Journal of Anxiety Disorders 28 (2014) 747–753

Contents lists available at ScienceDirect

Journal of Anxiety Disorders

Aversive learning and generalization predict subclinical levels of anxiety: A six-month longitudinal study

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ARTICLE INFO

Article history:
Received 25 April 2014
Accepted 4 September 2014
Available online 16 September 2014

Keywords:
Anxiety
Aversive learning
Discrimination learning
Generalization
Longitudinal study

ABSTRACT

The identification of premorbid markers of risk for psychopathology is one of the most important challenges for present-day psychiatric research. This study focuses on behavioral vulnerability factors that contribute to the development of anxiety. Little is known about the role of aversive learning and generalization in the development of pathological anxiety. In this study, a large student sample ($N = 375$) completed a differential aversive learning task followed by a test of generalization. Anxiety was assessed at that moment and after a six-month follow-up. Results showed that both predictors (discrimination learning and generalization) added significantly to the explained variance in anxiety symptomatology at follow-up. These results highlight the importance of longitudinal designs and indicate that screening for individual differences in aversive learning and generalization may foster prediction of anxiety disorders, paving the way for targeted prevention.

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According to diathesis-stress models, mental disorders arise from the interaction between vulnerability factors (i.e., diatheses) and life stress (e.g., Zvolensky, Kotov, Antipova, & Schmidt, 2005). These vulnerability factors may be characterized at the (neuro-)biological (e.g., anomalies in the amygdala-based fear circuitry in anxiety disorders; Shin & Liberzon, 2010), or behavioral level (e.g., negative attributional style in depression; Jacobs, Reinecke, Gollan, & Kane, 2008; irregularities in smooth pursuit eye tracking in schizophrenia; O'Driscoll & Callahan, 2010). Identifying vulnerability factors allows for accurate prediction and paves the way for targeted prevention (Beauchaine, 2009). The personal and societal costs of mental health problems are immense and predicted to increase (e.g., Murray et al., 2012). Thus, prediction and prevention of psychopathology is a major challenge for psychiatric research (World Health Organization Mental Health Action Plan, 2013). Identifying behavioral markers of psychopathology is particularly relevant. Assessing behavior is minimally invasive for the tested individual and is easily and cheaply applicable by the scientist-practitioner in the clinic. Hence, the detection of behavioral markers of risk for psychopathology provides both a theoretical and practicable answer to the challenges ahead.

The present study focuses on behavioral vulnerability factors for anxiety. One major pathway to anxiety disorders is aversive learning (Lissek et al., 2005; Mineka & Zinbarg, 2006). This is a form of associative learning in which an originally neutral stimulus (conditional stimulus; CS) comes to evoke fear reactions after pairings with an aversive stimulus (unconditional stimulus; US). Fear can be highly adaptive by motivating defensive reactions in the face of danger. Abnormalities in aversive learning, however, may contribute to the development of anxiety disorders (Lissek et al., 2005). These abnormalities may manifest as a deficit in discriminating between signals of danger and signals of safety. For instance, a panic attack bears symptomatic resemblance to a heart attack, but only the latter represents actual danger (Haddad, Pritchett, Lissek, & Lau, 2012). Thus, *impaired discrimination learning* between safety signals and danger signals may contribute to the development of anxiety symptoms. Deficits in discriminatory aversive learning have been demonstrated in individuals suffering from an anxiety disorder (e.g., Lissek et al., 2009; Grillon & Morgan, 1999), as well as in individuals with subclinical levels of anxiety (e.g.,

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http://dx.doi.org/10.1016/j.janxdis.2014.09.006
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Arnaudova et al., 2013; Chan & Lovibond, 1996; Haddad et al., 2012; Gazendam, Kamphuis, & Kindt, 2013; but see also Torrents-Rodas et al., 2013; Indovina, Robbins, Núñez-Elizalde, Dunn, & Bishop, 2011).

Maladaptive consequences of irrational fears are greatly multiplied by the generalization of aversive learning. Generalization occurs when a conditioned response is elicited by a stimulus different from but similar to the actual CS. Generalization reduces the need to rediscover contingencies that have proven to be important in the past (Hermans, Baeyens, & Vervliet, 2013). It becomes pathological, however, when the conditioned fear reactions are frequently elicited in the absence of actual threat. For instance, after a biting incident, an individual may react fearfully to the dog that was involved, but also to other, more or less similar dogs, or even to seeing a dog on television, which obviously represents no imminent threat. In the same logic, individuals who show increased *generalization* may be more prone to develop anxiety complaints. Differences in generalization have been demonstrated in individuals suffering from panic disorder, relative to healthy controls, with the former displaying stronger generalization (Lissek et al., 2010).

In order to test hypotheses about the role of discriminatory aversive learning and generalization in the etiology of anxiety disorders, longitudinal studies are critically needed (Kraemer et al., 1997). The present study is a prospective investigation of the relationship between anxiety and both aversive learning and generalization. This adds significantly to the current set of cross-sectional studies by testing whether the known deficits are consequences or antecedents of anxiety complaints (diagnostic markers or vulnerability factors, respectively; Beckers, Krypotos, Boddez, Effting, & Kindt, 2013). Moreover, the identification of premorbid markers of risk for the development of anxiety complaints requires, by definition, the use of non-clinical samples. The present study was conducted in a large group of first-year psychology students. Because the transition to university is accompanied by a set of stressors related to academics, finances, social interaction, and other issues, students are particularly interesting from a diathesis-stress perspective (Dyson & Renk, 2006; Gefen, 2010).

At a baseline assessment, we measured levels of self-reported anxiety and administered a differential aversive learning task followed by a test of generalization to all participants. After a six-month follow-up period, participants completed the anxiety measures again. Most cross-sectional studies have used individually selected levels of electrical stimulation on the arm as aversive US. For practical applicability purposes, we decided to use individually selected levels of aversive pictures of the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 2008). Also, we focused on simple verbal ratings as measures of aversive learning and generalization, instead of complicated psychophysiological measurements. These decisions ensure easy use and wide applicability in out-of-laboratory settings, which is critical for implementation of risk detectors.

The aversive learning phase consisted of two circles differing in size (Lissek et al., 2010), one of which (CS+) was contingently followed by negative emotional pictures (US). The other circle (CS−) was never followed by the US. The dependent variables were verbal US-expectancy and fear ratings that were collected during each circle presentation. We hypothesized that impaired differentiation in US-expectancy between the two circles would predict higher levels of anxiety six months later (statistically controlling for baseline anxiety). Following the differential aversive learning phase, various circles of different sizes between the CS+ and the CS− (generalization stimuli; GSs) were tested for their ability to elicit US-expectancy and fear ratings. We hypothesized that increased generalization would predict higher levels of anxiety six months later (statistically controlling for baseline anxiety).

1. Method

1.1. Participants

Participants were 375 first year psychology students at the University of Leuven, Belgium, who completed the differential aversive learning task and test for generalization. Twenty students could not be invited for follow-up because they failed to provide their anonymous ID before completing the questionnaires. Therefore, the analyses of Time 1 (T1) are based on 355 participants (288 women). Their mean age was 18.3 (SD = 1.2, range: 17–29). At Time 2 (T2), six months later, 273 participants (231 women) of the original 355 (77%) completed the follow-up questionnaires. All participants gave informed consent and received course credits for their participation.

1.2. Apparatus and stimuli

Stimuli were presented on a Dell desktop computer screen (48.3 cm). The stimulus sequence, the presentation of the stimuli, and the inter-trial intervals were controlled by Affect 4.0 (Spruyt, Clarysse, Vansteenwegen, Baeyens, & Hermans, 2010).

Based on the Lissek et al. (2010) conditioned generalization paradigm, two circles served as the conditional stimuli. For half of the participants, a small circle (5.08 cm) was the CS+, and a large circle (11.94 cm) was the CS−. For the other half, this was reversed. The generalization stimuli (GSs) were eight circles, with each GS increasing 15% in diameter starting from the smallest circle, thus creating a continuum of perceptual change between the smallest circle and the largest circle. The diameters, in centimeters, of the eight GSs were 5.84, 6.6, 7.37, 8.13, 8.89, 9.65, 10.41, and 11.18 respectively.

The unconditional stimuli (US) were pictures from the International Affective Picture System (Lang et al., 2008). Nine pictures were selected based on previously obtained arousal ratings in young adults (Grühn & Scheibe, 2008). Importantly, these nine pictures were divided into three categories that were created to obtain three different levels of US-aversiveness. In conditioning paradigms that employ an electrical stimulus as US, the intensity of the aversive stimulation during the experiment is usually not fixed, but instead chosen by participants before the start of the experiment in order to find a level of stimulation that is rated as highly uncomfortable but not painful. Likewise, in this experiment, the three categories of USs differed in aversiveness, allowing participants to choose between mild, moderate, or severe US aversiveness. The most aversive USs were pictures of a thoracotomy, a bloodied corpse and an aggressive dog, with a mean arousal rating of 7.4. The moderately aversive USs depicted a tribal mutilation, fecal matter, and a hospitalized infant, with a mean arousal rating of 5.9. The mild USs depicted a firearm, a cockroach, and a paper bag of vomit, with a mean arousal rating of 5.1.[1] All stimuli were presented on a white background in the center of the computer screen.

The experimental trials consisted of the presentation of a circle that was (in the case of a CS+) or was not (in the case of a CS− or a GS) followed by a US. The US was presented for 1000 ms immediately after termination of the CS+. The mean inter-trial interval was 2500 ms and ranged from 2300 ms to 2700 ms.

[1] The IAPS numbers for the most aversive USs were 1300, 3051, and 3250. For the moderately aversive USs, the IAPS numbers were 3300, 9042, and 9320. The mildest level of US-aversiveness consisted of Pictures 3241, 7380, and 9373.

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