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Reducing chronic anxiety by making the threatening event predictable: An experimental approach

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ABSTRACT

Panic disorder is characterized by both specific, phased fear and generalized, chronic anxiety. Standard extinction procedures are efficient in reducing specific fear. However, methods based on human conditioning research – that are capable of reducing chronic anxiety have not yet been thoroughly investigated. This study evaluates a new way of reducing chronic anxiety by signaling aversive events (or by making them more predictable). Using an experimental approach with healthy participants, specific fear and chronic anxiety were operationalized in a within-subjects fear-potentiated startle paradigm by, respectively, conditioning to a cue by presenting predictable shocks and conditioning to a context induced by unpredictable shocks. The results clearly demonstrate that context conditioning is reduced when a discrete cue is added that predicts the onset of the aversive event. The data suggest that making unpredictable events, such as for example panic attacks, predictable, may reduce the generalized and sustained anxiety that often complicates exposure treatment.

Introduction

Although fear may facilitate survival in threatening situations, fear responses can be defined as problematic and potentially disabling when these responses occur too frequently, occur in situations in which there are no objective threats, or cause the individual to suffer significant distress (e.g., American Psychiatric Association, 1994; Mineka & Zinbarg, 2006). People suffering from panic disorder (PD) experience recurrent panic attacks[1] that occur without their being aware of any specific cues or triggers that precede the panic attack (American Psychiatric Association, 1994). In addition, the PD patient develops substantial anxiety, worry, or concern to suffer another panic attack (American Psychiatric Association, 1994). For these reasons, it is worthwhile to find sufficient ways to reduce anxiety.

On the basis of ethological, clinical, and neurobiological evidence, many prominent researchers (e.g., Bouton, Mineka, & Barlow, 2001; Davis, 1992, 1998; see also Mineka & Oehlberg, 2008 for a recent review) proposed a fundamental distinction between two aversive motivational emotional states, namely fear and anxiety. *Fear* has been defined as stimulus-specific (Barlow, 2000; LeDoux, 1992; Marks, 1969), characterized by a phased response to an aversive, immediately threatening stimulus. *Anxiety*, on the other hand, is more sustained, more generalized, and future-oriented and is not associated with a specific discrete cue (i.e., free-floating). Instead, it is associated with the apprehensive anticipation of upcoming potential threats and has a more chronic course (Barlow, 2000; Bouton et al., 2001; Grillon, 2002; Grillon & Davis, 1997). Despite the fact that several psychopathological disorders exemplify cued fear (e.g., specific phobias), the hypervigilance and long-term signs of distress in some anxiety disorders could be better explained by chronic anxiety (e.g., Generalized Anxiety Disorder, GAD). Furthermore, recent research supports the idea that PD, but also other anxiety disorders like Posttraumatic Stress Disorder (PTSD) and Obsessive Compulsive Disorder (OCD), involve both specific fear and chronic anxiety (Zvolensky, Lejuez, & Eifert, 2000).

Contemporary models of human fear conditioning have been extensively used to study and understand the etiology, maintenance, and treatment of specific fears and phobias (Craske, Hermans, & Vansteenwegen, 2006; Hermans, Craske, Mineka, & Lovibond, 2006). In a typical cued *fear* conditioning paradigm, a neutral stimulus (conditioned stimulus, CS) is repeatedly followed by an aversive stimulus (unconditioned stimulus, US). After a number of pairings, the CS becomes a reliable predictor of the US and starts eliciting anticipatory fear responses (conditioned

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[1] Although the presence of recurrent unexpected panic attacks is essential for the diagnosis of PD (American Psychiatric Association, 1994), PD patients sometimes experience/report predictable panic attacks (Baker, Patterson, & Barlow, 2004).

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response, CR). However, this prototypical fear conditioning paradigm is not appropriate to study anxiety, given that anxiety is not triggered by an explicit cue, but instead is activated in a less differentiated way and is focused on future potential threat (Grillon, 2002).

Central to several models of *anxiety* is the notion 'unpredictability' (e.g., Barlow, 2000; Mineka & Kihlstorm, 1978). Animal studies have demonstrated that unpredictable aversive events increase anxiety more than predictable aversive events (for a review, see Mineka & Zinbarg, 2006). Unpredictable aversive events are very effective in inducing chronic anxiety (Barlow, 2000; Grillon, Baas, Lissek, Smith, & Milstein, 2004). Grillon and his coworkers (e.g., Grillon, Baas, Cornwell, & Johnson, 2006; Grillon & Davis, 1997) developed a paradigm in which they used fear-potentiated startle as dependent variable and an aversive shock as US. In fear-potentiated startle the amplitude of the startle reflex is modified by the current state of fear. In the basic between-subjects procedure of Grillon and colleagues (Grillon & Davis, 1997), one group of participants (i.e., paired/predictable condition) received paired presentations of the CS (blue light) and the US (aversive electrocutaneous shock), whereas another group (i.e., unpaired/unpredictable condition) received explicitly unpaired CS–US presentations. It was demonstrated that relatively more unpredictable aversive situations systematically led to more physiological anxiety than predictable situations. This was indicated by larger baseline startle responses to the experimental context in unpredictable compared to predictable conditions in an immediate test as well as in a test after a retention interval (Grillon & Davis, 1997). This observation is in accordance with Pavlovian conditioning/learning models (e.g., Rescorla & Wagner, 1972; see also Grillon, 2002; Vansteenwegen, Iberico, Vervliet, Marescau, & Hermans, 2008). Unsignaled USs are contingent upon the presence of the background context. As a consequence, the context should gain some associative strength with the US. Because the context is a long-lasting stimulus, this will lead to a chronic apprehensive anticipation of threat, resulting in *contextual fear* (Grillon & Davis, 1997). Furthermore, Grillon, Ameli, Goddard, Woods, and Davis (1994) demonstrated in a clinical group of PD patients an elevated baseline startle caused by the aversive context, but a normal fear-potentiated startle. Hence, uncued procedures that install contextual fear can be used as a laboratory model to study generalized and sustained anxiety. This contextual sensitization is characterized in persistent apprehensive anticipation about future danger that is typical for chronic anxiety (Grillon, 2002).

In order to reduce specific or cued fear in humans, standard extinction procedures have been proved to be successful (Craske et al., 2006; Vervliet, Vansteenwegen, & Eelen, 2004; see Foa and Kozak (1986) for an alternative habituation explanation). Generally, nonreinforced presentations of the (fear-eliciting) cue that was previously coupled with the aversive event extinguish the phased conditioned fear responses. This emphasizes the similarity between experimental extinction in humans and exposure treatments for phobias, where a robust decrease of phobic fear is commonly observed (Öst, 1997). The procedures are characterized by a disconfirmation of the expectation of the US that was previously established by predictors. Although often successful implemented in strongly controlled animal studies (e.g., Bitencourt, Pamplona, & Takahashi, 2008), standard exposure protocols may be difficult to translate to situations of chronic and generalized anxiety in humans, which are characterized by the absence of specific and phasic objects of fear. Because the context is per definition diffuse and long-lasting, it is not immediately clear whether extinction of contextual fear would be successful.

An alternative procedure for conducting exposure can be found in psychotherapeutic treatment procedures of PD, where perceived unpredictable panic attacks are put under control of internal cues that occur before the typical panic attack (Craske, Glover, & DeCola, 1995). Also, self-monitoring, as often described in treatment protocols for PD (e.g., Craske & Barlow, 2008), is an important component of assessment as it is of treatment of PD. Retrospective recall of earlier experiences with panic and anxiety, in particular when made under anxious circumstances, may possibly inflate estimates of panic intensity and frequency of the PD patient (Rapee, Craske, & Barlow, 1990). As a consequence, such increase may enhance worrying and apprehension about potential panic. On the contrary, self-monitoring can lead to more accurate estimates and can therefore contribute to an objective self-awareness (for a review of self-monitoring with panic and anxiety disorders, see Craske & Tsao, 1999). As such, objective self-monitoring can be seen as an analogous procedure of making stressors more predictable with the intention of reducing the anxiety levels and panic attacks. However, these procedures used in the treatment of PD have not yet been experimentally investigated. An experimental approach might be able to elucidate the underlying processes of the treatment procedures for PD patients and hence contribute to more effective treatment procedures.

In this study we examined whether increasing the predictability of the aversive stimulus (US) by presenting a novel stimulus that predicts the onset of the US would reduce the level of contextual fear. Two groups of participants were exposed to a within-subjects context conditioning procedure (also see Grillon et al., 2006; Vansteenwegen et al., 2008). We employed the human fear conditioning preparation, using an electrocutaneous stimulus as US and visual stimuli (geometrical figures) as CSs. Different contexts (i.e., predictable and unpredictable contexts[2]) were created by the display of images of different rooms on the background screen. Dependent variables were startle modulation and online US-expectancy ratings. When measured during the CSs, these dependent variables index conditioning to the cue and when measured during the intertrial interval (ITI) they indicate contextual conditioning (e.g., Iberico et al., 2008; Vansteenwegen et al., 2008). During the acquisition phase, we applied the procedure as used by Marschner, Kalisch, Vervliet, Vansteenwegen, and Büchel (2008), but we added fear-potentiated startle as an index of learning. Both groups received predictable shocks (immediately after one CS) in one context (picture of room A, the predictable context), whereas in

[2] There is no absolute, but a relative difference in predictability between the predictable and the unpredictable contexts. In strict sense, the moments that the USs could be presented were predictable in both contexts. In the predictable context, the USs were signaled by/paired with the offset of the CSs (100% reinforced; 2 USs/mini-block). In the unpredictable context, the participants received one, two, or three shock(s) on three different (but fixed) moments during the ITI of the mini-block (partial reinforcement; mean of 2 USs/mini-block), unsignaled and explicitly unpaired with the CSs. Hence, participants received seven different shock-combinations in the unpredictable context, whereas the shocks in the predictable context were presented signaled and on identical times (and thus more predictable) within each mini-block. However, the three moments that the USs could be presented in the unpredictable context were predictable from the basis of the passage of time after the onset of the mini-blocks and the explicitly unpaired CS–US presentations. Despite this possible temporal conditioning and in addition to the partial reinforcement schedule and the unsignaled US presentations in the unpredictable context, several other aspects of the procedure enhanced the unpredictability in the unpredictable context compared to the predictable context. Firstly, one third of the USs was presented before the first CS of the mini-block in the unpredictable context and these USs were therefore not predictable from the basis of the passage of time after the onset/offset of the CSs. The time interval (ITI) between two mini-blocks was randomized between 1 and 3 s with a mean of 2 s making counting of time more difficult. Secondly, the time intervals between CS and a possible following US in the unpredictable context were not the same for the first and the second CS-presentation, which is respectively 8.5 s after the first CS-presentation and 7 s before the second CS and 9.5 s after the second CS and 6 s before the end of the mini-block.