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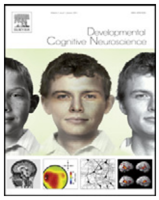

Psychosocial problems and recruitment of incentive neurocircuitry: Exploring individual differences in healthy adolescents

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ABSTRACT

Maturational differences in brain responsiveness to rewards have been implicated in the increased rates of injury and death in adolescents from behavior-related causes. However, much of this morbidity is related to drug intoxication or other externalizing behaviors, and may be concentrated in a subset of adolescents who are at psychosocial or neurobiological risk. To examine whether individual differences in psychosocial and behavioral symptomatology relate to activation of motivational neurocircuitry, we scanned 26 psychiatrically healthy adolescents using fMRI as they performed a monetary incentive delay task. Overall Problem Density on the Drug Use Screening Inventory (DUSI-OPD) correlated positively with activation of ventral mesofrontal cortex (mFC) during anticipation of responding for rewards (vs responding for no incentive). In addition, DUSI-OPD correlated positively with right ventral striatum recruitment during anticipation of responding to win rewards (vs responding for no incentive or to avoid losses of identical magnitudes). Finally, a psychophysiological interaction (PPI) analysis indicated that increased connectivity between nucleus accumbens and portions of anterior cingulate and mFC as a function of reward prospects also correlated with DUSI-OPD. These findings extend previous reports demonstrating that in adolescents, individual differences in reactivity of motivational neurocircuitry relate to different facets of impulsivity or externalizing behaviors.

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1. Introduction

1.1. Neuromaturational differences may account for adolescent vulnerability

Adolescents experience considerable injury due to behavioral causes (U.S. Centers for Disease Control). Hypersensitivity of motivational neurocircuitry to reward-predictive cues or reward deliveries (that is insufficiently checked by immature frontocortical executive control) has been postulated as neurodevelopmental risk factor (Galvan et al., 2006; Somerville et al., 2010; Casey and Jones, 2010). To investigate this possibility, cross-sectional comparisons have compared age-group differences in the responsiveness of mesolimbic incentive neurocircuitry to anticipation and receipt of rewards – specifically in the ventral striatum (VS) and the ventral mesofrontal cortex (mFC), where greater activation of these mesolimbic regions has been interpreted as greater degree of valuation of rewards or of affective reactions to rewards (see below).

1.2. Extant neurodevelopmental difference findings in reward sensitivity are mixed

To study reward processing in humans, functional magnetic resonance imaging (fMRI) paradigms in humans (e.g. Knutson et al., 2001) have been translated from those used in primate electrophysiological studies (Schultz, 2000,

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2007; Schultz et al., 2003). These experiments show that the VS activates in response to learned, reward-predictive instrumental cues (Knutson et al., 2001; Galvan et al., 2006). In addition, ventral mFC responds to reward deliveries (Knutson et al., 2003), and has activated as a final integrator of the expected or experienced value of several kinds of rewards – such as foods (Hare et al., 2009), odors (Rolls et al., 2010), small-immediate vs larger-delayed rewards (Kable and Glimcher, 2007), and perceived probability of winning money (Knutson and Cooper, 2005). The VS features significant anatomical (Haber and Knutson, 2010; Sesack and Grace, 2010) and functional (Cauda et al., 2011) connectivity with the mFC, in addition to significant connectivity with other limbic frontocortical structures such as insula and perigenual anterior cingulate cortex (ACC), which are frequently recruited by prospective (especially uncertain) rewards.

Extant neuroimaging findings on mesolimbic reward-processing differences between adolescents and other age groups, however, show mixed directionality. An initial comparison between healthy adolescents and young adults who performed a monetary incentive delay (MID) reaction-time task showed that compared to adults, adolescents had reduced activation of right nucleus accumbens (NAcc) by cues to respond for explicit amounts of money (Bjork et al., 2004), with no age difference in recruitment of mFC by reward deliveries. A subsequent study where subjects chose between cartoon images for an unspecified amount of money revealed greater VS recruitment by rewards in adolescents compared to adults and younger children (Galvan et al., 2006).

In gambling tasks, adolescents showed greater VS recruitment compared to younger adults by anticipation of rewards in a simulated slot-machine gambling task (Van Leijenhorst et al., 2010b), and when choosing a risky response option in a roulette-wheel like probability task (Van Leijenhorst et al., 2010a). Similarly, Ernst et al. (2005) reported greater VS sensitivity adolescent to reward deliveries and omissions in the wheel-of-fortune task. In a decision-making learning task with stochastic payoff probabilities for correct choices, adolescents showed an exaggerated VS response to unexpected reward deliveries and omission of expected rewards (i.e. prediction errors), as well as a greater limbic response to reward deliveries in general compared to younger children and adults (Cohen et al., 2010). However, a second developmental comparison using the MID task with a larger sample and improved methodology replicated the modest decrement in right VS recruitment by reward predictive cues in adolescents compared to adults (Bjork et al., 2010b). We suspect these divergent findings resulted from differences in stimuli, learning, or other behavioral contingencies between the tasks used (discussed in Bjork et al. (2010b)), as well as from design emphasis on the anticipatory vs consummatory components of the instrumental behavior (Geier et al., 2010).

1.3. Differences between adolescents in brain reward-responsiveness may also be critical

Age-dependent differences in reward processing, while important and intriguing in their own right, however, still leave a large amount of variance unexplained. An interesting complimentary question, then, is whether individual differences in brain recruitment by reward-predictive cues also relate to (or even regulate) individual differences in proclivity for risky behaviors or emotional reactivity. Individual differences in reward sensitivity (or its neural instantiation) among adolescents likely has public health implications in that a substantial portion of adolescent death and injury is attributed specifically to behaviors with a high hedonic or psychosocial payoff, such as speeding, violence, or intoxication with alcohol or other drugs, especially in social contexts. With regard to reward anticipation, persons with overly robust activation of motivational neurocircuitry by signals in the environment that a potential reward is available may be more prone to pursuing the reward despite potential risks associated with that reward (where either the generation or the invocation of a mental representation of the potential downside of the behavior is insufficient). With regard to reward consummation or delivery of rewards, individuals with overactive limbic (hedonic) processing or reward deliveries (such as drugs or alcohol) may be at risk for continued or escalating pursuit of that behavior.

Increased reward sensitivity in children at risk has been suggested by laboratory behavior. Subjects diagnosed with externalizing disorders like attention-deficit hyperactivity disorder (ADHD) or conduct disorder (CD) in childhood show increased behavioral (Newman and Wallace, 1993; Fonseca and Yule, 1995; Matthys et al., 1998, 2004; Lane and Cherek, 2001; Fairchild et al., 2009) and VS (Bjork et al., 2010a) sensitivity to deliveries of rewards or reduced sensitivity to punishments in laboratory tasks. In the real world, persons with these histories also show more reckless driving habits (Barkley et al., 1993; Fischer et al., 2007), and are at increased risk for abuse of drugs or alcohol (Fergusson and Horwood, 1995; Fergusson et al., 2007; Pardini et al., 2007) at follow-up. For example, young adult motorists with childhood histories of ADHD were more likely to suffer traffic accidents, speeding violations, and injuries at follow-up assessment compared to control subjects, where subjects with comorbid CD had the worst motor vehicle outcomes (Barkley et al., 1993).

In essence, it seems likely that among adolescents injured or killed due to behavioral causes, there is an over-representation of individuals with some combination of reward-sensitive or loss-insensitive neurocognitive traits. Notably, we found that among psychiatrically healthy adolescents, high scorers on a brief measure of sensation-seeking (e.g. willingness to bungee jump) showed greater recruitment of the VS by cues to respond to win rewards in another variant of the MID task (Bjork et al., 2008). Similarly, Buckholtz et al. (2010) reported that in healthy young adults, both recruitment of VS by MID reward cues (fMRI) and phasic dopamine responses to rewards in the VS (positron emission tomography) correlated positively with impulsive and antisocial behavior as indexed by the Pychopathic Personality Inventory (PPI) (Lilienfeld and Andrews, 1996).