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Research report

The neural signature of escalating frustration in humans

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A B S T R A C T

Mammalian studies show that frustration is experienced when goal-directed activity is blocked. Despite frustration's strongly negative role in health, aggression and social relationships, the neural mechanisms are not well understood. To address this we developed a task in which participants were blocked from obtaining a reward, an established method of producing frustration. Levels of experienced frustration were parametrically varied by manipulating the participants' motivation to obtain the reward prior to blocking. This was achieved by varying the participants' proximity to a reward and the amount of effort expended in attempting to acquire it. In experiment 1, we confirmed that proximity and expended effort independently enhanced participants' self-reported desire to obtain the reward, and their self-reported frustration and response vigor (key-press force) following blocking. In experiment 2, we used functional magnetic resonance imaging (fMRI) to show that both proximity and expended effort modulated brain responses to blocked reward in regions implicated in animal models of reactive aggression, including the amygdala, midbrain periaqueductal grey (PAG), insula and prefrontal cortex. Our findings suggest that frustration may serve an energizing function, translating unfulfilled motivation into aggressive-like surges via a cortical, amygdala and PAG network.

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From running and missing the bus to helplessly observing someone commandeer our taxi, daily life throws numerous obstacles in the path of our desired goals. Such events evoke frustration, which can escalate into aggression, in alignment with theories positing that frustrating barriers to the attainment of expected gratification instigate aggressive behavior (Berkowitz, 1989; Dollard, Doob, Miller, Mowrer, & Sears, 1939). Yet despite frustration's putative role in this process, its underlying neural systems remain unspecified. One proposal is that frustration reflects mild engagement of the reactive aggression system which increases in proportion to the intensity of the desire that is thwarted (Panksepp, 2005); however, this remains to be demonstrated.

Knowledge of the neural basis of reactive aggression comes largely from comparative research. Electrical and chemical stimulation studies and lesion studies in animals have identified a core aggression circuit comprising the amygdala, hypothalamus, and periaqueductal grey (PAG) (Nelson & Trainor, 2007; Panksepp, 2005). The area of PAG involved in aggression receives direct inputs from the hypothalamus, and from the medial prefrontal and insular cortices which have been proposed to have a role in evaluating the emotional content of frustrating events (Bandle, 1988; Panksepp, 2005). The prefrontal cortex has inhibitory connections to aggression-relevant regions of the amygdala, and both regions have been implicated in aggression-related psychiatric disorders (Blair, 2010; Davidson, Putnam, & Larson, 2000). Following the hypothesis that frustration induces reactive aggression, we predicted that the areas implicated in reactive aggression would be associated with frustration in humans.

Motivation or desire to attain a goal has been shown to affect the level of frustration and aggression when thwarted (Amsel, 1992; Dollard et al., 1939). We therefore used a parametric design that varied participants' motivation prior to blocking using two established strategies — the goal gradient principal, which shows an animal's desire to achieve a goal increases with increasing goal proximity (Hull, 1932; Shidara & Richmond, 2002), and the effort expended in reaching the goal (Pompilio, Kacelnik, & Behmer, 2006; Staw, 1976). Manipulations of goal gradient are frequently confounded with expended effort (Hull, 1932; La Camera & Richmond, 2008; Shidara & Richmond, 2002). Therefore, it is important to separate contributions of these prospective (proximity) and retrospective (expended effort) variables.

Human research shows that people's frustration is often displaced towards innocent bystanders or inanimate objects, for example, slamming a door or forcefully pressing the keys of a computer keyboard (Haner & Brown, 1955; Kapoor, Burleson, & Picard, 2007). Similarly, comparative research shows that a frustrating event has an invigorating effect on behaviors that immediately follow it (Amsel, 1992). Consequently, we used participants' key-press force to confirm the outcome (blocked or win) as an objective index of frustration in response to blocking (Kapoor et al., 2007). In addition, participants were also asked to rate their level of frustration after being blocked. Experiments 1a & b verified that our paradigm was effective in eliciting frustration, and that the level of frustration was related to the participants' motivation to attain the goal at the point of blocking. Experiment 2 used functional magnetic resonance imaging (fMRI) to address the neural basis of human frustration. We predicted that frustration would engage similar brain areas to those implicated in animal models of reactive aggression, and that mirroring the behavioral data, the level of engagement should be related to participants goal-directed motivation when blocked.

1. Experiment 1a (behavioral study)

1.1. *Materials and methods*

1.1.1. *Participants*

Twenty-seven healthy male volunteers (mean age and SD 23.4 $\pm$ 2.5) participated in Experiment 1a. All were right-handed and fluent English speakers. The study was authorized by the Hertfordshire Research Ethics Committee and informed written consent was obtained from each participant.

1.1.2. *Apparatus*

A specially designed pressure button box was used to record the force participants applied to the buttons and their reaction times (Magconcept® Sunnyvale, CA). The digitized force signal was recorded with a resolution of $\sim$.3 N (Newton). The sampling rate was 500 Hz. This allowed RTs to be measured to the nearest 2 msec. RTs were computed as the time at which the force first exceeded 2 N. This value is well within the range used by standard all-or-none response keys for recording RTs.

1.1.3. *Paradigm*

The multi-trial reward schedule task was composed of separate schedules comprising four (1/4, 2/4, 3/4, 4/4), three (1/3, 2/3, 3/3), two (1/2, 2/2) or one (1/1) trial(s). Participants were required to complete all trials in each schedule to obtain two pounds reward. Each trial was preceded by a two second presentation of a schedule cue indicating the number of trials that were left to complete (e.g., two filled boxes and two blank boxes represented two trials left to complete) (Fig. 1). Progress towards winning the reward was also indicated by the proportion of a two-pound coin that was visible.

After each schedule cue, participants were presented with an array of 3 arrows (i.e., ">>>" or "<<<") for 1 sec and were required to indicate the direction of the arrows as quickly and accurately as possible to advance through the schedule. Participants were told that the response criterion for each trial was set by the computer in an unpredictable fashion. If their RT was slower than the criterion or they responded incorrectly, the appropriate feedback ("Blocked") would be presented for 2 sec, and they would fail to win the reward. However, if they completed all trials in a schedule successfully they would win the reward and the feedback "Win" would be presented. In fact, the response criteria were predetermined so that participants lost about 14 times at each schedule state and won on about 33% of trials within each schedule (Fig. 2). Thus, if the feedback was predetermined to be negative, participants would be presented "Blocked" regardless of their actual RT. If the feedback was predetermined to be positive, participants would advance to the next trial in the schedule or