Context Conditioning and Behavioral Avoidance in a Virtual Reality Environment: Effect of Predictability

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Background: *Sustained anxiety can be modeled using context conditioning, which can be studied in a virtual reality environment. Unpredictable stressors increase context conditioning in animals. This study examined context conditioning to predictable and unpredictable shocks in humans using behavioral avoidance, potentiated startle, and subjective reports of anxiety.*

Methods: *Subjects were guided through three virtual rooms (no-shock, predictable, unpredictable contexts). Eight-sec duration colored lights served as conditioned stimuli (CS). During acquisition, no shock was administered in the no-shock context. Shocks were paired with the CS in the predictable context and were administered randomly in the unpredictable context. No shock was administered during extinction. Startle stimuli were delivered during CS and between CS to assess cued and context conditioning, respectively. To assess avoidance, subjects freely navigated into two of the three contexts to retrieve money.*

Results: *Startle between CS was potentiated in the unpredictable context compared to the two other contexts. Following acquisition, subjects showed a strong preference for the no-shock context and avoidance of the unpredictable context.*

Conclusions: *Consistent with animal data, context conditioning is increased by unpredictability. These data support virtual reality as a tool to extend research on physiological and behavioral signs of fear and anxiety in humans.*

Key Words: Associative learning, Pavlovian conditioning, predictability, psychophysiology

Conditioned fear theories have had a long tradition in contributing to understanding the origin and maintenance of anxiety disorders (Bouton et al 2001; Mineka and Zinbarg 1996). According to such theories, an unconditioned emotional response (UR) to an aversive unconditioned stimulus (US) becomes associated with cues present during the traumatic event, which, in turn, become conditioned stimuli (CS). Subsequent encounters with these cues trigger conditioned emotional responses (CRs) of fear and anxiety. According to Mowrer's two factor theory, fear and anxiety motivate a desire to seek safety, promoting and reinforcing avoidance behavior (Mowrer 1953). Mowrer's two-factor theory may no longer be accepted in its entirety, but avoidance remains integral to the theoretical basis of behavioral interventions (Wolpe 1982).

During fear conditioning, associations develop to both explicit and contextual cues present during acquisition. Animals that have undergone fear conditioning in which an explicit cue such as a light is repeatedly paired with an aversive event such as a shock will not only exhibit fear to the light (cued fear conditioning), but also to the experimental context (e.g., the cage; context conditioning). Although simple explicit cue-danger (e.g., light/CS-shock/US) associations are by far the most studied form of fear conditioning in humans, they do not model the symptoms of sustained generalized anxiety and anxious apprehension found in several disorders (Barlow 2000; Clark and Watson 1991; Grillon et al 1998).

By contrast, context conditioning captures important characteristics of anxiety disorders. Context conditioning models situations of uncued danger and sustained anxiety states (Grillon 2002). Context conditioning has also been proposed as a model for phobic avoidance (agoraphobia) in panic disorders (Gorman et al 2000). Moreover, cued and context conditioning have different neural bases, suggesting that they may indeed constitute distinct aversive states. Both types of conditioning rely on the amygdala, but unlike cued fear conditioning, context conditioning requires the integrity of at least two other structures, the hippocampus (Kim and Fanselow 1992; Phillips and LeDoux 1992) and the bed nucleus of the stria terminalis (BNST) (Sullivan et al 2004). It is noteworthy that the amygdala has been related to phasic responses to a threat cue, whereas the BNST mediates sustained responses to stressors (Walker and Davis 1997). In fact, Davis (1998) has labeled the phasic amygdala-mediated responses "fear" and the sustained BNST-mediated responses "anxiety," suggesting that cued and context conditioning could be used as experimental models of these two aversive motivational states.

Given the relevance of context conditioning for anxiety disorders, it is crucial to better understand both the conditions that promote context conditioning and the effect of context conditioning on emotional and behavioral responses in humans. One factor that affects context conditioning is the predictability of the aversive event (Rescorla and Wagner 1972). Animal studies have demonstrated that unsignaled (unpredictable) shocks produce more contextual fear than signaled (predictable) shocks (Fanselow 1980; Marlin 1981). In addition, when given a choice, animals will avoid contexts wherein shocks are unpredictable compared to predictable contexts, suggesting that unpredictable contexts are more aversive (Odling-Smee 1975a; 1975b).

Predictability is also a key variable in the etiology and maintenance of anxiety (Barlow 2000; Foa et al 1992; Mineka and Kihlstrom 1978). Predictability mitigates anxiety elicited by various types of threat. Unpredictable stressors produce a constellation of debilitating physiological and behavioral changes in animals that are not seen when the stressors are predictable: increased ulceration, weight loss, learning impairment, and enhanced symptoms of anxiety and avoidance (Mineka and Kihlstrom 1978). These results are based on animal investigations. Research in humans lags far behind pre-clinical studies and the results have been contradictory with reports that unpredictable stressors lead to increased anxiety (Feldner et al 2003; Zvolensky et al 1999), decreased anxiety (Averill et al 1977; Miller

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1979), or no significant differences (Averill and Rosenn 1972; Rothbart and Mellinger 1972; Vogeltanz et al 1999) compared to predictable stressors. In a review, (Miller 1981; page 230) concluded "the physiological and subjective data show that predictable aversive events probably cause higher anticipatory arousal than unpredictable events."

This conclusion, however, may be premature. Using the startle reflex as a measure of aversive states, we recently reported greater anxiety during anticipation of unpredictable shocks compared to predictable shocks (signaled by a cue; Grillon et al 2004). In addition, the DSM-IV-R makes a distinction between cued/predictable and uncued/unpredictable panic attacks, the latter leading to a high level of generalized anxious apprehension (Barlow 1988) and sustained anticipatory anxiety about future panic attacks (Rachman and Levitt 1985). Hence, it is possible that, like in animals, humans show greater context conditioning under unpredictable shocks compared to predictable shocks.

Major methodological hurdles impede efforts to implement measures derived from rodent context conditioning studies that rely on differential spatial contexts. In recent years, we have used engaging, computer-generated virtual reality environments to create different spatial contexts while keeping the subject stationary in the laboratory (Baas et al 2004). Virtual reality is an ideal tool to examine the effect of predictability, not only on subjective and physiological measures of anxiety, but also on behavioral responding because virtual reality provides the opportunity for subjects to navigate in virtual spaces.

The ability to allow subjects to behave freely in a controlled environment while still confined to the laboratory is a distinct advantage of virtual reality. Most research on emotion has relied on physiological responses and verbal reports with few examining overt avoidance behavior. The present study incorporated these three measures. Overt behavior is particularly significant for research on anxiety. Functional accounts of anxiety emphasize its role in avoidance of aversive stimuli. In addition, behavioral avoidance is a central feature of most anxiety disorders. Individuals who seek treatment for anxiety disorders do so primarily because their avoidant behavior interferes with normal daily functioning (Beck and Emery 1985).

The virtual reality environment used in this study was comprised of three separate rooms or contexts. These contexts were associated either with predictable shocks (signaled by a cue), unpredictable shocks, or no shock. Aversive responses were measured by subjective reports, the startle reflex, and overt behavior. We hypothesized that anxiety indexed by startle and subjective reports would be augmented in the unpredictable context compared to the predictable context. We also predicted that subjects would show conditioned behavioral responses when given a choice to re-enter the virtual rooms, choosing to enter the no shock context and to avoid the unpredictable context after being conditioned.

Methods and Materials

Subjects

Participants were 37 healthy volunteers, 16 females and 21 males (mean age 27.2; *SD* = 7.9 years) who gave written informed consent approved by the NIMH Human Investigation Review Board. They were divided into an acquisition-only (N = 14) and an acquisition-extinction (N = 23) groups (see below). Inclusion criteria included 1) no past or current psychiatric disorders as per Structured Clinical Interview for DSM-IV (First et al 1995); 2) no medical condition that interfered with the objectives of the study as established by a physician; and 3) no use of illicit drugs or psychoactive medications as per urine screen.

Stimuli and Apparatus

VR Environment. The software application (VR Worlds, Psychology Software Tools, Inc., Pittsburgh, Pennsylvania) consisted of several interconnected virtual environments (e.g., an urban area, an apartment complex, a subway system). A subset of these environments, a restaurant with a bar, a bank, and a casino was used to constitute the different contexts in the present study (Figure 1). These contexts were located on different sides of a common street. Each context contained a different style lamp associated with an 8-sec duration colored light (blue, green or yellow) that served as conditioned stimuli (CS). For a given subject, the lamp was associated with one color per context (e.g., bank/blue, casino/green, and restaurant/yellow). The color of the lights in each context was counterbalanced across subjects and contexts.

Psychophysiology System

Stimulation and recording were controlled by a commercial system (Contact Precision Instruments, London, Great Britain). The acoustic startle stimulus was a 40-ms duration, 103 dB (A) burst of white noise with a near instantaneous rise time presented binaurally through headphones. The eyeblink reflex was recorded with electrodes placed under the left eye. Amplifier bandwidth was set to 30–500 Hz. Electric shocks (up to 5 mA) were produced by a constant current stimulator and administered on the right wrist.

Design

A sequence of movements and events (scenario) in the different virtual contexts was pre-recorded. In a scenario, subjects were moved from one context to another through the street, entering and exiting through the front door. Note that subjects were not wearing a head-mounted device to enable them to control their own view of the environment. The VR was displayed either on a monitor (during familiarization and during the behavioral avoidance task) or on a large screen (during conditioning). They also were not free to navigate in the environment

Figure 1. Pictures of the virtual environment. The different virtual contexts were a bank, a casino, and a restaurant.