examine whether this change in self-concept in somatoform disorders is the result of having many health complaints, or whether they are actually the cause for having many health complaints. In addition they suggest that subliminal evaluative conditioning could be used to examine the causality of self-concept related to illness in symptom reporting. However, as our study in chapter 5 showed, careful consideration should be administered before using subliminal evaluative conditioning and it should always be used with a manipulation check.

CONCLUSIONS

Our studies did not find conclusive, that is, laboratory-based, evidence for the notion that the reporting of health complaints, especially pain, is increased by illness-related memory, as suggested by the symptom perception model (Brosschot, 2002; Brown, 2004; Rief & Barsky, 2005). This is possibly because of the techniques used to manipulate illness memory in this thesis turned out to be insufficient. Future studies should use (or invent) new techniques that are more valid to activate illness-related implicit memory networks, so that the hypothesized causal effect of illness memory on increased symptom reporting can be adequately examined. However, in ambulatory studies we showed some evidence in support of the hypothesis, including one priming intervention study that had the expected effects, at least in a subgroup, and a cross-sectional study. These findings still support the idea, that illness memory might play a role in symptom reporting. However, longitudinal studies in larger sample groups are necessary to provide real evidence of the possible causal role of illness memory in symptom reporting. Future studies examining MUS should examine whether activated illness-memory networks indeed causes increased attention towards bodily signals, or if this increased attention is caused by some other factors. We believe that our results offer several promising routes for future studies to examine the role of illness memory in the etiology of somatic complaints. The suffering of many patients with medically unexplained symptoms or subjective health complaints and their impact on our health care costs warrants this kind of research.

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Samenvatting
(Dutch summary)

De rol van ziekte-gerelateerd geheugen (ziekteschema) in het rapporteren van lichamelijke klachten

Het doel van dit proefschrift was om meer inzicht te krijgen in de factoren die een rol spelen bij het rapporteren van lichamelijke klachten. Mensen hebben vaak last van gewone gezondheidsklachten zoals hoofdpijn, rugpijn, of vermoeidheid zonder dat zij daarvoor naar de huisarts gaan. Deze zogenoemde 'subjectieve gezondheidsklachten' komen veelvuldig voor. Ihlebaek, Eriksen, en Ursin (2002) vonden dat in de maand voorafgaand aan een onderzoek, 96% van de ondervraagden in hun studie minstens één lichamelijke klacht had zoals hoofdpijn, nekpijn of verkoudheid. Vaak gaan deze klachten na een aantal dagen vanzelf weer over, en niet iedereen gaat voor deze klachten naar de huisarts. Bij de huisarts kan vervolgens voor een deel van de lichamelijke klachten een medische oorzaak gevonden worden, maar voor een substantieel deel niet, uiteenlopend van 32% (Marple, Kroenke, Lucey, Wilder en Lucas, 1997) tot 60.6% (Fink, Sørensen, Engberg, Holm, & Munk-Jørgensen, 1999). De term die voor deze klachten gebruikt wordt is somatisch onverklaarde lichamelijke klachten (SOLK) en deze klachten worden zowel in de huisartsenpraktijk als bij de verschillende medische specialismen in het ziekenhuis gevonden. Ieder specialisme heeft zo een eigen benaming voor een ziektebeeld waar geen medische verklaring voor is, zoals fibromyalgie bij reumatologie en chronisch vermoeidheidssyndroom bij infectieziekten (Hall, 2011).

Veel mensen hebben dus regelmatig last van een subjectieve lichamelijke klacht zoals hoofdpijn, waarvoor een substantieel deel van de mensen op bezoek gaat bij de huisarts (Eriksen, Svendsrød, Ursin, & Ursin, 1998; Eriksen & Ursin, 2004). Bovendien zijn deze klachten vaak de oorzaak van langdurig ziekteverlof en arbeidsongeschiktheid (Eriksen et al., 1998). Slechts een klein deel van deze mensen blijft langdurig last houden van een somatisch onverklaarde lichamelijke klacht of heeft last van meerdere klachten. Echter, omdat deze lichamelijke klachten - zonder aantoonbare medische oorzaak - wel van grote invloed zijn op de ziektekosten en op de kwaliteit van leven van diegene met deze klachten, is het van belang om deze klachten te reduceren (Brown, 2004; Eriksen et al., 1998).

In dit proefschrift is een theoretisch model getoetst dat een verklaring biedt voor hoe mensen een lichamelijke klacht kunnen hebben zonder dat daar een medische oorzaak voor is. Dit model (Brosschot, 2002; Brown, 2004; Rief & Barsky, 2005), dat het meest gedetailleerd is uitgewerkt door Brown (2004) suggereert dat cognitieve processen zoals aandacht en geheugen een rol spelen in de waarneming van lichamelijke signalen. Eerdere theoretische modellen gaven aan dat mensen meer lichamelijke klachten rapporteren doordat men onbewust meer aandacht heeft voor lichamelijke signalen en men daardoor deze lichamelijke signalen eerder waarneemt en voelt (Barsky & Wyshak,1990; Watson & Pennebaker, 1989). Deze signalen worden eveneens eerder geïnterpreteerd als een symptoom van een ziekte en daardoor gerapporteerd als klacht. Het model van Brown (2004) suggereert dat deze verhoogde

aandacht voor lichamelijke processen komt door een meer geactiveerd impliciet ('automatisch', 'onbewust') geheugennetwerk voor ziekte-gerelateerde informatie, ook wel ziekteschema genoemd. En doordat dit uiteindelijk leidt tot meer klachten, wordt het geheugennetwerk voor ziekte steeds meer geactiveerd en bevat het steeds meer informatie, wat uiteindelijk weer leidt tot het meer waarnemen van lichamelijke signalen, en zo ontstaat er een vicieuze circel. Het grootste gedeelte van deze vicieuze circel bestaat uit impliciete processen, dit wil zeggen dat dit onbewust gebeurt. Tevens is het zo dat dit proces is gebaseerd op de interpretatie van echte lichamelijke signalen en het dus niet zo is dat men een dergelijke klacht verbeeld heeft. Brosschot (2002) heeft gesuggereerd dat een verhoogde aandacht en geheugen voor ziekte-gerelateerde informatie (cognitieve bias) uiteindelijk mogelijk leidt tot een sneller en versterkt doorgeven van lichamelijke signalen (sensitisatie). Of andersom: het lichamelijk versneld en versterkt doorgeven van lichamelijke signalen (sensitisatie) leidt uiteindelijk tot het meer gevoelig worden in de aandacht en het geheugen voor ziekte-gerelateerde informatie (cognitieve bias).

In dit proefschrift is de validiteit getoetst van dit theoretische model waarin een geactiveerd ziektegerelateerd geheugen leidt tot het rapporteren van lichamelijke klachten. Onderzocht is of manipulaties van het impliciete geheugen voor ziektegerelateerde informatie leiden tot veranderingen in het rapporteren van lichamelijke klachten. Tevens is onderzocht of dit impliciete geheugen voor ziekte informatie een voorspellende waarde heeft voor het rapporteren van lichamelijke klachten.

Het activeren van ziekte-gerelateerd impliciet geheugen en het rapporteren van pijn

Om een causaal verband te kunnen aantonen tussen een meer geactiveerd impliciet geheugen voor ziekten en het rapporteren van klachten, hebben wij getracht om in gezonde proefpersonen een impliciet geheugen voor ziekte te activeren en vervolgens te kijken of zij eerder klachten rapporteren (Hoofdstuk 2). Dit hebben wij gedaan door middel van ‘subliminal priming’, dat wil zeggen het aanbieden van stimuli voor een zeer korte periode, waardoor men zich niet bewust is van het zien van deze stimuli. In onze eerste studie lieten wij verschillende woorden zien die te maken hadden met ziekte of neutrale woorden. Wij deden dat extreem kort (sneller dan 1/20 seconde) zodat proefpersonen zich niet bewust waren dat zij deze woorden hadden gezien. Daaropvolgend werden proefpersonen gevraagd om hun hand zo lang mogelijk in ijskoud water te houden, totdat zij het niet meer konden volhouden (maximum van 4 minuten). Als het model klopt zouden proefpersonen die onbewust ziekte-woorden te zien kregen, eerder pijn voelen en hun hand eerder uit het water halen in vergelijking met proefpersonen die neutrale woorden te zien kregen. In onze eerste studie werd dit inderdaad gevonden. Echter, omdat dit effect niet heel erg sterk was, de gebruikte vragenlijsten misschien van invloed waren op de priming, en omdat de gebruikte woorden misschien niet helemaal de juiste representatie waren van het concept

‘ziek’, hebben wij een tweede studie (Hoofdstuk 3) gedaan waarin wij de resultaten van onze eerste studie trachten te repliceren, dit keer met verbeterde methoden. In deze studie konden wij ons gevonden effect van de eerste studie echter niet repliceren en vonden wij dus geen verschil van het onbewust aanbieden van ziekte-gerelateerde woorden op pijntolerantie in vergelijking met het aanbieden van neutrale woorden.

Omdat wij in de eerste twee studies tegenstrijdige resultaten vonden, hebben wij in onze derde studie (Hoofdstuk 4) getracht om het impliciete geheugen voor ziekte sterker te manipuleren dan in onze eerste twee studies. Hiertoe hebben wij de methode ‘subliminale evaluatieve conditionering’ gebruikt, waarin een impliciet concept sterker wordt gekoppeld aan het impliciete 'zelfconcept'. Hiervoor lieten wij gezonde proefpersonen woorden zien die te maken hadden met ziekte in combinatie met het woordje ‘ik’, beide steeds subliminaal. Er wordt gedacht dat hoe sterker iemands geactiveerde impliciete zelfconcept overlapt met het geactiveerde impliciete schema voor ziekte en/of pijn, hoe meer diegene klachten zal rapporteren door een verhoogde aandacht voor lichamelijke signalen (Pincus & Morley, 2001). Echter, we vonden niet dat proefpersonen die onbewust woorden te zien kregen die te maken hadden met ziekte in combinatie met het woordje ‘ik’ een lagere pijntolerantie hadden dan proefpersonen die neutrale woorden te zien kregen of een ‘X’ in plaats van ‘ik’. Er werd wel gevonden dat mensen die gekenmerkt worden door in het algemeen weinig gefocust te zijn op zichzelf ('laag zelfbewustzijn'), in combinatie met het meer activeren van het zelf-schema, dat die een hogere pijntolerantie hadden dan mensen met een hogere zelf-bewustzijn. Een mogelijke verklaring voor het gevonden effect zou kunnen zijn dat mensen die het woordje ‘ik’ onbewust te zien kregen meer tijdelijk zelfvertrouwen kregen en zo langer de pijntaak konden volhouden. Vervolgstudies zijn echter nodig om de precieze werking uit te zoeken.

Omdat de eerste drie studies tegenstrijdige resultaten lieten zien, kon dat twee dingen betekenen: 1) de hypothese dat een geactiveerd geheugenschema voor ziekten van invloed is op het rapporteren van klachten is niet juist of 2) de technieken gebruikt in de eerste drie studies zijn niet effectief in het activeren van geheugenschema voor ziekte. De methoden van de eerste drie studies zijn veel gebruikt in eerdere studies die effectief bleken om gedrag onbewust te veranderen (bijvoorbeeld Kiefer, 2002; Levy, 1996; Pierce & Lydon, 1998; Lowery, Eisenberger, Hardin, & Sinclair, 2007). Dus we gingen ervan uit dat deze methoden goed zouden werken en het desgewenste effect zouden hebben. Echter, om de tweede verklaring uit te sluiten hebben we in de vierde studie (Hoofdstuk 5) onderzocht of subliminale priming die in de eerste twee studies gebruikt zijn inderdaad leidt tot een meer geactiveerd ziekteschema. Tevens onderzochten we of de subliminale evaluatieve conditioneringsmethode inderdaad leidde tot een meer geactiveerde link tussen ziekteschema en het zelfconcept. In het eerste gedeelte kreeg de helft van de proefpersonen onbewust ziekte woorden te zien en daarna werd gekeken of zij sneller ziektewoorden herkenden dan andere woorden op een zogenaamde lexicale decision

taak. Dit was niet het geval. In het tweede onderdeel van deze studie werd gekeken of de andere helft van de proefpersonen een impliciete associatie lieten zien voor ziekte en zichzelf, als zij vantevoren onbewust ziektewoorden te zien kregen in combinate met het woordje “ik”. Dit was ook niet het geval. Beide methoden bleken dus niet het desgewenste effect te hebben, en dus niet te voldoen aan het effectief manipuleren van het ziekteschema. Dit betekent dat we in de eerste drie studies niet hebben kunnen onderzoeken of de hypothese dat een geactiveerd ziekteschema leidt tot meer klachten klopt.

In het tweede gedeelte van dit proefschrift hebben wij op een andere manier de associatie tussen ziekteschema en het rapporteren van lichamelijke klachten onderzocht. Omdat manipulatie op onbewuste wijze van het ziekte schema niet effectief bleek, besloten wij in de vijfde studie (Hoofdstuk 6) om het ziekte-schema te manipuleren met bewust waargenomen stimuli (supraliminale priming). Ook besloten wij ditmaal het in het dagelijks leven te onderzoeken, met daadwerkelijk gerapporteerde klachten. Gezonde proefpersonen werden in twee groepen gedeeld. De ene groep kreeg een aantal dagen positieve gezondheidswoorden te zien terwijl zij een online computertaak deden. De andere groep kreeg neutrale woorden te zien. Alle proefpersonen werden gevraagd om aan het einde van de dag een vragenlijst in te vullen die lichamelijke klachten inventariseerde. Er werd gevonden dat de proefpersonen die de taak deden waarbij zij positieve gezondheidswoorden te zien kregen een significant lager aantal klachten hadden dan de proefpersonen die neutrale woorden te zien kregen. Echter, dit gold alleen voor de proefpersonen met de kenmerken laag 'negatieve affect' (de tendens om veel negatieve emoties te ervaren) of lage somatosensorische versterking ('somatosensory amplification', de neiging om lichamelijke signalen versterkt waar te nemen). Deze resultaten suggereren dat het direct activeren van een positief gezondheidsschema lichamelijke klachten kan reduceren in bepaalde subgroepen. Misschien dat de proefpersonen bij wie het niet werkte, namelijk zij die geneigd zijn om meer negatief affect te rapporteren of lichamelijke signalen versterkt waar te nemen, ook eerder geneigd zijn positieve gezondheidsinformatie te interpreteren als negatief. Dit zodat het past in hun ziekteschema, en dit zou tot gevolg hebben dat positieve 'gezondheids-priming' niet tot een klachtenreductie leidt zoals in de andere subgroepen.

In het laatste onderzoek (Hoofdstuk 7) is de hypothese dat activatie van een ziekteschema leidt tot meer gezondheidsklachten op nog een andere manier onderzocht, en dit keer bij zowel gezonde proefpersonen als bij proefpersonen met somatisch onverklaarde lichamelijke klachten (SOLK). In deze studie is gebruik gemaakt van een cross-sectioneel design om zo de temporele relatie tussen activatie van een ziekteschema en lichamelijke klachten te onderzoeken. De hypothese was dat proefpersonen met een chronisch geactiveerd ziekteschema ook meer lichamelijke klachten zouden hebben, en dat dit geactiveerde ziekteschema stabieler zou zijn (d.w.z. een sterke samenhang tussen de twee metingen) en de mate van lichamelijke klachten op een later moment zou kunnen voorspellen. Er werd inderdaad gevonden

dat proefpersonen met SOLK een sterker impliciet geheugen bias hadden voor woorden die met ziekte te maken hadden, en dus een sterker geactiveerd ziekte schema, in vergelijking met de groep gezonde proefpersonen. De gezonde proefpersonen lieten ook een impliciete geheugenbias zien voor ziektewoorden, deze bias was alleen minder sterk in vergelijking met de SOLK proefpersonen. Echter, deze bias was niet stabieler voor de proefpersonen met SOLK, en was niet gerelateerd aan meer lichamelijke klachten op hetzelfde meetmoment en het voorspelde ook niet het aantal lichamelijke klachten op een later meetmoment. Er werd in deze studie dus wel bewijs gevonden voor de hypothese dat SOLK samenhangt met een meer geactiveerd ziekte schema, maar geen bewijs gevonden voor de hypothese dat een meer geactiveerd ziekte schema is gerelateerd aan het rapporteren van een verhoogd aantal lichamelijke klachten op hetzelfde moment of een week later. Een mogelijke verklaring voor dit gevonden resultaat is dat de meetmomenten te kort na elkaar kwamen, waardoor er meer 'state' variantie is gemeten in plaats van 'trait' variantie. Misschien dat deze associatie wel gevonden zou kunnen worden als er een langere tijdsspanne tussen de meetmomenten zou zitten waardoor meer de samenhang tussen 'trait' variantie gemeten zou kunnen worden in plaats van de 'state' variantie.

Sterke punten en beperkingen van de onderzoeken

Één van de sterke punten van dit onderzoek is dat we hebben getracht om door middel van experimentele studies en met verschillende methoden het causale verband tussen impliciete geheugen voor ziekte-informatie en het rapporteren van lichamelijke klachten aan te tonen. Dit wordt al jarenlang gespeculeerd, maar er zijn tot nu toe maar weinig experimentele studies geweest die geprobeerd hebben om het causale verband aan te tonen. Het is lastig om een oorzaak- en gevolg-verband te onderzoeken omdat het omgekeerde ook plausibel is, namelijk dat het hebben van lichamelijke klachten automatisch leidt tot het hebben van een sterker impliciet geheugennetwerk voor ziekte-informatie. Veel studies hebben inderdaad gevonden dat mensen met SOLK een cognitieve bias hebben voor ziekte-informatie, maar het is onduidelijk of die bias een oorzaak of een gevolg is van het hebben van lichamelijke klachten.

Een ander sterk punt van dit onderzoek is dat we ons eigen onderzoek hebben geprobeerd te repliceren. In een replicatiestudie hebben wij niet hetzelfde resultaat kunnen repliceren, maar dit hebben wij wel gepubliceerd. Het is gesuggereerd dat veel meer onderzoekers dan tot nu toe hun studies waarin negatieve resultaten gevonden worden ter publicatie zouden moeten aan bieden, om het "file-drawer"-effect - het laten liggen 'in de la' van onwelgevallige resultaten - te reduceren (Lieberman, 2012).

In dit onderzoek hebben wij tevens rekening gehouden met twee alternatieve hypotheses: dat mensen meer lichamelijke klachten rapporteren omdat er sprake is van een meer geactiveerd schema voor sensaties of negatieve informatie in het algemeen. Deze alternatieve hypotheses zijn onderzocht omdat er gesuggereerd is dat mensen met meer negatieve gevoelens en gedachten ook meer aandacht hebben voor

interne stimuli en daardoor meer lichamelijke klachten rapporteren (Watson & Pennebaker, 1989).

Een ander sterk punt van dit onderzoek is dat er gebruik is gemaakt van verschillende methoden om de rol van impliciet geheugennetwerk voor ziekte-informatie op het rapporteren van lichamelijke klachten te onderzoeken. Deze relatie is niet alleen in de gecontroleerde setting van het laboratorium onderzocht, maar ook in het dagelijks leven. Bovendien zijn er verschillende priming-technieken gebruikt om het impliciete geheugennetwerk te manipuleren. En er is zowel in gezonde proefpersonen als proefpersonen met SOLK onderzoek gedaan naar deze relatie.

Tenslotte hebben we onderzocht of de methoden die gebruikt werden om het geheugennetwerk voor ziekte activeren inderdaad werkten. Een beperking van dit onderzoek is echter dat we dit laatste pas aan het einde van een serie experimenten hebben onderzocht. Het zijn weliswaar veel gebruikte methoden in de psychologie, en worden om die reden geloofwaardig geacht, maar ons vertrouwen bleek onterecht. Het was achteraf gezien beter geweest om meteen een manipulatiecheck te doen, zodat wij niet onnodig langer doorgingen met een ondeugdelijke methode. Hopelijk draagt ons onderzoek naar de werking van deze methode bij aan het ontwikkelen van een betere methode om het impliciete ziekteschema te manipuleren. In het onderzoek waarbij gebruik werd gemaakt van het manipuleren van een ziekteschema met behulp van bewust waargenomen stimuli (supraliminal priming) is er ook geen manipulatiecheck gedaan. Alhoewel we wel vonden dat er een bepaald effect was van deze methode op de uitkomstmaat, weten we nu niet zeker of dat inderdaad komt door onze manipulatie. Verder is ook een beperking dat we alleen twee opeenvolgende weken hebben gebruikt als meetperiode om de prospectieve, voorspellende rol van impliciete geheugennetwerk voor ziekte op het rapporteren van klachten te meten. Een andere beperking is dat we alleen priming met behulp van woorden hebben gebruikt. Het kan zijn dat er misschien andere resultaten waren gevonden als we andere stimuli zoals bijvoorbeeld plaatjes, hadden gebruikt.

Conclusies

Onze onderzoeken vonden geen sluitend bewijs voor de hypothese dat meer geactiveerde impliciete geheugennetwerken of schema's voor ziekte-informatie zorgen voor verhoogde rapportage van lichamelijke klachten. Dit komt met name omdat de technieken die gebruikt zijn om deze impliciet geheugennetwerken of schema's te manipuleren achteraf niet goed bleken te werken. Toekomstige studies zouden betere methoden moeten ontwikkelen om zo het daadwerkelijke causale verband tussen deze geheugennetwerken en rapportage van lichamelijke klachten te kunnen onderzoeken. In onze studies in het dagelijks leven vonden we wel enig bewijs die deze hypothese ondersteunt. Echter, longitudinale studies met grotere groepen proefpersonen zijn nodig om sterker bewijs te kunnen leveren voor deze hypothese. De resultaten van deze onderzoeken geven wel richting aan de stappen die nodig zijn om de rol van ziekteschema's in het rapporteren van lichamelijke klachten te onderzoeken. Het

verder onderzoeken van deze rol is belangrijk vanwege de slechte kwaliteit van leven in SOLK patiënten en is eveneens van maatschappelijk belang vanwege de impact van SOLK op onze maatschappelijke kosten.

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Publications
Curriculum vitae

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CURRICULUM VITAE

Esther Meerman was born in 1982 in Groningen, the Netherlands. After completing her high school education at the Stedelijk Gymnasium in Leiden, she started to study Clinical Psychology and Clinical Neuropsychology at the University of Amsterdam. From September 2004 she studied at the University of Toronto for one year as an exchange student. She received her master's degree from the University of Amsterdam in 2007. In 2008, she started her PhD research at the Clinical and Health Psychology department of Leiden University. In 2012, she began her postdoctoral training to become a licensed psychologist (Gezondheidszorgpsycholoog) at the hospital Kennemer Gasthuis, in Haarlem. She will be finished with this in April 2014.