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The perseverative cognition hypothesis: A review of worry, prolonged stress-related physiological activation, and health

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Abstract

Perseverative cognition, as manifested in worry and rumination, is a common response to stress, but biopsychological models of stress and health have largely ignored it. These models have generally focused on physiological activation that occurs during stress and have insufficiently addressed effects that occur in anticipation of, or following, stressful events. We argue that perseverative cognition moderates the health consequences of stressors because it can prolong stress-related affective and physiological activation, both in advance of and following stressors. We review evidence that worry, rumination, and anticipatory stress are associated with enhanced cardiovascular, endocrinological, immunological, and neurovisceral activity. The findings yield preliminary support for our hypothesis, suggesting that perseverative cognition might act directly on somatic disease via enhance activation via the cardiovascular, immune, endocrine, and neurovisceral systems.

Keywords: Prolonged physiological stress-related activation; Recovery; Worry; Rumination; Perseverative cognition; Literature review

Introduction

Worrisome thinking is a common response to stressful events, but for the most part, this construct has been mainly studied within the context of test anxiety in students and anxiety disorders. Worry plays a role in nearly all anxiety disorders and it is a basic feature of generalized anxiety disorder (GAD). Even in the area of anxiety, it was not until the 1980s that the potential etiological importance of the concept became recognized and systematically investigated (see Ref. [1]). In the case of rumination, extensive scholarly recognition of its role in psychopathology (mainly depression) is of an even more recent date [2]. In this paper, we will argue that worry, rumination, and related phenomena may play a much broader role; that is, they may be crucial factors in somatic health as well. We will present evidence that such cognitions have physiological sequelae that can lead to long-term health consequences, including cardiovascular disease (CVD) and other organic diseases. Furthermore, we will outline the diverse processes and mechanisms underlying these long-term health consequences, including currently known physiological and neurovisceral concomitants of worry. The article will begin with the definition and nature of worry, rumination, and related concepts and the crucial mechanism that these phenomena share, called *perseverative cognition.* Next, we will discuss the etiological role that perseverative cognition may play in somatic disease.

Worry, rumination, and perseverative cognition

Several definitions of worry have been given. Borkovec et al. [3,4] introduced a working definition of worry that appears to be most often used: Worry is a chain of thoughts and images, negatively affect-laden, and relatively uncontrol-

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lable. It represents an attempt to engage in mental problem solving on an issue whose future outcome is uncertain but contains the possibility of one or more negative outcomes; consequently, worry is related closely to fear process.

Thus, the definition highlights the role of both cognitive and affective substrates. An important component of this definition is the role of problem solving; worry may lead to constructive problem-solving strategies or, alternatively, to nonconstructive perseverative thoughts regarding the source of the anxiety or, e.g., anger. In this way, it prolongs or even exacerbates negative affect. This is also expressed in another regularly used definition of worry that is less related to psychopathology: Worry is primarily a constructive problem-solving process that is thwarted by cognitive predispositions (anxiety and others; [5]).

There are many definitions of rumination, all of which share the experience of having repetitive, intrusive, negative cognitions (see Ref. [6]). Some of these definitions are narrow, such as the definition of Nolen-Hoeksema [2] of depressive rumination: Behaviors and thoughts that focus one's attention on one's depressive symptoms and on the implications of these symptoms. Others are very broad, such as the view of Martin and Tesser [7] of rumination as (our paraphrasing) a class of conscious thoughts concerning one's goals and that recur in the absence of immediate environmental demands requiring the thoughts.

Worry, rumination, and many related cognitive processes in the literature, such as anticipatory stress and cognitive intrusions, are conceptually close but are usually not equated with one another. A common feature in these processes, and others, such as obsessions and (appetitive) craving, has been described as "repetitive thought", emphasizing the recurring nature of these processes [8]. The perspective that we assume in this article is somewhat different and concerns the somatic health consequences. The core feature of these repetitive cognitions that is responsible for the effects on somatic health is that they contain cognitive representations of a psychological problem, a difficulty, a crisis, or, in other words, a stressor. To refer to this central shared feature, we suggest the term perseverative cognition. Thus, we define perseverative cognition as the repeated or chronic activation of the cognitive representation of one or more psychological stressors.

Why perseverate?

The most concrete function attributed to worry is an attempt at constructive mental problem solving, although it may represent an unproductive and, perhaps, even a counterproductive attempt [5]. Davey [5] and coworkers found positive correlations between worry and problem-focused coping, but only after controlling for the effect of trait anxiety. Thus, worry appeared to be associated with a habitual tendency for attempted active problem solving combined with low confidence of success.

Tallis and Eysenck [9] proposed a tripartite function of worry: First, worry serves an alarm function, acting to interrupt ongoing behavior and directing awareness toward an issue demanding immediate solution. Second, worry may have a "prompt" function, maintaining awareness of unresolved threatening situations. Third, worry is thought to have a preparation function, anticipating threat and making the organism ready for a situation in which high or even vigorous motor activation is needed ('fight or flight'). For the most part, however, actual fighting or fleeing is rare; thus, worry or related manifestations of perseverative cognition theoretically leave the individual in a prolonged state of psychophysiological "action preparation", which is generally assumed to be the core of emotion [10–12]. A central notion of this article is that this prolonged state may have important long-term health consequences.

Perseverative cognition, somatic illness, and physiology

Studies of stress, coping, and disease have largely ignored worry, rumination, and other perseverative cognitive phenomena. The bulk of research in this area has involved either discrete stressors, such as life events or daily hassles, or discrete coping strategies, or both. When chronic stress has been studied, such as marital or social–economic stress, the emphasis has been mostly on the stimulus characteristics or the individual's perception of them and seldom on enduring cognitive processes that may act as mediators. One reason is that theoretical models that link stressors to health outcomes have been poorly specified. In particular, a complete model must account for the set of chronic pathogenic pathways that ultimately cause disease. Perseverative cognition may contribute to such pathways by both serving as a stressor in itself and by mediating the effects of psychosocial stressors. We shall discuss this seemingly hybrid nature of perseverative cognition in the sections to follow.

Thus, perseverative cognition might help to convert the immediate psychological and physiological concomitants of life events and daily stressors into prolonged physiological activation of several of the body's systems, which, in turn, has been argued to be necessary for the development of a chronic pathogenic state [13,14].

Another reason for the neglect of worry and perseverative cognition in stress research is that the dominant measures (such as life events and daily hassles) always focused on the past. During half a century of stress research, little explicit attempt at measuring anticipatory stress has been accomplished. As with perseverative cognition, we hypothesize that this too may be a consequence of the lack of theoretical precision as to the psychophysiological mechanism underlying the stress–disease link. There has been a particular failure to recognize the importance of prolonged activation, with some notable exceptions [13–16]. Most investigators continued to measure stressors as discrete events, and coping behavior as discrete and singular goal directed strategies,

without addressing the important question of whether and how some events or coping strategies have prolonged effects on physiology [17].

The role of perseverative cognition in stress-coping disease

Traditionally, coping strategies are usually regarded as moderators of stressor effects on health. That is, coping strategies are regarded as a means by which the effect of stressors is ameliorated by eliminating or avoiding the stressor, or by changing its meaning. Perseverative cognition, in contrast, can be thought of as a mediator, or a final pathway by which the stressor exercises its effects on the body's systems. It does this by virtue of its propensity to prolong the stressor itself, in a representational form that continues to activate the organism. Thus, we hypothesize that without perseverative cognition or a comparable mechanism that maintains a cognitive representation, which may operate to prolong the activation, a stressor cannot have an impact on the development of a chronic disease in a direct manner.

Within the framework of leading theories on emotion and cognition [10–12], perseverative cognition may be regarded as a prolonged state of action readiness for the individual. This represents a highly vigilant state, which may produce moderate but chronic levels of activation for the cardiovascular, hypothalamic pituitary adrenal, and immune systems, and for which extreme increases in physiological activation may not be observed. The crucial pathogenic property, therefore, in perseverative cognition is not its acute, short-term effects on any given system (i.e., intensity or amplitude), but rather its duration and the inadequate autonomic and emotional regulation associated with it. This idea is expressed in the simple scheme in Fig. 1. The scheme makes clear that short responses do not automatically lead to long responses; that is, there is no arrow in the scheme between short and prolonged responses. Prolonged responses only occur when the stressor's cognitive representation is prolonged, a process we call perseverative cognition.

Thus, rather than a "reactivity" model, in which the short-duration physiological spikes are thought to play the primary role in physiological changes, this represents an "allostatic load" model [14], which may be conceptualized better in terms of the "area under the curve," in which the total amount of stress induced physiological activation, over time, is regarded as the primary pathogenic pathway.

Although its role in the stress–disease process may be different than the role played by coping, perseverative cognition is theoretically related to coping. As said, one may regard perseverative cognitive processes as fruitless attempts at mental problem solving [5]. If one looks at the instruments used in most studies of coping and health, an implicit assumption seems to be that coping behavior is a matter of merely choosing among behavioral options. The instruments do not, however, assess dynamic dimensions that are relevant to the coping process, such as how long it takes respondents to make their decision, how long they vacillate between options or between actually performed behaviors, or whether they simultaneously tend to use more than one strategy.

Thus, we hypothesize that perseverative cognition can serve as a mediator or pathway, by which psychosocial stress may produce sustained activation of one or more physiological systems. Such activation is due, at least in part, to a prolonged state of action readiness generated by neural systems (see section on neurovisceral concomitants below) that, in close collaboration with the cognitive apparatus, detect and respond to threat. The cognitive apparatus normally allows us humans to problem solve without reflexive, direct behavioral consequences, i.e., "off-line", as it were.

Perseverative cognition and perceived control

A core cognition of this perseverative state is the perception that control over a stressor, i.e., one's ability to actively cope, is threatened. Perceived uncontrollability over threat or challenge and related concepts like hopelessness

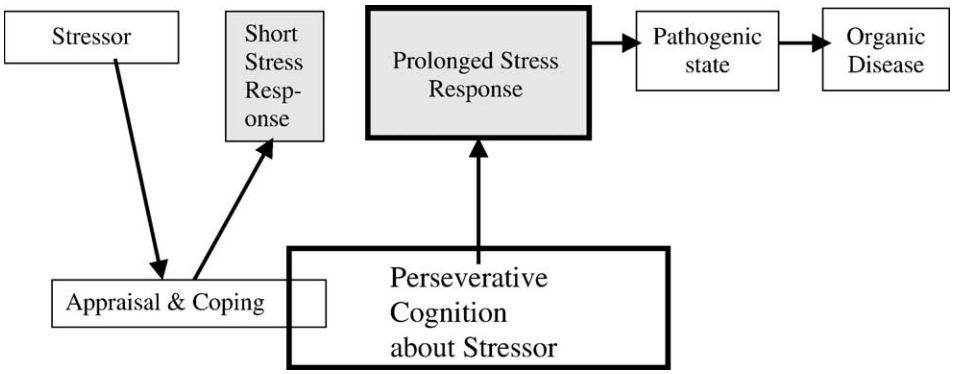

Fig. 1. Basic model of perseverative cognition mediating the effect of stress on organic disease. The difference in size of the two 'stress response' boxes reflects the notion that the hypothesized prolonged response lasts substantially longer than does the response during and immediately following a stressor. It does not reflect the exact relative difference in passage of time.

have been documented as critical determinants of pathogenic physiological states and final health problems (e.g., Refs. [18–20]). Theoretically, perseverative cognition is caused by perceived uncontrollability of a stressor: If a stressor is controllable, there is no need to worry or ruminate about it. At the same time, perseverative cognition prolongs the experience of uncontrollability: By prolonging the cognitive representation of the stressor, it also prolongs the cognitive representation of the stressor's uncontrollability and, finally, its physiological activation. This process can even be amplified when an individual has a high need for control (e.g., Ref. [21]) or a strong expectation that control is possible, i.e., a high internal locus of control.

In summary, we propose that perseverative cognition prolongs a stressor's effects by maintaining its cognitive representation, together with its degree of uncontrollability. This, in turn, sustains the physiological response to the stressor, which, over time, will lead to disease [13,15,16]. Several findings support the latter notion that prolonged physiological activity is a risk factor for disease [22–25].

Somatic disease and physiological activation

We will now focus on the available evidence concerning the potential pathogenic effects of perseverative cognition. There is recent evidence of the link between perseverative cognition and disease outcomes, as well as with physiological functioning that is relevant for the development of somatic disease. We will give an overview of the findings with worry and rumination, as well as those with anticipatory stress. With respect to the latter, we discussed above that a large part of perseverative cognition concerns anticipating future events. Although the idea of considering future stressors is absent in the bulk of stress research, it is obviously a possible way to cognitively "protract" stressor effects.

To understand the link between perseverative cognition and somatic disease and somatic complaints, it is necessary to identify the physiological pathways that are affected by this type of cognitive and related affective activity and that may serve as pathogenic influences. Siegle and Thayer [26] have recently reviewed the literature on the (neuro)physiological concomitants of depressive rumination. In this section, we shall briefly describe the results of studies that have shown that a broader range of perseverative cognitions, including worry, rumination, and anticipatory stress, produce effects on several such pathways, without going into the details of how these pathways can lead to disease. We based this review on a literature search over the last 30 years, using the abstracts, descriptors, and titles of the PSYCINFO and MEDLINE (PUBMED) databases, with terms referring to worry and rumination and anticipatory stress, combined with terms referring to somatic disease and physiological functioning. Due to space constraints, we have limited the latter to the most commonly used health-related parameters, i.e., cardiovascular, endocrinological, and immunological parameters. Words referring to worry and related concepts are extremely common and very frequently used in terms of cognitions concerning disease and its consequences, instead of its (co)determinants. Therefore, we had to inspect every single one of a vast quantity of abstracts to be able to select some of the studies described below and in Table 1. In this table, the studies that explicitly measured or manipulated perseverative cognition are displayed, together with their dependent variables, participants, operationalizations of perseverative cognition, design, main outcomes, and controlled variables. We only included studies concerning prolonged activation, i.e., during recovery from or anticipation to stress and continuous ('rest') levels. Below, we also discuss a number of studies showing the effects of anticipating stressors or effects of distraction after stressors. Although they strongly suggest the influence of perseverative cognition, the latter was not explicitly measured, and therefore, we did not include them in the table.

Somatic disease and somatic complaints

To date, only some studies have reported relationships between general somatic complaints and perseverative cognition (see Table 1). Trait, as well as state rumination and worry, was found to be related to self-reported illness symptoms in at least five studies [27–31], three of which used prospective designs [27,28,31]. One of these [27] reported that 1 week's total worry duration was prospectively related to health complaints in high school and college students. The authors also found that a worry reduction intervention appeared to decrease self-reported worry duration as well as these complaints. These effects too involved a range of different single somatic complaints, including lower back pain, neck pain, coughing/bronchitis, breathing difficulties, and stomach pains. In this study, trait worry was cross-sectionally related to somatic complaints. Another study [28] found that trait rumination was prospectively related to self-reported physical health problems 1 year later, but only for 20- to 35-year-old individuals and not 70- to 85-year-old ones. Yet, a third prospective study only found a cross-sectional effect on health complaints, and only when self-esteem was low, and failed to find an effect of trait rumination at the 8-week follow-up [31]. Cross-sectional relationships were found between the number of times that the participant worried about their 'conflicting goals' in 3 weeks and somatization [30] and between trait rumination [29] and health complaints. The latter effect was mediated by perceived stress. Two of the studies corrected for negative affectivity or trait anxiety. This suggests that, at least in two studies, the association was for, a large part, due to a "pure" tendency to worry/ruminate and not only to a tendency to express or experience negative affect. Thus, there is some suggestive evidence for a prospective relationship between perseverative cognition and an increase in a wide range of somatic complaints. One finding for anticipatory stress seems to be in line with these outcomes. In students anticipating an

Table 1
Overview of reviewed studies of associations between perseverative cognition and prolonged endocrine, immune, cardiovascular activation and skin conductance, somatic complaints, and disease outcomes

Outcome variables	Studies (first author)	Participants and sample size	Instrument measuring perseverative cognition	Design	Effects of perseverative cognition	Controlled variables
Somatic complaints and disease	Emmons, 1988 [30][a]	40 students (70.0% F)	State: # times "thinking about conflicting strivings"	Cross-sectional: Experience sampling (3 weeks)	More somatization	
	Rector, 1996 [31]	121 (58.7% F; gen. popul.)	Trait: ECQ-R	Cross-sectional/ longitudinal 8 weeks; Trait× Self-esteem	More somatic symptoms only combined with low self-esteem at baseline; no longitudinal effects	Sex, coping, LOC, emotional inhibition
	Kubzansky, 1997 [34]	1758 M (21–80 years; gen. popul.)	Trait: Worry about different domains	Longitudinal 20 years	Higher risk all types CHD and angina pectoris	Age, smoke, alcohol, BP, cholesterol, BMI
	Lok, 1999 [29]	327 (48.3% F; gen. popul.)	Trait: ECQ-R	Cross-sectional	More health complaints: Via perceived stress	Perceived stress, control, hassles
	Thomsen, 2004 [28]	196 young (27 years) and 314 elderly (75 years; 55% F; gen. popul.)	Trait: ECQ-R	Longitudinal 1 year	Young: More somatic symptoms at follow up, not at baseline; Old: No effect controll. f. NA and at follow-up	Sex, baseline symptoms, life events, NA
	Brosschot, in press [27]	171 high school students (81.3% F; 17 years)	Trait: PSWQ; State: # worry episodes and duration; six days/nights	Experience sampling and Exp. worry reduction; Cross-sect. and prospect.	Trait and state: More somatic complaints; strongest for worry duration; Worry reduction: less complaints	Trait anxiety, sex, age
Endocrine and immune responses	Rowland, 1987 [45]	16 M (27.5 years)	State: one item 'worried'	Correlational: During erotic movie	More plasma CORT, no effect prolactin, testosterone, luteinizing hormone	Drugs, illness
	Segerstrom, 1998 [40]	47 employees (53.2%; 45 years)	Trait: PSWQ	Prospective (2, 8, and 15 weeks after earthquake)	Lower # NK cells, but no effect on NKCA, Th, Tc, and B cells	Trait anx., IES, NA, age, caff., alc., smok., exercise, sleep duration
	Segerstrom, 1999 [41]	21 snake/spider fear students/staff (66.7% F)	Trait: PSWQ	Correlational: trait and recovery from feared object	Lower # NK recovery after fear, but no effect Th, Tc, B cells	Sex, age, alc., medic. needle/blood fear
	Young, 2001 [44]	47 F students; 19 years	Trait: RRS (short version)	Trait×Recovery from public speech and cognitive stressors	No effects on salivary CORT; but no increase in state rumination	Age, BMI, smok., alc., exercise, medic., menstr. period, psychiat. hist.
	Schlotz, 2004 [39]	219 (53.4% F; 49 years; gen. popul.)	Trait: TIACS–'worry during last year'	Cross-sectional; Salivary CORT on six mornings	Higher awakening CORT and increase during morning; Stronger on weekdays	Sex, time of day/week, sleep dur. and awak. time
	Thomsen, 2004 [42]	196 young (35.6% F; 27 years)/314[b] elderly (53.8% F; 75 years; gen. popul.)	Trait: ECQ-R	Cross-sectional	Only elderly: higher ## of leukocytes, lymphocytes, B-cells; No effect six other cell types, NKCA and no PHA effect controll. f. sadness and sleep quality	Sex, age, marital status, sadness, sleep quality

(*continued on next page*)

Table 1 (*continued*)

Outcome variables	Studies (first author)	Participants and sample size	Instrument measuring perseverative cognition	Design	Effects of perseverative cognition	Controlled variables
Cardiovascular activity and SCL	Dua, 1987 [54]	20 (17 students, 3 others)	Trait: one item scale; State: 'imagining worry'	Trait×Imagining worry vs. pleasant (within ss)	Imagining worry greater HR, no effects of trait or Trait×State, or on SCL	
	Roger, 1988 [53]	45 students (51% F, 20 years)	Trait: ECQ-R	Correlational: Recovery from cognitive stressor	Slower HR recovery 1st min after stressor	Neuroticism, extraversion, sex
	Lyonfields, 1995 [37]	15 GAD students and 15 non-GAD (66.7% F)	State: Worry induction and GAD	Worry Induction× GAD diagnosis	Lower HRV (MSSD) and higher HR during worry and in GAD patients	
	Thayer, 1996 [38]	34 GAD, 32 non-GAD	State: worry induction and GAD	Worry Induction× GAD Diagnosis	Lower HRV (MSSD and HF) and higher HR during worry and in GAD patients	Sex, age, ethnicity
	Segerstrom, 1999 [41]	21 snake/spider fear students/staff (66.7% F)	Trait: PSWQ	Trait×Feared Object	Trend toward slower HR recovery; No effects on SCL	Sex, age, alc., medic., needle/blood fear
	Chambers, 2000 [68]	118 (50% F; gen. popul.)	Trait: DAB-VR	Trait×Age	Higher resting BP, but only in older participants	Other DAB scales, NEO-PI, tr. anx., depress.; hypert. risk fact.
	Schwartz, 2000 [66]	30 (F and M; gen. popul.)	State: Thoughts related to anger recall	Correlational: Recovery after anger recall	Slower BP recovery after anger recall only in women	State anxiety
	Neumann, 2001 [52]	80 students (F; 19 years)	Trait: DRS	Correlational: Recovery after anger recall	Slower recovery of HR, CI, PEP and LF, not on SI, HRV, HF, LF/HF, TPR, BP	Disease / medic, BMI, smok., contraceptives
	Glynn, 2002 [69]	72 students (65.3% F)	State: Instructed rumination ("vivid recall of emotional task")	Recall vs. no recall of emotional vs. neutral tasks	Slower BP recovery controll. f. emot. recall vs. no recall and vs. nonemot. recall (highest for M);No HR effects	Task reactivity, sex, medic.
	Brosschot, 2003 [56]	73 (79.5%; 34 years; gen. popul.)	State: Worry episodes, hourly for 1 day	Experience sampling: Worry episodes	Lower HRV (MSSD) and higher HR	Coff., alc., smok., exercise, movement
	Vickers, 2003 [55]	84 dysphoric and 86 nondysph.. students (58.2% F; 20 years)	Trait: RRS	Trait Rumination× Dysphoria× Rumination Induction	No main or interaction effects on HR, BP, SCL	
	Suchday, 2004 [67]	40 M students	State: Angry rumination after anger provocation	Correlational: recovery after anger provocation	Slower recovery BP and HR indep. of expressors vs. nonexpressors	BMI, caff., alc., exercise

BMI: body mass index; BP: blood pressure; CI: cardiac index; CORT: cortisol; DAB-VR: Destructive Anger Behavior-Verbal Rumination scale; DRS: Dissipation Rumination Scale; ECQ-R: Emotional Control Questionnaire-Rehearsal: ruminating about past events; GAD: generalized anxiety disorder; HF: high-frequency power (0.15–0.4 Hz); HR: heart rate; HRV: heart rate variability; IES: Impact of Events Scale; LF: low-frequency power (0.04–0.15 Hz); LF/HF: ratio HF to LF; LOC: locus of control; NA: negative affectivity; NEO-PI: NEO personality index; NK-cells: natural killer cells; NKCA: NK-cell activity; PEP: preejection period; PHA: proliferative response to phytohemagglutinin; PSWQ: Penn Sate Worry Questionnaire; RRS: Ruminative Response Scale; SCL: Skin conductance level; SI: stroke volume index; Tc: T-cytotoxic cells; Th: T-helper cells; TIACS: Trier inventory for the assessment of chronic stress; TPR: total peripheral resistance.

[a] Numbers correspond to the numbers in the reference list.

[b] 86/185 for NK, 59/136 for PHA.

oral academic examination, Lacey et al. ([32]; not in Table 1) found enhanced somatic complaints, compared with a control group. The increases included headaches, sore throat, fatigue, nausea, earaches, and intestinal discomfort, and this increase in complaints correlated with weakening of some immune responses (see below). It is important to be aware of the

possibility that at least part of the increases in somatic complaints discussed in this section may not be due to prolonged physiological activation but to excessive worrying about health complaints themselves [33].

The only study that explicitly links worry to verifiable disease outcome was recently reported ([34]; see also Table 1), showing that a tendency to worry predicted a second myocardial infarction. More indirectly, worry is a core characteristic of several conditions that are known to be risk factors for CVD, such as anxiety disorders, trait anxiety, and depression (e.g., Refs. [35,36]). This, together with the finding that these risk factors share with trait and state worry a low vagal tone (an independent risk factor for CVD; see below), has led several authors to suggest that worry is a potential mediator of the CVD risk associated with anxiety disorders and depression [4,13,37,38].

Endocrine and immune responses

Chronic activation of the hypothalamic–pituitary–adrenal axis (mainly cortisol) has widely been thought to make individuals more vulnerable for disease states via suppression of the immune system and has many direct pathological effects, such as hippocampal degeneration, atherogenic facilitation, and dysregulation in calcium metabolism. Several studies have shown that trait worry and rumination are associated with elevated cortisol levels and altered immune responses (see Table 1). Recently, trait rumination was also found to be related to higher morning salivary cortisol, an effect that was stronger during working than weekend days [39]. Similarly, Segerstrom et al. [40] reported that participants high on trait worry, controlled for trait anxiety and posttraumatic stress responses (i.e., intrusion and avoidance), had fewer natural killer (NK) cells in the wake of the Northridge earthquake. In another study, Segerstrom et al. [41] showed that high trait worry was related to suppression of the expected increase in NK cells when exposed to a fearful situation, but not to higher heart rate (HR) or skin conductance (see below). Thomsen et al. [42] recently found that trait rumination was related to a higher number of several types of leukocytes, and this relationship was not mediated by negative affect (sadness). Both rumination and the immune increases were positively related to health care utilization. The authors interpreted these increases as reflecting general physiological activation, which is in line with the notion that mild acute stress may increase activity in some immune parameters, while more severe and chronic stress is more likely to be immunosuppressive [43]. Finally, one study did not find an association between a disposition to ruminate and recovery from a short laboratory speech task [44], a finding that the authors attributed to the failure of this task to cause rumination.

There was only one study of state worry with these dependent variables: Rowland et al. [45] found that worry during sexual stimulation was positively related to plasma cortisol levels.

Several studies showed endocrinological and immunological effects of merely anticipating stress. Spangler [46] showed significantly higher levels of salivary immunoglobulin A (s-IgA, a common marker of immune competence) during the anticipation of and recovery from an emotionally challenging real life stressor (examination), as compared with a similar laboratory stressor (memory test). These effects were also reflected in cardiovascular differences (see below) and, at least for the anticipatory differences, marginally significant in salivary cortisol. Importantly, the responses during the tasks (reactivity) were not significantly different from each other. More recently, Smyth et al. [47] showed that both current experience of a stressor and anticipating a stressor in the next hour, but not having experienced a stressor in the hour before, were associated with increased salivary cortisol. These effects were mediated by high negative affect and low positive affect. Consistent with our view of perseverative cognition as a "prolongator" and "exacerbator" of negative affect, it seems likely that differences in anticipatory worrying accounted for both the mood and cortisol effects. Lacey et al. [32] found that plasma cortisol levels were elevated among graduate students relative to matched control participants 1 h before the oral examination, but not 6–8 weeks earlier. In contrast, mitogen-stimulated (Con-A) lymphocyte proliferation (another common immune marker) was only reduced 6–8 weeks before the examination. Interestingly, one coping style, 'attempts at problem solving', correlated negatively with lymphocyte proliferation. These authors suggested that different biological processes might be at work during the changing time course prior to an expected stressor, with cortisol reacting to more proximal stressors, while immune changes may reflect long-term adaptation to the prolonged anticipated stressors.

Cardiac activity

Chronically enhanced HR is a risk factor for all-cause mortality [48], and reduced HR variability [HRV; an index of parasympathetic activity ('vagal tone')] is also an all-cause mortality risk factor (e.g., Ref. [49]) and has been specifically associated with an increased risk of hypertension and other cardiovascular disorders [50,51]. Thayer, Borkovec, and colleagues [37,38] have repeatedly demonstrated that both experimentally induced and dispositional measures of worry are associated with low HRV and high HR. Neumann et al. [52] showed that trait anger-rumination predicted slower recovery after anger recall for HR, cardiac index (cardiac output corrected for body size) responses, and two indices of sympathetic control of the heart, low frequency power of HRV and preejection period, but not for blood pressure (BP) and other cardiac variables, including HRV. Roger and Jamieson [53] showed that trait rumination, but not neuroticism, was related to slower HR recovery after cognitive stress tasks. Dua and King [54], however, found that state worry, but not trait worry, was related to high HR. Segerstrom et al. [41] too found only a

trend toward slower HR recovery, no higher HR, or skin conductance level (SCL) for trait worriers who were exposed to a fearful situation (see above), although they found some immunosuppressive effects, and Vickers and Vogeltanz-Holm [55] found also no relationship between trait rumination and HR and SCL, and also not with BP. In an ambulatory study, Brosschot et al. [56] showed reduced HRV and higher HR during periods of worry that occurred during the day, independent of other reported stressors and negative affectivity. In a simultaneous ambulatory study, Brosschot and Thayer [57] showed that negative emotional valence, and not emotional arousal, was related to sustained higher HR after emotional episodes, while only emotional arousal was related to initial reactivity to these episodes. The increase in HR due to negative emotion appeared to hold on even when the negative emotions itself were recovered, which suggest that the effect was due to perseverative cognition. Kamarck et al. [58] found a comparable effect with BP. Perseverative cognition was not measured in these studies, and therefore, they are not included in Table 1.

Several studies showed cardiac effects of anticipating stressors and are also not contained in the table. One study found that HRV was lower during anticipation of and recovery from an emotionally challenging real life stressor (examination), compared with a comparable laboratory stressor (memory test), while reactivity to both tasks was not significantly different [45,46]. Cortisol and IgA (see above), but not HR, showed the same effects. In the Brosschot et al. study [56], HR was higher and HRV lower during the night in participants that had experienced many daily stressors the day before as compared with those who reported a low number of stressors, suggesting a further effect of perseveration. A recent study by Hall et al. [59] showed that anticipating an oral speech that had to be delivered upon awakening in the morning appeared to decrease the levels of parasympathetic activity and increase sympathetic activity during the preceding sleep period. In a control group that did not anticipate the stressor, parasympathetic activity showed the normal sleep-related increase. Because the participants were objectively asleep according to polysomnographical measurements, these results suggest that nightly unconscious perseverative cognition (about the forthcoming stressor) might have accounted for these results.

Several of these findings seem to converge, suggesting that perseverative cognition is associated with decreased parasympathetic activity and increased sympathetic nervous system activity. The association with this potentially pathogenic state makes a disposition to worry or ruminate a likely and independent risk factor for CVD. The significance of perseverative cognition as a mediator may be broader, though. Low parasympathetic activity has also been found to characterize depression and anxiety disorders [37,38,60,61], which are conditions that are increasingly documented as important risk factors for cardiovascular and other diseases (e.g., [35,36]). Thus, as suggested above, worry and rumination may serve as a mediator of the relationship of anxiety and depression with CVD, via prolonged sympathetic activation due to chronic low parasympathetic control of the heart.

Blood pressure

High sustained BP is a risk factor for many diseases, including CVD and diabetes, and one of the most widely studied stress-related physiological parameters [17]. Most studies relating worry to BP recovery deal with hostility and anger. The reason for this is that hostility has been found to be a potent psychological risk factor for hypertension and CVD [62–64]. Studies of prolonged activation related to anger and hostility have a relatively long history. In a series of experiments in the 1960s, Megargee and Hokanson (see Ref. [65]) showed faster cardiovascular recovery in angered participants allowed to express anger, and this effect was generally replicated in the decades to follow by others (see Ref. [13]). Theoretically, due to the lack of response opportunity, angered individuals might have tended to ruminate over the frustrating situation, which might be the direct cause of their prolonged high CV activation. This is indeed what recent studies suggest. Several authors have shown that trait as well as state rumination about angering situations prolongs the BP elevation due to experienced anger (see Table 1). Schwartz et al. [66] and Suchday et al. [67] have reported that perseverative angry cognitions caused sustained BP following an anger recall task. During the post anger recall rest period, participants who self-reported continuing angry thoughts also showed poorer recovery to prestress BP baselines. In addition, they found that when they provided distractions (in the form of visually interesting stimuli), self-reported angry thoughts were fewer and, correspondingly, BP recovery was facilitated. Furthermore, Chambers and Davidson [68] found higher resting levels of systolic BP (SBP) in persons high on angry rumination. Only one study [52] found no effect of trait anger rumination on BP recovery after anger recall, but did find such evidence for several cardiac variables (see above). Together, these results are consistent with the hypothesis that angry cognitive perseveration mediates the disease risk of high hostile individuals. Although both inhibited and expressed anger have been implicated in the disease risk of hostility (see Ref. [63]), it has also been pointed out [13] that angering situations in which no socially appropriate response are possible are far more common than similar situations in which anger can be freely expressed. This implies that hostile persons are forced to inhibit their anger far more often than they are able to express it, while they are at the same time more vulnerable to these situations and will experience more anger in general. Given the findings with angry rumination reviewed above, it is likely that this leads to a high frequency of angry perseverative cognition in these individuals. Together with prolonged states of physiological activation, this makes them more prone to develop the pathogenic physiological state that can lead to CVD and other diseases.

We found two studies of perseverative cognition and BP levels not dealing with anger or hostility (see Table 1). Glynn et al. [69] showed slower BP recovery–but no effects for HR–following emotional tasks for participants who had to recall the emotional tasks versus those who recalled neutral tasks. On the other hand, as mentioned earlier, Vickers and Vogeltanz-Holm [55] found no relationship between trait rumination and BP, HR, and SCL.

For BP too, several indirect proofs for effects of perseverative cognition have been reported. Glynn et al. [69] found that while the magnitude of BP responses occurring during emotional (harassment) and nonemotional stressors was comparable among the tasks (i.e., reactivity), BP recovery following the stressor involving harassment was significantly poorer than that following the nonemotional stressors. Importantly, when participants were distracted and, therefore, were less able to ruminate, BP recovered more quickly. Anticipation before emotional events was associated with elevated BP in several studies, e.g., in participants anticipating PhD oral defense [71], dental procedures [72], and mental arithmetic [70]. Melamed found that a variable strongly related to worry and rumination, i.e., emotional reactivity, was positively correlated to rest BP [73], ambulatory BP [74], and to high-risk plasma lipids [75]. Interestingly, the latter relationship was not found for life stress.

The influence of type of operationalization of perseverative cognition and other moderators

As is shown in Table 1, a variety of operationalizations have been used for state as well as trait worry and rumination. The state instruments or manipulations are difficult to compare because of a lack of details in the reviewed articles. Still, the effects of states of perseverative cognition on symptoms and physiological activity appear to be very consistent across the seven studies that measured or manipulated them [30,38,45,46,56,66,67,69]. This is less the case for the trait versions. The most commonly used instruments in the reviewed studies are well-validated instruments: The Penn State Worry Questionnaire (PSWQ; [27,40,41]), Emotional control questionnaire-Rumination (ECQ-R; [28,29,31,42,53]), and the Ruminative response scale-Rumination (RRS-R; [44,55]). The designs and the dependent variables differ so much across the studies that no firm conclusion may be drawn with respect to which one has the strongest and most consistent associations with symptoms and physiological activity. Overall, however, there seems to be a slight tendency for the PSWQ (four studies) to show more consistent associations and to hold up better after controlling for other negative emotional traits and other variables. For the ECQ-R (six studies), the associations appear to be repeatedly dependent on other variables, such as self-esteem [31], perceived stress [29], and age, finding effects either for young [28] or for old individuals [42]. Finally, the two studies using the RRS-R did not find physiological effects. It is possible that the PSWQ shows slightly superior effect because, unlike the ECQ-R, it is assumed to measure somewhat more severe worrying, as in anxiety disorders. The other more 'clinical' scale, the RRS-R, pertains more to depressive disorders, and it is possible that depressive rumination has somewhat less outspoken physiological concomitants. Still, as mentioned before, the results are not easy not compare, and it is also not known how many unpublished negative results exist.

Notwithstanding these drawbacks, the results in Table 1 seem to indicate that perseverative cognition is associated with a range of health-related outcomes. It can also be concluded, with some caution, that these associations are dependent of the way in which it is operationalized, with the associations appearing the most consistent for the PSWQ. The effects for states of perseverative cognition seem to be more consistent than those for traits, even when the duration of these states varies across studies, from acute worry inductions to diary measures over several weeks. The health-related variables include both illness variables and physiological parameters from several bodily systems and is generally independent of demographic variables and other negative emotional traits, such as trait anxiety and neuroticism. Finally, there were no studies with objective disease outcomes, apart from one study showing prospective effects of worry on myocardial infarction [34].

Perseverative cognition: neurovisceral concomitants

Thayer and Lane [76] have recently outlined the neurophysiological concomitants of perseverative cognition. These concomitants directly involve the regulation of the autonomic nervous system and, therefore, are important in understanding how perseverative cognition can mediate the influence of stressors on a broad range of diseases. For this reason, we will go into some detail discussing the neurovisceral pathways involved and some of the evidence linking them to perseverative cognition. The network at issue is a network of reciprocally interconnected neural structures that allow the prefrontal cortex to exert an inhibitory influence on subcortical structures associated with what has been traditionally called defensive behavior (i.e., "fight/flight"). In the Introduction, we argued that this is similar to how emotion theorists would view negative emotion, i.e., as a state of psychophysiological "action preparation" [10–12]. Prefrontal inhibitory control on these subcortical structures allows the organism to flexibly regulate its behavior in response to changing environmental demands. For example, when faced with threat, the tonic inhibitory control of subcortical structures by the prefrontal cortex can be rapidly decreased (disinhibited), leading to sympathoexcitatory fight or flight responses necessary for survival. However, when this tonically inhibitory network is disrupted, a rigid, involuntary defensive behavioral pattern is allowed to emerge with its associated perseverative behavior manifesting in atten-

tional, affective, and autonomic inflexibility [76]. Thus, neurobiologically speaking, perseverative cognition represents the breakdown of a common reciprocal inhibitory cortical–subcortical neural circuit, i.e., a failure of potentially adaptive inhibitory neural processes. A recent neuroimaging study of the suppression of unwanted thoughts provides support for this model [77]. When this autonomic inflexibility is prolonged, the chronic pathogenic state necessary for the development of disease may ensue.

Structurally, the network in which these perseverative processes occur includes the anterior cingulate, insular, and ventromedial prefrontal cortices, the central nucleus of the amygdala, the paraventricular and related nuclei of the hypothalamus, the periaquaductal gray matter, the parabrachial nucleus, the nucleus of the solitary tract, the nucleus ambiguous, the ventrolateral medulla, the ventromedial medulla, and the medullary tegmental field [78]. These structures are reciprocally interconnected such that information flows in both directions, top–down and bottom–up, so to speak. The primary output of this network is mediated through the preganglionic sympathetic and parasympathetic neurons and, in this way, forms a neurovisceral mediator between disinhibitive, stress-related perseverative processes at the level of the brain and the causation of pathogenic states in the course of time. For example, in the case of the influence of perseverative cognition on CVD, one can think of a pathway in which perseveration at a higher level in the CNS leads to an imbalance at the level of the sinoatrial node of the heart. This node is innervated by the two autonomic branches that control the heart, via the stellate ganglia (sympathetic) and the vagus nerve (parasympathetic). The interplay of these inputs is the source of the complex variability that characterizes the healthy HR time series [79]. Thus, the output of this network is directly linked to HRV. As we briefly noted above, decreased HRV has been associated with an increased risk of hypertension and other cardiovascular disorders [51].

Conclusions

In this article, we provided the groundwork for a theoretical approach to the relationship between worry, rumination, anticipatory stress, physiological concomitants of these states, and health. We have introduced the term perseverative cognition to describe the core cognitive–emotional process involved in worry and rumination, thus allowing this concept to be applied to a wider range of emotional states and dispositions than has previously been done, including anticipatory stress. We have shown that perseverative cognition may play a much broader role in psychological and somatic health than has hitherto been appreciated. There is no doubt that humans are highly capable of storing and recalling the cognitions and affect associated with stressful and traumatic events; yet, our theories of stress and chronic illness have failed, for the most part, to take this into account. Thus, we have suggested that the physiological reactions that occur while the stressor is actually taking place may not be as important as the cognitive, representational perseveration that may occur long after the stressor itself has ended. We have summarized evidence suggesting that perseverative cognition is related to enhanced activity of a wide range of physiological parameters and also to somatic complaints and somatic disease. Furthermore, the neurovisceral processes and mechanisms that may underlie these consequences were outlined.

In conclusion, perseverative cognition may contribute to ill health by expanding the temporal duration of a stressor beyond the traditional reactivity period to include anticipation and recovery, thereby being the source of prolonged physiological activation. There is some evidence that perseverative cognition is related to prolonged activation and to somatic complaints, but evidence for objective disease outcomes is still largely missing. A possible limitation of our review is that there is an unknown quantity of studies with alternative cognitive–emotional phenomena that are also characterized by perseverative cognition, such as, perhaps, emotional reactivity [73–75] mentioned in the section on BP, which may also have physiological effects. We hope that this theoretical review will inspire other researchers to examine these phenomena in the context of our perseverative cognition hypothesis. There are several possible promising routes for future research in this area. First, it may be most fruitful to address cognitive perseverative states instead of traits, because the former appear to yield more consistent results. Furthermore, the two studies that seem to imply perseverative cognition during sleep [56,59] suggest the intriguing possibility of unconscious perseveration, which can have substantial physiological effects, perhaps even during waking periods. Finally, perseverative cognition, being a core element in anxiety disorders and depression, may be responsible for a major part of the effects of these disorders on somatic diseases (e.g., Refs. [35,36,80,81]) and physiological activation (e.g., Refs. [37,38,41,60,82–86]). Perseverative cognition may be the missing link in the relationship between psychosocial factors and the chronic pathogenic physiological state thought to be causally related to the development of disease.

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