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Review

Making a mountain out of a molehill: On the role of the rostral dorsal anterior cingulate and dorsomedial prefrontal cortex in conscious threat appraisal, catastrophizing, and worrying

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ABSTRACT

According to appraisal theories fear and anxiety are elicited by the subjective evaluation of a situation or internal state as threatening. From this perspective anxiety disorders result from maladaptive, exaggerated threat appraisals that over-estimate the threatening consequences of often innocuous stimuli and situations. When these threat over-estimations occur at the level of conscious processing, they are referred to as catastrophizing and worrying. Both are major pathogenic processes in many clinical theories of anxiety. Until recently, little has been known about the neurobiological basis of normal and pathological conscious threat appraisal. Here, we review functional neuroimaging studies which draw a consistent picture of the rostral part of the dorsal anterior cingulate (dACC) and the adjacent dorsomedial prefrontal cortex (dmPFC) as the likely key neural substrate of conscious threat appraisal. Moreover, findings of hyper-activation of the rostral dACC/dmPFC during catastrophizing and worrying emphasize its relevance to aberrant neural processing in anxiety disorders. These insights open a new avenue for improving the prevention and treatment of mental disorders that involve pathological appraisal.

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1. Introduction

Appraisal theories date back to Magda Arnold and her classic work on "Emotion and Personality" (Arnold, 1960). Appraisal theories posit that emotional reactions (understood as an orchestrated multi-level response involving physiological, hormonal, motor,

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subjective-experiential and cognitive changes) are the result of an evaluation (appraisal) process during which a stimulus or situation is interpreted in terms of its meaning to the organism (Arnold, 1960; Frijda, 1993; Lazarus, 1966; Roseman and Smith, 2001; Scherer, 2001). In other words, the type, quality and extent of an emotional reaction are not determined by simple, fixed stimulus-response relationships, but by the context-dependent, subjective analysis of the motivational relevance of a stimulus or situation. In this framework, anxiety, fear or panic result from the evaluation of a situation as highly threatening (Lazarus, 1966). Both conscious and unconscious processes are thought to contribute to stimulus appraisal (Leventhal and Scherer, 1987; Robinson, 1998). Unconscious, non-verbal threat appraisal presumably lies at the heart of phylogenetically old threat processing (LeDoux, 1985). Conscious appraisal, however, may be more dominant in unfamiliar and ambiguous situations (Lazarus, 2006) and introduces the possibility of more flexible threat processing, which has become a particularly valuable tool in the treatment of anxiety disorders.

Threat appraisals can be maladaptive and can lead to exaggerated fear responses by involving an over-estimation or over-interpretation of a threat. Though not directly referring to appraisal theory, the founding fathers of cognitive therapy have considered erroneous and biased threat appraisal a core feature of all anxiety disorders (Beck and Clark, 1997; Beck et al., 1985). Especially panic disorder is characterized by catastrophic misinterpretations of bodily sensations (Austin and Richards, 2001; Beck et al., 1985; Casey et al., 2004; Clark, 1986). Individuals with panic disorder evaluate innocuous bodily sensations in a catastrophizing manner: an increased pulse rate after climbing some stairs might, for example, be taken as evidence of an upcoming lethal heart attack, the subjectively perceived threat then elicits a further increase in pulse rate, resulting in a vicious cycle that can lead to a full-blown panic attack. Examples of other frequent and typical objects of catastrophizing are the normal feelings of nervousness and concentration problems before an important exam (inducing expectations of failure and performance anxiety), or the ambiguous or critical reactions of an audience and one's own signs of embarrassment (inducing social-phobic fears). Reiss and McNally (1985) conceptualized the tendency to catastrophize over bodily and mental arousal symptoms as anxiety sensitivity, or "fear of fear", and introduced a widely used questionnaire tool, the Anxiety Sensitivity Index (ASI), to assess this appraisal style in individuals.

Another form of biased threat appraisal, excessive worrying, involves negative estimates of more distant, uncertain and unpredictable dangers. Worry contents might also include external threats such as contracting a disease, losing one's job, becoming a victim of a crime or more general situations where the threat is not necessarily self-relevant, such as worries about the possibility of war in a different part of the world or the possible impending extinction of human life on Earth due to environmental problems. According to the Diagnostic and Statistical Manual of Mental Disorders, worrying is a core feature of generalized anxiety disorder and also accompanies certain forms of panic disorder. A questionnaire tool that is widely used to assess the individual trait-like tendency to worry, is Meyer et al.'s (1990) Penn State Worry Questionnaire (PSWQ).

While exaggerated threat appraisals may well occur at both the unconscious and conscious level, catastrophizing and worrying in the sense used in the clinical literature, requires the conscious perception of the to-be-over-interpreted stimulus and the generation of negative thoughts. Such maladaptive conscious threat appraisal does not only characterize the anxiety disorders but is also a key target in their treatment (Beck et al., 1985; Clark and Beck, 2010). Cognitive therapy tries to change erroneous conscious threat appraisal in favor of more elaborate and adaptive threat appraisal, thereby also diminishing the potential influence of any underlying maladaptive automatic information processing.

Given the theoretical importance of conscious negative threat appraisals in the development, maintenance and therapy of anxiety disorders, defining the neural networks mediating this process is an important step towards a better understanding, prevention and treatment of anxiety disorders. For instance, neural responsivity to threat stimuli in "catastrophizing areas" may predict whether a person is at risk of developing an anxiety disorder as well as the kind of treatment an anxious patient would respond to best. More interestingly, perhaps, is the possibility of targeting aberrant neural processing in such brain areas with the help of neurofeedback or neurostimulation tools, which may complement conventional psychotherapy and increase its efficiency or efficacy. In this review, we focus on the neural underpinnings of conscious threat appraisal and its extreme forms, catastrophizing and worrying. To provide a background, we first briefly discuss empirical findings about the causal role of conscious evaluative processes on normal as well as pathological fear/anxiety. We then review studies on the neural substrates of conscious threat appraisal and discuss recent findings of deviating neural processing during catastrophizing and worrying. Based on these results, we will argue that a relatively well circumscribed brain region situated in the rostral aspects of the dorsal anterior cingulate and the dorsomedial prefrontal cortex (rostral dACC/dmPFC), mediates these processes. We conclude with a list of open questions and suggestions. Addressing them may further advance our understanding of emotional processing under healthy and pathological conditions.

2. The role of conscious threat appraisal, catastrophizing and worrying in the generation of fear and anxiety

The central paradigm to study fear or anxiety generation via conscious evaluative processes is 'instructed fear', often also termed 'anticipatory anxiety' or 'threat of shock'. In instructed fear experiments, subjects are told that a defined cue (the 'conditioned stimulus' or CS in Pavlovian language) might be or will be followed within a certain time window by a harmful event such as a painful electric shock (the outcome or 'unconditioned' stimulus, US). In the purest form of instructed fear paradigms, the cue is never actually followed by the outcome, depriving subjects of learning the cue-outcome contingency through experience, as would be the case in Pavlovian conditioning. Yet, subjects typically show clear fear/anxiety reactions that can be measured through self-report, increases in skin conductance, heart rate or in the startle reflex response (e.g., Cook and Harris, 1937; Funayama et al., 2001; Holtz et al., 2012; Maier et al., 2012; Phelps et al., 2001). In these cases, the conscious knowledge of the cue-outcome contingency and the associated negative appraisal processes are the only plausible sources of the threat response. It has been argued that such learning via instructions is one of the major routes by which fear develops in humans (Olsson and Phelps, 2004).

Showing a causal relation between *exaggerated* conscious appraisal and *exaggerated* fear is more tricky. Essentially, one has to experimentally induce catastrophizing or worrying thoughts and show corresponding effects in fear responding. One study fulfilling this criterion was recently conducted in healthy subjects reporting trait-like high and low fear of cardiac symptoms (Telch et al., 2010). The authors introduced these subjects to a CO_2 inhalation challenge. In the experimental but not the control group the experimenter brought in a cardiac defibrillator briefly before the start of the CO_2 inhalation and explained the purpose of its presence as having to do with safety reasons. Subjects with high cardiac-related anxiety reported to appraise the presence of the defibrillator as threatening, in accordance with a successful