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A neural network that links brain function, white-matter structure and risky behavior

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ABSTRACT

The ability to evaluate the balance between risk and reward and to adjust behavior accordingly is fundamental to adaptive decision-making. Although brain-imaging studies consistently have shown involvement of the dorsolateral prefrontal cortex, anterior insula and striatum during risky decision-making, activation in a neural network formed by these regions has not been linked to structural connectivity. Therefore, in this study, white-matter connectivity was measured with diffusion-weighted imaging in 40 healthy research participants who performed the Balloon Analogue Risk Task, a test of risky decision-making, during fMRI. Fractional anisotropy within a network that includes white-matter pathways connecting four regions (the prefrontal cortex, insula and midbrain to the striatum) was positively correlated with the number of risky choices and total amount earned on the task, and with the parametric modulation of activation in regions within the network to the level of risk during choice selection. Furthermore, analysis using a mixed model demonstrated how relationships of the parametric modulation of activation in each of the four aforementioned regions are related to risk probabilities, and how previous trial outcomes and task progression influence the choice to take risk. The present findings provide the first direct evidence that white-matter integrity is linked to function within previously identified components of a network that is activated during risky decision-making, and demonstrate that the integrity of white-matter tracts is critical in consolidating and processing signals between cortical and striatal circuits during the decision-making process.

1. Introduction

Neuroimaging studies have shown that activation in the prefrontal cortex (PFC), striatum, and insula is important for maintaining the neural representations of risk and reward (Paulus et al., 2003; Kuhnen and Knutson, 2005; Rao et al., 2008; Kohno et al., 2013), but how structural connectivity between these brain regions influences risky decision-making and associated neural function is unclear. Activity in the insula is associated with tracking risk (Ishii et al., 2012; Naqvi et al., 2014; Paulus et al., 2003; Kuhnen and Knutson, 2005), and patients with insula lesions make choices that reflect insensitivity to the odds of winning on gambling tasks (Clark et al., 2008). In addition, projections from the midbrain to the striatum signal the presence of motivationally salient events, and anticipatory dopaminergic responses modulate risk preferences (St Onge and Floresco, 2009; Sugam et al., 2012). Afferents from the PFC to the striatum facilitate shifts in decision-making on the basis of reward contingencies in rodents (St Onge et al., 2012); and in humans, corticostriatal functional connectivity has been associated with right dorsolateral PFC (rDLPFC) function during risky decision-making (Kohno et al., 2014). Notably, anatomical studies of nonhuman primates have identified white-matter pathways that link the striatum with the PFC, insula and midbrain (Lynd-Balta and Haber, 1994). It is therefore plausible that structural connectivity between the striatum and these three regions may be critical for integrating the signals that shape adaptive decision-making.

Few studies have examined the association between white-matter integrity and risky decision-making. Impairments on the Iowa Gambling task are linked to lower fractional anisotropy (FA), an index of white-matter integrity, of the superior longitudinal fasciculus, corticospinal tract, and superior corona radiata in cocaine-dependent participants (Lane et al. 2010), and in frontal, parietal, occipital, and callosal regions across samples of healthy and alcohol-dependent

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participants (Zorlu et al., 2013). These studies have begun to detail the importance of white-matter integrity in reward-based risky decision-making, but the links between structural connectivity and functional brain activation have not been directly examined.

Relationships between structural connectivity and functional activity have been observed in studies combining diffusion tensor imaging (DTI) and functional magnetic resonance imaging (fMRI) (Bennett and Rypma, 2013), consistent with the view that brain function parallels structural connectivity. It was recently shown that coherence of a tract connecting the anterior insula and nucleus accumbens was correlated with reduced risk-taking, indexed by a participant's preference for positively-skewed gambles, and that this association was mediated by activation in the nucleus accumbens (Leong et al., 2016). The goal of the present study was to assess how structural connectivity within a broader network influences network-wide activation during risky decision-making.

Decision-making and neural activation were modeled using The Balloon Analogue Risk Task (BART) (Lejuez et al., 2002) paired with fMRI. During the BART, participants can pump a balloon for greater potential gain while risking the loss of accumulated earnings. In each trial, the alternate choice is to cash-out and retain earnings accrued. White-matter pathways connecting the striatum to the rDLPFC and anterior insula were selected on the basis of previous findings that activation in these regions was parametrically modulated by levels of risk and reward on the BART (Kohno et al., 2013). In addition, two studies paired transcranial stimulation with the Risk Task (Rogers et al. 1999), showing that risky choices were influenced by stimulation of the rDLPFC. Specifically, risk-taking behavior was affected by repetitive transcranial magnetic stimulation over the right but not the left DLPFC (Knoch et al. 2006) and by anodal stimulation over the right DLPFC coupled with cathodal stimulation over the left DLPFC with no changes in behavior when anodal stimulation was applied to the left DLPFC coupled with cathodal stimulation over the right DLPFC (Rogers et al. 1999). Therefore, FA was determined in white-matter pathways connecting the striatum with the rDLPFC, anterior insula and mid-brain.

Previous studies have shown that poor decision-making on the Gambling Task, a test in which risk-taking leads to a smaller amount of earnings, is negatively associated with FA in white-matter tracts (Lane et al. 2010), but taking more risk as the trials progress on the BART is an adaptive strategy that produces a more positive outcome (Dean et al. 2011). In addition, resting-state functional connectivity between the rDLPFC and striatum is positively related to the sensitivity of rDLPFC activation to levels of risk during decision-making (Kohno et al., 2014), and rDLPFC function is positively associated with overall performance (Kohno et al., 2013). Given these findings it was expected that FA would be positively associated with the modulation of activation in the rDLPFC, striatum and insula by risk.

2. Methods

2.1. Participants

Forty healthy, right-handed research volunteers (18–51 years of age: mean=27.83 SD=1.79; 10 female) participated in this study, which was approved by the UCLA Office of the Human Research Protection Program. Each participant provided written informed consent prior to enrollment. Exclusion criteria, determined by a physical examination and psychiatric evaluation using the Structured Clinical Interview for DSM-IV, were: systemic, neurological, cardiovascular, or pulmonary disease; head trauma with loss of consciousness; any current Axis I psychiatric diagnoses except nicotine dependence; and current use of prescribed psychotropic medications. Participants who tested positive for cocaine, marijuana, methamphetamine, benzodiazepines, or opiates by urine toxicology were excluded, as were those with MRI contra-indications.

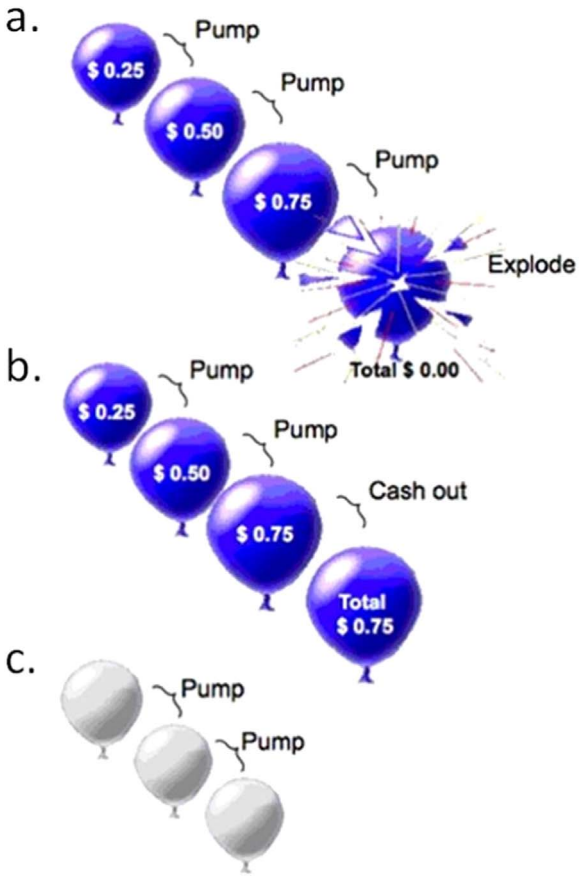

Fig. 1. *Balloon Analogue Risk Task*. a. Pumping an active balloon increases potential earnings but carries risk of balloon explosion and loss of earnings accumulated during the trial. b. If participants cash out before the balloon explodes, they retain the earnings accumulated. c. White balloons, which do not increase in size with pumping, do not explode, and are not associated with reward potential, are presented in control trials (see 2. Methods).

2.2. Balloon analogue risk task

A version of the BART (Lejuez et al., 2002), adapted for event-related fMRI, was used (Fig. 1). Red or blue balloons were presented on active trials, and white balloons were presented on control trials. Participants were instructed that when an active balloon was presented, they should choose between pumping the balloon for a potential increase in earnings ($0.25/pump) or cashing out to retain the earnings accumulated during that trial. Either choice was registered by a bar press. Pumping increased the size of an active balloon and accumulated earnings, or resulted in the balloon exploding and forfeiture of unrealized earnings accumulated during the trial. Trials included all pumps starting with the first presentation of a balloon and ended with the choice to cash out, which resulted in a 2-s display of the total earned or in a balloon explosion followed by a 2-s display of an exploded balloon with the message, “Total=$0.00”. Prior to scanning, participants were informed that red and blue balloons were associated with monetary reward and that they would receive their winnings after scanning, but not that the number of pumps to produce an explosion was pre-determined. For each active balloon trial, that number was determined from a uniform probability distribution, ranging from 1 to 8 and 1 to 12 pumps for red and blue balloons, respectively. Participants were informed that the white balloons did not explode and were not associated with potential reward, and that they should pump each white balloon until the trial ended. The white balloon trials were used to control for activation related to motor activity and visual