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Psychophysiological reactivity during uncertainty and ambiguity processing in high and low worriers



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ABSTRACT

Background and objectives: Intolerance of uncertainty (IU) has been linked to Generalized Anxiety Disorder (GAD), but studies experimentally manipulating uncertainty have mostly failed to find differences between GAD patients and controls, possible due to a lack of distinction between uncertainty and ambiguity. This study therefore investigated reactivity to ambiguity in addition to uncertainty in high worriers (HW) and low worriers (LW). We hypothesized an interpretation bias between the groups during ambiguity tasks, while uncertainty would facilitate threat processing of subsequent aversive stimuli.

Methods: HW (N = 23) and LW (N = 23) completed a paradigm comprising the anticipation and perception of pictures with dangerous, safe, or ambiguous content. Anticipatory cues were certain (always correct information about the following picture) or uncertain (no information). Subjective ratings, reaction times and skin conductance responses (SCRs) were recorded.

Results: HW rated particularly ambiguous pictures as more aversive and showed longer reaction times to all picture conditions compared to LW. SCRs were also larger in HW compared to LW, particularly during uncertain but also safe anticipation. No group differences were observed during perception of stimuli.

Limitations: All participants were female. HW was used as subclinical phenotype of GAD.

Conclusions: Intolerance of ambiguity seems to be related to individual differences in worry and possibly to the development of GAD. Threat-related interpretations differentiating HW and LW occurred particularly for ambiguous pictures but were not accompanied by increased autonomic arousal during the picture viewing. This disparity between subjective rating and arousal may be the result of worrying in response to intolerance of uncertainty, restraining physiological responses.

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1. Introduction

Generalized Anxiety Disorder (GAD) is a common anxiety disorder with a lifetime prevalence of 4–6% (Beesdo, Pine, Lieb, &

Wittchen, 2010; Kessler, Petukhova, Sampson, Zaslavsky, & Wittchen, 2012). However GAD pathophysiology has been relatively understudied in comparison to other anxiety conditions, possibly due to the lack of a specific anxiety inducing stimulus or event for GAD sufferers, making experimental studies more difficult to design. Current theories of GAD propose that the anticipation of negative experiences relates to the high levels of worry observed in those with GAD. The intolerance of uncertainty model of GAD (Dugas, Gagnon, Ladouceur, & Freeston, 1998) states that patients tend to overestimate the risk and negative consequences of situations and that this overestimation of risk is especially evident in uncertain situations (i.e., those lacking explicit information about the further course of events). It has therefore been proposed that intolerance of uncertainty (IU) underpins the relationship between

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uncertainty and excessive worry in GAD. IU is suggested to arise from a combination of enhanced activation of internal representations of uncertain information and the threat-related interpretations of such information (Dugas et al., 2005). This model is supported by empirical data showing positive associations between IU and worry (Buhr & Dugas, 2006).

Several studies indicated that biased information processing occurs during uncertainty. Studies in healthy individuals have shown negatively biased expectancies of aversion following uncertain anticipation cues (Sarinopoulos et al., 2010) and subsequent increased negative mood ratings towards aversive pictures (Grupe & Nitschke, 2011). Healthy individuals also showed increased response times and decreased response accuracy with increasing uncertainty (Krain et al., 2006). On a psychophysiological level, uncertainty during anticipation has also been associated with increased skin conductance responses (SCRs) during perception of aversive stimuli (Grupe & Nitschke, 2011). On a neural level, recent findings suggest the processing of uncertain anticipation is modulated by prefrontal areas (Clauss et al., 2014; Motzkin, Philipp, Wolf, Baskaya, & Koenigs, 2014) and is executed in distinct neural processes and brain regions (Grupe & Nitschke, 2013; Grupe, Oathes, & Nitschke, 2013). For example, areas implicated in emotion regulation such as the anterior cingulate cortex (ACC) and orbitofrontal cortex (OFC) have been reported to show increased activation during anticipation (Critchley, Mathias, & Dolan, 2001). In contrast, the insula has been reported to show decreased activation (Sarinopoulos et al., 2010). Higher insula and amygdala responses to aversive pictures were also found when their presentation followed an uncertain cue and ACC activity during the anticipatory phase was inversely associated with these responses (Sarinopoulos et al., 2010).

However, similar investigations on biased processing during uncertainty have not found differences between high worriers or GAD patients and healthy controls. In these studies, patient and control groups did not differ on a behavioral (Krain et al., 2008; Yassa, Hazlett, Stark, & Hoehn-Saric, 2012) or psychophysiological level (Grillon et al., 2009; Yassa et al., 2012). Differential functional brain activations between GAD patients and controls were reported by Yassa et al. (2012) but have not been observed in other investigations (Krain et al., 2008; Mochcovitch, da Rocha Freire, Garcia, & Nardi, 2014). Given this data, one urgent research question is why these studies failed to find differential group effects as predicted by current models.

We propose that IU should be carefully distinguished from intolerance of ambiguity (IA), a closely related concept that has been confused with IU in the past (Grenier, Barrette, & Ladouceur, 2005). According to Grenier et al. (2005) and more recently Carleton (2012), both concepts share a biased interpretation of situations or stimuli as threatening. For IU, the causes of threat are in or are referring to the future, whereas for IA the causes of threat are in or referring to the present. With these temporal differences between both concepts in mind, some authors argue that IA is the part of IU pertaining to possible current threat (Carleton, 2012) whereas IU is related to a possible imminent future threat. As such situations containing uncertainty or ambiguity have been described in different terms regarding the source of subjective insecurity experienced in both cases. For instance, uncertainty has been described as “unknowable” (Carleton, 2012, p. 940) in this respect, while ambiguity has been described as “characterized by equivocal or ambiguous features” (Grenier et al., 2005, p. 596). Based on such differences, there appears to be potential for a delineation of both concepts besides just temporal differences which can be experimentally tested. In our experimental conceptualization, based on the above literature, uncertainty is characterized by an absence of available information on the outcome of the situation. In contrast,

ambiguity is characterized by contradictory or ambivalent information available on the situation. We propose that the combined effects of uncertainty and ambiguity in a given situation compose the marked information processing bias that differentiates GAD patients from healthy controls. Studies of threat biases in children and adolescents (Lau et al., 2012) and in adults with GAD (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & van Ijzendoorn, 2007) consistently revealed biases in various stages of information processing. These stages included reactions towards stimuli of possible threat as well as threatening interpretations of ambiguous situations. However, only one experimentally based study (Simmons, Matthews, Paulus, & Stein, 2008) investigated ambiguity, using a ‘wall of faces’ task. The authors reported longer response times as well as increased neural activation in the insula during ambiguity, which was also found to be correlated with IU. This study used a non-clinical sample. For other samples, levels of processing, or tasks, no experimental studies were available so far. The need for further research on that topic was also demanded by a recent review which described an unpublished study on the temporal order in the association between IA and IU (Rosen, Ivanova, & Knaeuper, 2014).

The current study aimed to examine reactivity to more distal and to more proximal potential threat, i.e. uncertainty (during anticipation) and ambiguity (during perception), in high worriers (HW) as a subclinical phenotype of GAD compared to low worriers (LW). Skin conductance responses (SCR) were examined as psychophysiological correlates, as they are considered a useful autonomic marker of anticipatory anxiety (Boucsein, 1992) and information processing activity (Spinks & Siddle, 1985). By integrating work from related research (Aikins & Craske, 2001; Dugas et al., 2005; Nitschke et al., 2009; Sarinopoulos et al., 2010; Schienle, Kochel, Ebner, Reishofer, & Schafer, 2010; Schwerdtfeger, 2006), we developed a paradigm that involved presentation of certain and uncertain anticipation cues, subsequently followed by pictures showing scenes of positive, aversive or ambiguous valence. On a behavioral level, we hypothesized that HW compared to LW would rate ambiguous scenes as more aversive and show slower reaction times (RTs) for negative scenes following uncertain cues compared to scenes following certain cues. On a psychophysiological level, we expected HW compared to LW to show increased tonic and phasic SCRs during ambiguity but not during uncertainty, as well as during danger/ambiguity perception after uncertain cues compared to danger perception after certain cues.

2. Methods

2.1. Development of the picture set for the paradigm

The pictures used in the study (safe, danger or ambiguous) were either chosen from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2008) on the basis of their valence and arousal ratings or were generated by our research group. Pictures with ambiguous content related to typical worry topics (e.g., health or finances). A preliminary set of 196 pictures were evaluated online by student volunteers ($n = 53$, 21% male) ranging in age from 18 to 36 years ($M = 23.47$; $SD = 4.2$). Each picture was rated for valence (from 0 = “most pleasant” to 8 = “most unpleasant”) and arousal (from 0 = “not arousing” to 8 = “most arousing”) using a modified version of the Self-Assessment Manikin Scale (Bradley & Lang, 1994), in which the five original ratings were supplemented with four intermediate ratings. Participants also rated how anxious the picture scene made them (from 0 = “not at all” to 8 = “extremely”), how dangerous they judged the scene (from 0 = “safe” to 4 = “ambiguous” to 8 = “danger”), and how difficult it

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