Neurobiology of Learning and Memory 123 (2015) 50–57

Contents lists available at ScienceDirect

Neurobiology of Learning and Memory

journal homepage: www.elsevier.com/locate/ynlme

High trait anxiety during adolescence interferes with discriminatory context learning

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ARTICLE INFO

Article history:
Received 10 November 2014
Revised 27 March 2015
Accepted 5 May 2015
Available online 14 May 2015

Keywords:
Adolescence
Anxiety
Context conditioning
Development
Individual differences

ABSTRACT

Persistent adult anxiety disorders often begin in adolescence. As emphasis on early treatment grows, we need a better understanding of how adolescent anxiety develops. In the current study, we used a fear conditioning paradigm to identify disruptions in cue and context threat-learning in 19 high anxious (HA) and 24 low anxious (LA) adolescents (12–17 years). We presented three neutral female faces (conditioned stimulus, CS) in three contingent relations with an unconditioned stimulus (UCS, a shrieking female scream) in three virtual room contexts. The degree of contingency between the CSs and the UCSs varied across the rooms: in the predictable scream condition, the scream followed the face on 100% of trials; in the unpredictable scream condition, the scream and face appeared randomly and independently of each other; in the no-scream condition the CS was presented in the absence of any UCS. We found that the LA adolescents showed higher levels of fear-potentiated startle to the faces relative to the rooms. This difference was independent of the contingency condition. The HA adolescents showed non-differential startle between the CSs, but, in contrast to previous adult data, across both cue types displayed lowest startle to the unpredictable condition and highest startle to the no-scream condition. Our study is the first to examine context conditioning in adolescents, and our results suggest that high trait anxiety early in development may be associated with an inability to disambiguate the signalling roles of cues and contexts, and a mislabelling of safety or ambiguous signals.

1. Introduction

Anxiety problems are common, persistent, and debilitating, exerting huge costs for individuals and society (Olesen, Gustavsson, Svensson, Wittchen, & Jonsson, 2012). Understanding the mechanisms by which anxiety problems arise or abate has therefore become a priority (Beddington et al., 2008). At least half of adult anxiety problems will have their onset by the age of 18 years (Gregory et al., 2007), and by focusing on early individual differences, we can develop a model that enables anxiety to be addressed early, with the aim of reducing long-term burden. In addition, on-going changes in brain function during adolescence exert long-term influences on patterns of behaviour in adulthood (Burnett, Sebastian, Cohen Kadosh, & Blakemore, 2011). This substantial neural development may shape how persistent fears emerge in a way that may contrast with how they emerge in adults.

In adult anxiety models, conditioning theory has highlighted the role of associative learning between explicit cues and aversive outcomes in producing fear responses. High-anxious adults show greater fear to a threat cue (conditioned stimulus (CS+); a stimulus which has been followed by an aversive unconditioned stimulus (UCS)) than their low-anxious counterparts (Lissek et al., 2005), and also manifest more fear to non-threat cues (CS−; a stimulus which is never followed by a UCS). Such fear responses to CS− cues in high-anxious adults have been attributed to stimulus generalisation (Dunsmoor, Mitroff, & LaBar, 2009; Haddad, Pritchett, Lissek, & Lau, 2012; Lissek et al., 2008, 2009).

Although conditioning of discrete cues seems best suited for explaining transient fear states in both anxious and low-anxious individuals, context conditioning, or conditioning to diffuse non-specific 'background' cues, has been used to explain situations of more generalised and sustained fear responses, in other words, anxiety. Previous work with healthy adults suggests that contextual fear is greater under conditions when the CS/UCS association

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http://dx.doi.org/10.1016/j.nlm.2015.05.002
1074-7427/

is less predictable, that is, when the UCS does not reliably follow the CS (Grillon, Baas, Cornwell, & Johnson, 2006). A small body of literature investigating contextual fear in anxious adults tentatively suggests that the enhanced response under unpredictable circumstances is even greater in high anxious individuals (Baas, 2012).

While developmental perspectives on anxiety emphasise the importance of extending this work to adolescents, the limited available data in this area focuses more on children than adolescents (Craske et al., 2008; Field & Storksen-Coulson, 2007; Waters, Henry, & Neumann, 2009) – and none, to our knowledge, pertains to contextual (as opposed to cued) fear responses. One reason for the paucity of fear conditioning studies in adolescents is balancing practical and ethical considerations. Electrical shocks, the most powerful UCS in adults, may not be appropriate for adolescents. Less noxious UCSs however, such as loud sounds and unpleasant photographs, whilst useful in working with children, provoke minimal fear in the adolescent age range (Lau et al., 2008). To address this problem, a paradigm which has recently been introduced uses a piercing female scream as the aversive UCS. The 'screaming lady paradigm' has been successfully used in both healthy and clinical non-adult populations both in the US and the UK (Haddad et al., 2012; Lau et al., 2008, 2011). Lau and colleagues used this procedure in a sample of anxious and low-anxious adolescents and found that while all adolescents could discriminate between threat and safety cues, anxious adolescents show enhanced fear to both (Lau et al., 2008). It remains to be determined whether high anxious adolescents generalise their fear to the context in which the fear conditioning occurs, and the extent to which anxiety-associated differences emerge under predictable and unpredictable conditions.

The current study combined the screaming lady paradigm (Lau et al., 2008) and a discriminative cued-conditioning paradigm, with measures of context learning (Grillon et al., 2006) to investigate differences in cue and context threat learning in high anxious and low anxious adolescents. Here, three neutral facial expressions appeared under one of three contingency conditions. In the predictable scream contingency condition (P), the CS+ was always followed by the scream, whereas in the unpredictable scream contingency condition (U), a different face (CS_U^-) and the scream appeared pseudo-randomly with a minimum gap of 2 s between them. In the no scream contingency condition (N), a third face served as the CS_N^- but no screams occurred. To index fear, we used fear-potentiated startle (FPS) that is electromyography of the eye-blink startle reflex to an airpuff. Fear-potentiated startle responses represent a low-invasive, easily controllable measure of fear. Moreover, the operational procedure is comparable in humans and animals, which is particularly attractive as the underlying neural networks are well-documented in the animal model (Grillon, 2002). Based on previous models of CS/Context conditioning interactions (e.g. Rescorla & Wagner, 1972), we expected to observe a differential FPS response to the discrete CS+ cue and the CS− cues, and between the three contexts (independent of individual anxiety levels) due to the different CS–UCS contingencies. Specifically, we predicted greater contextual FPS to U relative to P and N, and expected to observe greater cued startle response to the CS+ relative to the CS− (independent of contingency condition). Importantly, based on prior data on cue conditioning and stimulus generalisation in anxious vs. low-anxious individuals, we predicted that (1) HA adolescents would show increased FPS responses to the discrete CS+ and both CS− cues than LA adolescents independent of contingency condition and that this group difference may be particularly large for the CS− cues and (2) HA adolescents would exhibit greater FPS responses to the room context cues, and based on adult data, tentatively, this anxiety-related difference would be greatest to the room in the unpredictable contingency condition.

2. Methods

2.1. Participants

For the current study, we created a large recruitment pool of 2000 children and adolescents from local schools, who were screened for state and trait anxiety levels (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1970). Participant selection then focused on the highest and lowest scoring 5% of the sample (based on the trait anxiety score). The final sample reported here consisted of 43 participants, of whom 24 were low anxious (LA) (mean age: 14.0, SD: 1.2 years, 7 female) and 19 were high anxious (HA) (mean age: 14.6, SD: 1.6 years, 9 female). See also Table 1 for trait and state anxiety distribution in the two groups. An additional 6 LA and 11 HA participants were tested but not included in the current analyses due to technical difficulties leading to incomplete/invalid data (5 participants), or lack of reliable eye blink responses (i.e., blinks on less than 75% of trials, 12 participants). Participants self-reported no history of psychiatric illness or learning difficulty, which was corroborated by the school. Informed consent was obtained from the participant's primary caregiver, and informed assent was obtained from all participants prior to testing. The study was approved by the local ethics committee at the University of Oxford. All participants received a £10 Amazon voucher for taking part in the study.

2.2. Psychophysiological apparatus

We recorded the fear-potentiated eye-blink startle reflex in accordance with guidelines set out in Blumenthal et al. (2005). Stimulation and recording were controlled by Psychlab (Contact Precision Instruments, London, UK) and E-prime 2.0 software (Psychology Software Tools, Pittsburgh, PA). Electromyography (EMG) recordings of the eye-blink startle reflex were made with two 4 mm Ag–AgCl electrodes placed beneath the left eye over the orbicularis oculi muscle, approximately 25 mm apart. A third electrode was placed onto the tip of the nose and served as a baseline reference. EMG activity was sampled at 1000 Hz, with amplifier bandwidth set to 25–500 Hz. To elicit the fear-potentiated eye-blink response, we used a 40 ms air-puff startle probe of medical grade compressed air, delivered to the centre of the forehead through a polythene tube (2 m long, 32 mm inside diameter), affixed approximately 1 cm from the skin by way of a headpiece worn by the participant. The headpiece allowed the participants to move their head while maintaining constant placement of the air-puff. A visor was positioned between the polythene tube and the participant's eyes to prevent the air-puff from reaching the cornea. A solenoid valve with an AC switch controlled delivery of the air-puffs. Prior to testing, air pressure was set at 0.7 bar initially (measured at the level of the regulator), but this was adjusted for each participant individually. Pressure was set at the minimal level required to elicit reliable blinking during a test block of six successive startle probe presentations.

2.3. Conditioning paradigm

We combined a classical, discriminative cued-conditioning paradigm (Lau et al., 2008) with a context variable. Photographs of three female faces with neutral expressions from the NimStim face stimulus set[1] served as specific threat-cue (CS+) and safety-cues (CS−), each appearing in one of three contexts (three pictures of rooms in a house, see Fig. 1). The UCS was a 95 db. female

[1] Development of the MacBrain Face Stimulus Set was overseen by Nim Tottenham and supported by the John D. and Catherine T. MacArthur Foundation Research Network on Early Experience and Brain Development.