International Journal of Psychophysiology 98 (2015) 59–64

Contents lists available at ScienceDirect

International Journal of Psychophysiology

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

Demographic factors predict magnitude of conditioned fear

Blake L. Rosenbaum [a], Eric Bui [a,b], Marie-France Marin [a,b], Daphne J. Holt [a,b,c], Natasha B. Lasko [a,b], Roger K. Pitman [a,b], Scott P. Orr [a,b], Mohammed R. Milad [a,b,c,*]

[a] The Department of Psychiatry, Massachusetts General Hospital, Boston, MA, United States
[b] Harvard Medical School, Boston, MA, United States
[c] The HST-MIT Athinoula A. Martinos Center for Biomedical Imaging, Charlestown, MA, United States

ARTICLE INFO

Article history:
Received 18 November 2014
Received in revised form 21 May 2015
Accepted 26 June 2015
Available online 4 July 2015

Keywords:
Fear conditioning
Demographics
Classical conditioning
Education
Extinction
Skin conductance

ABSTRACT

There is substantial variability across individuals in the magnitudes of their skin conductance (SC) responses during the acquisition and extinction of conditioned fear. To manage this variability, subjects may be matched for demographic variables, such as age, gender and education. However, limited data exist addressing how much variability in conditioned SC responses is actually explained by these variables. The present study assessed the influence of age, gender and education on the SC responses of 222 subjects who underwent the same differential conditioning paradigm. The demographic variables were found to predict a small but significant amount of variability in conditioned responding during fear acquisition, but not fear extinction learning or extinction recall. A larger differential change in SC during acquisition was associated with more education. Older participants and women showed smaller differential SC during acquisition. Our findings support the need to consider age, gender and education when studying fear acquisition but not necessarily when examining fear extinction learning and recall. Variability in demographic factors across studies may partially explain the difficulty in reproducing some SC findings.

1. Introduction

Classical conditioning has been used to explore fear-based learning associated with clinical anxiety (Grillon and Morgan, 1999; Pitman and Orr, 1986) as well as to elucidate mechanisms associated with the psychopathology of several psychiatric disorders, including posttraumatic stress disorder (PTSD) (Blanchard et al., 1996; Garfinkel et al., 2014), obsessive compulsive disorder (OCD) (McLaughlin et al., 2015; Nanbu et al., 2010), and schizophrenia (Graham and Milad, 2011; Milad and Quirk, 2012). A typical fear-conditioning paradigm involves the pairing of a neutral cue (conditioned stimulus, CS) with an aversive stimulus (unconditioned stimulus, US), such as an electric shock, that produces an unconditioned response (UR). Subsequent to a series of CS–US pairings, presentation of the CS comes to elicit a conditioned response (CR) when presented alone. In human fear conditioning, physiological measures such as startle, heart rate, or skin conductance (SC) are commonly used to measure the CR (Jovanovic et al., 2012; Orr and Roth, 2000; Vervliet et al., 2004). During extinction training, when the CS is no longer paired with the US, the CR will diminish, i.e. extinguish, over repeated presentations. Both increased fear conditionability and the diminished ability to extinguish fear have been suggested to be involved in the pathophysiology of anxiety disorders (Milad and Quirk, 2012; Pitman et al., 2012; Rauch et al., 2006; Shin and Liberzon, 2010).

Substantial individual differences in conditionability characterize human fear conditioning studies. Some individuals rapidly acquire a strong CR that is relatively specific to the fear cue; others may acquire a CR that generalizes to non-conditioned cues, while still others fail to acquire a CR. It has been suggested that genetic, developmental and personality factors contribute to individual differences in conditionability (Hettema et al., 2003; Merrill et al., 1999). Several studies have examined the relationship between conditioned fear responses and various personality traits, especially anxiety. For example, a recent study of 46 healthy Puerto Rican subjects found that the combination of self-report measures of personality traits and measures of physiological reactivity predicted as much as 45% of the variance observed during fear conditioning (Martinez et al., 2012). Similarly, Otto and colleagues reported that self-report measures of anxiety symptoms, mood, and personality explained about 28% of the variance in fear conditioning (Otto et al., 2007).

The potential effect of demographic factors such as age, gender and education on fear conditioning is generally treated as nuisance variance in fear-conditioning studies. Consequently, studies often seek to match experimental and control groups for these variables so as to mitigate their possible influence(s) on the findings. It is unclear whether matching for these variables does, in fact, reduce variance in the conditioning indices being measured. And even if matched within a particular

* Corresponding author at: Department of Psychiatry, Massachusetts General Hospital, 149 13th St, CNY 2614, Charlestown, MA 02129, United States.
E-mail address: milad@nmr.mgh.harvard.edu (M.R. Milad).

http://dx.doi.org/10.1016/j.ijpsycho.2015.06.010
0167-8760/

study, differences in demographic characteristics between laboratories are difficult to avoid and could potentially contribute to the lack of consistent findings across studies. In order to address this issue, we have pooled data from 222 participants that were studied in our laboratory over the past several years. This sample includes healthy participants, as well as PTSD, OCD and schizophrenia patients who underwent the same differential conditioning procedure that used SC as the measure of conditioned fear (Holt et al., 2012; Milad et al., 2009). Given the relative lack of previous research examining this domain, it is difficult to hypothesize which of these demographic factors may be associated with the acquisition and extinction of fear-conditioned SC.

2. Materials and methods

2.1. Participants

141 healthy controls and 81 patients (OCD, n = 21; PTSD, n = 40; schizophrenia, n = 20) who were recruited for one of three different studies and underwent the same two-day fear conditioning protocol while in an fMRI scanner were studied. The age range for all participants was 18 to 67 years old. Neuroimaging and psychophysiological data from these participants related to the neurobiology of fear extinction in healthy subjects (Linnman et al., 2011a, 2012; Milad et al., 2007a,b) and in the different clinical populations (Holt et al., 2012; Linnman et al., 2011b; Rougemont-Bucking et al., 2011) have been previously published.

2.2. Fear conditioning paradigm

A detailed description of the fear conditioning paradigm is available elsewhere (Milad et al., 2007b). Briefly, participants were presented with images of two different rooms that provided the visual context, one specific to acquisition and one specific to extinction for 3 s. Each context contained a lamp that was first presented in the off position and that then “turned on” to one of three colors: blue, red, or yellow. The colors represented different conditioned stimuli (CSs) that signaled whether or not the participant would receive an electric shock (CS+) or no shock (CS−) and were presented for 6 s. The shock was delivered through two electrodes placed on the right hand and lasted 500 ms, immediately following offset of the CS+ presentations. The shock level was previously selected by the participant to be “highly annoying but not painful.” Day 1 of the protocol consisted of Habituation, Conditioning (acquisition), and Extinction Learning phases, and Day 2 consisted of Extinction Recall and Renewal phases. During the Habituation phase, the two CS + s (4 trials each) and the CS− (4 trials) were presented within both the conditioning and extinction context; no shocks were delivered during this phase. In the Conditioning phase, participants were presented with two CS+s (for example, one might be represented by a red light and the other represented by a blue light) within a specific conditioning context and paired with the electric shock (8 trials for each CS+, 62% partial reinforcement). The CS− (for example, a yellow light) was presented without shocks (16 trials). All CS's were counterbalanced and presented in a pseudo-random order. In the Extinction Learning phase, only one of the CS+s was extinguished (CS + E), in a novel extinction context and without shocks. The other CS+ was not presented and remained unextinguished (CS + U). The CS + E (16 trials) and CS− (16 trials) were both presented during extinction learning. On the following day, during the Extinction Recall phase, the CS + E (8 trials), the CS + U (8 trials), and the CS− (16 trials) were presented within the extinction learning context (without the US), whereas during the Renewal phase the three CSs were presented in the conditioning context (without the US). As part of the protocol and prior to fear conditioning, participants completed several questionnaires including the Beck Anxiety (BAI) and Depression Inventories (BDI), the Anxiety Sensitivity Index (ASI), and the State-Trait Anxiety Inventory (STAI-T).

2.3. Skin conductance recording

A SC response (SCR) was calculated by subtracting the mean SC level (SCL) during the 2 s immediately preceding CS onset from the highest SCL recorded during the CS presentation. This algorithm differs slightly from the standardized method for calculating SCRs because a negative value can be produced. Therefore, throughout the text, “SCR” and “change in SC” are used interchangeably. Each SCR was square-root transformed; for negative SCRs, the square-root of the absolute value of the SC change was obtained and then the negative sign was replaced. These data were then averaged across respective CS+ and CS− trials. Differential responses were calculated by subtracting the average SCR to the CS− trials from the average SC change to the respective CS+ (both E and U) trials.

2.4. Data analyses

All data used in the analyses were previously collected and compiled into a master database containing demographic, SCR, and psychometric data. Because the distribution was not normal in these populations, age was dichotomized into an older (≥29 years old) and a younger group (<29 years old) using a median split. The actual median value was rounded to the closest whole number. Similarly, education was dichotomized into a lower education group (<16 years of education) and a higher education group (≥16 years of education). Sixteen years of education is equivalent to the completion of a Baccalaureate degree in the United States. Data analyses were initially conducted for all experimental phases (Conditioning, Extinction Learning, Extinction Recall, and fear Renewal). Because there were no significant relationships between the demographic variables for phases other than Conditioning, the analyses presented below focus on the Conditioning phase alone. For this phase, separate 2 × 2 × 2 analyses of variance (ANOVA) were conducted that included: patient status (patient, healthy control) as a between-group factor; stimulus type (CS+, CS−) as a within-subject factor; and demographic variable: age (younger, older), gender (men, women), or education (low, high) as a between-subject factor. Significant interaction effects were then decomposed using additional ANOVA or independent sample t-tests, as appropriate. A series of multiple regression analyses were used to examine whether age, gender and education predicted SC change to the CS− and CS+ presentations, as well as the differential SCR, after adjusting for patient status. All analyses were performed using SPSS v22.

3. Results

For the entire sample (n = 222), the mean age (standard deviation) was 35.6 (15.2); 126 of the participants (56.8%) were women. The majority of participants had an education of 16 years or more, (n = 131, 59%) and 108 (48.6%) were 29 years of age or older. The overall range of education was 8 years to 24 years.

3.1. Effects for age

3.1.1. Conditioning

A 3-factor ANOVA (patient status, age, stimulus) produced a marginal main effect for age ($F(1,218) = 3.49$, $p = .062$), indicating a larger change in SC for the older group. There was no significant stimulus × age interaction ($F(1,218) = 1.95$, $p = .164$). There was no significant main effect or interactions involving patient status (all F's(1,218) < 1, p's = ns) There was a significant main effect for stimulus as well ($F(1,218) = 111.85$, $p < .001$). In order to decompose the stimulus × age interaction (See Fig. 1), SCRs to the CS+ and CS− were separately compared between the two age groups. Results of these comparisons showed that SCRs to