The continuum of consciousness in cardiovascular stress research : an experimental expedition

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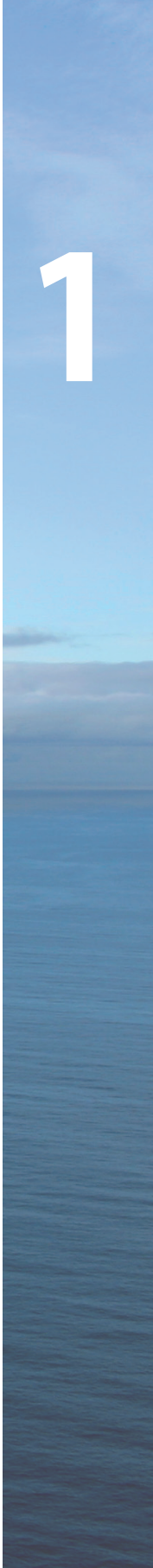
Chapter 1

Introduction



Cardiovascular (CV) diseases are prevalent and place a major burden on individuals and health care resources. Treatment is usually aimed at traditional risk factors such as diabetes mellitus, smoking, and physical inactivity (1). Psychological stress has been found to negatively affect health and contributes to the development and worsening of somatic diseases, such as CV diseases (e.g., 2-7), but the underlying mechanisms are still unclear (e.g., 8,9). It is widely recognized that these adverse consequences are largely the result of chronic stressors and impaired physiological recovery (10-16). One of the mechanisms underlying this relationship is thought to be the ongoing cognitive representations of the stressor, which is referred to as perseverative cognition. Perseverative cognition can manifest itself for example as worrying (17-21). However, these perseverative cognitions do not fully explain the effect of psychological stress on health-relevant outcomes (e.g., 22-25). It has been suggested that stress-related cognitions can also occur outside of awareness, which is referred to as unconscious stress (26-28). In the current thesis, the effect of stress-related cognitions occurring outside of awareness on physiological activity is explored with a systematic review and a series of experimental studies to enhance our understanding of the relationship between psychological stress and health.

In this Chapter, I will elaborate on the three main components of this thesis; stress, awareness, and health-relevant parameters. This is followed by a discussion of the main methodological issues that play a key role in this area of research. Finally, I will introduce the content of the remainder of this thesis in an outline.

The concept of stress

Research on psychological stress has been hindered by a lack of consensus on the definition of *stress* (e.g., 29,30). Consequently, a wide range of operationalizations of psychological stress is used, such as perceived stress, worry, anxiety, or anger (e.g., 17,20,31-33). According to Levine and Ursin (1991, 34), these operationalization are all valid methods to test specific stress-related hypotheses, but an overarching formal definition is called for. The idea of a formal and systematic definition was further developed into the cognitive activation theory of stress (CATS; 16), which defines *stress* based on four components: stress stimuli (or stressors), stress experience (i.e., appraisal), the (nonspecific) stress response, and the feedback from the stress response which generates stress-related behavior and cognition. In CATS, the stress response is an adaptive process that induces increased arousal and concurrent behavioral and physiological changes. This occurs when the organism detects a situation that does not meet its expectancies, which constitutes the stressor. When the organism is unable to cope with the situation the response is maladaptive, which leads to continuous arousal, and may lead to negative cognitive states such as helplessness, hopelessness, and negative affect resulting from the continuous negative physiological feedback. Notably, the CATS emphasizes the general and nonspecific nature of the

physiological and affective response to stress stimuli (16). If one reads this definition closely, it becomes apparent that the psychological aspects encompasses often segregated concepts such as cognition or emotion, as the CATS assumes that all of these responses are part of the (mal)adaptive processes. Within this framework, any stimulus that induces negative affect is seen as a stressor. So, stress is considered to be a psycho-biological response set to a stressor. In the current thesis, the psychological aspects of the response as described by the CATS are further explored to explain its relationship with somatic disease.

The stress response is quickly activated in response to a stressor, but when one further appraises this stressor as something that should be dealt with effectively, the activation of the stress response is short-lived and is not likely to result in adverse health consequences (35). However, when the stressor is appraised as something that cannot be coped with, it will result in sustained arousal that is detrimental to one's health (10,11,13-16). Moreover, if we cannot, for some reason, adequately resolve the discrepancy in what was expected (*set values*) and the reality (*actual values*), the stress response, psychologically and physiologically, is continued (16). The stressor induces ongoing stress-related cognitions (e.g., worry). The perseverative cognition hypothesis states that these cognitions result in physiological activation for the duration of the cognition (17,18). These prolonged stress-related cognitions have been found to increase cardiovascular (CV) and hormonal activity in the laboratory and in real life (for a review see 21). However, in most studies, perseverative cognition explains only a part, or in some studies even none, of the prolonged CV responses to stressors (e.g., 21,23-25). Thus, although prolonged stress-related cognitions are important to evaluate as a factor in the etiology of somatic diseases, additional factors should be explored.

Psychological stress beyond self-report

In 1939 Alexander (36) suggested that unconscious processes may be involved in health-related processes. More specifically, his Specificity Theory entailed that unconscious conflicts could lead to somatic diseases such as hypertension. Although this psychoanalytic idea could not be verified with experimental studies, the idea that self-report does not fully capture associated threats to health is still an area of interest in psychosomatic medicine (for an overview see 28). Research on psychological stress relies mainly on self-report, but as mentioned above this approach has not yet led to identifying a sufficiently specified mechanism underlying the detrimental prolonged physiological responses to stressors (e.g., 15,21). Moreover, research suggests that as people may be unaware of their emotions, self-report questionnaires on affective states are likely to be insufficient (e.g., 37). Furthermore, there is evidence of stressors during the day leading to physiological activity during sleep, when there is no conscious cognition (e.g., 15,22,38), which suggests that factors beyond self-report may play an

important role. Hence, it has been proposed that people may not be aware of, or are unable to report on, part of their affective state (28), even when faced with health-relevant changes in the physiological state. This has been referred to as *unconscious stress* (26,27). It is suggested that stress-related cognitions may also occur outside of awareness. In fact, research on unconscious processes in other fields suggests a role of these processes in for example attitudes, self-esteem, emotions, central nervous system activity, decision making, and affective evaluation (39-47). Moreover, extending the reasoning of the CATS and PC hypothesis, these active representations of a stressor are hypothesized to simultaneously elicit physiological stress responses without the individual being aware of this process or even of the existence of these representations. This prevents active coping with the stressor, which may result in ongoing adverse physiological activation. In other words, even stressors that are not consciously noticed or cannot be reported on, may induce affective and bodily responses that may eventually lead to serious health problems. This is called the unconscious stress hypothesis, and forms the central hypothesis of this thesis.

The unconscious: A level of awareness

Psychology as a science has a long history of studying *the unconscious*. The repression theory of Freud has received considerable attention within and outside of the scientific community and referred to the unconscious as a different state of the mind that inhibited negative associations to prevent the conscious self from experiencing mental distress (see for a review 48). Experimental work was done in this area by for example Jung (1907, 49) and Peterson and Jung (1907, 50) (see also Chapter 2). Ever since these early studies, there has been an ongoing debate on the definition of consciousness (e.g., 51). Nowadays, an influential perspective is that consciousness should be thought of as a continuum in which multiple levels of awareness exist (40,43,51,52). According to Kihlstrom (1987, 53; 1993, 52) on one end of this continuum we have the mental states that are represented in phenomenal awareness, that is, conscious awareness. It can be assessed with questionnaires or introspection. The other end remains an enigma, with representations that are not available to phenomenal awareness, which is epitomized by the lack of a clear definition. For example, it has been defined as processes that occur while attention is directed elsewhere (in the case of decision-making; 42) and automatic activation (in the case of attitudes; 43).

Furthermore, different methodologies have been used to assess this end of the continuum of consciousness, such as subliminal presentation or implicit measures (53). Moreover, as suggested by for example LeDoux (1996, 54) and Wiens and Öhman (2010, 51) research on affective phenomena should not be limited to subjective indicators, because converging evidence from multiple indicators is much more persuasive of the existence of changes in the psychological state. However, in a large body of research on awareness not this theoretical notion of a continuum is conveyed, but

rather a dichotomy of unconsciousness versus consciousness (as elaborated on by for example Fazio & Olson, 2003, 43). Underlying this dichotomy lies the assumption that processes can be either conscious or unconscious, which, considering all evidence (e.g., 52,55,56), seems unlikely.

This thesis acknowledges that consciousness should be viewed as a continuum. Consequently, the operationalizations of unconscious processes are not meant to capture one end of a dichotomy and should be interpreted as addressing several levels of awareness other than what can be reported. Focusing on other levels of awareness beyond self-reports may help in explaining the variance in stress-related physiological responses. Moreover, although in the current thesis we have tried to address several levels of awareness with a range of methods chosen from the existing literature, it is not assumed that the realm of consciousness is limited to the levels on which these methods assess affective phenomena.

Inducing unconscious stress

To explore the role of unconscious processes in the relationship between stress-related information and (prolonged) physiological activation, we have taken two approaches; inducing and measuring unconscious stress.

Unconscious stress can be induced by activating the stress response outside of one's awareness, that is, by presenting a stressor below the threshold of awareness (i.e., subliminally). In experimental research, a common method to manipulate unconscious processes is subliminal priming, which has been shown to affect behavior, affect, and brain activity (e.g., 57-60), but also elicits CV changes (61-63). Even presentation times of 20 ms or shorter can elicit these effects (e.g., 64,65). The mechanism of subliminal priming relies on the activation of the associated evaluation of the prime once the prime is presented (66). The presented stimuli are usually sounds, images, and words (67). In the current context the associated evaluation of the prime should be stress-related. When presenting stress-related stimuli subliminally and measuring physiological responses, the unconscious stress hypothesis can be tested, that is, increased physiological responses to subliminal stress-related primes would provide evidence of unconscious stress. As discussed, psychological stress entails a range of negative affective cognitions, which can be specific (such as the word 'angry') but also nonspecific (such as a series of threatening words). However, the use of these stimuli requires the assumption that they elicit a certain level of psychological stress in all individuals, which is not necessarily true for each word and in each individual.

An alternative method that better ensures the induction of comparable stress-related cognitions to the same stimulus across participants is the use of a fear conditioning paradigm. This paradigm consists of pairing a stimulus with an aversive unconditional stimulus, such as a shock. The automatic physiological response to the aversive stimulus is thought to also occur in response to the (now) conditional

stimulus after repeated pairing (e.g., 45,68). The nonspecific state of vigilance and physiological activation that is induced by this method can be interpreted as a stress-response in line with learning-based stress theories (e.g., 16,69-72). In other words, by using a fear conditioning procedure, a (temporary) stressor can be created. By subsequently presenting the conditional stimulus subliminally and measuring the concurrent physiological changes, the unconscious stress hypothesis can be tested: Does the subliminally presented conditional stimulus (i.e., the stressor) increase physiological activity? In the past, increased autonomic nervous system activity to subliminally presented fear conditioned stimuli has been found (73), but no health-relevant parameters, such as blood pressure, have been addressed. In the current thesis, subliminal presentation of both previously validated stress-related stimuli and fear conditioned stimuli were used to induce unconscious stress.

Measuring unconscious stress

The second approach to testing the unconscious stress hypothesis is by measuring unconscious stress. Stress-related cognitions can be measured at different levels of awareness. In general, measures are designed to generate scores reflecting certain attributes of a person (74). To measure constructs outside of awareness implicit measures are applied. These measures use a procedure that prompts the subject to produce an automatic response that provides information about the assessed construct. Automatic in this context refers to "the absence of certain goals, awareness, substantial cognitive resources, or substantial time" (74). In this conceptualization of implicit measures it is stipulated that it is the measurement that is implicit and not the construct itself (see also 39,43). An implicit measure that is very prominent at present is the Implicit Association Test (IAT, 75). It was originally designed to measure implicit prejudices but has been adapted to suit other purposes and is increasingly used to measure implicit affect, referred to as the affective IAT. During an affective IAT, participants have to categorize stimulus-words that relate to the attribute of interest, for example *anxiety* vs. *calmness,* into target categories that relate to for example the *self* (e.g., me, I) or *others* (e.g., they, his) (76). The response index that is derived from the reaction times is thought to reflect the intensity of the attribute under investigation measured implicitly. Although debate is still ongoing concerning the correct interpretation and implementation, there seems to be consensus that these implicit measures do add to findings with self-report measures (75, 77-81).

Several studies have used implicit measures in relation to physiological measures during and after experimental stress inductions. For example higher negative affectivity measured with the IAT has been associated with higher BP and heart rate (HR) and lower heart rate variability (HRV; 76,82). In this thesis, other implicit measures that may be associated with the physiological correlates of psychological stress are evaluated. First, the Implicit Positive and Negative Affect Task (IPANAT; 83-85) was used, in which

participants have to indicate to which extent an artificial word has a certain affective value to them. Responses are thought to be a result of *affect infusion* (86), which means that representations of affective states at any level of awareness influence the affective value attributed to ambiguous stimuli. The responses are thought to reflect the activation of a certain affect. Previous studies have indicated that the negative affect subscale of the IPANAT was related to stressor-specific cortisol responses and higher levels of the cortisol awakening response (85,87). Regarding CV responses, correlational data have related the subscale to slower recovery of blood pressure after a stressor that was not found with the self-reported measure of affect (88). The possible practical and theoretical implications of these findings warrant further research.

Second, we used a Lexical Decision-making Task (LDT; 89), which is a common measure to capture *automatic vigilance*. In this task participants have to respond to a string of letters by indicating whether it represents a "word" or a "nonword". The actual words are positive, negative, or neutral in nature. Faster responses to a category indicate greater accessibility. It is thought that the affective representation that is activated enhances this accessibility, which leads to a quicker perception and processing of the presented stimuli of the category that is represented and is known as automatic vigilance (81). In earlier studies, automatic vigilance for negative information as measured with the LDT was found to be related to slowed recovery of HR (90). In the current thesis, these implicit measures are assumed to respond to induced psychological stress by increased negative affect on the IPANAT and shorter reaction times to negative words in the LDT.

These particular tasks were chosen for several reasons. First, the IPANAT and LDT use a series of emotion words covering the two ends of the spectrum of affect, negative and positive, rather than preset categories as in for example the IAT. In contrast to the IAT, both tasks are clinically applicable since the scores have a meaning at the individual level, and its administration procedure is straight-forward and brief. The IPANAT in particular directly assesses affect without having to extract it from affect-related self-concepts or attitudes (74,81,91). Importantly, these measures have the potential to be implemented on a mobile device for intervention purposes. Taken together these advantages and previous findings suggest that the IPANAT and LDT might be suitable candidates as implicit measure of psychological stress. Moreover, implementing measures that assess affective constructs such as psychological stress at an implicit level might provide the field with an additional tool to explain the occurrence, development, and progress of prolonged physiological activity that ultimately leads to (CV) disease. The explanatory value of these implicit measures, in addition to self-report measures, is explored in the current thesis.

Notably, in the studies where we tested if measures of unconscious stress could explain prolonged physiological activity after a stressful experience, we used stress-inductions to elicit the psychological and physiological stress response (92). In the

studies, we choose to administer two widely used stress-induction procedures. One was a mathematical task with anger harassment. The procedure was similar to that of a previous study (88), which found a relation between the negative subscale of the IPANAT and slower recovery of BP. However, that study lacked a control condition and firm conclusions regarding the IPANAT would be premature. The other procedure that we used was an anger recall task, which is a well-documented stress-induction task that is known to elicit CV responses (93).

Physiological correlates of (unconscious) stress

In the relationship between psychological stress and CV health, several outcome measures are of importance. CV activity can be expressed in various parameters that represent different aspects of the physiological state, but only those that are addressed in this thesis are described here. Blood pressure (BP) is most often expressed in SBP, the highest level of the pressure at the systole (i.e., contraction) of the heart, and DBP, the lowest level of the pressure at the diastole (i.e., relaxation) of the heart. Hypertension is diagnosed with a SBP of 140 mmHg or higher (160 mmHg when older than 60 years) and/or a DBP of 90 mmHg or higher (94). Mean arterial pressure (MAP) can be calculated from these two indices and is a more general vascular index that has been related to the baroreceptor activity (95). Heart rate (HR) is the number of heart beats per min (95). Heart rate variability (HRV) indicates the variability in timing of the heartbeats and fast fluctuations in this timing (especially when these occur within the frequency range of respiration) is thought to represent activity of the parasympathetic nervous system. In general, a higher HRV is considered healthy and is expected to be lower in response to stress-related stimuli (96). Furthermore, total peripheral resistance (TPR) is an index of resistance of the blood flow through the organism. Low TPR has been related to the development of CV disease and all-cause mortality (97,98). Additionally, TPR is thought to represent a specific dimension of the stress experience: A higher TPR would be associated with the experience of *threat* rather than *challenge* (99,100). Noninvasively it can only be calculated using other CV parameters (96).

In the different experiments described in this thesis, we have used SBP, DBP, and HR to focus on immediate physiological changes, but in Chapters 3, 6, and 7 we looked at other indices of CV activity (MAP, TPR, and HRV) that help to more specifically clarify the specific state of the organism. All of these outcome measures have been described in relation to adverse consequences for health (e.g., 101,102). Furthermore, in the systematic review and the fear conditioning study we have also looked at skin conductance responses, as this is a common outcome measure in this research area (103), which we believe provides the necessary context for the outcomes of the study.

Main goals and outline

To sum up, by examining the CV responses to (subliminally presented) stressors and measuring psychological stress with self-report and implicit measures, this thesis will address whether unconscious stress can further explain the physiological response to a stressor.

In this thesis, a series of experimental studies is described using samples of healthy young adults, as an initial step to address the validity of the unconscious stress hypothesis. The central aim of these studies was to induce psychological stress and measure responses in physiological activity, but the methodology to address unconscious stress differed between studies. **Chapter 2** describes the systematic review of studies in which stress-related and stress-unrelated stimuli were presented subliminally, while peripheral physiological parameters were measured. In Chapters 3 and 4, we describe two studies in which we executed a subliminal priming paradigm on CV activity. More specifically, the study in **Chapter 3** tests the effect of subliminal threat words versus that of neutral words on CV activity. In **Chapter 4**, a study is described in which we presented the subliminal word 'angry' [woedend] and 'relax' [ontspan] to test the effects of this manipulation on CV activity. This study aimed to replicate the finding by Hull et al., (2002, 62), who observed that subliminally presenting the word 'angry' enhanced CV activity compared to the word 'relax'. However, as discussed above, the use of stress-related stimuli in subliminal priming paradigms offers an important limitation: it assumes pre-existing affective associations with the presented stimuli. However, these associations can differ greatly between individuals. In order to overcome this, we have tried to create a stressor with equal valence across participants in the study described in Chapter 5. In this study, we used a fear conditioning paradigm to create an association between neutral images and an aversive stimulus, a mild electrical shock. This association would create a physiological stress response that we expected to occur during a test phase in which these neutral images (CS+) were presented subliminally but without the shock, as compared with stimuli that were not paired with a shock (CS-).

In addition to these studies in which we looked at subliminally presented stress-related stimuli, we performed several experiments using measures beyond self-report after a stress-induction to assess the relationships with CV activity. In **Chapter 6** the Implicit Positive and Negative Affect Test was used after mental arithmetic that had to be performed with and without negative feedback. **Chapter 7** describes the associations of a Lexical Decision-making Task with CV responses after the recall of an anger or happiness evoking situation. In **Chapter 8** the findings of the studies are discussed to elaborate on the concept and challenges of the unconscious stress hypothesis. Together, these chapters provide a primary overarching approach in examining the relationship between psychological stress and health on the continuum of consciousness.