SECURITY-MOTIVATION IN OBSESSIVE-COMPULSIVE DISORDER

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A Thesis Submitted to the School of Graduate Studies in Partial Fulfillment of the Requirements for the Degree Doctor of Philosophy

McMaster University DOCTOR OF PHILOSOPHY (2012) Hamilton, Ontario(Neuroscience)

TITLE: Security-Motivation in Obsessive-Compulsive Disorder AUTHOR: Andrea Hinds, B.Sc. (McMaster University) SUPERVISOR: Professor H. Szechtman NUMBER OF PAGES: (10 chapters, 142 pages)

ABSTRACT

We present the results from a series of experiments which support a novel hypothesis for a special motivational circuit underlying both the detection and response to potential threat, and the typical symptoms of Obsessive-Compulsive Disorder (OCD). Szechtman and Woody (2004) proposed that the Security-Motivation System (SMS) has two primary responsibilities: surveillance of the environment for subtle cues that may indicate the potential for danger, and motivation towards avoidance of this harm through participation in appropriate behavioural motor programs. To determine the parameters under which the SMS operates, we designed and implemented several novel paradigms for examining both typical and atypical response of the SMS to potential threat in a number of populations. It was demonstrated that the SMS is specifically activated after exposure to cues that suggest the possibility of harm to the self or others, such as via threats to personal safety or contaminated objects. Once activated, the SMS can only be disengaged through participation in the appropriate motivated corrective behaviour – such as hand washing or checking for danger. Results showed that this essential termination feedback cannot be substituted with cognitive strategies, and that in the absence of these behaviours, activation of the SMS persists; the consequence of incomplete SMS termination strongly resembles the stereotypic compulsions in OCD. Indeed, results demonstrated that patients with OCD are unable to achieve satisfaction from task completion after corrective behaviour, resulting in continued SMS activation, after exposure to stimuli specific to the patients' symptom profile. Our collective results

provide a solid foundation for the view of OCD as a dysfunction of Security-Motivation, and indicate that the SMS is indeed an essential circuit for potential threat detection.

The author wishes to acknowledge Dr. Henry Szechtman for his supervision and guidance in the completion of this research. A special thank you also to Dr. Erik Woody, Dr. Michael Van Ameringen, and Dr. Louis Schmidt for providing expertise and advice, and to Dr. Marie Coroneos for her assistance in data acquisition and analysis. We also wish to thank Dr. Stephen Porges for training and consultation for the use of MxEdit and CardioBatch/CardioEdit software essential for data collection and analysis.

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LIST OF ABBREVIATIONS AND SYMBOLS

BDI: Beck Depression Inventory

CBT: Cognitive Behavioral Therapy

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition

ECG: Electrocardiography

EMG: Electromyography

HRV: Heart Rate Variability

MINI: Mini International Neuropsychiatric Interview

OCD: Obsessive-Compulsive Disorder

PI-WSUR: Padua Inventory – Washington State University Revision

RMS: Root Mean Square

RSA: Respiratory Sinus Arrhythmia

SCID: Structured Clinical Interview for DSM-IV

SMS: Security-Motivation System

VR: Virtual Reality

Y-BOCS: Yale Brown Obsessive Compulsive Scale

DECLARATION OF ACADEMIC ACHIEVEMENT

The research outlined here represents work undergone towards fulfillment of graduate requirements for which the author has been primarily responsible. Paradigm and study design were completed under the guidance of the graduate committee. Statistical analysis was completed with guidance from Dr. Henry Szechtman. Patient recruitment was completed with guidance from Dr. Michael Van Ameringen. All aspects of study implementation, including participant recruitment and screening, development of experimental materials, data collection, as well as data editing and analysis, were completed by the author.

CHAPTER 1: SECURITY-MOTIVATION

I. Motivation Toward Threat Detection

Hebb (1966) defines motivation as the organization of one's actions toward a single goal for the purpose of increasing species survival, and it can be best understood as a measure of the level of overall activation of an organism. Cardinal, Parkinson, Hall and Everitt (2002) describe motivation in terms of a complex interaction between emotion, interpretation of the environment, and the ultimate acquisition of one's goals. Motivation towards the removal of aversive stimuli or emotions (such as anxiety) via active coping mechanisms or increased vigilance is thought to originate from the appraisal of demands and constraints in one's environment that result in the evaluation and perception of threats to physical well-being (Lazarus, 1993; Nash & Thebarge, 2006; Schneiderman, Ironson & Siegel, 2005); here, stress is conceptualized as an imbalance between the perceived demands and resources available to an individual, resulting from any challenge or threat, either real or perceived, to the normal functioning of the biological system (Nash & Thebarge, 2006). The resulting activation of hypothalamic, pituitary and adrenal functions (the HPA axis) in response to physiological and psychological stressors reflects an attempt to restore balance. While the short-term impact of HPA activation on the central nervous system may be beneficial to the organism, long-lasting or exaggerated release of glucocorticoids can have detrimental effects on the appropriate response of the individual to stressors over time.

Unlike fear, which results from the indication of explicit, defined danger, and elicits specific threat avoidance action plans, anxiety is a state of general distress that may be directed at stimuli that are non-specific and undefined. It is well established that a number of different species rely on essential environmental cues to signal the presence of possible threats to the individual; many of these cues, however, indicate only *inferred* risk (as opposed to perceptible, manifest threats such as physical contact with a predator) and therefore carry some level of uncertainty as to the actual presence of the threat (Szechtman & Woody, 2004; Boyer & Lienard, 2006). Examples include an odor or visual cue indicative of the possible presence of a predator, or of the possibility that an individual or object is diseased or contaminated. Species-typical behaviours direct the individual toward the avoidance of potential threats to safety; in humans, such behaviours include washing after exposure to a potential contaminant, and checking that one's home is secure (Szechtman et al, 2004; Boyer et al, 2006). The cost associated with the risk of predation and infection are incredibly high – avoidance of individuals that are potentially infected, for example, greatly reduces the possibility of contracting bacteria, viruses or other parasites (Kavaliers, Choleris, Agmo & Pfaff, 2004). As a result, behaviours that are key for a species' survival – such as foraging, mating, and social interaction – are also heavily influenced by the desire to avoid these risks. The detection and amelioration of potential threats may have serious evolutionary implications, as the consequences of its failure (such as an impact on the capacity for reproduction, disability, or even death) are potentially quite severe (Choleris, Clipperton-Allen, Phan & Kavaliers, 2009). The importance of such a detection system for the survival of the species suggests that it is relatively primitive and specialized toward the specific challenges to fitness that a species may face (Szechtman & Woody, 2004). Of particular interest is contamination from pathogens or other invisible agents; it is suggested that many behaviours have evolved specifically to cope with the risk of infection and exposure to disease (Choleris et al., 2009). Given the evolutionary imperative to detect and avoid potential threats to fitness, and serious consequences of ignoring or misinterpreting relevant cues, it is likely that the brain is ideally networked to efficiently deal with such information.

Cardinal, Parkinson, Hall and Everitt (2002) emphasize the dichotomy between motivational systems responsible for relatively unconscious, security-based actions (thought to be evolutionarily older) such as the avoidance of harm, and more recently developed cognitive processes which drive complex motivations, such as long term goal formation. While this and other models exist to address the general response of a security circuit towards stress, we are interested in the proposal that *specific* challenges to safety may operate via distinguishable motivational circuits; further, we propose that a special motivation system exists to prepare for action against potential threats as distinct from direct threats to safety, and to deal with the particular challenge of creating an environment that is as secure for the individual as possible.

II. Function of the Security-Motivation System

In 2004, Szechtman and Woody proposed that the detection, appraisal and avoidance of potential threats to the organism are tasked to a special system, termed the "Security-Motivation system (SMS)". Others have since described an analogous circuit, such as Boyer and Lienard (2006), who termed it the "Hazard-Precaution system". All mammalian motivations have specific end goals, that of the SMS being self-preservation. As this system is proposed to deal specifically with indirect cues (rather than obvious evidence of danger), the SMS functions by organizing behaviours that probe for such threat cues – particularly those that have been recurrent threats throughout our ancestral history (such as disease) (Szechtman & Woody, 2004). In order for such a system to be effective, it must be very sensitive and highly tuned to specific input, due to the high fitness cost of ignoring cues that predict a tangible threat. For potential threats to be accurately assessed, this motivational circuit must also be adept at cue appraisal under a number of different contexts and rapid in its processing of information of potential relevance for survival (Boyer & Lienard, 2006). As opposed to tangible dangers, the focus on ambiguous, unclear or partial stimuli – often from several different sources (Blanchard, Hynd, Minke, Minemoto & Blanchard, 2001) – is a more demanding task, and relies heavily on the inference that there is a deviation from conditions that are indicative of safety (Szechtman & Woody, 2004). Both the features of the threat, and its context, may influence the appraisal and response to cues (Blanchard et al, 2001).

Activation of security motivation in response to such cues must also be sufficient to motivate the individual towards the production of appropriate threat-avoidance behaviours, induce a state of wariness about one's surroundings (Szechtman & Woody, 2004) and initiate an appropriate action plan. Corrective behaviours aimed at reducing or eliminating a threat would be species-typical, and must be appropriate for the particular type of threat detected; for example, if the cues indicate the presence of a predator or pathogen, the response may be checking or washing, respectively.

Once activated, proper termination of the system is necessary to prevent a continuously heightened level of anxiety, hyper-vigilance, and excessive participation in avoidance behaviours. Security-Motivation is unique, however, in the sense that there are no definite cues for the removal of *potential* danger; since the presence of threat is, by definition, on the basis of individual interpretation and assessment of ambiguous cues, there is no concrete sensory evidence that a treat is no longer present (Szechtman & Woody, 2004). For this reason, it is proposed that there is some internal sense of task completion, or feeling of satisfaction and confidence that a potential threat has been appropriately dealt with, that accompanies participation in corrective behaviours; Szechtman and Woody (2004) termed this “yedasentience” and define this sense of knowing as the terminating signal for SMS activation. Under this theory, the sense of task completion associated with corrective motor outputs produces a rapid disengagement of the SMS. In the absence of yedasentience, SMS activation may naturally decay over time, allowing the system to eventually return to its base state; however, this process is thought to be inefficient and much slower, taking a significantly longer period of time to elicit SMS deactivation. Thus, the proper functioning of the Security-Motivation circuit is, in this view, highly reliant on feedback from completion of security-based behaviours.

III. Neurobiology of Security Motivation

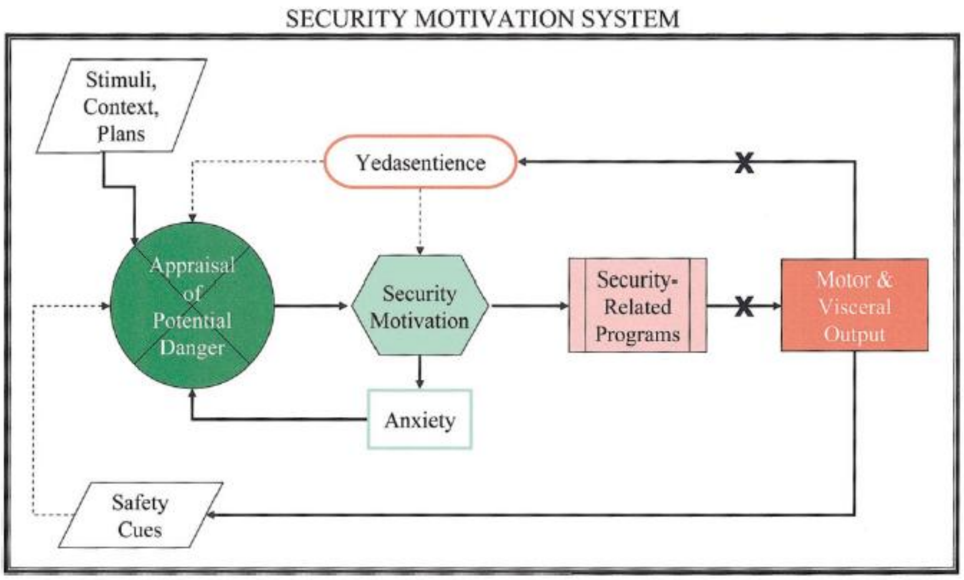

Figure 1: A model of the Security-Motivation, representing communication between the major functional components. X's represent points in the circuit where dysfunction could lead to disturbance to Security-Motivation function. (Szechtman & Woody, Obsessive-Compulsive Disorder as a Disturbance of Security-Motivation, *Psychological Review, 111*(1), 111-127, 2004. Published by APA, reprinted with permission.)

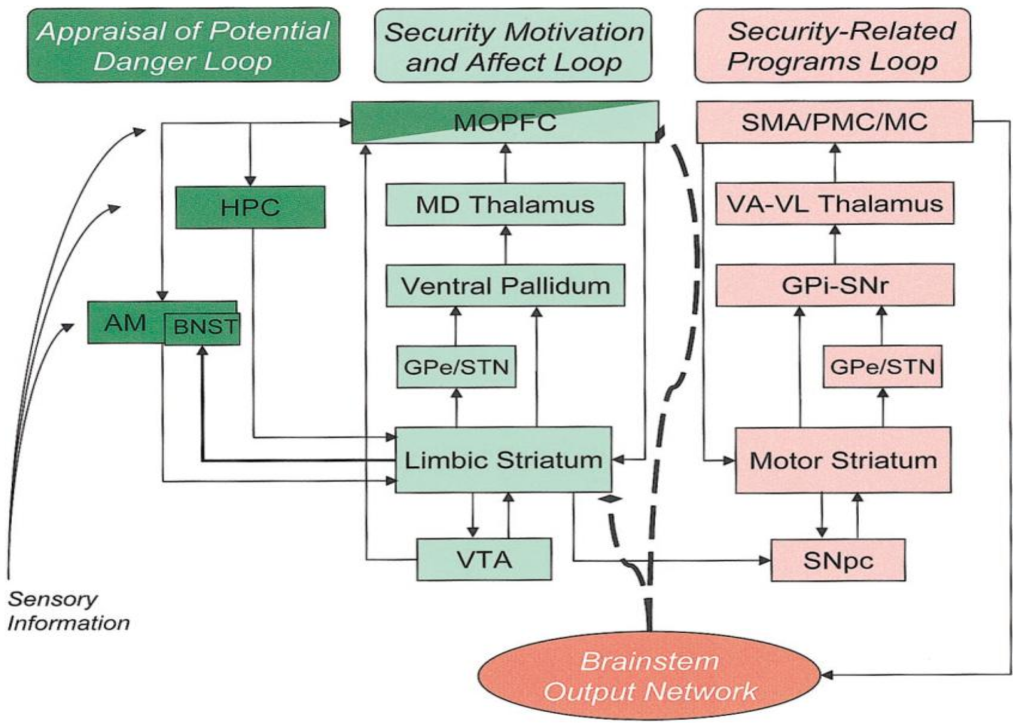

Figure 2: A model of the neural substrates comprising each component of the Security-Motivation system. (Szechtman & Woody, Obsessive-Compulsive Disorder as a Disturbance of Security-Motivation, *Psychological Review, 111*(1), 111-127, 2004. Published by APA, reprinted with permission.) HPC = hippocampus; AM = amygdala; BNST = bed nucleus of the stria terminalis; MOPFC = medial and orbital prefrontal cortex; MD Thalamus = mediodorsal thalamic nucleus; GPe = external segment of the globus pallidus; STN = subthalamic nucleus; VTA = ventral tegmental area; SMA = supplementary motor area; PMC = premotor cortex; MC = motor cortex; VA-VL Thalamus = ventroanterior and ventrolateral thalamus nucleus; GPi = internal segment of the globus pallidus; SNr = substantia nigra pars reticulata; SNpc = substantia nigra pars compacta.

Neurophysiologically, the Security-Motivation circuit is comprised of several interconnected components involved in the appraisal of danger, affect, and the production of motor programs (see Figure 1). The structures sub-serving each functional component are hypothesized to include those known to be involved in primary motivational systems; previous literature has emphasized the role of the limbic system (in particular, the amygdala and hippocampus), thalamus, basal ganglia and frontal cortex in initiating and engaging in goal-directed behaviours (van Marle, Hermans, Qin & Fernandez, 2009; Boyer & Lienard, 2006; Szechtman & Woody, 2004) (see Figure 2). Here we highlight the proposed neurobiology and functional role of each component:

Appraisal of Potential Danger is hypothesized to correspond to areas typically associated with the evaluation of the environment and identification of threat, and processing of motivational stimuli. Its main role is the regulation of vigilance and assessment of cues as representing a deviation from the normal state. The amygdala, hippocampus, bed nuclei of the stria terminalis, and medial orbital prefrontal cortex match this description, typically considered crucial for motivation and emotional processing. The amygdala in particular has been implicated in associating emotional context to stimuli, conditioned learning, and in motivation towards defensive behaviours (Szechtman & Woody, 2004). In order for stimuli to be properly assessed, their context – including memory for previous encounters and expected consequences – must also be considered, functions also attributed to these brain regions. The Appraisal circuit is necessary for activation of security motivation and downstream threat-avoidance motor outputs.

Security Motivation and its corresponding state of anxiety, once activated by the detection of a potential threat, are proposed to motivate the organism toward an appropriate action. Similar to other defined motivational circuits, it is comprised of projections between the limbic striatum, basal ganglia and cortex, and drives both motor and sensory responsiveness (Szechtman & Woody, 2004). Activation of this component is suggested to direct the individual towards the selection of an appropriate motor pattern as well as produce a sustained motivational state – in this case, anxiety and uncertainty of one's safety – until a termination signal is elicited.

Security-Related Programs are generated in response to security motivation, and organize species-typical action patterns. Such motor sequences are thought to involve the basal ganglia and thalamocortical projections, including an important role for the dorsal striatum and midbrain dopaminergic neurons in motor sequencing (Szechtman & Woody, 2004). Security programs are implemented through communication with the brainstem and its subsequent control over motor activity. Finally, Yedasentience – the feeling of knowing after successful completion of a corrective motor act – is thought to provide the essential negative feedback to security-motivation and its correlate of anxiety. The motor circuits which regulate defensive or protective acts may utilize serotonergic pathways for this feedback, as serotonin has been established as having a role in behavioural suppression (Soubrie, 1986).

CHAPTER 2: RELATIONSHIP OF SECURITY-MOTIVATION TO OBSESSIVE-COMPULSIVE DISORDER (OCD)

I. Definition of OCD

The distinctive security-based behaviours associated with Security-Motivation (directed towards avoidance of potential threat) bear a strong resemblance to the stereotypical motor patterns seen in a particular anxiety disorder – Obsessive-Compulsive disorder (OCD). Szechtman and Woody (2004) proposed that the etiology of OCD has its roots in fundamental dysfunction of the Security-Motivation system.

Obsessive-Compulsive Disorder is an anxiety disorder that is characterized by recurrent thoughts or obsessions that are most often concurrent with repetitive or stereotyped compulsive actions. Obsessions and compulsions are typically related to concerns involving threat to the safety of oneself or others; common obsessions are focused on the potential for contamination, preoccupation with bringing harm to a friend or loved one, and doubt over the security of one's surroundings. Similarly, the associated compulsive behaviours reflect a desire to eliminate these threats, and include frequent checking (repetitive actions related to security and orderliness) and excessive washing and cleaning (of hands, other body parts, or possessions; Reed, 1985). More common that previously thought, an approximate 1-2% of the population is diagnosed with OCD symptoms considered excessive and severe enough to seriously and negatively affect one's quality of life (DSM-IV-TR; American Psychiatric Association [APA], 2000). The age of onset for OCD is typically in the early to mid 20s; OCD may be diagnosed based on the presence of obsessions or compulsions alone, and the manifestation of these symptoms is highly variable. While symptoms related to checking and washing are most common in clinical populations, the majority of patients present with multiple types of obsessions and compulsions (Rasmussen & Eisen, 1992). However, patients are often diagnosed as having a particular subtype of OCD, based on the most predominant compulsive symptom they present with; thus, patients are often classified as "checkers", "washers" or "hoarders". OCD is also highly comorbid with other mood and psychiatric disorders according to DSM-IV criteria. OCD patients may meet criteria for major depressive disorder, social or other phobias, generalized anxiety disorder, trichotillomania and/or panic disorder, and may suffer consequences of alcohol or illicit drug abuse.

Symptoms of Obsessive-Compulsive Disorder may be reduced in frequency and severity with pharmacological treatment (commonly anxiolytics and antidepressants) to manage chronic anxiety, and/or behavioural therapy techniques. However, treatments are often only moderately effective, and symptoms may worsen or reappear after major life stressors, such as personal loss or injury (Boyer & Lienard, 2006). Considering the significant burden of OCD, it is imperative to develop a more complete understanding of the neurobiological mechanisms underlying this disorder (Szechtman & Woody, 2004).

II. Cognitive Model of OCD

Various conceptual models of Obsessive-Compulsive Disorder have attempted to account for the underlying causes behind its classic symptoms, as well as the high variability in clinical presentation associated with this disorder. Much research into the neurological basis for Obsessive-Compulsive Disorder has suggested that it reflects a disorder of cognitive functioning. In 2004, Tsao and McKay described OCD as a disorder of dysfunctional appraisal of one's environment – specifically, that tendencies toward obsessive and compulsive behaviours are associated with a hypervigilance and increased sensitivity to stimuli expected to elicit a disgust response. This view was echoed by Stein, Arya, Pietrini, Rapoport and Swedo (2006), who describe the typical OCD symptoms as reflecting an inability to appropriately process emotions relating to disgust. They define OCD as disorder of hypersensitivity, a byproduct of incorrectly interpreting the environment, and viewing innocuous stimuli as posing a threat to health or safety. One problem with this view is that it assumes that the anxiety associated with OCD is synonymous with disgust, in some cases using anxiety as a direct measure of disgust; while there is certainly a relationship between these emotional states, they are not interchangeable. It has been demonstrated that anxiety alone predicts compulsive behaviour in OCD patients, and that these patients can easily distinguish between their anxiety toward a contaminated object and their feelings of disgust (Cougle, Wolitzky-Taylor, Lee & Telch, 2007). Further, disgust is associated only with cues for contamination; it is not clear how other OCD subtypes, such as ordering or checking, may be accounted for under these models.

This cognitive view of OCD is supported by a number of other researchers. McKay (2006) similarly described OCD as a bias towards "safe" situations, developed as a cognitive response to a fear of contamination and heightened memory for unpleasant events; under this theory, exposure to disgusting or dangerous stimuli in one's past creates a desire to avoid any object or environment which may act as a "cue" for that threat. The individual would be hypersensitive to such situations, and when such stimuli cannot be avoided, tolerance for this exposure is low, resulting in heightened anxiety and exaggerated compensatory behaviours. However, this model fails to explain the presence of compulsions in the absence of obsessions (Rasmussen & Eisen, 1992). There is, in fact, a lack of solid evidence that OCD patients display any consistent concurrent dysfunctions of cognition – such as perceptual or memory disorder – that might be expected to accompany such a serious disruption in normal cognitive processing. Further, the cognitive perspective of OCD suggests that patients would tend to obsess over objects or situations that posed the most viable threat, or those that had posed an actual, serious threat to their safety at some point in their history (or that of their loved ones) in order for such a learned aversion to develop. In reality, the type and content of safety-related obsessions and compulsions that are most often seen in OCD are significantly skewed towards older, more evolutionarily relevant threats (such as disease or predation) that the individual may never have encountered, as opposed to more likely modern threats (such as guns or car accidents) (Boyer and Lienard, 2006). However, the view of OCD as a cognitive disorder has been supported by the success in using cognitive behavioural therapy (CBT) to reduce OCD symptoms. This may include habituation via repeated exposure to cues, such as contaminated objects, and prevention from engaging in the desired compulsive acts.

If OCD is, indeed, a dysfunction of appraisal, it would be expected that patients would endorse their ultimate analysis of a particular stimulus or situation, whether or not they are ultimately correct; washing one's hands excessively, for example, should reflect their belief that their environment is, in fact, contaminated (even if it is not). This model conflicts with a prominent feature of OCD – that patients are often cognitively aware that their concerns are excessive or unnecessary, but still feel compelled to comply with them. This "ego-dystonic" nature of OCD (behaviours that are inconsistent with the individual's cognitive understanding) (Julien, O'Connor and Aardema, 2007) suggests that obsessions are not *caused* by a dysfunction in appraisal. In addition, if compulsions reflect a natural (albeit unnecessary) response to a perceived threat, participation in these behaviours should effectively eliminate anxiety, at least for a short period of time until a new threat is detected. One might then expect compulsions to be reasonably appropriate in duration, resembling a normal response to a threat, but dysfunctional in frequency (as a higher sensitivity to the possibility of threat would result in a much higher amount of time spent dealing with such threats); in contrast, there is little evidence in the literature to suggest that OCD patients have unrealistic perceptions of their environment. In contrast, patients appear to be selective in the objects or situations that they develop compulsions toward, and compulsive behaviours are generally longer than normal in duration (Szechtman & Woody, 2004). The fact that patients persist in engaging in compulsive behaviours despite the fact that they are often ineffective in relieving anxiety supports the idea that OCD is not simply a disorder of hyper-excitability.

III. OCD as a Disorder of Security-Motivation

Recent literature suggests an alternative explanation for the development and expression of Obsessive-Compulsive Disorder; Szechtman and Woody (2004) posit that this disorder reflects a motivational dysfunction, specifically related to the special motivational circuit responsible for potential threat detection, the Security-Motivation system. In contrast with the more established view of OCD as a byproduct of impairment in cognition and reasoning abilities, this hypothesis suggests that OCD has a more evolutionarily relevant basis in security-motivation. There is growing evidence to support the idea that the typical behaviours seen in OCD likely reflect subtle dysfunctions in an essential motivation. It is well established that the focus of obsessional anxiety seen in OCD – concerns for safety and protection from potential threat – is similar in content to normal safety-based motivation experienced in the general population (Abramowitz, 2006); where patients appear to differ is in the subjective experience of anxiety associated with these thoughts, and the frequency and duration of its associated corrective behaviours. OCD behaviours are centered around safety concerns that may have had serious consequences in our evolutionary history (for example, hoarding food, checking for predatory animals, or avoiding unhygienic or ill members of the group). This supports the view of OCD as a disorder of essential motivation, wherein such “extreme” behaviours may have conferred an evolutionary advantage for survival, allowing the disorder to persevere in the population (Boyer & Lienard, 2006). OCD-like behaviours have persisted, not only in humans, but in a number of other species as well, all involving repetitive motor programs aimed at threat prevention (Stein, Dodman & Moon-Fanelli, 1996).

If, in fact, the etiology of OCD results from dysfunctions in motivation, the question of interest then becomes determining *where* in the security-motivation circuit this dysfunction arises. When patients afflicted with Obsessive-Compulsive disorder are asked to describe their state of mind during the experience of obsessions and compulsions, they generally do not indicate a sense of being overwhelmed by the urgency or severity of their obsessions, but rather an inability to exert control over the engagement in the associated repetitive acts. They describe themselves as “not having the willpower to stop”, and being unable to have “self control [and] stop wasting time” on these acts (Reed, 1977), leading some to liken OCD to a disorder of impulse control. Importantly, such depictions of OCD emphasize the dissociation between the performance of security behaviours and the normal capacity of these behaviours to effectively attenuate anxiety. For this reason, Szechtman and Woody (2004) conceptualize OCD as a disorder of stopping. In this view, compulsions are abnormally repeated due to perseveration of the Security-Related programs component of the Security-Motivation circuit (where appropriate motor plans for potential threat response are produced) or as a result a dysfunction in the appropriate feedback from these motor behaviours on the termination of Security-Motivation.

If security-related actions fail to generate a “feeling of knowing”, the Security-Motivation or Appraisal of Potential Danger modules of the Security-Motivation system (SMS) (and its associated anxiety) would remain activated. Although patients may be cognitively aware that they have participated in the corrective act, and thus realize that their continued anxiety is unwarranted, the disturbance in the SMS negative-feedback pathway and lack of SMS termination would compel them to continue the behaviour. The sites of potential dysfunction indicated in Figure 1’s model of SMS communication highlight how disordered feedback to motor outputs or Yedasentience may result in such perseveration. In this way, these behaviours may become ritualistic and habitual for the sufferer, despite providing no genuine relief. Patients describe continuing these actions in an attempt to "feel just right", suggesting a reliance on yedasentience to determine when to stop. A study examining the effect of blocking the feeling of knowing through hypnosis (Woody, Lewis, Snider, Grant, Kamath & Szechtman, 2005) showed that a lack of yedasentience elicited OCD-like behaviours (prolonged anxiety and production of compulsive acts) in non-clinical participants. This model also helps to explain the ego-dystonic nature of OCD, wherein a conflict exists between intact cognitive appraisal of the environment (objectively, external cues for potential threat may no longer be present, indicating that the patient is most likely out of danger) and the subjective experience that security-related actions have not yet removed the threat.

CHAPTER 3: TESTING THE SECURITY-MOTIVATION HYPOTHESIS OF OBSESSIVE-COMPULSIVE DISORDER

I. Measurement of Security-Motivation

If Obsessive-Compulsive Disorder (OCD) does, indeed, reflect a disturbance of a hardwired motivational circuit, we should be able to determine the neurophysiological components responsible for symptom presentation by manipulating the function of the Security-Motivation system (SMS). The prediction that OCD is a disorder of deactivation does not exclude the possibility that deficits in motivation, appraisal or motor programs also exist, and may contribute to the manifestation of symptoms. It is important for the constructs of the SMS to be explored in both clinical and non-clinical populations in order to effectively compare threat detection, appraisal and effect of threat removal behaviour between groups.

Since anxiety is an essential component of security-motivation (constituting the affective output of its activation), it is proposed to be an effective measure of activation of the SMS. Tracking anxiety over time in human participants in response to contamination- or safety-threat exposure is pertinent to the proper understanding of how particular cues trigger, and maintain activation of, the Security-Motivation system. By monitoring the time-course and fluctuation of anxiety during corrective responses, such as washing or checking, it may be better understood how dysfunction in its dynamics may relate to OCD behaviours.

A consideration of Porges' polyvagal theory (Porges, 2001) provides a rationale for tracking heart rate variability as a physiological, relatively objective measure of anxiety. The autonomic nervous system consists of the sympathetic and parasympathetic branches which act antagonistically to regulate homeostasis; sympathetic output mobilizes the body for action and defense behaviours during times of stress, while parasympathetic output serves to conserve energy. The major parasympathetic output from the brain – the vagus nerve – innervates the visceral organs, and is essential for regulation of the cardiac rhythm and decrease in heart rate. Porges proposes that the vagal nerve itself has two branches: the unmyelinated branch, responsible for immobilization behaviours when faced with imminent threat, and the myelinated branch which inhibits arousal and facilitates a relaxed state in the absence of danger cues (Porges, 2007a) (See Table 1).

ANS Component	Behavioural Function	Neural Pathway
Myelinated vagus	Social communication Inhibition of arousal	Stems from the nucleus ambiguous of the brain stem
Sympathetic-adrenal system	Mobilization (active)	Stems from the spinal cord sympathetic nuclei
Unmyelinated vagus	Immobilization	Stems from the dorsal motor nucleus of CN X

Table 1: The three subsystems of the polyvagal theory (Porges, 2007a).

Furthermore, it is suggested that the myelinated vagus acts as a "vagal brake", modulating the impact of the sympathetic system on the cardiac rhythm. When attention is shifted to the potential for threat, the influence from the parasympathetic system is reduced in order to allow for increased sympathetic readiness in case of an actual need to mobilize energy for defensive action.

Importantly, innervation of the heart by the vagus nerve results in heart rate variability (HRV) – variation in the inter-beat heart rate pattern. Acute stress or anxiety lowers vagal tone, withdrawing vagal input to the heart and allowing for increased sympathetic input; in fact, if the vagal brake is chronically deficient or nonfunctional, the individual would be in a constant state of physiological readiness, an unending state of emergency (Porges, 2007b). Reduced vagal tone, in turn, lowers cardiac variability (Austin, Riniolo & Porges, 2007). Thus, by measuring HRV, we can determine the level of parasympathetic activity; here, HRV is quantified as a measure of respiratory sinus arrhythmia (RSA) (Porges, 2007b). Importantly, RSA change represents a pure index of vagal brake withdrawal unlike other measures of the cardiac rhythm such as heart rate, which is also affected by other parasympathetic and sympathetic inputs. This is important, as we are interested specifically in the input from the unmyelinated vagus to the cardiac pattern.

Evidence from the literature supports the measure of heart rate variability (HRV) as an indication of SMS activity concurrent with the experience of anxiety. Reduced HRV has been associated with the experience of negative emotional states, and chronically lowered HRV may be indicative of a higher risk for the development of mood or anxiety disorders (Porges, 2001). In addition, acute psychological stress has been shown to reduce HRV in a laboratory setting in response to anxiety-inducing situations (either natural or manufactured), such as exposure to traumatic images or participation in demanding cognitive tasks (Pieper, Brosschot, Van Der Leeden, & Thayer, 2007).

A shift towards increased sympathetic output is also associated with increased heart rate; therefore heart rate changes are also be indicative of increased anxiety, and may be tracked along with HRV measures. However, motivation towards threat avoidance is not expected to elicit full physiological reactions needed for fight or flight, so measures of parasympathetic withdrawal (HRV) are expected to more reliably reflect Security-Motivation activation as compared to heart rate.

The literature also supports the relationship between movement of the facial muscles and the expression of emotional state. Activation of the corrugator supercilli – located above the eyebrow – is associated with the furrowing of the brow in expressions of discomfort and disgust in emotionally unpleasant situations (Wolf, Mass, Ingenbleek, Kiefer, Naber & Wiedemann, 2005). Studies using facial electromyography (EMG) have shown a direct correlation between corrugator activation and the self-reported experience of discomfort (Bradley & Lang, 2000), which is largely involuntary. Therefore, measurement of corrugator activity can provide an additional measure of negative affect in response to potential threat exposure.

II. Experimental Design

In order to observe the time-course of anxiety and Security-Motivation activation after threat exposure, it is essential that the cues are relevant to security motivation, that they represent *potential* threats rather than actual, specific threats, pose a valid threat to self-preservation or safety, and are species appropriate. As indicated previously, safety concerns in both clinical and non-clinical human populations are largely focused on the threat of contamination (resulting in illness or death), attack by an aggressor, or causing harm to the self or others. Cues that are commonly associated with these threats include: foul odors, dirt and bodily fluids (contamination), unsecured doors and locks (aggressive attack) and indication that one has failed to neutralize a hazard (for example, smoke indicative of a fire that could cause serious harm). In reproducing valid threats in a laboratory setting, is it necessary to balance a desire to elicit authentic belief in the potential for the threat with the ethical consideration of ensuring that no *true* threat is present. Due to this constraint, many previous studies exploring the effect of threat exposure, particularly in the context of Obsessive-Compulsive disorder (OCD), have used stimuli which mimic threat cues in an unrealistic way. For example, the use of synthetic bodily fluids (water labeled “saliva” or rubber vomit) present threat cues that may be easily determined to be (or even defined as) fake (Tsao & McKay, 2004). In this case, it is not possible to accurately conclude that the responses generated to these cues would resemble those produced by mechanisms underlying the management of genuine threats.

Of the most common potential threat cues relevant for human study, those indicating contamination via germs or disease are arguably the easiest to control and manipulate experimentally (Szechtman and Woody, 2006). Concern about contamination involves a feeling of endangerment after exposure to people, places or objects that are perceived to be diseased or infected. Fecal matter, blood and vomit are commonly indicated as extremely salient cues, likely due to their association with states of parasitic or viral infection. In order to use effectively contamination stimuli for the study of security-motivation, there must be the perceived potential for acquired illness rather than simply the perception of the stimulus as being “disgusting”. Although the experience of disgust is often linked to that of contamination, and both may elicit similar reactive avoidance behaviours and affective states, they are not synonymous; contamination exists in the absence of disgust (and vice versa) and, importantly, stimuli invoking pure disgust are not necessarily perceived as a threat to health and safety (Rachman, 2004). For example, a pile of rotting meat may be disgusting, but it may not become a contamination threat unless touched or ingested. Contamination cues are often also more dependent on context (for example a stained toilet seat or used bandage that one may imply has been in contact with bodily fluids) rather than overt visible cues. This distinction is especially important because individuals who are highly sensitive to contamination cues tend to have a lower threshold for disgust, labeling something as “disgusting” or attributing properties of disgust to neutral objects more readily (Tsao & McKay, 2004).

Experimental monitoring of security-motivation relies also on the capacity for the measurement and manipulation of corrective behaviours; in addition, it is imperative that the behaviour of interest is both a valid representation of the naturally observed motivated response and can be reliably recreated in the lab environment. Washing or cleaning after contact with potential contamination threat is a predictable, highly homogeneous response that is also easily tracked.

Checking behaviours in response to potential safety threats are similarly common in humans, but are more difficult to control in a laboratory setting. Simulating a potentially dangerous situation in the lab can be done, but the threat must be realistic, and must invoke the participant to experience genuine doubt about their own safety. Checking most naturally occurs in response to personal spaces or objects - for example, OCD patients with checking compulsions are more inclined to perform compulsive checks in familiar environments, with behaviours directed towards items of personal value or significance; this generally includes one's own home (or that of a loved one). There is a large variety in the number and type of things that ultimately compel one to check. Some may routinely check doors or locks, others monitor electrical appliances, while another may be more concerned with checking that they have not unwittingly harmed a loved one. This makes generalizing a stimulus as invoking "checking" more difficult. Monitoring checking behaviours by using places or objects relevant to each individual participant is possible; an early study of compulsive checking determined that preventing the performance of security behaviour in response to a personally relevant checking-related obsession significantly increased subjective distress (Rachman & Roper, 1976). However, this design sacrifices control and consistency between subjects, and home-based studies often cannot utilize physiological recordings, instead relying on subjective ratings of anxiety.

To our knowledge, the literature involving the neurophysiology of potential threat detection and amelioration in human populations is limited, and reflects a lack of a sufficient paradigm for testing and manipulating threat exposure in a way that is naturalistic and properly controlled. The present body of research contributes several experimental paradigms designed to aid in advancing the study of security motivated behaviours and evaluate the hypothesis that the symptoms of OCD may be explained by Security-Motivation dysfunction.

CHAPTER 4: EXPERIMENTAL TEST OF THE EFFECT OF WASHING BEHAVIOUR ON SMS ACTIVATION

I. Basis for the Study

The results of this study were previously published in the peer-reviewed article entitled: Hinds, et al.: **The psychology of potential threat: properties of the security motivation system.** *Biological Psychology* 2010, 85(2): 331-337.

We established an experimental paradigm to test the prediction that the Security-Motivation system (SMS) responds to potential threat, and address the following specific research questions:

1) Can we observe activation of the security-motivation system in response to potential threat stimuli exposure? We hypothesized that contact with a stimulus containing cues for potential threat would act as a trigger for activation of Security-Motivation output. This should be observable as heightened anxiety (the affective correlate of SMS activation) and motivation to perform threat-removal behaviours.
2) Is this SMS activation specific to threat-related cues as opposed to being generalized to all stimulus contact? Our theory suggests that neutral cues which do not carry information about the potential for harm would not be effective in activating security motivation and security-related behaviours.
3) Does engagement in precautionary behaviour deactivate the SMS, once activated, by generating a negative feedback signal for SMS termination? We predicted that the completion of the appropriate behaviour produces the sense of task completion ("yedasentience"), deactivating the system and eliminating anxiety. We further hypothesized that preventing or delaying participation in corrective behaviours creates a prolonged anxiety due to the inability to inhibit the activated SMS.
4) Is the measurement of respiratory sinus arrhythmia (RSA) an appropriate and objective index of security-motivation activity? The time-course of SMS activation, decay and termination should be observed as a fluctuation in heart rate variability (HRV) with lowered HRV indicative of a heightened state of anxiety.

For this protocol to be effective, we needed to select, create and test a stimulus that could effectively activate Security-Motivation and thus represent a viable potential threat. In addition, we needed to control and manipulate the ability to participate in the corresponding security-based behaviours, monitor the effects of these manipulations on anxiety (SMS output), and determine all aspects of experimental timing.

II. Experimental Paradigm

a. Variables

Our first independent variable was the type of stimulus used for activation of the Security-Motivation appraisal system that would contain sufficient environmental cues for potential threat. It must pose no real harm to the individual (for ethical reasons), but still elicit genuine wariness of threat. Based on ease in manipulation and generalization, it was decided that the potential danger most appropriate was that of illness and disease; thus the stimuli of interest should contain cues for contamination. This stimulus needed to be convincing as a potentially dirty, germ-carrying object which looked, felt and smelt realistic. Development of the stimuli followed a process of trial and error, involving numerous modifications and variations on typical contamination threats. Early attempts involved the use of a novel concoction, a recipe designed to mimic the appearance and smell of human vomit. Ultimately, this stimulus was determined to be inappropriate for our study as it was not feasible to convince participants that it represented an authentic potential threat; it also likely elicited disgust responses due to the overt nature of the cues rather than security-motivation activation. Since bodily fluids are most readily associated with the transfer of disease, we decided to use diapers (expected to contain such fluids) as our stimuli. Real, clean baby's diapers were made to appear used and discarded through a number of modifications. A recipe was created for dirtying the diapers:

1) Diapers are opened and filled with water to create heaviness
2) Diapers are reclosed and sprayed with a mixture of water and ammonia (to create the odor of urine)
3) Diapers are stained subtly with yellow food coloring and chocolate
4) Diapers are handled to create the appearance of wear

To facilitate physical contact, seven diapers (manipulated as described above) were placed into a garbage bin labeled "Pediatrics" to create one contamination stimulus – a collection of discarded diapers. Immediately before experimentation, the diapers and bin interior were sprayed with a combination of water, ammonia and baby oil to create a texture and odor representative of contaminated waste that had been in contact with infants. By time of contact, no moisture remained, and no transferable residue was present on the stimuli.

A control condition was required for comparison between threat-related and neutral, non-safety-based cues with regards to elicitation of Security-Motivation activity. This stimulus needed to be in no way associated with contamination or any other variations of potential threat. After testing several options (including a bin filled with hand soap, and box of shredded paper, and water scented with rose oil), we selected clean, unused Styrofoam packaging peanuts as our control. This stimuli was easy to acquire and replace, and did not have any distinct texture or odor. For contact, the

Styrofoam peanuts were placed in a garbage bin identical to that used for the diaper stimuli, but without the label of “Pediatrics”.

Our second variable was the amount and timing of the behavioural actions in response to potential threat exposure. Manipulation of the security-motivated behavioural output (the action taken to remove the potential threat) was vital to our hypothesis to determine its role in controlling Security-Motivation activity. The appropriate motor output in response to contamination is washing or cleaning; hand washing, then, was determined as the behaviour of interest in response to contact with either the soiled diapers or packaging peanuts. The point during the experiment at which the participant was permitted to wash was expected to impact the time at which the Security-Motivation system was shut off. We controlled hand washing by restricting washing to a set time limit in one subset of participants, and delaying washing in the other. One issue raised was the fact that the protocol called for instructions in which one group was washing while the other group (for whom washing was delayed) was doing nothing. This was problematic as it presented a possible confound - it allowed for the possibility that physical activity in general (rather than the specific behaviour of washing) could account for the differences between groups. To correct for this discrepancy, instructions for a physical motor task were included, to be completed in lieu of washing for participants for whom washing was delayed. Several tasks were piloted, including manipulation of a puzzle; ultimately, a motor task mimicking the actions of hand washing without soap or water was designed, ensuring that this action closely resembled that which was being performed by the other group, yet did not provide any cognitive distraction.

Combination of the variables (washing condition and stimulus contacted) yielded four distinct experimental groups: Diaper/Wash Permitted, Diaper/Wash Delayed, Styrofoam/Wash Permitted and Styrofoam/Wash Delayed. The dependent variable of interest was the level of anxiety at each of the defined time points during the experiment.

b. Protocol

It was required that the experiment be set up in such a way as to best observe and track the dependent variable of anxiety fluctuation and security-motivation activation over time. Participants were recorded continuously over the course of approximately 15 minutes, wherein four distinct time points of interest were determined, each consisting of two minutes of observation. They were labeled as:

Baseline: Initial recording of baseline physiological measures (baseline anxiety)

After Exposure: Recording of measures after stimulus contact

After Fixed Task: Recording of measures after 30sec wash (or motor task)

After Free Wash: Recording of measures after unlimited washing

Interrupting these periods of interest were the periods of contact with the stimuli, instructions for participants and the actual activity of hand washing or motor task completion. The time-course of the experiment went as follows:

0-120 sec Subject's baseline measurements are recorded for exactly 2 minutes

120-240 sec Subject is given instructions for contact with stimuli (approximately 2 minutes)

240-360 sec Subject is in contact w/ stimuli for exactly 2 minutes

360-420 sec Stimuli are removed, subjects are given further instructions (approx 1 min)

420-540 sec Subject rests, focusing on hands, measurements are recorded for exactly 2 minutes

540-570 sec Subject is permitted to complete hand washing or motor task for exactly 30 sec

570-690 sec Subject rests again, same as before, measurements taken for exactly 2 min

690-800 sec Subject is permitted to wash hands for as long as they want

800-920 sec Subject rests, measurements taken for exactly 2 min

The independent variable "time of washing" determined whether washing was permitted at time 540-570 sec above. Manipulation here resulted in the period **After Fixed Task** in which some participants had washed while others had not. In accordance with our hypothesis, this should create individuals for whom the act of washing has elicited a sense of task completion (the washers) along with individuals who have not effectively dealt with the potential threat exposure (the non-washers). Thus, this timeline was optimal for observing the effect of engaging in threat removal behaviour (hand washing) on anxiety elicited by an activated Security-Motivation system.

Participants remained seated for the duration of the experiment, and rested quietly during the four observation periods with eyes closed. Resting before and after threat exposure ensured that any observed change in autonomic and psychological measures was due solely to experimental manipulation. Any unsolicited activity – such as physical movements or sensory stimulation – could confound our measurement of autonomic regulation. Movement also creates data artifacts due to the nature of our physiological recording. In addition, removing visual stimulation ensured that the participant was not exposed to any additional environmental information that may inadvertently alter the experience of the contamination threat cues; this could include anything that might signal an alternative threat, safety cues, or anything that could elicit a conflicting motivational state. To reduce these confounds, participants were given the following instructions during all four resting periods:

> "During this time, I would like you to sit as still as possible, with your hands resting in your lap, and your eyes closed. Try not to be distracted or let your mind wander. Ideally, we would like you to clear your mind - however this is not an easy task. Focus on how you are feeling, and where you are, right now. Relax as naturally as possible, and try not to manipulate your breathing, posture or muscle tone."

At the point of stimulus exposure, participants were given further information about the stimulus itself, and instructions for making physical contact with the diapers (or Styrofoam control) by submerging their left hand and arm into the bin. Instructions for threat exposure were as follows:

> "I want you to place your left hand into this pail full of [Styrofoam/Diapers], and tilt the pail towards you with your right hand. Nothing else is in the pail besides what you can see. Keep your hand in the pail until I instruct you to stop. Please keep your hand moving around and reach all the way to the bottom of the pail. Do not remove your hands from the pail until the 2 minutes is up and keep your eyes open at all times. Your actions should be similar to what you would do if you had dropped something into the bin, and were searching for it with your hand.

> I want you to think about how the diaper pail looks and feels. Keep your eyes focused on your hand at all times. Continue to contact the [Styrofoam/Diapers] with your hand, and think about how it feels to be touching them until I instruct you to stop. I want you to focus your attention on your hand at all times, really concentrating on your contact with the stimulus and think about how your hand feels, and whether or not you feel dirty or contaminated."

Participants were then instructed to remove their hand from the bin and proceed with the three comparative time points of interest: After Exposure, After Fixed Task and After Free Wash. During each of these times, participants were asked to focus attention on their hand, and the potential for it to be contaminated.

Hand washing and drying was permitted at least once during the duration of recording (during the Fixed Task for those in the wash condition, and during the Free Wash for both conditions). Participants were able to complete hand washing with minimal additional movement by being seated in the immediate proximity to a sink which was reachable by rotating of their chair, and remained seated for the duration of washing. The sink was fitted with an automatic, motion-activated faucet preset to deliver a consistent flow of warm water at about 25°C, as well as an automated soap dispenser. During washing, participants were asked to use whatever routine they would normally follow, to ensure that the behaviour would impact Security-Motivation in the same way that it would in a natural setting. The actual amount of time spent hand washing was recorded.

c. Participants

The participants were 76 university students and other individuals in the general public between the ages of 18-65, who were recruited via advertisements posted in the McMaster University campus and University Hospital, and on the university website. Their mean age was 24.6 years (SD = 7.4), and their mean body weight, height and BMI were 64.4 kg (SD = 10.2), 1.68 m (SD = 0.09), and 22.7 kg/m^2 (SD = 2.6), respectively. All participants were prescreened to ensure that they met inclusion criteria. Participants were excluded if they answered “yes” to any of the following:

- A previous diagnosis or treatment for a disorder or abnormality of the heart or respiratory system (due to the use of cardiac and respiratory measures as our dependent variable).
- Any known allergies that could be triggered by contact (due to the direct contact with stimuli that had been treated with cleaning products, oils, and foods).
- Any previous or current diagnosis or treatment for mood, personality or psychotic disorders – for example, depression, obsessive-compulsive disorder, panic disorder or schizophrenia (due to the potential confound of anxiety or mood disorder on the normal processing of threat information).

Participants were also required to refrain from caffeine, nicotine and other stimulants for at least 2 hours prior to the study, and were asked not to participate if they were currently ill or taking any over-the-counter medication. This was due to the potential effect of these drugs on the cardiac rhythm. This information was provided previous to attending the experimental session and was reconfirmed before beginning the study.

Participants currently taking other medications were not excluded, but medication history and information was recorded in case of potential effects on physiological function; most common was the use of oral contraceptives. Non-clinical status was confirmed through participation in a brief questionnaire derived from the Structured Clinical Interview for DSM Disorders in which participants were asked to report any symptoms suggesting a history of psychiatric disorder.

Each participant was randomly assigned to one of the four experimental conditions, subject to the constraint of allowing each group to have a comparable number of each gender (57 females and 19 males completed the study, with 4-5 males and 13-15 females per group) and to ensure an approximately equal age composition across groups.

III. Measurements

a. Physiological Recordings

We were interested in the fluctuation of heart rate variability (HRV), heart rate and facial movement as a function of the stimulus to which participants were exposed and their ability to engage in hand washing. All physiological data were collected using the Biopac Acquisition Unit (BSL PRO MP 35) which was customized for the recording of electrocardiography (ECG), electromyography (EMG), and respiratory data in our participants. ECG provides a measure of the cardiac pattern, and is influenced by respiratory patterns. EMG from the facial muscles provides a measure of corrugator activation (facial response to compelling or disgusting stimuli).

EMG data were collected using three adherent electrodes placed on the forehead – two about the left corrugator supercilli muscle (immediately above the inner boundary of the eyebrow, spaced approximately one inch apart), and one ground electrode in the center of the forehead. Data were collected via analog input channels at a sample rate of 2000 Hz, with filter rates as determined by Biopac presets as appropriate for EMG recording. Raw data were automatically converted to root mean square (RMS), a measure of EMG power wherein each data point was averaged over 500 samples, reducing data noise, to obtain an average measure of muscle contraction. RMS scores were extracted directly from the Biopac data output.

ECG was recorded via two adherent electrodes placed on the inner ankle of both feet (just above the ankle bone), and one electrode on the inside of the right wrist. Data were collected at a sample rate of 2000 Hz with filter rates as appropriate for adult ECG recording according to Biopac presets. Respiratory sinus arrhythmia (RSA, our measure of heart rate variability) was not directly obtainable using the acquisition software, and required a more sophisticated program. The raw ECG data were extracted from Biopac and converted to a form readable by Porges' MxEdit software (Brain-Body Centre, University of Illinois, Chicago) (Porges, 2007b) and edited within this program. The RSA index of vagal tone (as calculated from cardiac inter-beat intervals) and corresponding scores for heart rate variability (HRV) were calculated using MxEdit. Editing of raw heart rate data was completed manually according to approved guidelines (Brain-Body Centre, University of Illinois, Chicago) which require no more than 5% of the raw data be edited, in order to conserve data validity. Since our measurements were collected from participants at complete rest, recording artifacts requiring editing were extremely rare, and well below the suggested 5% limit. Any data sets containing significant artifacts produced through either machine or human error resulted in that set being discarded. The final MxEdit output produced an average HRV and heart rate score for each two minute recording segment of ECG data (four segments per participant).

Due to the nature of the Biopac recording system, once recording began it could not be paused without altering the data calibration; therefore, it was required that each data acquisition be taken as a continuous recording for the entire duration of physiological monitoring. As such, about half of each data file included usable data (the four 2-minute resting recordings of interest) while the other half reflected the data recordings taken in between these time points (for example, during instructions and washing times). These unnecessary data were removed during data processing in MxEdit.

b. Subjective Measures

To assess the participants' subjective experience of potential contamination and motivation to participate in corrective behaviours, a rating questionnaire was created. Upon completion of the study, participants were asked to reflect back to the **time of stimulus contact** and rate their subjective level of discomfort, feeling of contamination, and urge to wash on a scale of 0-10 (See Figure 3).

HOW WOULD YOU RATE YOUR LEVEL OF DISCOMFORT & FEELING OF BEING CONTAMINATED DURING CONTACT WITH THE WET & SOILED DIAPERS?

Please Rate on a scale of 1 to 10: 1 – Not at all disgusted, 10 – Extremely disgusted

1 2 3 4 5 6 7 8 9 10

HOW STRONGLY WOULD YOU RATE YOUR COMPULSION TO WASH YOUR HANDS AFTER CONTACT WITH THE WET & SOILED DIAPERS?

Please Rate on a scale of 1 to 10: 1 – Not at all compelled, 10 – Extremely compelled

1 2 3 4 5 6 7 8 9 10

Figure 3: Sample questionnaire for participants. For control groups, the phrase "Wet & Soiled Diapers" was replaced with "Styrofoam Peanuts".

All participants were also asked to complete the Padua Inventory Washington State University Revision (PI–WSUR) (Burns, Keortge, Formea & Sternberger, 1996) upon completion of the experiment. The PI-WSUR is a self-report inventory consisting of 39 questions about the type and strength of obsessive-compulsive symptoms, but was given to non-clinical participants in order to assess their perception of potential threats in normal daily life. Separate subscales within the PI–WSUR relate to either washing or checking concerns; by scoring the response to the subset of questions relating to washing, we could determine the individual's level of preoccupation with exposure to germs and the threat of personal contamination.

All participants were expected to score within the normal range on the total Padua and within the washing subset. The average total score for individuals without OCD is approximately 22 and average contamination score is approximately 7 (Burns, Keortge, Formea & Sternberger, 1996). Although a high PI-WSUR score does not necessarily suggest a clinical diagnosis, this information was important for assessing individuals with higher than average aversions to potential contamination. Since the average total PI-WSUR score for individuals with Obsessive-Compulsive disorder is approximately 55, and 14 for the contamination score, we determined that the PI-WSUR score for eligible participants must not exceed 38 (one standard deviation above the total mean) and that their score on the contamination subset must not exceed 12 (one standard deviation above this mean). This ensured that our participant sample could be reliably distinguished from the clinical or sub-clinical population.

IV. Results

Recalling that the purpose of this experiment was to observe the dynamics of the proposed Security-Motivation system (SMS) in response to potential threat and participation in corrective behaviours, the principal data of interest in this experiment are the SMS measures after stimulus contact (diapers or Styrofoam), after prescribed behaviour (controlled hand washing or sham wash/motor task) and after unlimited free washing. Our hypothesis of the role of security-motivation in response to contamination threat suggested that contact with the soiled diapers would activate the SMS, producing a motivated state of anxiety directed at removal of the threat, which would only be deactivated through hand washing.

Statistical analysis for physiological data was performed only on recordings during the predetermined rest periods. We discarded any physiological data that were incomplete or unreadable due to equipment malfunction or improper positioning or adherence of electrodes. As per MxEdit protocol (Porges, MxEdit manual), a maximum of 5% of the total cardiac data may be edited to correct for artifacts in order to maintain validity of the data. Therefore, any data that required extensive editing were also discarded. We also compared subjective ratings and mean wash times between experimental groups.

Raw respiratory sinus arrhythmia (RSA) scores were converted to reflect RSA change from baseline by subtracting the RSA values at the time periods of interest from their baseline scores; in this way, higher scores reflect a larger decrease in RSA. A larger reduction in RSA is, in turn, reflective of a greater loss of heart rate variability, reduced activity of the vagal brake, and higher levels of SMS activation. Therefore, an increase in RSA change suggests increased anxiety/SMS activation, while a decrease in RSA change suggests lowered anxiety/SMS deactivation. All statistical data were entered into SPSS software to determine statistical significance. RSA change data was analyzed with a repeated measures multivariate analysis of covariance (MANCOVA), using time point of measurement as the within-subjects factor, condition and stimulus as between-subject factors, and baseline RSA, age, and sex as covariates.

As predicted, the three-way interaction of Stimulus, Prescribed Behavior, and Time of Measurement was statistically significant, $F(2, 68) = 13.78$, $p < .001$ for RSA change. Figure 4 shows the relevant adjusted means.

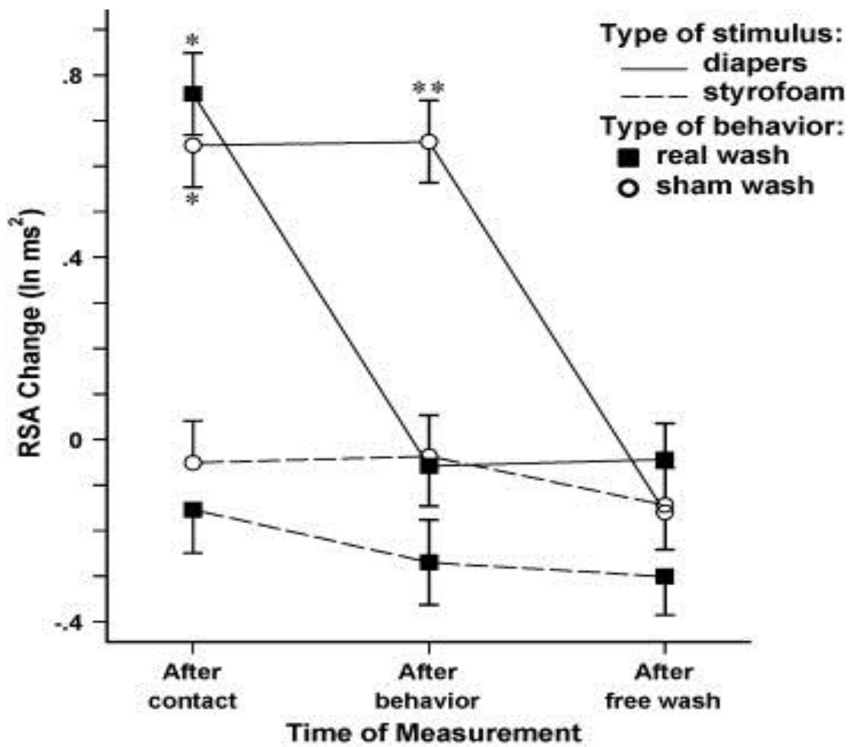

Figure 4: Effect of behaviour on terminating SMS activity. *$p<0.05$ vs groups in the Styrofoam stimulus condition at the same time; **$p<0.05$ vs the other 3 groups at the same time of measurement. Error bars represent 1 SE.

(Hinds, Woody, Drandic, Schmidt, Van Ameringen & Szechtman, The Psychology of Potential Threat: Properties of the Security Motivation System, *Biological Psychology*, *85*, 331-337, 2010. Published by Elsevier, reprinted with permission.)

Analysis of EMG power showed an extremely high level of corrugator activity during stimulus exposure, both to the contamination and control stimuli. This was expected due to the fact that the eyes were open during contact, and the participant was actively concentrating on, and expressing an emotional reaction to, the stimuli. While the pattern of EMG remained significantly heightened after exposure, activity decayed slowly to baseline regardless of hand washing, and did not differ significantly between groups based on type of exposure. Of note, retrospective review of the paradigm demonstrated that participants may have been inadvertently affected by the placement of the facial electrodes leading to a potential confound of the results. While the electrodes were non-invasive, the electrode leads pulled slightly on the skin due to their weight; given that the face is sensitive, this may have posed a distraction. Sweat on the brow was also more likely to cause the electrodes to become loose, despite the removal of moisturizing agents and makeup products from the face prior to recording. It is possible that the residual EMG activity reflects habitual and subconscious movement of the muscle in response to a persistent tactile stimulation rather than a display of anxiety or disgust.

Subjective rating scores and wash times served as a check to verify that the diapers elicited higher subjective discomfort and motivation to participate in hand washing than did the Styrofoam peanuts. A 2x2 analysis of variance was used to compare mean scores on subjective ratings and time spent washing between groups. Stimulus and Prescribed Behaviour were between-subject variables. The mean ratings of discomfort were significantly higher for those who had contacted the diapers in comparison to those who had been exposed to Styrofoam, for main effect of Stimulus, $F(1,80) = 344.94$, $p<0.001$. Urge to wash after stimulus exposure was also significantly higher for those in the diaper condition, for main effect of Stimulus, $F(1,80) = 263.14$, $p<0.001$. Participants exposed to diapers also washed for a significantly longer period of time (measured in seconds) during the Free Wash as compared to those in the Styrofoam groups, regardless of whether or not washing had previously been permitted, for main effect of Stimulus, $F(1,80) = 59.06$, $p<0.001$. See Table 2.

	Contamination-Wash	*Contamination-Sham*	*Control-Wash*	*Control-Sham*
Rating of Discomfort	7.20±1.61	6.25±1.92	1.35±0.81	1.10±0.31
Rating of Urge to Wash	7.85±1.46	7.70±1.98	1.95±1.39	2.05±1.47
Free Wash Time (in sec)	17.10±8.59	29.60±9.32	7.00±3.24	14.30±6.86

Table 2: Mean ±SD values for subjective ratings and free wash times.

V. Implications

As predicted, exposure to a potential threat suggesting contamination elicited a significant change in RSA, a measure of heart rate variability, which persisted until an appropriate behaviour to alleviate the threat was completed. Anxiety remained elevated in delay-wash individuals across both time periods monitored before washing was permitted, and participants permitted to wash earlier showed a significant drop in anxiety back to baseline levels after washing. Once washing occurred for all individuals, all resting physiological measures of anxiety showed a significant return to baseline levels. The reliance on washing to produce sufficient recovery of RSA and removal of SMS activity supports the hypothesis that this behaviour supplies the internal termination signal for the SMS. Activation was not seen after exposure to a neutral stimulus, suggesting that this activation is specifically associated with security-based motivation, which corresponds to our hypothesis that situations or objects which do not present a cue for potential danger should not activate the Security-Motivation system; participants exposed to Styrofoam neither experienced anxiety (the system output) nor benefited by engaging in the terminating washing behaviour. The increased discomfort rating and wash times for those exposed to diapers (as opposed to Styrofoam) are consistent with the expectation that potential threat cues elicit both anxiety and wariness of the environment, as well as a motivation toward threat removal.

The results of this study provide the basis for a solid understanding of the parameters of Security-Motivation activation and disengagement, and allows for a more sophisticated and specific analysis of the system, including the susceptibility of the termination feedback loop to cognitive involvement, and the variability of these results between populations. Of particular interest is the comparison of non-OCD participants with those diagnosed with obsessive-compulsive disorder, due to the expected role of the SMS in this disorder.

CHAPTER 5: EFFECT OF MANIPULATION OF COGNITIVE APPRAISAL OF POTENTIAL THREAT ON THE SMS

I. Basis for the Study

The results of this study were previously published in the peer-reviewed article entitled: Hinds, et al.: **The psychology of potential threat: properties of the security motivation system.** *Biological Psychology* 2010, 85(2): 331-337.

We have gathered evidence in support of the hypothesis that participating in behaviours directed towards the amelioration of potential threats acts as the essential termination signal for Security-Motivation system (SMS) activation. While our previous findings have demonstrated that SMS activity persists in the absence of corrective threat removal, they do not provide definitive proof that performance of precautionary behaviour is *necessary* to deactivate security motivation and that the SMS cannot be similarly shut down via other methods. Thus, we established an experimental paradigm to address the following research question:

> Can participation in a cognitive reevaluation of the potential threat stimuli effectively terminate SMS activation in place of feedback from threat-removal behaviour? We hypothesized that the activated system requires corrective action to return to baseline, and that cognitive feedback on security motivation would be ineffective. This should be observable as maintenance of an activated state after contact with a potentially threatening stimulus despite later cognitive feedback that the threat is invalid.

To support our hypothesis, we needed to demonstrate that cognitive strategies are not effective substitutes for corrective behaviour – in other words, that attempts to shut off the activated Security-Motivation system via cognitive processes are ineffective. This required the development of a protocol to introduce an alternative strategy for shutting down the SMS by altering the interpretation of experimental stimuli.

II. Experimental Paradigm

a. Variables

As we were interested in activation of the Security-Motivation system (SMS), we needed our stimulus to contain potential threat cues, and therefore used a version of our stimuli of diapers made to appear contaminated. Real, clean baby's diapers were modified using the following recipe:

1) Diapers are opened and moistened internally with a small amount of water
2) Diapers are closed and sprayed with water externally
3) Diapers are handled to create the appearance of wear

Pilot work discussed in the next chapter showed that this level of stimulus was sufficient to activate the SMS. As in our previous studies, diapers (manipulated as described above) were placed into a garbage bin labeled "Pediatrics" to create one contamination stimulus – a collection of discarded diapers. Type of Termination Behaviour was also a variable of interest, as we created a time point at which as some participants were permitted to wash without delay (washing-based termination), while others were reliant on cognitive strategies to cope with threat exposure (cognitive-reappraisal-based termination). The dependent variable was again the level of anxiety at each of the defined time points during the experiment.

The independent variable of interest for this study was not the stimulus itself, but rather the information *about* this stimulus that participants were provided. Of importance was both the type of information given (what they were told about the stimulus), and the timing of its delivery. To determine if the SMS could still be activated in the absence of a valid contamination threat, and if it could be deactivated through cognitive rather than behavioural strategies, we developed three experimental groups that differed in when they got information negating threat, and whether they were permitted to engage in corrective washing (the Fixed Wash):

Group 1: This group was provided with information negating the possibility of potential threat *before* contact with the stimulus; they also were permitted to engage in a corrective Fixed Wash after contact.

Group 2: This group was given the same information for negation of the contamination threat as Group 1, but it was provided only *after* exposure to the stimulus, and *in place of* the corrective Fixed Wash. In this case, cognitive re-evaluation of the threat (via new information) was, itself, the corrective behaviour.

Group 3: This group, acting as a control condition, was given no information at any time negating the possibility of potential danger, and engaged in a Fixed Wash; this condition was the same as the original washing condition as tested in the study of experimental manipulation of security-motivation (Chapter 4).

b. Protocol

To determine the effect of cognitive reappraisal of contamination threats on activity of the Security-Motivation system (SMS), we created a paradigm in which we could observe if these cognitive strategies altered the expected time-course of SMS activation and disengagement. It was required that the experiment be set up, as in our previous studies, to observe and track the dependent variable of anxiety fluctuation and security-motivation activation over time. Participants were recorded continuously over the course of approximately 15 minutes, wherein four distinct time points of interest were determined, each consisting of two minutes of observation. They were labeled as:

Baseline: Initial recording of baseline physiological measures (baseline anxiety)

After Exposure: Recording of measures after stimulus contact

After Fixed Task: Recording of measures after 30sec wash or 30 sec of cognitive reappraisal of the stimuli.

After Free Wash: Recording of measures after unlimited washing

Interrupting these periods of interest were the periods of contact with the stimuli, instructions and appraisal information for participants and the actual activity of hand washing. The time-course of the experiment went as follows:

0-120 sec	Subject's measurements are recorded for exactly 2 minutes
120-240 sec	Subject is given instructions for contact with stimuli (approximately 2 minutes).
240-270 sec	**Subject is either given information about innocuousness of stimuli, or no additional information**
270-390 sec	Subject is in contact w/ stimuli for exactly 2 minutes
390-450 sec	Stimuli are removed, subjects are given further instructions (approx 1 min)
450-570 sec	Subject rests, focusing on hands, measurements are recorded for exactly 2 minutes
570-600 sec	**Subject is either given information about innocuousness of stimuli, or permitted to complete hand washing for exactly 30 sec**
600-720 sec	Subject rests again, same as before, measurements taken for exactly 2 min
720-840 sec	Subject is permitted to wash hands for as long as they want
840-960 sec	Subject rests, measurements taken for exactly 2 min

The three groups differed in whether knowledge that the diapers were innocuous was provided at time 240-270 sec above, 570-600 sec above, or not at all. This design was optimal for observing the effect and timing of cognitive evaluation of stimuli on the SMS. The effect of cognitive evaluation of the stimulus given before versus after contact could be compared, as could the effect of giving this cognitive information after contact versus the effect of participating in corrective washing. The latter contrast is especially important for testing whether cognitive reappraisal after contact can substitute for corrective behaviour in the deactivation of the SMS.

Participants remained seated for the duration of the experiment, and rested quietly during the four observation periods with eyes closed. As in our previous studies, they were instructed to relax naturally and avoid becoming distracted, while focusing attention on their state of mind. At the point of stimulus exposure, participants were given further instructions for making physical contact with the diapers by submerging their left hand and arm into the bin. For participants in the group that got the threat-negating information before contact, the following additional information was given:

> "The diapers you will be touching appear dirty and used, but they are actual clean and unused, and in no way contaminated. The appearance of being used and discarded has been created by crumpling the diapers and simply wetting them with clean water."

After two minutes of contact, participants were instructed to remove their hand from the bin. All participants then proceeded with the three comparative time points of interest: After Exposure, After Fixed Task (washing or receipt of threat-negating information) and After Free Wash. During the Fixed Task, participants in the group that got threat-negating information were given the same information as described above for the before-exposure group, rather than washing. During each of the recording times, participants were asked to focus attention on their hand, and the potential for it to be contaminated.

Hand washing was permitted during the Fixed Wash (for two of three groups), and during the Free Wash (for all groups); the protocol for hand washing did not change from our previous studies in which participants rotated towards an automatic, motion-activated faucet while remaining seated for the duration of washing. During washing, participants were asked to use their normal routine, and the actual amount of time spent hand washing was recorded.

c. Participants

Participants were 45 (36 female and 9 male) individuals in the general public between the ages of 18-65, recruited through ads posted in the University hospital and online. The mean age was 26.5 years (SD = 8.2), and mean body weight, height and BMI were 66.6 kg (SD = 11.7), 1.71 m (SD = 0.07), and 22.8 kg/m^2 (SD = 3.1), respectively. All participants were screened for eligibility as in our original study protocol: exclusion on the basis of psychiatric, cardiac or respiratory disorder, or allergy, and avoidance of stimulants at least 2 hours before participating in the study. Subjects taking medications for conditions other than those listed above were not excluded, but medication history was recorded. Each participant was randomly assigned to one of the three experimental conditions, subject to gender constraint and attempts to avoid differences in age composition between groups. 15 participants (12 women and 3 men) were in each group.

III. Measurements

a. Physiological Recordings

From our previous studies, we determined RSA (as a measure of heart rate variability) to be the most robust and consistent measure of activation of the Security-Motivation system. Therefore, we were again interested in the fluctuation of heart rate variability (HRV) as a function of the timing and type of stimulus information provided to participants. All physiological data were collected using the Biopac Acquisition Unit (BSL PRO MP 35) customized for the recording of electrocardiogram (ECG) and respiratory data. As in our original paradigm (Chapter 4), ECG was recorded via electrodes on the ankles and wrist with sample and filter rates appropriate for adult ECG recording. Raw ECG data were extracted and then edited in MxEdit analysis software for the calculation of the RSA index of vagal tone and corresponding heart rate variability scores. Output produced a final average HRV for each two minute recording segment of ECG data (four segments per participant).

b. Subjective Measures

To assess the participants' subjective experience during the duration of physiological recording and exposure to the diaper stimulus, a rating scale was created. This scale was developed as an expansion of the rating questionnaire, which asked participants to retrospectively self-report their affective state during stimulus exposure (on a scale of 0-10). There were three significant revisions made to improve the validity of this rating scale (see Figure 5).

1) Subjective ratings were gathered at four points during the experiment, rather than only once at the completion of the study as a whole. Ratings were recorded

immediately after stimulus contact, and then at the end of each of the following two-minute physiological recording periods (After Exposure, After Fixed Task and After Free Wash). This revision permitted a more complete picture of the time-course of affective state across the duration of the experiment, and as a direct correlate of security motivation state.

2) The self-report ratings were converted from an interval scale (where subjects had to choose a distinct number to represent their feeling state) to a continuous, linear scale (where participants placed themselves on a continuum). Participants were asked to indicate on the line where they rated themselves on the measure, according to a defined description for the highest and lowest points. This allowed for more specificity and accuracy in the ratings, as well as the ability to reflect smaller fluctuations in affect.

3) A specific measure of anxiety state was requested, to specifically focus on the affective state most associated with SMS activation. Ratings for sense of contamination and urge to wash also remained. To determine the subjective experience of security motivation termination via hand washing, participants were also asked an additional question following both periods of washing in which they rated their internal sense of self-satisfaction from completion of the task.

The linear scale was 15cm long, so the point at which the participant placed his or her mark on the line was measured as a distance from point ‘0’ (the left-most point on the line), and labeled as a score in millimeters. Time spent washing at each of the two wash periods was also recorded.

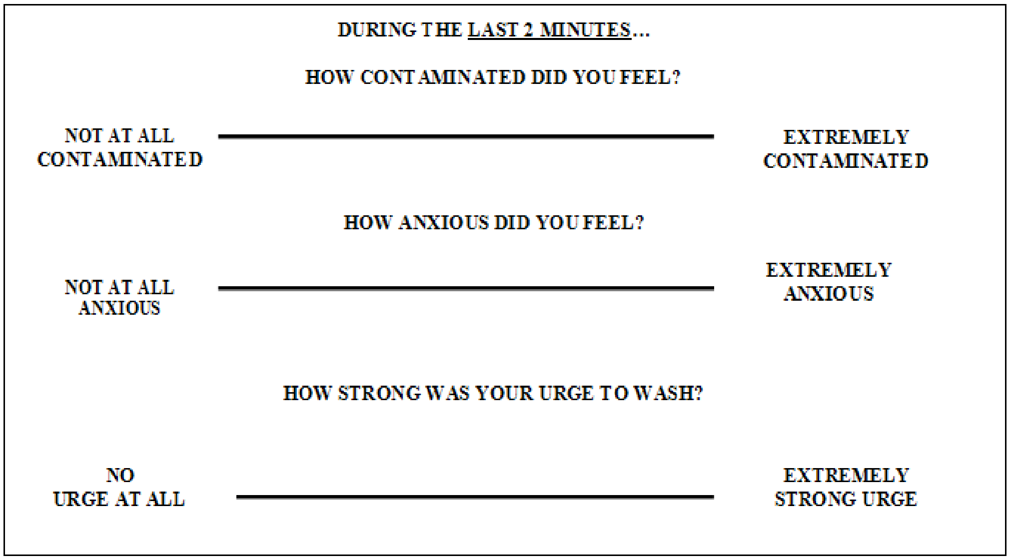

Figure 5: Sample linear scale for participants.

All participants completed the Padua Inventory (PI-WSUR) upon completion of the experiment to determine the individual's everyday tolerance to germs and contamination, and to classify individuals scoring significantly higher than the expected average scores for the total Padua and washing subset (as described in Chapter 4); cutoffs were a total score of 38, and contamination score of 12.

IV. Results

The purpose of this experiment was to observe the results of our experimental manipulations on the dynamics of Security-Motivation in response to potential threat and participation in corrective washing. The principal data of interest here are the measures of SMS activity after contact with lightly soiled diapers and after both controlled and unlimited hand washing, and controlled cognitive reevaluation, all dependent on when and if it is known that the diaper contamination has been manipulated. Our hypothesis that true contamination threat is necessary for SMS activation suggested threat exposure to visual and tactile cues for contamination without their association with real potential threat would be ineffective at eliciting security-motivation. Importantly, we predicted that this manipulation would only prevent SMS activity *before* exposure; the expectation was that removing threat validity after the SMS was already active would be "too late" – at this point, cognitive reappraisal or attempts to consciously deactivate security motivation would fail, and behavioural output would be required to return the system to baseline.

Statistical analysis for physiological data was performed on recordings collected during the four rest periods of interest. Any physiological data that were incomplete or unreadable, or required excessive editing was discarded. Raw respiratory sinus arrhythmia (RSA) scores were converted to reflect RSA change from baseline by subtracting the RSA values at the time periods of interest from their baseline scores for statistical analysis. We also compared subjective ratings and mean wash times between experimental groups.

RSA change data were analyzed with a repeated measures multivariate analysis of covariance (MANCOVA), using baseline RSA, age, and sex as covariates. There were two significant effects - the main effect of Group, $F(2, 39) = 9.49$, $p < .001$, and the interaction of Group with Time of Measurement, $F(4, 78) = 10.98$, $p = .001$. Subjective ratings for urge to wash, anxiety, and sense of contamination were analyzed as a within-subjects factor using a MANCOVA; age and sex were used as covariates. As in the RSA data, for the ratings, the main effect of Group, $F(2, 40) = 33.78$, $p < .001$, and the interaction of Group with Time of Measurement, $F(4, 80) = 39.52$, $p = .001$ were again significant. The lack of significant interactions with the factor of type of subjective rating indicated that these effects generalized across all three types of subjective ratings.

Figure 6 shows the time-course of RSA change and affective ratings as a function of information exposure and type of SMS-terminating behaviour. Immediately following contact with the diapers, the two groups that had not received information negating potential harm showed significantly greater activation than the group that had received this information before contact. At the time After Fixed Task, the period after either fixed wash, or cognitive reassessment, the group receiving information negating potential harm at this time demonstrated significantly elevated SMS activity as compared to the other two groups, who had completed a period of hand washing. Thus, the attempt to deactivate security-motivation after threat exposure using a cognitive strategy was *not* an effective substitute for corrective activity (in this case, hand washing). All measures returned to baseline after participation in the appropriate hand wash behaviour (during the free wash) for all groups.

Figure 6 also shows the adjusted means for the total subjective rating score at each of the time points of interest, as an additional measure of Security-Motivation activation and affective state of anxiety. As was seen for RSA change, hand washing was the only behaviour successful at deactivating the SMS – a comparison between the washing groups with the pre-exposure information group shows that ratings remained elevated only after exposure to the cognitive strategy.

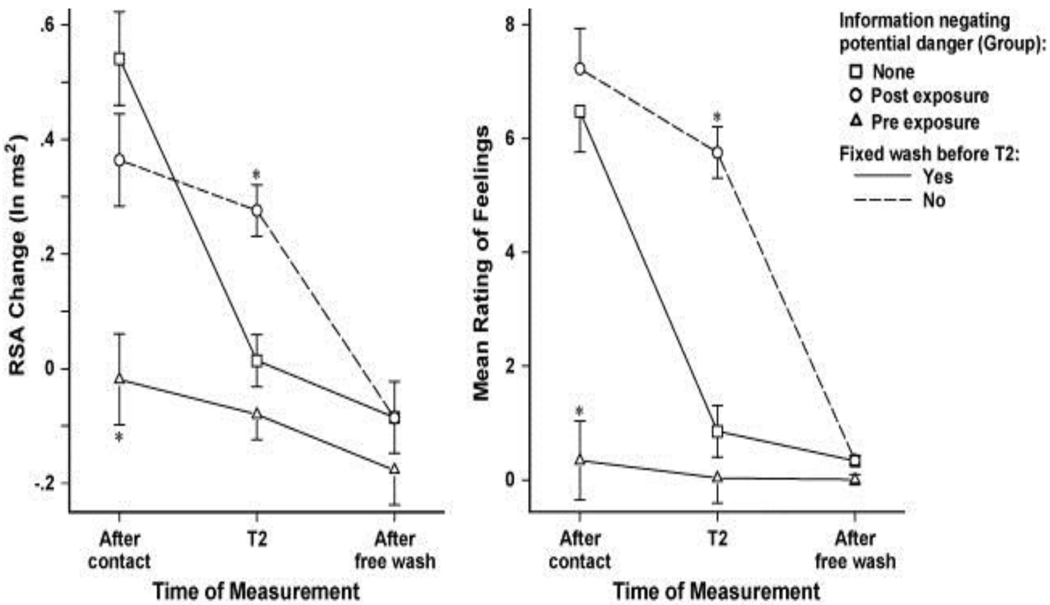

Figure 6: Effect of cognitive reappraisal of threat validity on SMS activity. T2 represents period after either fixed wash, or the provision of information negating potential harm. *p<0.05 compared to the other two groups at time of measurement. Error bars represent 1 SE. (Hinds, Woody, Drandic, Schmidt, Van Ameringen & Szechtman, The Psychology of Potential Threat: Properties of the Security Motivation System, *Biological Psychology, 85*, 331-337, 2010. Published by Elsevier, reprinted with permission.)

V. Implications

Measurement of both objective and subjective measures demonstrated, as predicted, that deactivation of the Security-Motivation system (SMS) requires corrective behaviour, which cannot be substituted with cognitive reappraisal strategies. Comparison of the effect of pre- versus post-exposure supplementation of threat appraisal with additional cue-related information showed that the timing of information presentation was the essential factor in whether it had an effect on SMS activity. This activity was measurable as the persistence of both anxiety and RSA change.

The results of this study imply that the SMS feedback and feeling of satisfaction produced by participation in motor behaviour, as outlined in the Security-Motivation hypothesis (Szechtman and Woody, 2004), is the dominant mode of quick and complete SMS termination. Further, the anxiety and wariness elicited by security motivation is strong enough to overwhelm the rational, cognitive evaluation of the environment; once one is in a state of readiness for engaging and managing a potential danger, the SMS does not appear to be able to deactivate solely on new information alone. In this way, there seems to be specific "rules" that the SMS abides by. The SMS appears to be very selective in its activation, responding to a range of relevant cues rather than a general sense of discomfort; once activation occurs, however, the system is committed to this decision, remaining decidedly inflexible to the influence of higher order cognitive input (even if this new information is relevant, and would significantly alter stimulus appraisal in the future). This pattern makes sense in view of the importance of this special motivational circuit for preventing serious threats to health and safety. Wariness and anxiety are strong indicators that something is amiss; making the decision to ignore those signals on the basis of new or more complete information may make sense rationally, but the extremely high cost of doing this in error may have limited this influence on the SMS over time. The results that we have generated through this study, then, help to form a more complete understanding of the role of security motivation and the parameters of control under which the system operates.

CHAPTER 6: MANIPULATION OF SECURITY-MOTIVATION IN OCD-AFFLICTED INDIVIDUALS

I. Basis for the Study

The results of this study were previously published in the peer-reviewed article entitled: Hinds et al.: **When too much is not enough: obsessive-compulsive disorder as a pathology of stopping, rather than starting.** *PLoS One* 2012, 7(1):e30586.

Our previous research based on the Security-Motivation hypothesis has provided evidence for the existence of this special system - a circuit specializing in the detection of, and response to, potential threats - in humans. Further, our research has demonstrated that security-based motivation is activated based on exposure to threat cues, such as signals for contamination, and that behaviours aimed at removing these threats act as the essential termination signal for the system. Our current objective was to establish the physiological and cognitive factors that may underlie dysfunction of the Security-Motivation system (SMS). By extending our findings to clinical populations – specifically those suffering from Obsessive-Compulsive disorder (OCD) symptoms – we may identify the role of the SMS in the development and production of OCD tendencies.

Much of our understanding of the SMS was based on studies in which its activity was studied for a relatively short period of time, and in which participation in corrective behaviour was completely effective in providing SMS termination feedback. Moving forward, we wanted a better understanding of how SMS activation persists over time in the prolonged absence of this feedback signal, particularly in circumstances in which the corrective behaviour is present, but ineffective. Although the SMS is proposed to require corrective actions toward potential threat, it is also expected that in the absence of corrective behaviour the activated SMS and corresponding anxiety follows a natural (but much slower) course of decay, returning the system to baseline if given enough time. This type of decay was an important consideration, particularly if we presume that certain types of motivation disorders reflect a reliance on this method of SMS termination due to dysfunction in the appropriate behavioural mechanisms. For details, then, on SMS decay, we looked to previous work conducted in our lab (Ana Drandic, Masters' Thesis). In this body of research, it was hypothesized that normal participants, in the absence of correction action, would show a very slow rate of recovery from SMS activation. Physiological measures and self reports of anxiety were expected to be significantly affected by potential threat exposure, an effect that would gradually wane over time. Interestingly, results showed that a time lapse of more than 20 minutes after potential threat exposure was insufficient to observe a return to baseline heart rate variability levels for participants who had been exposed to potentially contaminated stimuli. Thus, the results obtained by Ana Drandic (Masters' Thesis) revealed a very slowly decaying pattern of SMS activity in the absence of behavioural feedback.

The heightened anxiety and compulsion to wash seen in non-OCD participants disallowed from washing after contamination exposure is strikingly similar to that seen in Obsessive-Compulsive participants with washing-based symptoms. In addition, the role of anxiety in the appraisal and response to threat is also well understood as an essential component of normal motivation and affective output of the SMS. OCD is classified as an anxiety disorder, indicative of the fact that its classic symptoms are related to abnormalities in the expression or control of anxiety.

This lends credibility to the claim that OCD behaviours are exaggerations of the normal SMS mechanisms; however this dysfunction may be one of activation (a starting problem, where there is a pathological intensity of SMS excitation upon potential threat exposure), or one of stopping (where the normal SMS termination process fails). We established an experimental paradigm to test the prediction that the obsessions and compulsions associated with safety-related threats seen in OCD reflect dysfunction of the Security-Motivation system, and to address the following research questions:

1) Is activation of security-motivation in response to potential threat exposure in individuals afflicted with OCD different from that seen in non-OCD controls? We hypothesized that persons with OCD do not show disordered SMS activation, so that contact with a stimulus containing threat cues would trigger the SMS to a comparable degree in both those with OCD and controls. The type and intensity of threat cues, then, were not expected to affect the degree of SMS activity elicited.

2) Does engagement in precautionary corrective behaviour effectively generate a feedback signal for deactivation of the SMS, once security-motivation is activated, in OCD-afflicted individuals? We predicted that OCD reflects a disorder of stopping, so that the completion of the appropriate behaviour is unable to produce a sense of task completion. This should be observable as prolonged SMS activation (decreased heart rate variability) and experience of anxiety as compared to controls, despite similar corrective action, due to an inability to inhibit the active SMS.

To test these hypotheses, we needed a protocol to control, manipulate and monitor SMS activation in response to a relevant stimulus and the participation in the corresponding security-based behaviours, in both clinical and non-clinical populations.

II. Experimental Paradigm

a. Variables

As in our original study on the experimental manipulation of Security-Motivation (Chapter 4), the first independent variable was the type of stimulus used for activation of the Security-Motivation appraisal system via potential threat cues. Based on the success in our earlier paradigms, it was determined that the most appropriate stimulus was that which carried associated cues for contamination; concern for contamination is also one of the most highly reported subtypes of Obsessive-Compulsive disorder. We had shown strong results with the use of our soiled diapers, but we wanted to ensure that our manipulation of this contamination stimulus was most appropriate for the paradigm. As we were also interested in the effect of stimulus intensity (exposure to different variations and levels of contamination cues) on the differences between persons with OCD and controls on SMS measures, we needed subtle variations of our stimulus for presentation.

For these additional considerations to the experimental design, we consulted a previous body of work completed in our lab (Ana Drandic, Masters' Thesis). In this paradigm, the researchers explored SMS activity in normal participants after altering the contamination cues for the diaper stimulus to different degrees, creating distinct "levels" of stimulus intensity. In this study, participants were assigned contact with one of seven contamination intensities, ranging from the lowest exposure condition of clean Styrofoam (as used in previous studies as a control) to highly exaggerated cue exposure (see Table 3).

CONTAMINATION LEVEL	STIMULUS	STAIN
LEVEL 0	WHITE STYROFOAM PACKING BITS	NO
LEVEL 1	DIAPERS	NO (DRY, CLEAN)
LEVEL 2	DIAPERS	WATER
LEVEL 3	DIAPERS	WATER YELLOW FOOD COLOURING
LEVEL 4	DIAPERS	WATER AMMONIA SCENT YELLOW FOOD COLOURING
LEVEL 5	DIAPERS	WATER AMMONIA SCENT YELLOW FOOD COLOURING BROWN STAINS
LEVEL 6	DIAPERS	WATER AMMONIA SCENT YELLOW FOOD COLOURING BROWN STAINS IMMITATION FECES IMMITATION FECES SCENT

Table 3: Definition of stimulus intensity "Levels" as a measure of type and degree of associated cues.

It was hypothesized that the effect of contact on heart rate variability and subjective measures would correlate with stimulus intensity. Only Level 1 (dry diapers), Level 2 (wetted diapers) and Level 3 (wetted and discolored diapers) stimuli showed this trend, however, with these three levels differing strongly on physiological and subjective response consistent with the implied level of threat. As expected, Level 0 (Styrofoam) did not activate the SMS. The results of this study showed that contamination stimuli with relatively low levels of cues (and increased ambiguity for the actual contamination status of the object) were most effective for tracking changes in SMS activity over time.

For the current study, we chose the test three different levels of contamination stimulus intensity, selected to induce the most robust effect on the SMS and to differ in the level of implied threat of contamination. Thus contamination stimulus was defined as one of the following three levels:

Level 0: Control (no contamination threat) – clean, dry Styrofoam packing peanuts

Level 1: Contamination threat – dry diapers, opened and crumpled

Level 2: Contamination threat – diapers opened and crumpled, slightly weighted with a small amount of water inside the diaper, and wetted on the outside with water

Seven diapers were manipulated as described for levels 1 and 2 and placed into separate bins labeled Pediatrics. A similar bin was used for the control level, and filled with Styrofoam.

The second variable of interest was the participant type – normal control or OCD individual – as outlined below in “Participants”. We were most interested in the point after which hand washing was permitted, as this behaviour was predicted to have differing effects on the controls as compared to the OCD-afflicted persons. Therefore, all participants were exposed to both a period of restricted washing, and one of unlimited washing. Combination of these variables (stimulus intensity and participant type) yielded six distinct experimental groups: three levels of OCD-afflicted participants (Level 0, 1 or 2 exposure) and three levels of Control participants (Level 0, 1 or 2 exposure).

b. Protocol

To observe and track the dependent variable of security-motivation activity and anxiety over time, as a function of threat exposure, we repeated our measurement protocol developed in the study Experimental Manipulation of Security Motivation (Chapter 4). The times of measurement were labeled as:

Baseline: Initial recording of baseline physiological measures (baseline anxiety)

After Exposure: Recording of measures after stimulus contact

After Fixed Wash: Recording of measures after 30sec wash

After Free Wash: Recording of measures after unlimited washing

No changes were made to the experimental timing; however we eliminated the variable of wash condition as all participants engaged in the fixed wash. The time-course of the experiment went as follows:

0-120 sec	Subject's measurements are recorded for exactly 2 minutes
120-240 sec	Subject is given instructions for contact with stimuli (approximately 2 minutes)
240-360 sec	Subject is in contact w/ stimuli for exactly 2 minutes
360-420 sec	Stimuli are removed, subjects are given further instructions (approx 1 min)
420-540 sec	Subject rests, focusing on hands, measurements are recorded for exactly 2 minutes

540-570 sec Subject is permitted to complete hand washing for exactly 30 sec

570-690 sec Subject rests again, same as before, measurements taken for exactly 2 min

690-800 sec Subject is permitted to wash hands for as long as they want

800-920 sec Subject rests, measurements taken for exactly 2 min

Participants rested quietly during the four observation periods with eyes closed, and remained seated throughout the experimental recording. At the point of exposure, participants were given instructions for making contact with one of the three stimuli types by submerging their hand into the bin. Participants proceeded with the three comparative time points (After Exposure, After Fixed Wash and After Free Wash) in which they were asked to focus on their potential for having been contaminated, and their subjective experience. Hand washing was completed at an automatic sink during the Fixed Wash and Free Wash periods. During washing, participants were encouraged to use their normal washing routine.

c. Participants

We recruited individuals to participate in the study as either a Control participant (normal, non-clinical subjects as utilized in our studies to date) or OCD participant (meeting diagnostic criteria as outlined below). In total, 57 individuals with OCD and 57 non-OCD controls completed the study, with 41 females and 16 males in each group. All participants were between the ages of 25-65, and were prescreened to ensure that they met the general inclusion criteria: no previous diagnosis or treatment for heart or lung abnormalities or reported contact allergies. As in previous studies, participants were required to refrain from stimulants for at least 2 hours prior to the study and were disallowed from completing the study if they were ill or taking non-prescription medications. Exclusion on the basis of current pharmacological treatment was determined to be too restrictive, as it was expected that many of the OCD participants would be currently taking medications to manage their condition, and selecting only non-medicated individuals would severely limit our pool of eligible subjects. Therefore, use of prescription medications was permitted, and the experimenter recorded all current treatments for each participant.

OCD participants were recruited through the McMaster University Medical Centre Anxiety Disorders Clinic or through advertisements in the hospital and in the general community. Thirty-three OCD participants were recruited directly through the clinic, based on their medical history and confirmation of diagnosis by their clinician. Retrospective clinical chart review was approved by the McMaster University and Hamilton Health Sciences Institutional Review Board for the development of a pool of potential research participants based on their specific symptom profile. Inclusion in the study was based on a primary diagnosis of Obsessive-Compulsive Disorder (OCD) as determined previously by a physician using the Structured Clinical Interview for DSM-IV (SCID). This questionnaire has been validated as an acceptable measure for the diagnosis of mood and psychiatric disorders. Since this paradigm was concerned with exposure to contamination threat, eligibility as an OCD participant was also dependent on the expression of washing obsessions and compulsions as the predominant symptom subtype. On average, clinically diagnosed OCD patients with washing symptoms score a 14 on the PI-WSUR washing subset (Burns, Keortge, Formea & Sternberger, 1996); to be confident in our classification as "washers" and to ensure that the OCD participants recruited were actively experiencing washing-based symptoms, we set this average score of 14 as our minimum cutoff to qualify for the experiment. In addition, we needed a valid method for confidently distinguishing "washers" from other subtypes; OCD-afflicted individuals needed to score within the normal range for the PI-WSUR checking subset (no more than a score of 14, reflecting one standard deviation above the mean), and for OCD behaviours unrelated to checking or washing, such as thoughts about harm to the self or others (a cutoff score of 17; Burns et al., 1996).

Twenty-four additional OCD participants were recruited from outside of the clinic, through external advertisements, based on a self-report of OCD. Confirmation of this diagnosis was made through use of the Mini-International Neuropsychiatric Interview (MINI) which provides a reliable diagnosis of mood or psychiatric disorders, including OCD. These participants also completed the Yale Brown Obsessive Compulsive Scale (Y-BOCS) for determination of symptom severity and degree of disturbance of OCD symptoms on daily functioning. A minimum score of 16 (indicative of "moderate OCD") was required for confirmation of diagnosis. Similarly to those recruited directly from the clinic, participants responding to advertisements were prescreened for washing and checking Padua scores. All participants supplied information about their current treatment status (including individual or group therapy) and medication history within the past year. Upon completion of the study, they completed the PI-WSUR and their total score was recorded. Participants were informed that participation in this study in no way constituted treatment for their disorder, and would remain confidential; no information regarding participation or completion of the study was provided to their clinicians or recorded in their medical history.

Non-OCD participants were recruited through advertisements posted in the McMaster University Medical Centre, university campus, or on the McMaster website. These participants selected to match the overall age and gender of their counterparts in the OCD group, and reported no previous or current diagnosis or treatment for any mood or behavioural disorders. To support non-clinical status, participants were given the PI-WSUR upon completion of the study to ensure that the total score on this measure did not exceed one standard deviation above the mean for normal populations and that the score on the contamination subset did not exceed 12 (as determined in previous studies). Since OCD participants had been given a battery of questionnaires (either prior to, or during experimental testing), control subjects completed a similar evaluation for the purpose of ensuring they appropriately fit the classification as non-clinical (for any disorder) and provided similar information as did the OCD-afflicted individuals. We used a computerized questionnaire developed and validated by the McMaster Anxiety Disorder Clinic, the MacScreen (Dr. M. Van Ameringen). The MacScreen was similar in structure to the MINI and was completed in confidence in the lab in tandem with the Padua Inventory. Upon completion of the MacScreen, a summary was supplied to the experimenter to indicate if the participant met criteria for any disorders associated with the MINI. If so, the participant was excluded. Although not a diagnostic test, the MacScreen provided an additional validation of the accuracy of each participant's self report of clinical status.

Each participant was randomly assigned to one of the three experimental levels for stimulus exposure (Styrofoam, Dry diapers or Wetted diapers). This was subject to the constraint of approximately equal gender composition across groups, with 12-16 females and 5-6 males per group.

III. Measurements

Fluctuation of heart rate variability (HRV) over time (indicative of security-motivation activity) was recorded using the Biopac Acquisition Unit (sampled at 2000 Hz) in accordance with our previous measurement presets and processes (Chapter 4). Raw data were extracted and converted for input into Porges' CardioEdit and CardioBatch software for editing and analysis (Brain-Body Centre, University of Illinois, Chicago). The CardioEdit and CardioBatch are updated and modernized programs comparable in function to MxEdit, which we used previously. This software was selected for improved ease of use and greater control over data editing. The average RSA index of vagal tone was collected for each two minute recording segment (four per participant).

Participants' subjective experience of anxiety, urge to wash, and sense of contamination, as well as satisfaction gained from hand washing, were collected immediately after stimulus contact, and again at the end of each two-minute physiological recording period (After Exposure, After Fixed and After Free). We used a linear scale where ratings were scored in millimeter distance from point '0' for these measures. Time spent washing at each of the two wash periods were also recorded. At the conclusion of the experiment, self-report scores on several psychological questionnaires (as described above for Participant screening) were also collected.

IV. Results

The purpose of this experiment was to observe and compare the dynamics of Security-Motivation (SMS measures and subjective ratings) in response to contamination threat between clinical and non-clinical populations. The data of greatest interest are for the three points of measurement after stimulus exposure, where direct comparisons between groups for the effect of hand washing on the SMS may be made. Our hypothesis that OCD reflects dysfunctional SMS termination suggested that contact with either of the diaper stimuli would activate Security-Motivation to a similar degree for both the Control and OCD groups, but that, once activated, hand washing would be an ineffective tool for shutting down the system for the OCD group only.

Statistical analysis was performed on physiological measurements taken during the predetermined rest periods, subjective ratings and mean wash times between the experimental groups. Raw RSA data were converted to reflect change from baseline. Increases in cardiac data change reflect increased anxiety and SMS activation.

RSA change data were analyzed with repeated measures multivariate analysis of covariance (MANCOVA). Time point of measurement was the within-subjects factor, with stimulus level and participant type as between-subject factors. Covariates were baseline RSA, age and sex. As predicted, the three-way interaction of Group (OCD or Control), Stimulus (Level) and Time of Measurement was statistically significant, $F(4, 210) = 4.48$, $p < .01$, as was the interaction of Group and Time of Measurement, $F(2,$

104) = 23.11, $p < .001$ for RSA change. See Figure 7 for a graph of the relevant adjusted means.

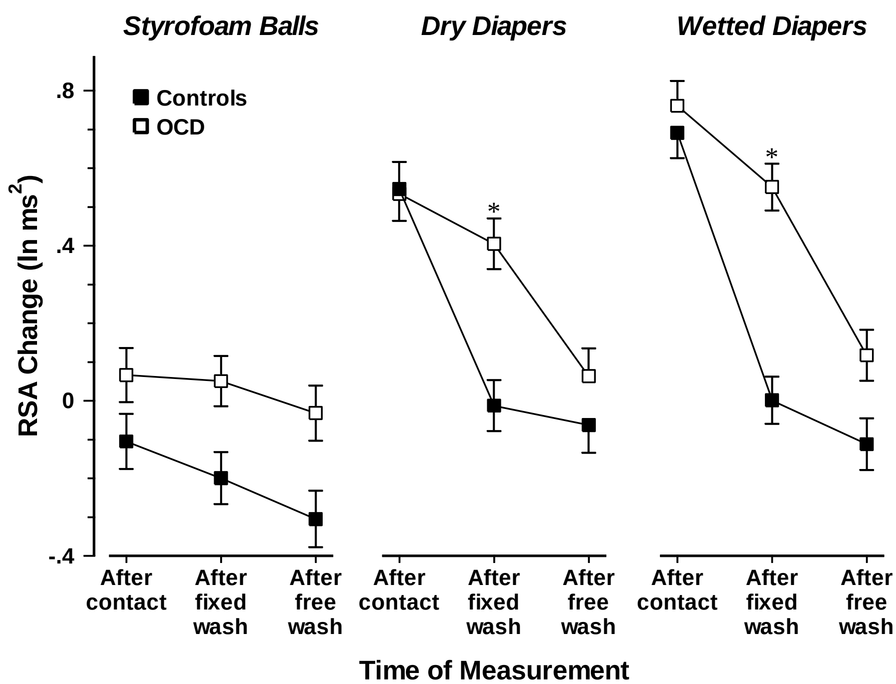

Figure 7: Effect of stimulus contact and hand washing on RSA as a function of participant type (OCD with washing compulsions vs. non-OCD controls). *p<0.05 compared to the other two groups at time of measurement. Error bars represent 1 SE. (Hinds, Woody, Van Ameringen, Schmidt & Szechtman, When Too Much is Not Enough: Obsessive-Compulsive Disorder as a Pathology of Stopping, *PLoS ONE, 7*(1), Epub. Published by the Public Library of Science, reprinted with permission.)

As expected, there was no significant difference between the OCD individuals and the control participants in initial SMS response to either contamination stimulus; both groups responded with comparable SMS activation towards the two contamination stimuli (diapers), and did not respond to the control stimuli (Styrofoam). These results do not support the view of OCD as s disorder of starting, wherein the SMS would show a heightened sensitivity towards potential threats and would be expected to show significantly higher activation towards the diaper stimuli. In comparing SMS activity after the 30-second fixed wash, however, engagement in corrective behaviour was significantly less effective at reducing the RSA change in the OCD group as compared to the controls after exposure to either of the two contamination stimuli. This finding supports our hypothesis that OCD is a disorder of SMS stopping, and that the capacity for behavioural output to elicit negative feedback for the termination of security motivation activity is disrupted in these persons. Nonetheless, those with OCD did see a significant return of RSA towards baseline after the unlimited free wash; this suggests that this prolonged washing did provide some relief of SMS activity for these individuals.

Subjective ratings were measured as an additional measure of the affective correlates of security-motivation over time – anxiety, and motivation towards threat removal. MANCOVA analyses of ratings of anxiety, urge to wash and feeling of contamination compared the change in these scores across each time point. The interaction of Group and Time of Measurement was not significant for either ratings of anxiety (Figure 8) or urge to wash (Figure 9), indicating that the OCD group and controls did not differ with regards to the effect of stimulus exposure and hand washing on these measures. The interaction of Group and Time of Measurement was, however, significant for the subjective rating of contamination over time, $F(2, 105) = 12.48$, $p < .001$ (Figure 10). Groups did not differ on their initial rating immediately following stimulus contact, but OCD persons showed a tendency towards elevated feelings of contamination after exposure to diapers at either stimulus intensity, despite hand washing. Therefore, this would suggest that, in the OCD group, washing was not as effective in terminating the feeling of contamination associated with the activated SMS. Although OCD participants and normal control show comparable trends in most subjective ratings, those with OCD had significantly higher overall raw scores when ratings were collapsed across all time points (Figure 11). This may be explained by a general elevation in anxiety for the OCD group wherein sufferers experience a non-directed sense of wariness about their surroundings as a learned response to the consequence of exposing themselves to events that may trigger their obsessions or compulsions. A general heightened anxiety could also help to explain the trend for OCD-afflicted individuals to have lowered resting RSA scores, and lowered HRV, overall.

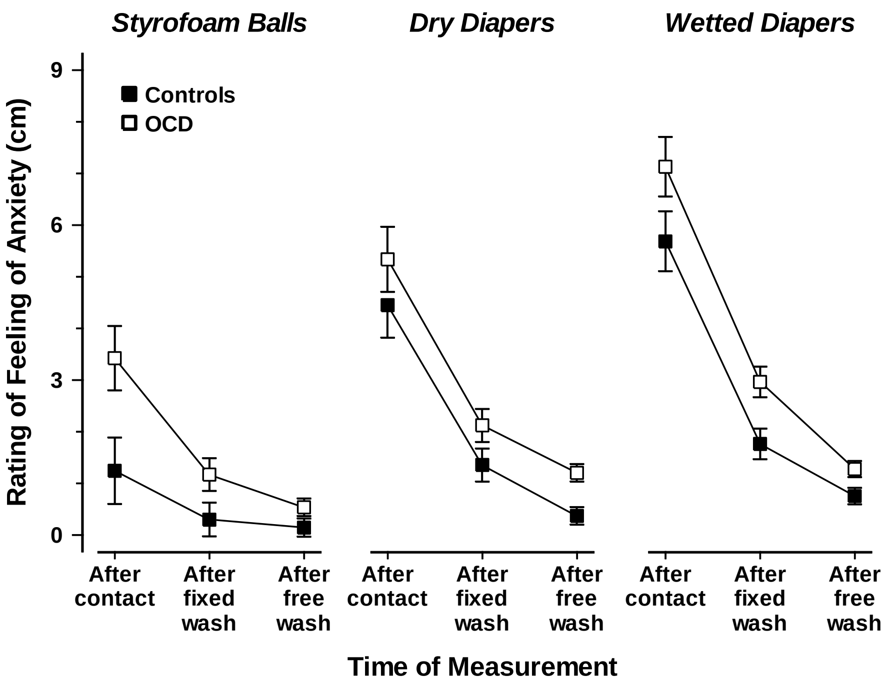

Figure 8: Ratings of feeling of anxiety over time – comparison of OCD with washing compulsions vs. non-OCD controls. (Hinds, Woody, Van Ameringen, Schmidt & Szechtman, When Too Much is Not Enough: Obsessive-Compulsive Disorder as a Pathology of Stopping, *PLoS ONE, 7*(1), Epub. Published by the Public Library of Science, reprinted with permission.)

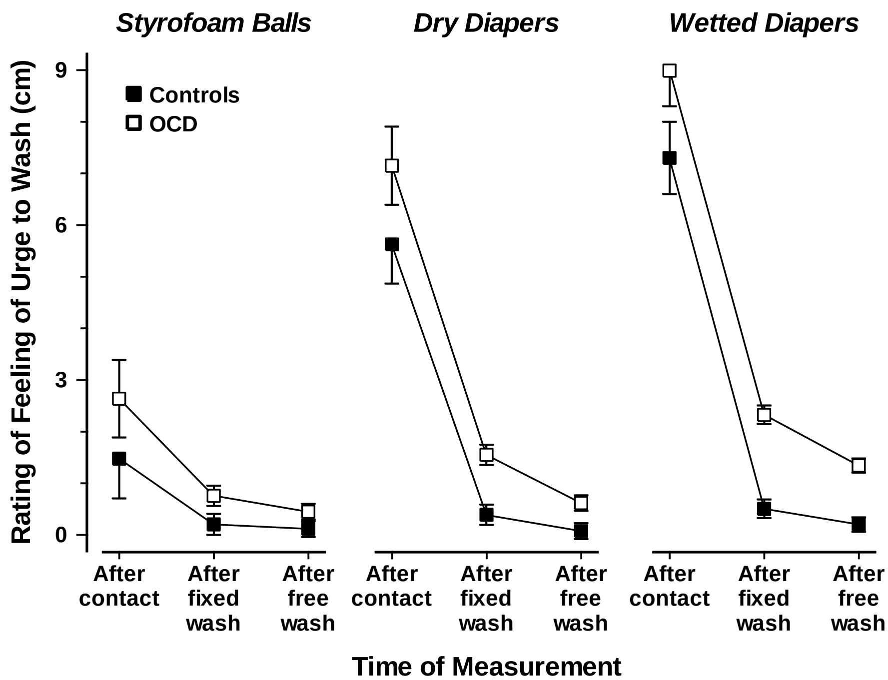

Figure 9: Ratings of feeling of urge to wash over time – comparison of OCD with washing compulsions vs. non-OCD controls. (Hinds, Woody, Van Ameringen, Schmidt & Szechtman, When Too Much is Not Enough: Obsessive-Compulsive Disorder as a Pathology of Stopping, *PLoS ONE, 7*(1), Epub. Published by the Public Library of Science, reprinted with permission.)

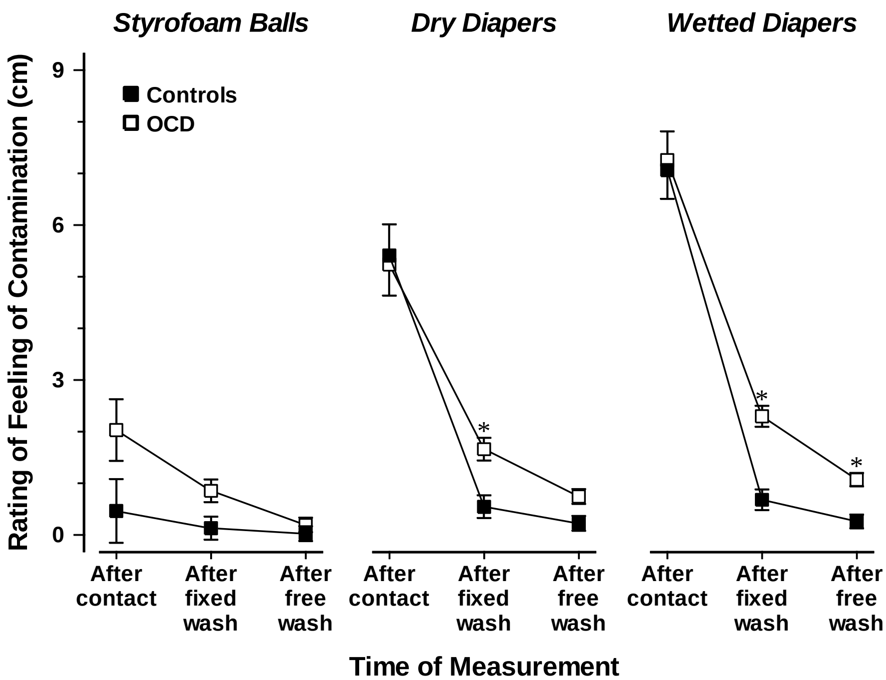

Figure 10: Ratings of feeling of contamination over time - comparison of OCD with washing compulsions vs. non-OCD controls. *p<0.05. Error bars represent 1 SE. (Hinds, Woody, Van Ameringen, Schmidt & Szechtman, When Too Much is Not Enough: Obsessive-Compulsive Disorder as a Pathology of Stopping, *PLoS ONE, 7*(1), Epub. Published by the Public Library of Science, reprinted with permission.)

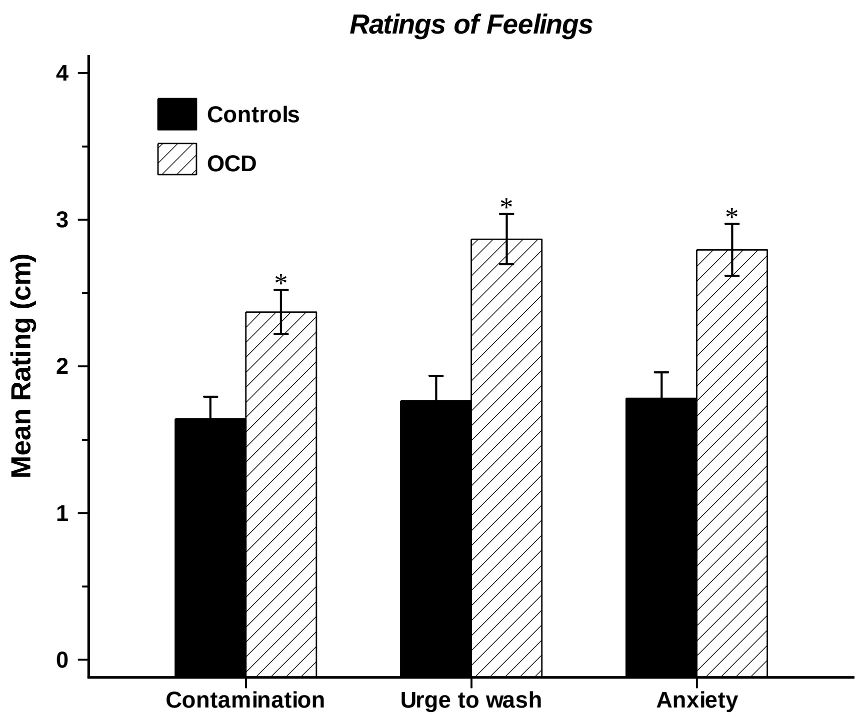

Figure 11: Ratings of feelings by category (collapsed across all time points) - comparison of OCD with washing compulsions vs. non-OCD controls. *p<0.05. Error bars represent 1 SE.

Wash duration and sense of satisfaction after washing were compared between groups for each of the two relevant time points (After Fixed Wash and After Free Wash). A MANCOVA of wash duration with age and sex as covariates yielded a significant interaction of Group, Stimulus, and Time of Measurement, $F(2, 106) = 8.34$, $p < .001$ and interaction of Group and Time of Measurement, $F(1, 106) = 37.98$, $p < .001$. The same effects were seen for the measure of satisfaction (Group, Stimulus, and Time of Measurement - $F(2, 106) = 3.13$, Group and Time of Measurement - $F(1, 106) = 30.01$, p

< .001) (See Figure 12). These results demonstrate that, after exposure to contamination stimuli, persons with OCD washed significantly longer but were also significantly less satisfied with this wash. Even when permitted to wash for as long as desired, this effect remained – substantially longer periods of washing were still ineffective at inducing an appropriate sense of task completion. In fact, normal controls tended to wash longer during the first time washing was permitted after exposure (the Fixed Wash), with their wash time dropping off sharply on the second wash (a product of already achieving satisfaction); OCD-afflicted persons showed the opposite trend – wash times were significantly longer when time was unlimited. These data support the hypothesis that OCD-afflicted individuals are unable to obtain satisfaction or a sense of task completion after performance of safety-related behaviours.

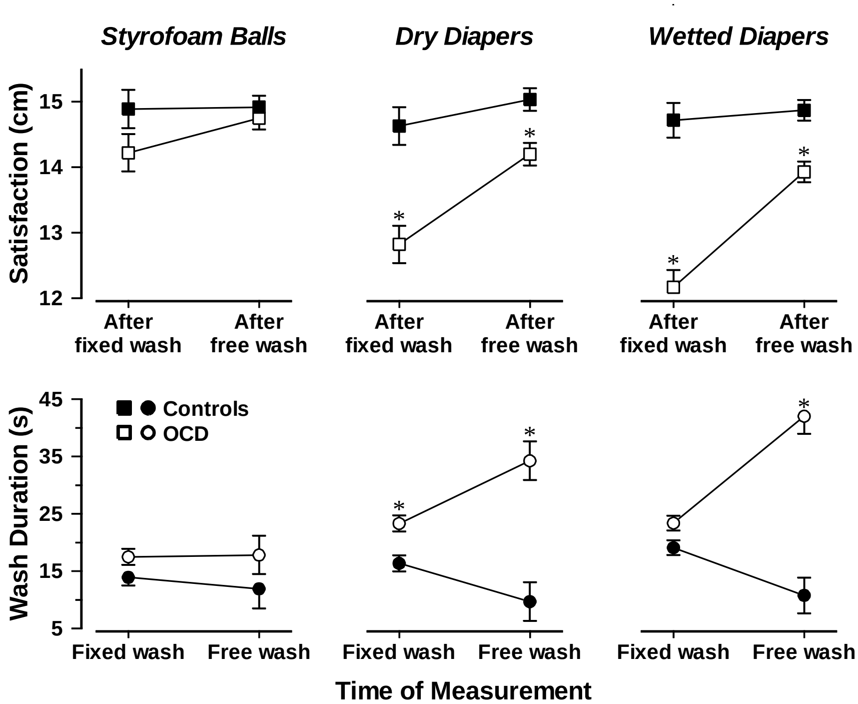

Figure 12: Rating of satisfaction and wash duration over time - comparison of OCD with washing compulsions vs. non-OCD controls. *p<0.05. Error bars represent 1 SE. (Hinds, Woody, Van Ameringen, Schmidt & Szechtman, When Too Much is Not Enough: Obsessive-Compulsive Disorder as a Pathology of Stopping, *PLoS ONE, 7*(1), Epub. Published by the Public Library of Science, reprinted with permission.)

Since all OCD-afflicted persons were actively symptomatic at the time of study participation, many participants in this group indicated regular use of medication specifically for the treatment of these symptoms. Pharmacological treatment of OCD is fairly diverse, and those diagnosed with OCD are often treated with dopaminergic antagonists and/or serotonergic agonists. This treatment may also be supplemented with anxiolytics. To ensure that the possible effect of different medication types and dosages was not confounding our results, we compared participants on the basis of medication classification. Those with OCD were grouped according to Medication type: no medication (12 participants), antidepressants (32 participants), and clonazepam (9 participants). Four participants were not classified because they were taking a mixture of both antidepressant medication and clonazepam. We did not observe any significant effects of Medication Type on RSA, or interaction with the variables of Stimulus or Time of Measurement. Therefore, we were confident in grouping our OCD participants for analysis without further consideration of medication status.

V. Implications

As we expected, OCD-afflicted individuals responded similarly compared to controls on measures of SMS activation to potential threat and neutral stimuli, but differed in the capacity for SMS termination via corrective behaviour. After exposure to contamination threat, RSA change from baseline, a measure of security motivation activation, persisted in those with OCD despite participation in active hand washing, as did their sense of being contaminated. The specificity of this dysfunction supports the view of OCD as a motivational disorder, based in difficulty obtaining satisfaction from behaviours aimed at deactivation of the Security-Motivation system. These results are the first to characterize OCD as a disorder of a normal motivational circuit rather than a cognitive hypersensitivity to potential threat, and to lend support to the Security-Motivation theory of OCD (Szechtman & Woody, 2004). Our results have implications for future research into the neurobiological abnormalities underlying the typical presentation of OCD, and may help to provide a basis for novel and more effective treatment strategies.

For this experiment, we considered only the washing subtype of Obsessive-Compulsive Disorder, as the focus and concern of this study was in contamination exposure and washing compulsions. However, this does not allow for generalization of these results to all individuals with OCD, as it is possible that alternative symptom subtypes (such as checking and hoarding) operate via unique neurophysiological mechanisms or due to a different location of dysfunction in the Security-Motivation circuit. Future study is required to better determine the specificity of our conclusion that OCD reflects a disorder of SMS stopping.

CHAPTER 7: SPECIFICITY OF SMS DYSFUNCTION – INVESTIGATION OF OCD SUBTYPES

I. Basis for the Study

The results of this study were previously published in the peer-reviewed article entitled: Hinds et al.: **When too much is not enough: obsessive-compulsive disorder as a pathology of stopping, rather than starting.** *PLoS One* 2012, 7(1):e30586.

We have provided evidence that dysfunction in the normal Security-Motivation circuit (specifically, the component controlling stopping of the activated SMS) underlies obsessive-compulsive disorder. We also distinguished this from a general disorder of hypersensitivity to potential threats, or dysfunctional activation of the SMS towards a particular subset of threat cues. To date, our research has focused on contamination-based triggers for the SMS, which has been an effective paradigm for observing SMS activity in OCD washers. However, other subtypes of OCD do not involve concerns with contamination, and focus instead on other threats to safety. While our findings have demonstrated that OCD washers follow the pattern of physiological activity that we predicted, it is not clear whether this dysfunction is generalized to all OCD sufferers, or if it is specific to the subset of participants for whom contamination is the predominant concern (washers).

In the comparison of many dimensions of symptom presentation or clinical features other than primary concern (such as psychiatric comorbidity, age of onset and course of the illness), washers and checkers do not differ significantly (Fontenelle, Mendlowicz & Versiani, 2005). Thus, it is reasonable to infer that both checking and washing OCD compulsions stem from a common neuropathology and similar site of SMS disturbance. However, the distinct subtypes of “washers” and “checkers” can be reasonably distinguished on the basis of symptom presentation, which remain relatively stable over time, leading OCD sufferers to express difficulty with only a particular repertoire of security concerns. It is also known that individuals with different subtypes of OCD show unique patterns of neural activity during participation in threat avoidance and evaluation of the environment (Rauch, Whalen, Curran, Shin, Coffey, Savage, et al., 2001). It is likely, then, that there is a neurophysiological basis for the specificity of threat concern, which may be directly related to Security-Motivation circuitry. We established an experimental paradigm to clarify and address the following research question:

> Does the disturbance to SMS functioning which results in OCD behaviour result in a general dysfunction towards potential threats, or a specific pattern of dysfunction related to one particular type of threat? In other words, will OCD-afflicted persons whose predominant symptom is checking show a stopping deficit in response to the threat of contamination (which is unrelated to checking)? We hypothesized that the stopping deficit is specific to the type of threat that is characteristic of the person's symptoms such that washing-related behaviours would not be affected in these individuals.

If this hypothesis is correct, the SMS response towards contamination should be intact for OCD checkers, and thus their pattern of activity should reflect a *lack of disordered function*, resembling that of normal, non-clinical controls.

II. Experimental Paradigm

a. Protocol

To examine the specificity of disordered SMS termination in OCD, we repeated our measurement of SMS activity as a function of threat exposure as outlined in the Manipulation of Security-Motivation in OCD-Afflicted Individuals (Chapter 6). Periods of measurement were:

Baseline: Initial recording of baseline physiological measures (baseline anxiety)

After Exposure: Recording of measures after stimulus contact

After Fixed Wash: Recording of measures after 30sec wash

After Free Wash: Recording of measures after unlimited washing

No changes were made to the experimental timing or wash condition; however, we chose to eliminate the variable of stimulus. From the three contamination levels used in our previous OCD study (level 0 Styrofoam, level 1 dry diapers, and level 2 wet diapers), we selected the wet diapers for this study, as this stimulus was the most potent and produced the highest SMS response. Because the variable of interest was participant type, the significant revision for this protocol was in the pre-screening of participants to create two experimental groups – a non-clinical Control and an OCD group with the appropriate “checking” OCD symptom profile (see ‘Participants’).

b. Participants

In total 13 OCD-afflicted persons and 15 controls completed the study, with 9-10 females, and 4-5 males in each group. All participants were aged between 25-65 years and met prescreening criteria for healthy cardiopulmonary function and restraint from stimulants or non-prescription medications before completing the study. Medication use was reported to the experimenter.

Participants with OCD were recruited through the McMaster University Medical Centre Anxiety Disorders Clinic, or through advertisements in the hospital and in the general community. Five participants were directly recruited from the clinic, based on medical chart review and previous clinical assessment. They were included if they had a primary diagnosis of Obsessive-Compulsive Disorder (OCD) by a trained physician, reflected in their results on the SCID. Eligibility for the OCD group was also dependent on the predominant expression of checking obsessions and compulsions. As for the washing-subtype participants, in order to qualify, participants were required to score, at minimum, the average for OCD patients on that particular subset of the Padua Inventory – Washington State University Revision (PI-WSUR); for the checking subset, the patient average is 20. In addition, participants had to score similarly to non-OCD controls for the PI-WSUR washing subset (a score of 12 or below). This was to ensure that they were currently experiencing checking-based symptoms, and could appropriately be labeled as "checkers".

Eight OCD-afflicted participants were recruited via external advertisements outside the clinic, and their inclusion was based on self-report of OCD. Confirmation of diagnosis followed as for the previous OCD study, using the MINI, Y-BOCS and prescreening for washing and checking Padua scores. Upon completion of the study, participants completed the PI-WSUR to obtain a total score. OCD participants were given identical information as was provided to the washing subset on the nature of the study and its confidentiality (see Chapter 6).

Non-OCD participants were recruited through advertisements, and selected to match the overall age and gender of the OCD group. They reported no diagnosis for mood or behavioural disorders, and non-clinical status was confirmed using the PI-WSUR total score (as previously described) and MacScreen neuropsychological battery as described for the previous patient based study (Chapter 6). Assignment to the Control or OCD group was based solely on these prescreening measures and was therefore not randomized.

III. Measurements

We measured changes in the RSA measure of heart rate variability (HRV) as a function of exposure to contamination stimulus as outlined previously (Chapter 4). Raw data were analyzed with CardioEdit and CardioBatch software (Brain-Body Centre, University of Illinois, Chicago) with RSA calculated for each two minute recording segment. Participants' subjective ratings of anxiety, urge to wash, and sense of contamination after contact, and after each physiological recording period were also measured, along with washing time during both wash periods.

IV. Results

This experiment sought to compare the motivated response to contamination threat between non-clinical controls, and OCD participants with checking-related symptoms. By making this comparison, we are indirectly comparing the response to two different subtypes of OCD participants ("washers" and "checkers") in an identical paradigm (since the response of OCD washers to these conditions has already been determined). In this way, we can observe if our previous results generalize to population of OCD-afflicted individuals as a whole. The data of interest is for the three points of measurement after stimulus exposure, where we can compare the effect of corrective behaviour on SMS termination between groups. Statistical analysis supports our prediction that disordered SMS termination after hand washing is specific only to OCD-afflicted persons for whom washing is a predominant feature of their symptom expression.

RSA data were converted to reflect a change from baseline and analyzed using a multivariate analysis of covariance (MANCOVA), with baseline RSA, age, and sex as covariates. Time point of measurement was the within-subjects factor and participant type the between-subject factor. The two-way interaction of Group (Control or OCD) with Time of Measurement was not significant $F(2, 22) = .10$. No significant difference between groups was seen in the subjective ratings, or in wash duration and satisfaction after washing.

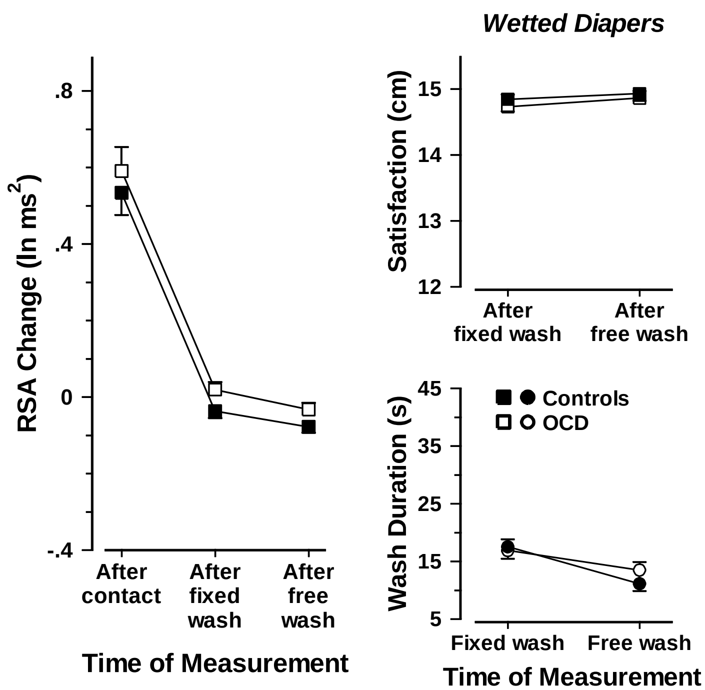

Figure 13: Effect of Hand Washing on RSA as a Function of Participant Type (OCD with checking compulsions vs. non-OCD controls). (Hinds, Woody, Van Ameringen, Schmidt & Szechtman, When Too Much is Not Enough: Obsessive-Compulsive Disorder as a Pathology of Stopping, *PLoS ONE, 7*(1), Epub. Published by the Public Library of Science, reprinted with permission.)

Figure 13 presents the adjusted means for RSA change, satisfaction, and wash duration. In essence, the OCD group in this study responded the same as controls to the experimental manipulation. These results are in stark contrast to the dramatic differences observed between OCD-afflicted persons and controls on the same paradigm when the OCD group was classified as washers (Chapter 6), even though the only difference between this and the previous study is the symptom subtype. These results strongly imply that the SMS stopping deficit in OCD is **only seen** when the threat-removal behaviour elicited is of the type that corresponds to the individual's symptom profile.

V. Implications

The results of this study demonstrate that the deficits that underlie disturbances in Security-Motivation activity and symptom presentation in Obsessive-Compulsive Disorder are not generic. In other words, the stopping deficit in OCD appears to be specific to the type of threat implied by the person's symptom profile. This is consistent with the hypothesis that the specific symptoms and focus of obsessions and compulsions seen in each subtype of the disorder have their basis in distinct, although related, SMS circuits. One implication of these results is that neuroimaging and neurocortical studies of OCD need to take account of different subtypes, because these subtypes may have somewhat distinct neural underpinnings.

CHAPTER 8: EXPERIMENTAL TEST OF THE EFFECT OF CHECKING BEHAVIOUR ON SMS ACTIVATION

I. Basis for the Study

Our research to date has provided much evidence for the effective activation of Security-Motivation via exposure to contamination-based triggers and the use of hand washing as the appropriate SMS-terminating behaviour. We have explored SMS response to this type of potential threat in a variety of populations due to its relative ease in manipulation and applicability for our experimental paradigms. However, contamination is not the only concern of security-motivation, but merely one of a larger repertoire of potential threats to health and safety that may be evaluated on the basis of subtle environmental cues. Therefore, to generalize our findings on the role and function of the SMS as a special motivational circuit tasked for the detection of and response to *all* potential dangers, it is pertinent to demonstrate its activation towards a greater variety of threat cues. To further validate our previous research, we wanted to develop an experimental paradigm which utilized cues that would elicit the corrective behaviour of checking. Checking is a relatively common response to threat, and importantly, is also one of the most common subtypes of Obsessive-Compulsive Disorder (OCD). In particular, we hoped to develop a checking-based paradigm for the comparison of OCD and non-OCD individuals akin to our washing paradigm.

There are several types of potential threats that may be expected to elicit behavioural checking – these include the suspected presence of intruders and the possibility of having failed to complete an essential task, such as locking one's door or eliminating a source of fire. A commonality between threats that reliably predict a checking response is that they induce a sense of uncertainty towards something that the individual feels personally responsible for. As described previously, development of an appropriate paradigm to induce or control this sense of responsibility and subsequent checking is difficult; unlike contamination (which may be experienced anywhere), personal responsibility is often highly tied to context, namely, situations that are personally relevant (and therefore highly variable between individuals). In a previous study that examined the performance of security-related behaviours in a laboratory setting, it was determined that the evaluation of such threats as harmful was diminished when not in an appropriate setting (Coles, Heimberg, Frost & Steketee, 2005). To evaluate the effectiveness of previously attempted paradigms, we looked to previous work conducted in our lab (Ana Drandic, Masters' Thesis). This research attempted to elicit and track SMS activity as a function of exposure to safety threat and participation in corrective checking related specifically to the threat of fire and personal injury.

In this unpublished study, participants' SMS activity was measured in response to exposure to a potential safety threat and engagement in corrective checking. For this task, the potential threat exposure was being directly responsible for the proper inspection of laboratory equipment that they were told could be a dangerous hazard. In different versions of the study, this hazard was described as a potential for fire (if an electrical appliance was not correctly turned off) or possibility for personal injury (if an electrical device they were handling was not correctly labeled as faulty). In both paradigms, the equipment was described as being potentially dangerous and warnings were given to enhance the believability of the threat. It was expected that in non-OCD persons the course of SMS activity would approximate what was seen for our washing paradigm – decrease in heart rate variability and increase in anxiety after exposure to the threat, until participation in corrective behaviour (in this case, checking), upon which the measures should return to baseline. However, these paradigms did not produce the desired effects, as HRV and anxiety did not significantly change in response to these stimuli or to checking. The researchers discussed several possible flaws with the experimental design that we took into consideration for our current attempt at creating a plausible checking paradigm:

1) It is possible that the type of threat or context of the threat exposure was not appropriate for activation of the SMS. The amount of cognitive processing and information given to participants may have removed the necessary subtlety and interpretation of cues that allows this threat to be *potential* rather than *overt*.
2) Situations that elicit wariness about personal threat are more potent in familiar environments. This makes it more difficult to elicit natural responses in the laboratory.
3) Participants likely doubted the authenticity of the threat situation, and the likelihood that the experimenter would allow them to be in any real harm. It may have also seemed implausible that the subject would be legitimately responsible for dangerous equipment, particularly in a hospital setting.

Building on these previous attempts, we developed an experimental paradigm to test the prediction that the Security-Motivation system (SMS) responds to the potential threat of task failure and risk to personal safety, and to address the following specific questions:

1) Can we observe and track activity of Security-Motivation in response to exposure to potential safety threats, as we did with threats of contamination? We hypothesized that contact with stimuli containing such cues would trigger activation of the SMS and be observable via physiological and psychological measures and the motivation to perform threat-removal behaviour.
2) Does engagement in the behaviour of checking deactivate the SMS once activated towards this type of threat? We predicted that checking is the appropriate behavioural output to provide feedback for termination of SMS activity and elimination of anxiety. As in the washing paradigm, blocking participation in this corrective action should prolong SMS activity.

For an initial test of these hypotheses, we needed to create a potential threat situation or stimulus that could effectively activate Security-Motivation and elicit checking, and to manipulate the ability to participate in this checking. The main variable of interest was the type of stimulus or situation to be used for activation of the SMS in order to represent a threat normally associated with the act of checking. It must elicit genuine wariness and threat appraisal while not actually posing harm to the individual. As described above, this posed the difficulty of developing a situation that was believably threatening given the limitations of setting and authenticity. Since posing a direct threat to the participant had been unsuccessful in the previous attempts in the lab (Ana Drandic, Masters' Thesis), we decided to use the more indirect threat of potential failure in a critical task. This is a valid safety related threat in situations where an individual may believe that something they have done (or not done) is ultimately responsible for causing harm to another person. Such threats are more potent when the harm may come to someone personally important to the individual, such as a friend or loved one. An example of this type of threat would be the possibility of having forgotten to take a particular precaution to ensure the safety of a child whom one is responsible for. The key aspect was developing a stimulus situation in which the supposed demand on the participant was reasonable – the subject must feel a legitimate sense of ownership for the task, and be unable to rationalize deferring this responsibility to the experimenter.

Work by Arntz, Voncken and Goosen (2007) used a task that involved sorting medications in order to elicit checking behaviours and the experience of high personal responsibility in response to the possibility of negative outcomes. On the basis of this work, we developed a paradigm which uses the possibility of failure on a critical pill-sorting task as the potential threat for SMS activation and induction of corrective checking.

Pilot Protocol

In a pilot version of this study, participants were asked to complete a sorting task in which they were responsible for the sorting and distribution of medications that they were told were to be directly administered to patients. Here, the potential threat was that making critical errors in the task could have health consequences to a vulnerable population. Participants were given a mixture of pills of assorted colours and shapes and instructions for dividing the pills into daily doses for two different patient groups (each with a slightly different required combination of pills) for a total of 10 patients. During threat exposure, the sorting task had already been completed, so the nature of the threat was in recall of the task completion and the suggestion of doubt to elicit wariness about the possibility of having made a critical mistake on the task. This also involved the suggestion of the serious consequences of this failure, as seen in the following excerpt:

> "I am going to ask you to think back to the pill sorting task that you completed earlier… We are particularly interested in high-consequence situations – situations where completing the task correctly or incorrectly could potentially have higher than average consequences. In this case, if you made mistakes in sorting the pills – for instance, mixing up the correct combination of color, shape and number - a patient could have a potentially serious reaction which could have health consequences… Often, even when people believe they have completed an important task correctly (in this case, mixing the medications properly), when they later go back to check, they find that their memory of doing the job correctly was flawed…"

Twenty participants between the ages of 18-65 (mean age of 32.0 years) were recruited from the general public for the pilot project. We were interested in whether exposure to the potential for critical failure on this task would elicit an anxiety response and SMS activation, and whether this SMS activation would be affected by corrective checking. However, the pilot data using RSA and subjective ratings indicated that this paradigm was not effective at eliciting activation of the SMS. Moreover, although participants did express a desire to complete the task correctly, they did not appear to consider the potential for failure as a security-motivated threat.

In this paradigm, a key factor is participants' belief that they were truly responsible for the safety and welfare of patients through their actions during the sorting task. In fact, a majority of participants expressed doubt in the realism of this situation – it seemed improbable that ill individuals would be given critical treatment without verification by a licensed physician or caregiver. In retrospective review of the data, participants who *did* believe the study's context (as reported through sense of personal responsibility for the safety of the patients in question) also show the predicted pattern of SMS activity over the course of the experimental recording. This suggested that we might be able to improve our paradigm by increasing the believability of the potential threat situation.

In addition, the task may have been too easy, or too easily completed, to effectively elicit any real sense of doubt. Most participants expressed a high level of confidence after task completion and a low likelihood of having made any errors, despite the supposed high consequence of the task. Only six pills were sorted into each patient cup, and the pills were distinct enough in colour, shape and size that the chance of making an actual error on the task was highly unlikely. Therefore, we expected that increasing task difficulty would create more ambiguity towards successful completion and a greater sense of wariness in the potential threat of task failure.

Hence, we made a second attempt at the development of a critical task paradigm that might prove to be useful to track and manipulate the activity of the SMS in the average population.

II. Experimental Paradigm

a. Variables

As in our initial pilot-project paradigm, the potential threat was the possibility of making critical errors in a pill sorting task which could ultimately have severe consequences. The first variable was the type of exposure – to either the threat condition, or a neutral control condition. To create a more appropriate potential threat condition, we modeled our pill sorting task and subsequent threat exposure more closely on the work described by Arntz, Voncken and Goosen (2007). In their study, Arntz et al. (2007) made modifications to a task (originally developed in 1995 by Ladouceur et al.) in which participants were asked to sort pills on the basis of a novel classification system where the predominant feature for sorting was colour. Participants were given a large assortment of medications with different appearances, and were asked to methodically put all pills of the same colour together. During this task, the subjects were given information about the importance of completing the task correctly, and on completion, the amount of time spent checking for accuracy was recorded. The researchers found that checking was not induced when the participants were simply told that the task was important and would affect the outcome of the development of the new pill classification system; this suggests that participants in this condition did not consider failure on the task to be a potential threat. The researchers then investigated the effect of greatly enhancing the sense of personal responsibility and potentially critical consequences of task failure by providing subjects with an additional story to provide details about the essential role of the participant and critical nature of the study, as well as the direct dependence on the participant to succeed. Participants were told that the investigators were developing the use of a pill classification system for use in underdeveloped areas where illiteracy and inability to follow written instructions was creating many dosing errors and serious medical consequences. They were further informed that their participation would directly influence the use of this new system because they were required to demonstrate that *anyone* could complete the task properly. When responsibility was enhanced in this way, the researchers saw a significant effect on anxiety and desire to complete checking behaviours.

We created a similar pill classification task and examined participant response to the threat of failure on this critical task as opposed to a non-critical control situation. In the Threat condition, participants completed a sorting task under the guise of a beta test for a new method of color-coding medications on the basis of dosage. Instructions for this task indicated that the task was meant to determine if this new system would be effective for reducing critical dosing errors. In the Control condition, participants completed a similar sorting test where the stimulus was innocuous candy; therefore this was not expected to be considered a critical task. Details of the tasks are discussed below (see Protocol).

The second variable was the amount and timing of checking in response to the potential threat of possible erring on the critical task. Corrective checking was restricted to certain points during the experiment, and for a set amount of time (as was done for hand washing in previous studies). Checking was manipulated by delaying this measure in one subset of participants creating Check and Delayed Check conditions. The dependent variable of interest was SMS activity at each of the defined time points during the experiment.

b. Protocol

A key distinction for this paradigm as compared to the washing protocol was in the distinction between two separate components: completion of the critical task, and tracking of the SMS. Participants were first exposed to the critical task before physiological recording, and then exposed to the potential threat stimuli of interest (the possibility of having failed in this task) during the measurement of SMS activity.

During the initial task, participants completed one of two possible sorting-based tests. For the Threat condition, subjects were told that they were being recruited to act as a "beta tester" for a new method for sorting medications in order to determine if the system was effective and simple enough to be successful. They were given the following story about their role in the study:

> "We are trying to reduce the amount of serious reactions that occur when people do not take prescription medications properly. In most cases, these are unintentional errors, where the patient confuses the dosage; this is especially true when the patient is taking two or more medications… Research has shown that one of the main mistakes people make when taking multiple prescriptions is that they mix up the times that these pills are to be taken. To eliminate this problem, these pills have been color coded according to the time they are to be taken. Pills that are to be taken in the morning are colored PINK. Pills that are to be taken in the afternoon (lunchtime) are colored WHITE. Pills that are to be taken in the evening are colored BLUE. This means that for any one prescription, the bottle

may contain different colored pills…[Once sorted, all similarly colored pills are taken together]…The most important component of this system is in the original sorting – that the right number of each pill by color is placed into the pillbox at the start of the week… In front of you are 7 prescriptions that Patient X has been given. Your job is to sort the pills that they are to take for one (1) week into the provided pillbox. Each bottle is labeled with the dosage."

For the Control condition, participants were given the following information:

"We are interested in strategies people choose when completing a sorting task. In front of you is a container of candy to be sorted into 7 servings. We are using this pillbox for sorting, so each compartment on the pillbox will represent one serving. The label on the container tells you how many of each color candy to put in each serving.

For the pill sorting task, participants were given the seven clear vials of pills, each containing one month's worth of the hypothetical "prescription" and labeled with the dosage for sorting. For example, prescription one read "one (1) pill, two times (2x) per day", and contained both pink and blue pills. This indicated that the participant was to sort one pink pill and blue pill for each day; the color indicated that one pill would be for a morning dose (the pink pill) and one would be for an evening dose (the blue pill). They were also provided a pillbox with seven compartments, labeled Sunday through Friday, to place each day's pills in. The seven prescriptions were labeled as follows:

Prescription 1: One (1) pill, two times (2x) per day

(contained pink and blue pills)

Prescription 2: One (1) pill, two times (2x) per day

(contained white and blue pills)

Prescription 3: One (1) pill, three times (3x) per day

(contained pink, white and blue pills)

Prescription 4: Two (2) pills, one time (1x) per day

(contained pink pills)

Prescription 5: One (1) pill, one time (1x) per day

(contained white pills)

Prescription 6: One (1) pill, three times (3x) per day

(contained pink, white and blue pills)

Prescription 7: One (1) pill, one time (1x) per day

(contained blue pills)

For the candy sorting task, participants were given a large, clear bag of pill-shaped candies of assorted colours (red, orange, yellow, green, blue and white), labeled with instructions to put "five (5) red candies, five (5) blue candies, and four (4) white candies into each serving". They were also given a pillbox for sorting, identical to that used for the pill-sorting task. Both groups were told that they were to complete the sorting task as quickly and accurately as possible, and to inform the experimenter when they felt the task was complete. After completion, sorted pills or candies were set aside and participants continued with the physiological recording portion of the experiment.

To maximize consistency between experimental groups and ensure that any significant group differences were based solely on the level of threat associated with the task (and not some aspect of handling of the stimuli), both stimuli were sorted into identical pillboxes and handled in the same manner. The color distribution between pills and candies was also the same – ultimately, when the task was completed correctly, each day on the pillbox contained exactly 5 red, 5 blue and 4 white pills or candies.

In order to monitor fluctuation in anxiety and SMS activity over time, we used our protocol already designed for the experimental manipulation of security motivation with washing threats (Chapter 4). In place of exposure to contamination, threat exposure here was in elicitation of self-doubt for successful completion of the critical sorting task. Participants were recorded over approximately 15 minutes to collect measurements for the four time points of interest. As in the previous study, they were labeled as:

Baseline: Initial recording of baseline physiological measures (baseline anxiety)

After Exposure: Recording of measures after threat exposure (task recall)

After Fixed Task: Recording of measures after 45sec check or no checking

After Free Check: Recording of measures after unlimited checking

These measures were interrupted by periods of task recall, instructions and the activity of checking. The time-course of the experiment was as follows, similar to the wash paradigm:

0-120 sec	Subject's measurements are recorded for exactly 2 minutes
120-360 sec	Subject is given instructions and script for recall of task and self-doubt (approximately 4 minutes)
360-420 sec	Subjects are given further instructions (approx 1 min)

420-540 sec	Subject rests, focusing on task, measurements are recorded for exactly 2 minutes
540-585 sec	Subject is permitted to check for sorting accuracy for exactly 45 sec (Check group) OR checking is delayed (Delay group)
585-705 sec	Subject rests again, same as before, measurements taken for exactly 2 min
705-800 sec	Subject is permitted to check for as long as they want
800-920 sec	Subject rests, measurements taken for exactly 2 min

The independent variable "time of checking" determined whether checking was permitted at time 540-585 sec above, resulting in the time **After Fixed Task** in which some participants had checked while others had not. This allowed for observation of the effect of engaging in checking behaviour on anxiety elicited by an activated Security-Motivation system towards the potential for task failure. As in the washing paradigm, participants remained seated for the duration of the physiological recording portion of the experiment, resting quietly during all four recording periods of interest.

Recall of the critical beta test (or control sorting task) and description of the consequences of task failure were presented to the participant in order to elicit self-doubt during the period of threat exposure. Since our concern was for enhancing the participant's sense of responsibility and believability in the importance of the task, we created a more thorough description of the importance of the critical task for subjects in the Threat condition:

> "Think back to the Beta test that you completed earlier. I want to give you some more information about the Beta testing. The group of patients of particular

> interest for this program are those with cancer. Often, cancer patients or their caregivers must administer combinations of medications that can have very serious health consequences if not taken properly. Children are especially vulnerable to dosing errors, and their caregivers do not often have previous experience distributing medications. As a result, physicians often prescribed lower dose medications or require patients to have medications administered in hospital. This diminishes the effectiveness of the treatment, and costs both the patients and the health care system significantly. In a previous study to test the effectiveness of the pill sorting procedure, the results were alarming – participants in the test made many mistakes. After reviewing the data, we found that the task is harder to do correctly than people think it is. We also know that people's memory of completing an important task can be flawed – for example, believing that something was done correctly (i.e. turning off a stove, or locking the door) when in fact, it was not. Often, participants believed that they had done the task perfectly, and were surprised to find that they had made potentially dangerous mistakes. In the rest of this experiment, we want you to help us improve the pill sorting procedure so that people don't make dangerous, and even potentially fatal mistakes."

For those in the Control condition (candy sorting), participants were simply asked to recall the sorting task. It was important that no information was given to this group that could be considered as a suggestion of task failure. Even though we did not expect participants in this group to be concerned with their sorting performance (as it had no association with responsibility for the safety or welfare of others, and was therefore not considered a relevant stimulus for SMS activation), we wanted to ensure that this did not present a possible confound. Participants may experience a general desire to be helpful, to genuinely assist the experimenter, and to do a good job in the study, even if the task itself is irrelevant; therefore, belief that one has failed, even if the consequence is low, may induce anxiety and therefore make it more difficult to differentiate the groups on the condition of Threat Exposure.

Checking was permitted during the Fixed Task for those in the Check condition, and during the Free Check for all participants. During this time, participants were given a cup containing a sample assortment of the pills or candies that reflected the correct sorting for each day based on the instructions. If completed correctly, each section of the pillbox contained 14 pills or candies, which allowed for relative ease in checking, as participants could confirm accuracy without having to empty the pillbox and could distinguish between the three colours fairly easily. In comparison to our earlier pill-based paradigm, checking in the current study required the participant to be more thorough and took more actual evaluative effort, as we increased the number of each item in the cup from six to fourteen. There was also a greater variety of pill types in this study as compared to our previous attempt, with seven distinct medications rather than only four.

c. Participants

Through general advertisements (at McMaster University and in the general community), we recruited 88 participants between the ages of 18-65 for completion of the study. The mean age was 29.2 years (SD = 5.4), weight was 62.5 kg (SD = 9.6), and height was 1.69m (SD=0.08). Participants were excluded from the study if they had consumed stimulants or non-prescription medications within 2 hours of completing the study, or if they reported any of the following:

- A previous diagnosis or treatment for a disorder or abnormality of the heart or respiratory system
- Previous or current diagnosis of mood or personality disorder
- Regular exposure to (through work, etc), or handling of, medications (to avoid the potential confound of previous exposure on the sense of task responsibility)

Each participant was randomly assigned to one of the four experimental groups: Pill-Check, Pill-Delayed Check, Candy-Check, or Candy-Delayed Check, subject to the constraint of gender composition. Seventeen participants were assigned to each of the candy-related groups (12 females and 5 males per group), and 27 participants were assigned to each of the two pill groups (20 females and 7 males per group).

III. Measurements

a. Physiological Recordings

In order to parallel our washing-based paradigm, we tracked the change in heart rate variability (HRV) in response to threat exposure and ability to engage in corrective checking. All physiological data were collected using the Biopac Acquisition Unit via adherent electrodes on the ankle and wrist (ECG recording). Data were collected under the same settings as for previous studies. Raw cardiac data were edited and analyzed using Porges' CardioEdit and CardioBatch software, with RSA calculated for each 2 minute time point of interest.

b. Subjective Measures

We assessed participants' subjective experience at each time point after threat exposure similarly to how we did for the washing-based study. A new linear rating scale questionnaire was created for the assessment of confidence in task performance (completing the sorting task accurately), anxiety for the critical nature of their involvement, urge to check and satisfaction with checking (in the two post-checking measurement periods) (see Figure 14). Scores were indicated on a 15cm scale and converted to a score in millimeters distance from score of 0. The questionnaire was also generic – it does not mention either the pills or candies – and was therefore identical for *all* participant groups.

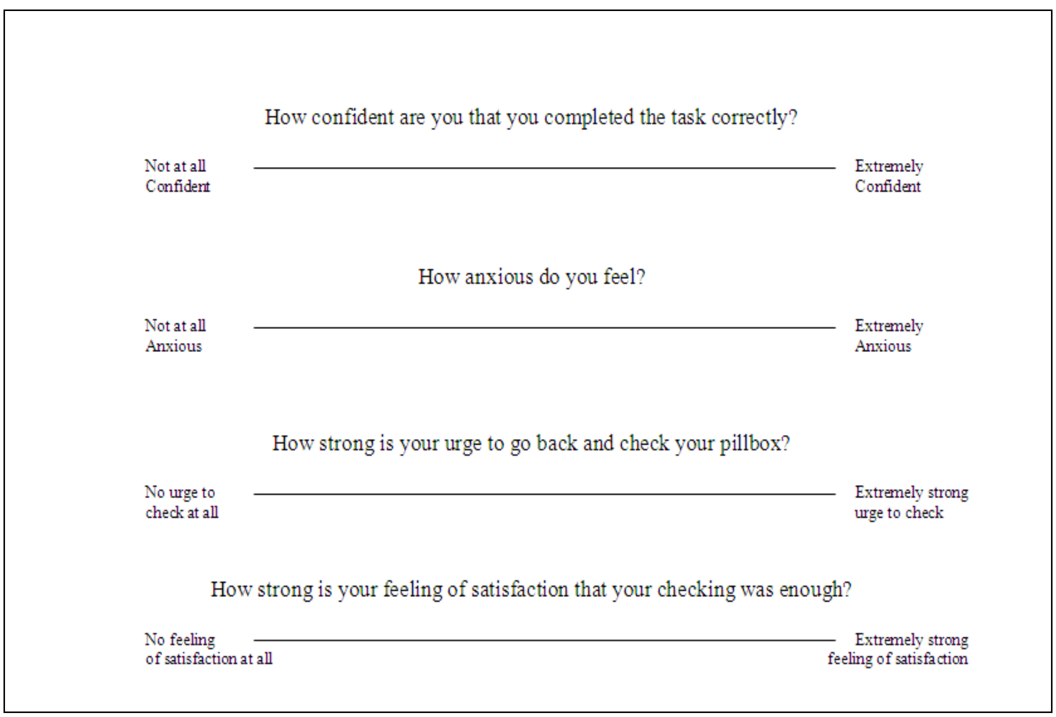

Figure 14: Linear scale questionnaire for all participants.

Upon completion of the experiment all participants also subjectively rated their everyday experiences by completing the Padua Inventory - Washington State University Revision (PI–WSUR). We scored the total responses, as well as just those related to the subset of checking threats for determination of individual tolerance for potential threats in their everyday life. All participants were expected to score within the normal, non-clinical range (within one standard deviation from the non-clinical average); therefore, the cutoff score on the PI-WSUR checking subset for eligibility was 14.

IV. Results

With this experiment, we hoped to observe a significant effect of exposure to the possibility of failing at a critical, and highly consequential, task and an effect of corrective checking on the dynamics of Security-Motivation. Therefore, the main data of interest are the measures of SMS activity immediately following exposure, and after the fixed checking period. We predicted that corrective checking would be necessary for the appropriate termination of the SMS after its activation by the threat of task failure, but that checking would be irrelevant when the responsibility associated with the task was low (as the SMS was not expected to be elicited in this situation).

Analysis was performed on the physiological recordings and subjective data collected for each participant at the four time points of interest, as well as the duration of time spent checking. Individuals were classified according to Threat Stimulus (Pill or Candy) and Behavioural Condition (Checking or Delayed Checking). RSA change data were analyzed with a repeated measures multivariate analysis of covariance

(MANCOVA). Time point of measurement was the within-subjects factor and threat stimulus and behavioural condition were between-subjects factors. Baseline RSA, age, and sex were covariates. Subjective ratings over time were also analyzed.

As in the comparable washing study (Chapter 4), the three-way interaction of Threat Stimulus, Behavioural Condition and Time of Measurement was statistically significant for RSA change, $F(2, 80) = 36.97$, $p<.003$ (See Figure 15). This interaction was also significant for the subjective rating of Confidence in Task Performance, $F(2,81) = 29.12$, $p<.001$ (see Figure 16) and Urge to Check, $F(2,81) = 12.85$ (see Figure 17). The pattern of results for all of these measures shows that in the high-consequence condition (involving the pills), there was activation of the SMS after the threat exposure, and this activation only decreased substantially when the participants were allowed to check. These results exactly parallel the earlier ones found with non-OCD groups using the washing paradigm.

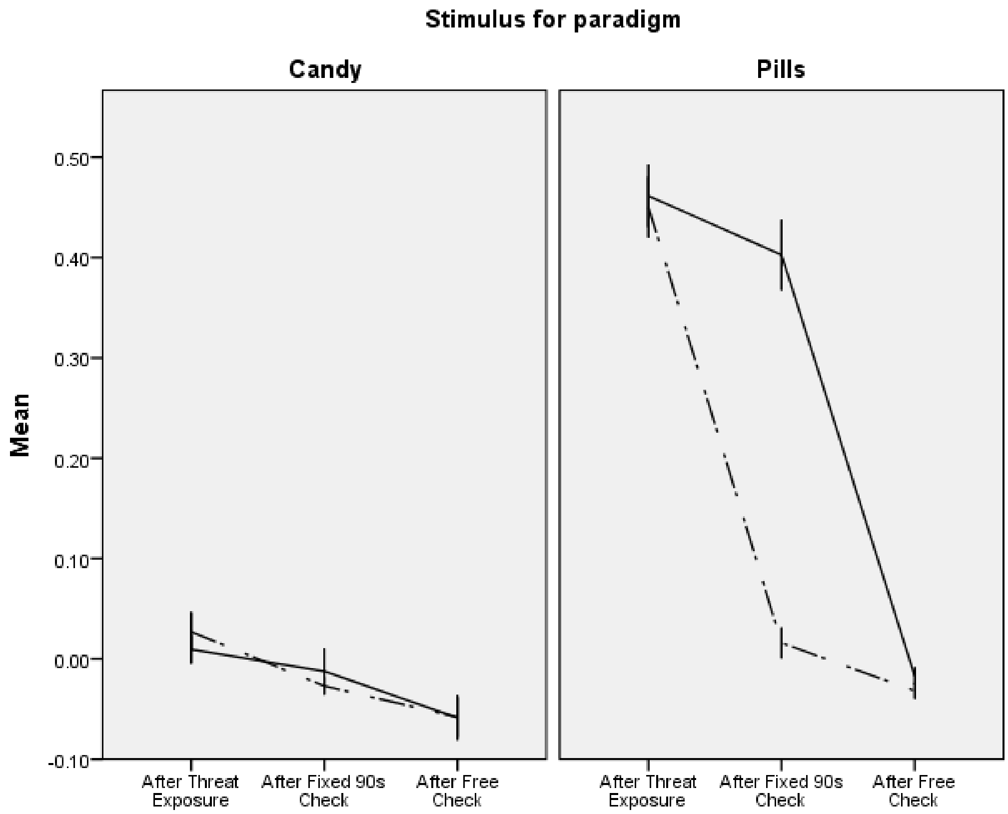

Figure 15: Effect of behaviour on terminating SMS activity – RSA change from baseline. Dashed line represents those in the Checking groups; Solid line represents those in the Delayed Checking groups. Error bars represent 1 SE.

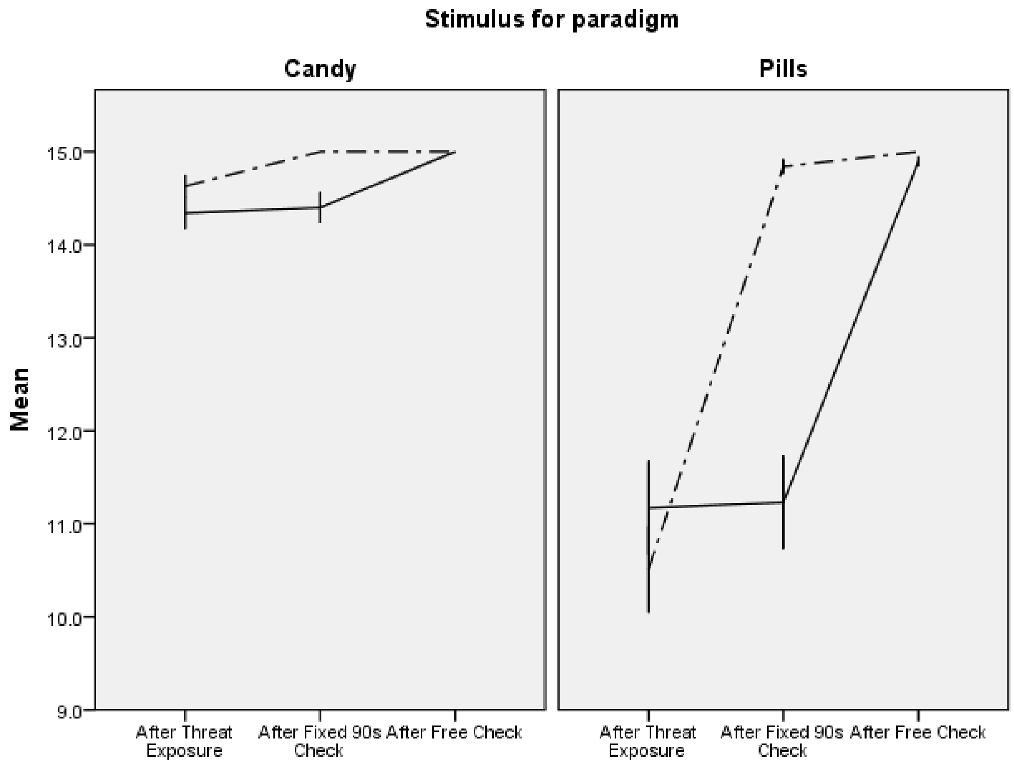

Figure 16: Mean ratings of confidence. Dashed line represents those in the Checking groups; Solid line represents those in the Delayed Checking groups. Error bars represent 1 SE. *p*<.05 for comparison of Pill-Delayed Checking group with other three groups at After Fixed 90s Check.

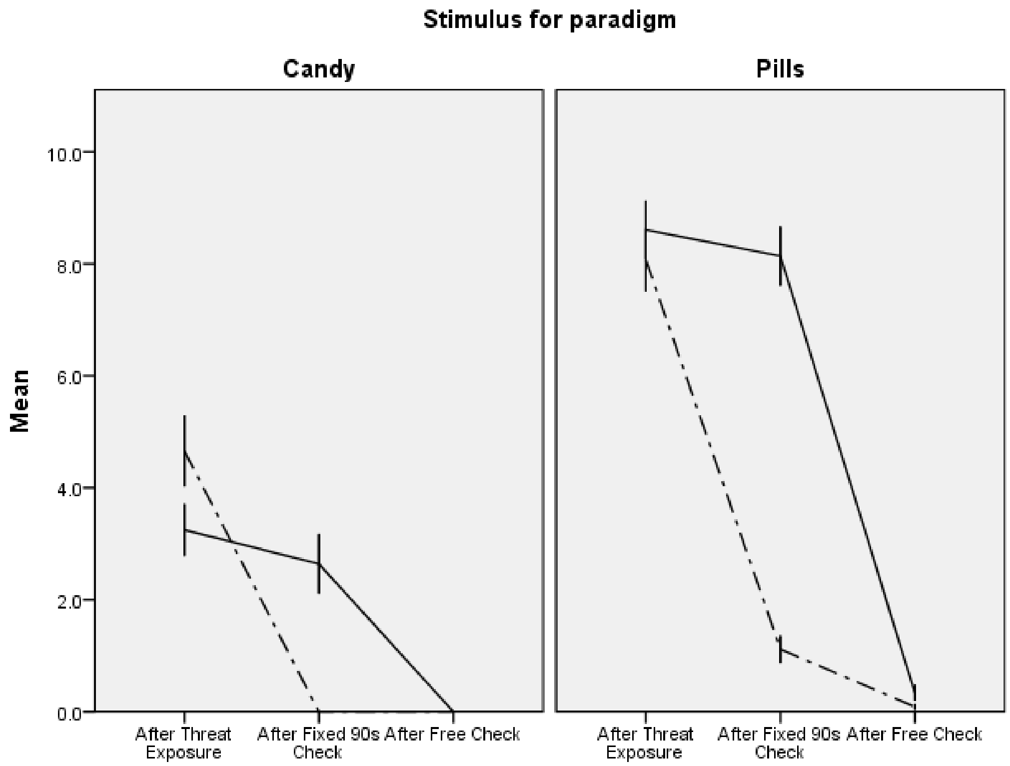

Figure 17: Mean ratings of urge to check. Dashed line represents those in the Checking groups; Solid line represents those in the Delayed Checking groups. Error bars represent 1 SE. $p<.05$ for comparison of Pill-Delayed Checking group with other three groups at After Fixed 90s Check.

V. Implications

Our revised paradigm to test the effect of exposure to potential task failure has shown that the SMS is indeed activated towards this threat when the sense of personal responsibility is high and task failure is associated with serious consequences. The SMS appears to be highly tuned to the validity of the potentially threatening situation, responding not only to the cues themselves, but also the context and validity of serious consequences. Further, the deactivation of this system, once activated, requires engagement in the appropriate corrective behaviour of checking for the presence of critical errors; in the absence of this behaviour, anxiety and SMS activity remain high, measurable as elevated RSA change from baseline and a higher urge to engage in checking (as measured via self-report). These results mirror the SMS termination and sense of satisfaction induced by hand washing in response to potential contamination threats, as seen in our original experimental manipulations of security-motivation.

Ultimately, the successful development of an effective and useful tool for tracking the response of the SMS toward critical task failure and corrective checking has bolstered the validity of our hypotheses. We have demonstrated conclusively that our observations to date reflect a broader role for the SMS in the detection and amelioration of a variety of potential threats, not simply focused narrowly on the realm of contamination. In addition, our results support the hypothesis that potential threats need not reflect a risk to the health or safety of the individual themselves in order to be of relevance to the SMS; rather, this system appears to respond just as effectively to threats which impact the overall safety of the group to which the individual belongs, or feels a sense of responsibility towards protecting. This raises a number of interesting evolutionary questions about the nature and function of such a system – one that expends energy in producing behaviours aimed not only at the removal of dangers to the self, but also the protection of the collective whole, either directly or indirectly. It is possible that a better understanding of the *ultimate* consequences (either real or perceived) of security-motivation failure will better elucidate the relationship between the various functions tasked to the SMS. Importantly, our recent paradigm also allows us to extend our research to explore checking-based behaviours in specific populations, including those afflicted with disorders of compulsive checking.

CHAPTER 9: FUTURE RESEARCH

I. Effect of Stimulus Re-Exposure on Security-Motivation

While we have explored several important aspects of the Security-Motivation system, our current research has focused on singular exposures to threat – that is, the response to one threat, at one particular point in time, independent of conflicting or competing information. The question of how the SMS responds to multiple or concurrent threats raises several interesting hypotheses for future study. In particular, one unexpected observation on the response of OCD-afflicted individuals to unlimited corrective behaviour provides an impetus for exploring the impact of stimulus re-exposure on the duration and intensity of SMS activity. In our previous study (see Chapter 6), the OCD group reported an incomplete sense of satisfaction after washing during the unlimited "free wash", despite the fact that the autonomic index of SMS activity indicated that the washing was sufficient to return the system to baseline (indicating that this behaviour was at least partially effective at ameliorating SMS activation). This inconsistency lead us to hypothesize that that the SMS "stopping" mechanism may reflect the activity of multiple subsystems that operate under unique timeframes to produce both immediate and delayed effects on SMS activity. It is possible that the short-term response to participation in corrective behaviour for as long as desired produces an immediate reduction of physiological preparedness and increase in vagal input (restoration of normal HRV), whereas production of a lasting subjective sense of satisfaction occurs over a longer period of time. In other words, those with OCD may be able to use an increase in corrective behaviour to compensate for their deficiency by producing a transient effect on the SMS that, unfortunately, does not generate a more stable signal for satiation. If this is true, *complete* deactivation of the SMS (once activated in these persons) may still be significantly prolonged.

It is possible, then, that this time after unlimited motor output reflects a critical period where the SMS is in a state of recovery that is yet incomplete for OCD washers (as compared to controls for whom recovery would be virtually instantaneous following corrective behaviour). During recovery, it may be that the SMS is hypersensitive to re-activation by new or repeated potential threats; if so, exposure would produce a pattern of activity that reflects the effect of causing the SMS to reactivate while still in a heightened state from its previous exposure. To further investigate this hypothesis, we would hope to establish a paradigm that would track SMS activity after exposure to both an initial potential threat and subsequent threat exposures. Manipulation of the timing and intensity of subsequent exposures could help establish under what conditions the SMS is hypersensitive (or, conversely, tolerant) to new potential threats, and when each new exposure elicits SMS activity indicative of an independent, unrelated event.

In a preliminary test of our predictions, we examined the effect of a secondary contamination threat immediately following a primary exposure to contamination in both OCD washing individuals and non-OCD controls. Participants were run through two subsequent sets of physiological recording (and concurrent subjective ratings) to observe the effects of reactivation of the SMS. More specifically, participants were run through the experimental paradigm as described in Chapter 4 for tracking the effect of washing on RSA. Immediately after completing an unlimited wash in response to cues for potential contamination, the entire recording paradigm was repeated.

For this preliminary study, we explored the effect of two alternative patterns of contamination exposure: one in which the stimulus remained unchanged between the first and second exposure, and one in which the stimulus was of a different intensity. This allowed us to measure SMS reactivation after exposure to a stimulus that is either a repetition, or a variation of the original. Using the contamination stimuli from our original OCD study (both wetted and dry diapers), we created four distinct groups on the basis of participant type (OCD or non-OCD control) and re-exposure stimulus intensity (see Table 4).

	FIRST EXPOSURE	***SECOND EXPOSURE***
OCD	Level 2	Level 2
	Level 2	Level 1
Controls	Level 2	Level 2
	Level 2	Level 1

Table 4: Experimental groups for pilot study.

Fifty-six participants aged 25-65 were recruited (28 persons with OCD and 28 non-OCD controls) and assigned to one of the two conditions for secondary exposure (identical or reduced intensity). Recruitment and screening was conducted as established for our previous clinical studies. Participants completed the protocol as outlined in Chapter 6 (Manipulation of Security-Motivation in OCD Individuals) with change in heart rate variability measured for four time-points of interest (Baseline, After Exposure, After Fixed Wash, and After Free Wash). In all groups, the second run followed **immediately** after completion of the first.

We were not interested in the effects during the first exposure (except as validation for our earlier results) as this was expected (and confirmed) to follow the predicted pattern as seen in our earlier OCD-centered studies: SMS activity returned to baseline immediately following hand washing in control participants, and remained elevated despite this washing for OCD participants (after contamination exposure). For determination of the effect of re-exposure, we were only interested in whether the SMS change from the starting baseline differed during the second exposure as compared to the first. We expected controls to respond to the second threat in a way that was consistent with the response to the same threat when experienced independently if SMS activation is completely terminated at time After Free Wash, it should be free to reactivate when re-exposed. Therefore, previous exposure to a higher potency threat was not expected to affect the response to subsequent threat of similar or lower intensity. This hypothesis was supported as the mean RSA values at the time-points of interest did not significantly differ between runs, $p>.05$. Patents were expected to show sensitization towards the second exposure, resulting in a pattern of activity identical to the first exposure, but with a higher intensity (the effect of SMS hypersensitivity). The data did not support this hypothesis. Like controls, OCD-afflicted individuals responded as though the second exposure was an independent event and RSA did not differ between runs, $p>.05$ (see Table 5). In fact, both persons with OCD and controls showed a trend towards *desensitization* (although not significant) after re-exposure to an identical stimulus; this suggests that the intensity of the secondary threat may be important in determining the SMS response when two potential threats are detected in close succession.

These results also provided compelling evidence for relatively high test-retest reliability in the analysis of HRV – raw HRV score, as well as HRV change in response to the environmental cues, remained consistent within subjects over each consecutive exposure.

REACTIVATION TOWARDS IDENTICAL STIMULUS				
	OCD		Controls	
	First Run	Second Run	First Run	Second Run
Baseline	6.20±1.26	6.23±1.24	6.95±1.24	7.09±1.28
After Exposure	5.53±1.24	5.67±1.18	6.30±1.19	6.61±1.26
After Fixed Check	5.71±1.24	5.82±1.20	6.96±1.25	7.13±1.36
After Free Check	6.17±1.27	6.27±1.24	7.05±1.31	7.17±1.30
REACTIVATION TOWARDS LOWER INTENSITY STIMULUS				
	OCD		Controls	
	First Run	Second Run	First Run	Second Run
Baseline	5.69±0.83	5.62±0.81	7.22±0.78	7.28±0.74
After Exposure	5.15±0.84	5.19±0.80	6.58±0.62	6.72±0.62
After Fixed Check	5.20±0.79	5.31±0.80	7.22±0.76	7.29±0.77
After Free Check	5.61±0.80	5.60±0.80	7.28±0.75	7.33±0.73

Table 5: Mean ±SD values for RSA.

In contrast to our initial hypothesis, incomplete deactivation of security-motivation (as seen in OCD populations) does not necessarily contribute to a state of hypersensitivity toward subsequent threat cues. There are several possible explanations for these findings, each with their own implications for further investigation. If it is the case that the incomplete disengagement of the SMS through hand washing as seen in OCD does **not** produce sensitization to future threats, we may consider why this would not occur and what alternative mechanism might prevent this sensitization. Perhaps it is a general phenomenon that the SMS cannot be elicited for reactivation if already engaged; in other words, it is possible that the effect of residual SMS activity is not in enhancing the response to future threats but rather, preventing additional response. In this case, the system would be ineffective at dealing with multiple threats at one time. Evolutionarily, this may have benefits, such as being effective at concentrating energy on one threat rather than dividing behavioural output between several tasks. Such a setup would also have detriments though, such as failing to appraise a crucial threat in favour of attending to one of lesser importance. In the case of SMS dysfunction, sensitization could have serious consequences – if the system became increasingly sensitized to each concurrent threat, a barrage of threats at one time and layering of increasingly hyper-responsiveness could overwhelm the system. Therefore, it may be advantageous to prevent sensitization of the SMS, a process which may be completely intact in persons with OCD.

An alternative interpretation of our findings is that there were inherent flaws in the methods used to test threat re-exposure. In this paradigm, the secondary contamination threat was very similar to the initial threat (dry as opposed to wet diapers). Exposure to a contamination threat that had already been encountered in the very recent past did not have the same impact as if this threat were novel. It is possible, then, that the SMS has developed in such a way that threats that are more novel and require more effort for appraisal are better able to elicit activity. This would support the view of the SMS as a system that is specially tuned to detecting and evaluating change. If our results can be explained as our secondary exposure representing insufficient change, it is possible that dramatically different results could be seen if the re-exposure stimuli contained a unique set of cues (for example, a source of contamination unrelated to diapers) or was of a different type of threat altogether.

In future, it would be beneficial to explore the factors that may influence SMS reactivation, such as stimulus intensity, timing between exposures, and type of potential threat. It is possible that altering the type of subsequent contamination exposure, increasing the time between exposures, and activating the SMS via a different subset of threat (for example, exposure to the potential for critical task failure immediately after exposure to contamination threat) could elicit a different pattern of results than was obtained in our pilot experiment. We may also be interested in exploring if test-retest reliability remains high when the duration between testing increases by hours or days, on subsequent testing visits.

II. Security-Motivation in OCD-Afflicted Individuals with Checking Symptoms

The successful development of a potential threat exposure paradigm now allows us to effectively repeat any of the studies outlined in the previous chapters, adjusting the focus from contamination and washing to critical task failure and checking (with the noted exception of the aspects of these studies that examined the effect of stimulus intensity – we currently have no method of adjusting the critical threat stimulus to reflect distinct levels of cue presentation). This would be valuable in demonstrating generalizability of our research methods, effectively mirroring the effects of population variability, cognitive reappraisal, clinical dysfunction, SMS reactivation, and behavioural specificity that we saw with contamination exposure and hand washing in our pill sorting responsibility task.

At present, we are actively exploring what is arguably the core basis for this body of work – the impact of SMS dysfunction on the development of obsessive-compulsive disorder symptoms. As we did for people with washing-based OCD using exposure to contamination (see Chapter 6), we expect to compare SMS activity between OCD-afflicted individuals with predominant checking symptoms and normal controls using our newly developed checking-based paradigm. Like OCD washers, we hypothesize that checkers will be unable to use engagement in corrective checking behaviour to provide essential feedback termination on the activated SMS after exposure to a relevant potential threat. Recalling that SMS dysfunction in the contamination protocol was specific to OCD washers (wherein OCD checkers were essential non-clinical for this task), it is of interest if any dysfunction seen towards corrective checking would be similarly subtype-dependent. We do not predict that individuals with washing compulsions would show an abnormal SMS response to threats of potential task failure (or any other potential threats unrelated to contamination and the risk of illness) and subsequent corrective checking. To test these hypotheses, we are currently recruiting non-clinical controls, OCD-afflicted persons meeting criteria for washing concerns, and OCD persons meeting criteria for checking concerns (as outlined in our previous discussions for inclusion and exclusion criteria). We hope to demonstrate that the typical obsessions and compulsions seen in OCD reflect *specific* patterns of dysfunction in crucial elements of the special security-motivational circuit, particularly the elements that underlie and control the essential negative feedback mechanisms for effective system disengagement.

Pilot work with OCD-afflicted individuals has begun – to date, we have compared the response of three non-OCD controls and three people meeting diagnostic criteria for OCD with compulsive checking as their predominant symptom, on the responsibility task paradigm as outlined in Chapter 8. The results of this preliminary data show that, as predicted, RSA change does appear to remain elevated in OCD checkers after exposure to critical task failure threat and engagement in corrective checking (as compared to controls, where threat-removal behaviour is sufficient to alleviate SMS activity). By continuing to increase the sample size for this study, we can determine if these results are reliable.

Although we have had success using RSA change as an index of SMS activity and heart rate variability, future research into the impact of manipulations on SMS activity may also benefit from additional physiological and psychological measures. Such indices may include other autonomic measures, such as blood pressure, and additional sympathetic measure as a complement to heart rate. Galvanic skin response, or skin conductance response (SCR) – a measure of the electrical resistance or conductivity of the skin is another useful and relatively simple autonomic measure. Literature has demonstrated the impact of emotionally significant content on electrodermal activity (Smith, Low, Bradley & Lang, 2006). In addition, analysis of video recordings of individuals participating in the surveillance and detection of threat cues may be useful in classifying typical responses and stereotypical facial expressions associated with anxiety

(Cunningham, Kleiner, Wallraven & Bulthoff, 2005). Non-invasive collection of sweat and saliva as described by Marques, Silverman & Sternberg (2010) may also be used to provide an indication of the release of cortisol and other biomarkers for the measurement of stress-related endocrine fluctuation. The concurrent use of several measures can provide further validity for the autonomic changes that correspond with SMS activity.

III. Additional Measures of Checking Behaviour

Although we have had success with the development of our paradigm for the induction of checking behaviour, we must also consider the possibility that task failure and the generation of a sense of personal responsibility is not a specific enough threat to be considered relevant only to compulsive checkers (as opposed to other OCD subtypes). While it is established that this threat does elicit checking, it may be that this particular type of checking can be differentiated from that which normally follows cues for threats to security (that may cause direct injury). Cues for the potential breach of responsibility, or failure in one's "duties" to protect the self or others, are indeed an appropriate trigger for the SMS, but may differ from traditional potential threats in that their consequences are indirect (and in fact may be less personalized, as the individual in this case is not *solely* responsible – when the responsibility is shared, so too are the consequences). It could be argued that exposure to contamination does also elicit a sense of personal responsibility, in preventing the continued spread of disease, or becoming the source or cause of illness for another person. In essence, SMS activation and motor-output generation in response to potential threat cues with *direct* consequences may be very specific (contamination leads to illness, and exposure to aggressors or unsafe conditions leads to injury) and compartmentalized (washing or checking); however, activation towards threats with *indirect* consequence may be more generalized. Thus it is possible that an individual with dysfunctional response mechanisms towards safety threats, for example, may have a normal response to contamination threats (as seen in the stark distinction between OCD washers and checkers when exposed to the same contamination stimulus) but a relative dysfunction in their response to the more general possibility of having failed to protect others or having "let down" the group. Perhaps, then, the "potential threat" in our checking paradigm is not actually the threat of reduced safety but rather, the threat of responsibility itself. In this case, the act of checking would effectively terminate the activated SMS, not because the behaviour had helped to eliminate a threat to someone's welfare, but simply because it had eliminated the individual's responsibility for that welfare.

Recent work has demonstrated the promise in using an alternative strategy for the testing and measurement of checking behaviour in response to potential threat exposure – the use of computer-based virtual reality (VR) simulation programs (Kim, Kim, Cha, Park, Rosenthal, Kim et al., 2010). The use of VR as a tool for the treatment of a number of disorders, including phobias and other anxiety disorders, is growing, as it allows for complete control over the exposure, as well as consistency between participants. VR works by presenting a simulated environment that the participant can freely interact with, permitting the individual to complete tasks or be involved in situations that might otherwise be impractical in a laboratory setting. Once an individual is immersed within a VR "world", their movements in the real world are reflected as a change in the VR environment. For example, one could have the experience of walking up a tall flight of stairs, or leaning out over a steep cliff, experiences that could allow someone with a fear of heights to gradually exposure themselves to these environments without restriction. Similarly, individuals with specific contamination or safety obsessions may be able to exposure themselves to these threats in a controlled manner. Kim et al. (2010) describe the extension of this technology for the specific analysis of compulsive behaviours in OCD populations, exposing both afflicted and non-afflicted participants to a series of checking-related tasks within the virtual setting and measuring the number and frequency of compulsive acts. Participants were instructed to navigate both a virtual office and home, and simulate the completion of several everyday safety-related tasks that would require checking for accuracy. This included unplugging electrical appliances, locking a door, and turning off a gas burner.

While this study simply tracked checking behaviours, it is reasonable to predict that such a simulation could be a useful tool for the manipulation of potential threat exposure and participation in corrective behaviour as we have done naturally to date. Using VR could allow for practically unlimited possibilities in the design of potential threat stimuli, in any of the modalities (contamination, safety, task failure, etc) of interest. It may even be possible to create personally relevant virtual environments since this factor can have such a significant impact on the relevancy of the situation (Kim, Kim, Cha, Park, Rosenthal, Kim et al., 2010). It is important to note that the indication of "presence" (the degree to which participants feel immersed in the virtual environment) is, on average, quite high, with participants easily able to approach the simulation as though it were reality (Kim et al, 2010). Therefore, we suggest that investigating the development and use of such technologies in tandem with our preexisting potential threat paradigms would be an ideal next step in the investigation of the role of the SMS in both normal threat detection and the perseverance of typical OCD behaviours.

CHAPTER 10: GENERAL CONCLUSIONS AND OVERALL SIGNIFICANCE

The experiments described here have been published in two peer-reviewed scientific journals (with another publication in preparation) and represent a significant body of work dedicated to the understanding of the Security-Motivation system as it relates to Obsessive-Compulsive Disorder (OCD). Our research has provided evidence for a special motivational system in humans that is specifically tuned to the appraisal of, and response to, potential threat cues. We have also supported the prediction that this circuit plays an essential role in the development and presentation of typical OCD symptoms, and have characterized OCD as a disorder of SMS stopping rather than of hypervigilance, inappropriate cue appraisal, or cognitive impairment. In addition, we have noted that this stopping impairment appears to be specific to SMS activity in response to a particular subset of potential threat, with OCD individuals showing deficit only towards stimuli that are personally relevant for their distinct cluster of symptoms. These results support a perspective on the nature of the dysfunctional stopping mechanisms that may underlie OCD that differs from other research to date on the topic. Previous research has described the perseveration of OCD-typical behaviours as reflecting deficits in inhibition or impulsivity (for example, Zeeb, Floresco & Winstanley, 2010; Chambers, Garavan & Bellgrove, 2009) rather than a problem with satiety and the normal termination of motivated arousal after goal attainment. An impairment in the sense of task completion as described here differs from the proposed pathological impairment of executive cognitive control over motor response as described by Verbruggen and Logan (2009) and Dalley, Everitt and Robbins (2011) (among others), in which the frontal cortex is unable to control or interrupt ongoing behavioural actions, allowing for their perseveration. Finally, we have demonstrated that engagement in the *appropriate* corrective behaviour is the essential termination feedback signal for the activated SMS, and cannot be substituted by cognitive effort or alternative behavioural tasks.

Through our research, we have also developed several experimental paradigms that have proven successful for the tracking and manipulation of the SMS. These paradigms present appropriate potential threat cues within a controlled environment in a manner that is both reliable and valid for future testing of SMS parameters.

The present results also lend credence to the study of the biological mechanisms that are proposed to underlie both normal and abnormal SMS circuitry. Our results suggest that the focus may need to shift from pathology of the orbitofrontal-basal-ganglia circuit (Saxena, Bota & Brody, 2001; Stein, Goodman, & Rauch, 2000) towards the exploration of circuits that may be indirectly causing hyperactivity in this pathway through a failure to inhibit its function. Since the negative feedback signal for goal attainment comes directly from the performance of security-related behaviour itself, areas of hypoactivity that may ultimately lead to SMS dysfunction include brainstem sites that provide proprioceptive feedback from task performance to the limbic striatum and prefrontal cortex (areas directly responsible for cue appraisal and security-motivation).

It is evident that detection and appraisal of potential threat cues and the subsequent motivation and action plan to remove such threats is a complex and dynamic process, and one that may be especially prone to dysfunction via physiological or neurochemical disturbances during development. Here, we have focused on one potential outcome of such dysfunction, the production of repetitive corrective acts that are characteristic of compulsions in OCD. Currently, the implications of this research on the treatment and diagnosis of OCD remain theoretical, with its predominant value being the advancement in understanding the neurophysiological circuitry underlying the persistence of its stereotypical symptoms. The link between SMS activity and the presentation of OCD symptoms may be relevant, though, for the development of future behavioural and psychopharmacological strategies. The current predominant therapy technique involves exposure with response prevention (ERP), which builds tolerance for potential threat exposure by training the patient to develop tolerance for potential threat exposure and modify his or her interpretation, and response to, threat cues. In essence, ERP provides symptom relief by targeting the initial SMS *activation* and cue appraisal – the starting component of security-motivation. Modifying SMS in this way does passively impact the mechanism of stopping by modulating the SMS pathway as a whole. We suggest, however, that more appropriate and effective treatment therapies would be those that specifically target the site of dysfunction and include techniques to directly compensate for the weakened or missing stop signal. While still theoretical, this may include some method of training or manipulation that directly enhances the patients' experience of motor output-generated feedback for termination of the SMS, or improves the interpretation or response to such feedback. Research has already suggested a role for hypnosis in the manipulation of confidence and satisfaction associated with task completion (Woody, Lewis, Snider, Grant, Kamath & Szechtman, 2005) and self-regulation and biofeedback for disorders involving autonomic dysregulation (Moravec, 2008). Such strategies may be important and useful supplements to traditional cognitive-behavioural therapies;

The development of workable scientific paradigms for the testing and manipulation of contamination and safety based stimuli (and the respective output behaviours of washing and checking) has provided greater insight into the biological and psychological mechanisms underlying response to these threats both in clinical and non-clinical samples. While checking and washing do represent the most common symptoms seen in OCD, behaviours such as hoarding and arranging are also quite prominent and have not been specifically addressed here. Our current work provides a framework for the creation of an appropriate stimuli and experimental protocol for the testing of these behaviours and their relationship to SMS dysfunction; however organizing and arranging are thought to arise in response to a threat of potential disruption to personal order, a situation that is both extremely context dependent (as it relates strongly to the individual's sense of their personal space) and highly variable. Although we have provided some excellent tools, the study of these subtypes of OCD in the context of SMS activity is likely to require more sophisticated and specific control over the environment and threat presentation, such as with the use of VR or home-based studies. Still, the results of our current studies may allow us to speculate on the relationship between the different types of potential threat whose detection and removal relies on the SMS, how distinct threats are managed by this system, and how specific dysfunction to one or more SMS response circuits may be disordered while others are left in tact.

In general, it is of interest to understand what factors influence the proper functioning of a special security-based motivational system and the implications of such a system on the production and maintenance of critically important survival behaviours. The analysis of risk in the environment is likely affected by a number of biological, contextual and psychological factors through development and over the course of one's lifespan, each contributing to the way in which potential threats are interpreted and dealt with. Although we have focused our research on human populations, it is important also to note that these findings are expected to generalize to all living creatures for which safety is an evolutionary concern, and may be similarly monitored through the use of species-appropriate experimental design. While we have focused on the role of negative feedback in control of the SMS, we may also consider to what degree and in what manner potential threat cue detection and appraisal is modulated by the SMS, and how this might affect the selection of appropriate behavioural outputs. Even baseline SMS activity is highly variable, with consistently low heart rate variability and resting RSA possibly indicative of chronic states of anxiety.

We believe the SMS is sensitive to change in environmental consistency for determination of the presence of potential threat; however, it is not yet clear what the "rules" are for deciding if the SMS should activate, and in what manner. It is probable that there is some threshold to be met for SMS activation, based perhaps on the accumulation of graded assessments, each independently evaluating some aspect of the environment, and the contextual nature of potential threat cues. It is logical that some mechanism must underlie this decision-making process, to ensure that the SMS does not remain inactive at a critical time (leaving the individual unprepared for a life-threatening situation) or, alternatively, activate too readily (motivating the organism to action unnecessarily, and at the cost of participating in other more relevant tasks). The system should also be able to shift focus readily, for example, in the situation where the individual is exposed to competing threat cues, or a new threat is encountered before removal of an initial threat is complete. It is likely that these determinations are based, at least in part, on the ultimate consequences of threat exposure. We are not yet certain how, or if, the system prioritizes its responses on the basis of cue potency and the relative effect on fitness if threat removal fails; for example, it might be predicted that threats with a high cost (such as severe illness or death) may have a greater bearing on the SMS than those with more subtle consequences (such as minor injury, destruction of property, or loss of status).

It is also likely that the interpretation of environmental cues is highly subjective, influenced by individual experiences and learned responses over the course of the lifetime which serves to modulate and calibrate the SMS. The accumulation of memories for life events is expected to have a significant influence on motivated states and consequent behaviours. This variability may affect how the system deals with the ambiguous nature of potential threat cues, particularly in circumstances where cues may be providing conflicting or competing information, and impacting the SMS via multiple sensory modalities at one time. It is also unclear whether the SMS is a system that is relatively rigid and innate (as suggesting by the conserved nature of SMS-eliciting stimuli over the course of evolution), or to what degree it may be modified by one's culture, social contexts, and early developmental experiences. In addition, there is a significant body of literature to suggest that both sex and age influence the parameters of security-motivation, and that changes in circulating hormone levels (in particular, typical female hormones such as progesterone) are essential modulators of threat appraisal and avoidance in both animals and humans (Choleris, Clipperton-Allen, Phan & Kavaliers, 2009; Conway, Jones, DeBruine, Welling, Smith, Perrett, et al. 2007; Fessler, Eng & Navarette, 2005; Fessler & Navarrete, 2003).

Our work on the Security-Motivation hypothesis and its extension to the study of Obsessive-Compulsive Disorder has helped illuminate the normal psychological processes that are related to security-based precautionary behaviours, and has contributed to the understanding of both the normal functioning of the Security-Motivation system and to our understanding of some typical behaviours seen in psychological disorder as reflecting psychopathology of Security Motivation.

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