



The fine line between ‘brave’ and ‘reckless’: Amygdala reactivity and regulation predict recognition of risk



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ABSTRACT

Background: High sensation-seekers (HSS) pursue novelty even at the cost of self-harm. When challenged, HSS are less anxious, show blunted physiological (cortisol, startle) and neurobiological (prefrontal-limbic) responses, and devalue aversive outcomes. Here, we investigate how these features interact under conditions of physical danger, in distinguishing between adaptive and maladaptive approaches to risk.

Methods: We recruited a cohort of individuals who voluntarily sought out recreational exposure to physical risk, and obtained serial cortisol values over two time-locked days. On the ‘baseline’ day, we scanned subjects’ brains with functional and structural MRI; on the ‘skydiving day,’ subjects completed a first-time tandem skydive. During neuroimaging, subjects viewed cues that predicted aversive noise; neural data were analyzed for prefrontal-limbic reactivity (activation) and regulation (non-linear complexity), as well as cortical thickness. To probe threat perception, subjects identified aggression for ambiguous faces morphed between neutral and angry poles.

Results: Individuals with prefrontal-limbic meso-circuits with less balanced regulation between excitatory and inhibitory components showed both diminished cortisol/anxiety responses to their skydives, as well as less accurate perceptual recognition of threat. This impaired control was localized to the inferior frontal gyrus, with associated cortical thinning. Structural equation modeling suggests that sensation-seeking is primarily mediated via threat-perception, which itself is primarily mediated via neural reactivity and regulation.

Conclusions: Our results refine the sensation-seeking construct to provide important distinctions (brain-based, but with endocrine and cognitive consequences) between the brave, who feel fear but nonetheless overcome it, and the reckless, who fail to recognize danger. This distinction has important real-world implications, as those who fail to recognize risk are less likely to mitigate it.

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Introduction

For any organism, novelty provides both potential benefits as well as potential costs: an animal that ventures out of known territory may find a new source of food, yet it may also expose itself to predation. As such, evolutionary selection may have favored a spectrum of novelty-seeking behavior within a species, as different circumstances make different attitudes towards risk more or less adaptive.

‘Sensation-seeking,’ in humans, is a personality construct characterized by the pursuit of novelty, even at the risk of increased social, financial, or physical harm (Zuckerman, 1994). High sensation-seekers

(HSSs) have received clinical attention because they are more likely than low sensation-seekers (LSSs) to engage in personally and socially destructive behavior such as drug abuse (Dennhardt and Murphy, 2013; Ersche et al., 2013; Marvel and Hartmann, 1986; Zuckerman, 1986), gambling (Estevez et al., 2013; Harris et al., 2013; Stanton et al., 2001), and promiscuity (Newcomb et al., 2011; Stanton et al., 2001). However novelty seeking, as a character trait, may also be disproportionately represented among populations (e.g., emergency room physicians, surgeons (Hojat and Zuckerman, 2008), firemen (Levenson, 1990), bomb squad technicians) that our society tends to view as altruistic, and even heroic. Here, we hypothesize that individuals who pursue a dangerous activity with full awareness of its risks (‘the brave’), versus those who pursue the same activity blind to its risks (‘the reckless’), are not simply two sides of the same coin, culturally distinguished post hoc simply by virtue of whether their impact is ultimately pro or anti-social. Rather, they represent qualitatively

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heterogeneous approaches to risk, which are neurobiologically, physiologically, and cognitively distinct.

Human and animal studies have established that threat assessment is regulated by a control circuit, with the amygdala and prefrontal regions providing dominant excitatory and inhibitory components, respectively (Phelps and LeDoux, 2005). From a control systems perspective, a healthy prefrontal-limbic circuit should be sufficiently flexible to respond to environmental threat, yet sufficiently constrained to efficiently return to baseline following perturbation. Because flexibility and constraint of the circuit affect the dynamics of the hemodynamic time-series, characterization of these dynamics can be used to quantify circuit-wide regulation. Theoretical work by ourselves (Rădulescu and Mujica-Parodi, 2014) and others (for review, see (Bullmore et al., 2009; Gisiger, 2001; He et al., 2010)) demonstrate that when control systems are optimized for both responsiveness and homeostasis, signal outputs are self-similar or *fractal*, with time-series that follow a power law for both excitatory and inhibitory nodes, balanced at a critical point between order and complexity (see *Methods* section). As circuits become increasingly dysregulated, signal complexity for affected nodes deviates from that critical point (Rădulescu and Mujica-Parodi, 2014), as observed in trait anxiety (Tolkunov et al., 2010), schizophrenia (Rădulescu et al., 2012), autism (Lai et al., 2010), epilepsy (Daneshyari and Kamkar, 2010), and aging (Suckling et al., 2008). Different brain states (He, 2011) and disorders may each reflect distinct regulatory circuit dynamics. However, the unique signature for each brain state and disorder derives from the specific circuit, feedback function (e.g., positive versus negative, strength, lag), and node affected, as well as whether deviation from the critical point shifts towards greater or lesser complexity (Rădulescu and Mujica-Parodi, 2014).

This study was designed to test whether one hallmark feature of HSS—reduced response to threat (De Pascalis et al., 2007; Joseph et al., 2009; Kruschwitz et al., 2012)—is predicted by prefrontal-limbic dysregulation, via its effect on threat perception. We recruited a cohort of first-time tandem skydivers—individuals who all willingly chose recreational exposure to physical risk. The study consisted of two testing days ('baseline' and 'skydive'), between 7 and 14 days apart, and time-locked to control for diurnal variability. On the baseline day, we obtained functional and structural MRI as well as personality measures. On the skydiving day, the subject jumped from 4 km (13,000 ft). On both testing days, subjects provided serial endocrine (cortisol, epinephrine, beta endorphin, testosterone) measurements and self-reported levels of state anxiety and euphoria. Neuroimaging data were analyzed for prefrontal-limbic reactivity (fMRI activation in anticipation of aversive bursts of loud white noise) and system-wide regulation (power spectrum scale invariance, a measure of signal complexity), as well as cortical thickness. We measured threat perception using a separate signal-detection task, in which subjects were asked to identify affect-valence for ambiguous faces morphed by degrees between neutral and angry expressions. Structural equation modeling mapped the relationship between sensation-seeking and neural, endocrine, and cognitive measures.

Methods

Participants

The Institutional Review Board at Stony Brook University approved this study; all participants provided informed consent. Thirty (12 female) healthy adults between the ages of 18 and 48 ($M = 24.69 \pm 7.27$) participated in the primary study; an additional $N = 22$ (2 female) healthy adults between the ages of 18 and 46 ($M = 22.45 \pm 7.48$) participated in a pilot fMRI-skydiving study reported in Appendix A. Participants were recruited from individuals who contacted Skydive Long Island (Calverton, NY) to schedule their first-time skydives. Potential participants were screened for drug usage, neurological/psychiatric histories, and MR exclusion criteria. Participants

provided information regarding age, gender, height and weight, and filled out questionnaires designed to measure different measures of personality related to risk aversion. These questionnaires included the NEO Personality Inventory (PAR, Lutz FL), Perceived Stress Scale (Cohen et al., 1983), Attitudes Towards Risk Questionnaire (Franken et al., 1992), State-Trait Anxiety Inventory (STAI: Mind Garden, Menlo Park, CA), and the Sensation-Seeking Scale (Zuckerman and Link, 1968). For the primary study, trait anxiety scores ranged from 20 to 53 ($M = 33.07 \pm 7.11$) while sensation-seeking scores ranged from 16 to 35 ($M = 24.85 \pm 4.68$); and detailed subject information for the pilot study is provided in Appendix A.

fMRI task

Pilot testing, in an independent sample of $N = 22$ first-time tandem skydivers, established that fear peaked in anticipation of—rather than in response to—the jump, and that cortisol response to that anticipatory period correlated with amygdala activation in response to fearful faces (see Appendix A). Therefore, for this study we used a neuroimaging task previously shown to elicit subjective threat anticipation, with associated activation of the amygdala and insula (Carlson et al., 2011). The *Anticipation of Aversive Events Task* consisted of a 20 trial block design, in which each trial consisted of a 1000 ms cue (red \otimes for 'aversive,' blue \odot for 'benign'), followed first by a 16 s countdown, and then by a 1000 ms auditory stimulus. Aversive cues predicted a burst of 100 dB white noise, while benign cues predicted a burst of 55 dB white noise. Inter-trial intervals were jittered between 4000 and 8000 ms, during which time subjects viewed a white fixation cross on a black screen. Total task time was 8 min.

MRI acquisition and analysis

Subjects were scanned on 3 T Siemens Trio ($N = 18$) or Philips ($N = 12$) MRI scanners at the Stony Brook University SCAN Center using 12-channel SENSE parallel head coils (post-hoc analyses, the results of which are provided in Appendix A, show that the use of two scanners did not significantly impact our results). Data were acquired using 232 T2*-weighted echo planar single-shot images covering the whole brain with the following parameters: TR = 2500 ms, SENSE factor = 2, TE = 22 ms, Flip angle = 83°, Matrix dimensions = 96 × 96, FOV = 224 × 224 mm, Slices = 36, Slice thickness = 3.5 mm, Gap = 0. Standard pre-processing procedures were performed using the Statistical Parameter Mapping software (SPM5), including image realignment corrections for head movements, slice-timing corrections for order of slice acquisition, normalization to standard 2 × 2 × 2 mm MNI space, and spatial smoothing with a Gaussian FWHM 6 mm filter. Using the general linear model in SPM5, first-level single-subject statistical maps were created from contrasts (17 s anticipatory cue block that combined 1 s cue plus 16 s countdown, for aversive versus benign conditions) and auditory events (0 s, for aversive versus benign conditions). At the second-level, cortisol reactivity values for each of the three time-periods were included as regressors of interest.

To quantify circuit-wide regulation via the degree of complexity in the signal, we calculated its power spectrum scale invariance (PSSI) using parameters that we previously optimized for fMRI time-series (Rubin et al., 2013). Outputs that are self-similar or *fractal* have frequency spectra $S(f)$, which follow a power law: $S(f) \propto f^{-\beta}$, with the critical point between order and complexity defined by $\beta = 1$ (*pink noise*) (Gisiger, 2001). Shifts towards greater chaos or greater persistence are defined as towards $\beta = 0$ (*white noise*) or $\beta = 2$ (*brown noise*) respectively. Using modeling and simulations of a prefrontal-limbic meso-circuit, we previously have shown that control systems with balanced excitatory and inhibitory components produce outputs with PSSI closer to pink noise, whereas control systems with less effective inhibitory feedback produce PSSI closer to white noise (Rădulescu and Mujica-Parodi, 2014).

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