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Review

Altered risk-related processing in substance users: Imbalance of pain and gain

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ABSTRACT

Background: Substance use disorders (SUDs) can be conceptualized as a form of risk-taking behavior with the potential for highly aversive outcomes such as health or legal problems. Risky decision-making likely draws upon several related brain processes involved in estimations of value and risk, executive control, and emotional processing. SUDs may result from a dysfunction in one or more of these cognitive processes.
Methods: We performed a systematic literature review of functional neuroimaging studies examining risk-related decision making in individuals with SUDs. A quantitative meta-analysis tool (GingerALE) and qualitative approach was used to summarize the imaging results.
Results: Meta-analysis findings indicate that individuals with SUDs exhibit differences in neural activity relative to healthy controls during risk-taking in the anterior cingulate cortex, orbitofrontal cortex, dorsolateral prefrontal cortex, striatum, insula, and somatosensory cortex. In addition, a qualitative review of the literature suggests that individuals with SUDs may have altered function in the amygdala and ventromedial prefrontal cortex.
Conclusions: The neuroimaging literature reveals that several neural substrates involved in the computation of risk may function suboptimally in SUDs. Future research is warranted to elucidate which computational processes are affected, whether dysfunctional risk-related processing recovers with sobriety, and whether different drugs of abuse have specific effects on risk-taking.

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1. Introduction

Substance use disorders (SUDs), which can refer to abuse or dependence, have profoundly negative impacts on society, including increased rates of morbidity and mortality, disrupted family relations, and a high cost to taxpayers (Nicosia et al., 2009). Recent research has suggested that differences in the neural processing of risk may underlie SUDs (Fishbein et al., 2005; Rogers et al., 1999), making it an important topic for improved understanding of addictive behaviors. Economists define risk as a selection among options with variably distributed outcomes (Lane and Cherek, 2000; Leland and Paulus, 2005; Slovic, 2000). Importantly, this definition of risk implies that an individual knows the probability and magnitude of the outcome associated with each option. This conceptualization differs substantially from the broader meaning of risk used by clinicians and the lay public, which incorporates experiential uncertainty but also emphasizes the potential for large ('catastrophic') negative consequences over positive outcomes (Schonberg et al., 2011). As a result, different experimental tasks have been used to probe risk-taking decision making depending upon whether they explore risk as defined by economists or risk more broadly. Although it is possible that common brain mechanisms may be identified in the future, current investigations of risk-taking in SUDs should attend closely to the different conceptions of risk that underlie experimental measures.

Implicit in the definition of SUD is the increased engagement in naturalistic risk-taking behavior, i.e., substance use despite uncertain adverse consequences. There is some experimental evidence that stimulant users engage in more risk-taking behaviors than non-users (Dom et al., 2006; Leland and Paulus, 2005) and that risk-taking propensity correlates with years of substance use (Rogers et al., 1999). Experimental studies also suggest that treatment for SUDs may reduce risk-taking behavior. For example, a group of 81 substance users undergoing inpatient treatment for dependence (e.g., cognitive training and a group-based 12-step program) showed significantly decreased risk taking behavior as measured by the Balloon Analog Risk Task (BART; Lejuez et al., 2002) after 30 days of inpatient treatment relative to their behavior on the BART at the beginning of treatment (Aklin et al., 2009). Furthermore, the degree to which individuals are willing to engage in risk-taking behavior may be an important factor in SUDs. For example, BART risk-taking behavior was a better predictor of drinking problems in a sample of 75 undergraduates than measures of impulsivity or delay-discounting (Fernie et al., 2010). Therefore, the degree of risk-taking may be associated with the severity and prognosis of SUDs.

This systematic literature review aims to provide a preliminary answer to the question, "Are there brain activation differences that distinguish individuals with SUDs from healthy comparison groups during risk-taking decision-making?" We propose that dysfunctions of several neural substrates may result in inappropriate computation of risk in individuals with SUDs. These dysfunctional processes could include: (1) altered valuation of options in ventromedial prefrontal cortex (VMPFC) and outcomes in orbitofrontal cortex (OFC) and striatum; (2) poor estimation of uncertainty and risk in anterior cingulate cortex (ACC) and insular cortex, (3) diminished executive control in dorsolateral prefrontal cortex (DLPFC); (4) reduced influence of emotional salience in amygdala; and (5) attenuated somatic markers in somatosensory cortex.

2. Methods

2.1. Design

We conducted a meta-analysis of available studies to determine whether brain regions outlined in our hypotheses differed consistently across studies. An extensive literature search revealed only a small number of studies, limiting the generalizability of the present analysis. In consequence, our review should be considered an early attempt to organize the literature rather than a definitive account. To supplement the meta-analysis, we also discuss the findings of relevant studies within the context of the addiction literature.

2.2. Literature search

A search of several databases (Medline, Google Scholar, Psych Info and Web of Science) was performed to identify potential studies up to 01/24/2013 for inclusion. Search terms included: "risk taking" <or> "decision making" <or> "Iowa Gambling" <or> "Cambridge Risk" <or> "Balloon Analog" <or> "Wheel of Fortune" <and> "substance-related disorders" <or> "drug abuse" <or> "drug dependence" <or> "alcohol" <or> "cocaine" <or> "amphetamine" <or> "heroin" <or> "opiate" <or> "stimulant" <or> "nicotine" <or> "marijuana" <and> "neuroimaging" <or> "neural" <or> "fMRI" <or> "PET." Following the database search, the reference lists of relevant studies were explored for additional research. This process yielded 24 studies potentially eligible for meta-analysis (see Table 1).

2.3. Inclusion and exclusion criteria for meta-analysis

Studies were included if they met the following four criteria: (1) examination of a SUD group; (2) use of functional neuroimaging methods: either functional magnetic-resonance imaging (fMRI) or positron-emission tomography (PET); (3) inclusion of a risk-taking measurement; and (4) examination of activation during the decision phase of risk-taking (rather than the outcome phase). Given the limited number of studies available, all substances were grouped together, including alcohol, tobacco, marijuana, cocaine, heroin and amphetamine. SUD diagnosis could be current or in remission. The combination of fMRI and PET studies within a single meta-analysis has precedent in the literature, as both techniques observe changes in blood flow related to task performance (zu Eulenburg et al.,