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Attention to pleasant stimuli in early adolescence predicts alcohol-related problems in mid-adolescence

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ABSTRACT

Attenuated responses to natural rewards have been found to predict subsequent substance use among dependent populations, suggesting that this may be a premorbid risk factor for later problematic substance use. However, research on adolescent risk-taking suggests that exaggerated, rather than blunted, reward responsiveness predicts later substance abuse. Acoustic startle-induced event-related potentials (ERP) were recorded in a sample of 11–13 year-olds while they viewed affective pictures, and participants were reassessed four years later regarding alcohol use and experience of alcohol-related problems. Increased attenuation of the amplitude of the P300 component of the ERP during viewing of pleasant pictures, relative to amplitude during neutral pictures (an indicator of increased attention to pleasant pictures), predicted increased likelihood of alcohol-related problems at follow-up. These findings further support research indicating that increased reward responsiveness predicts risky behaviours in adolescence, with anhedonia primarily a consequence of substance dependence.

1. Introduction

There is growing evidence that reduced responsiveness to natural reinforcers predicts future drug use among substance-dependent samples. Specifically, reduced responsiveness to pleasant images has been found to correlate with increased alcohol cravings in detoxified alcoholics (Wrase et al., 2007) and to predict higher levels of substance use over the subsequent 6 months in samples dependent on alcohol (Heinz et al., 2007), heroin (Lubman et al., 2009), and tobacco (Versace et al., 2012). Utilising event-related potential (ERP) indices of attention to pleasant, unpleasant, neutral, and drug-related pictures, Lubman et al. (2009) found that in opioid-dependent participants, reduced attention allocation to pleasant pictures (relative to heroin-related pictures) predicted increased likelihood of frequent (weekly or more) heroin use 6-months later. Similarly, Versace et al. (2012) found that in smokers attempting to quit tobacco, a pattern of ERP responsiveness characterised by reduced attention to pleasant (but not unpleasant, neutral, or cigarette-related pictures) predicted reduced likelihood of abstinence at 10-, 12-, and 24-week follow-ups. Further support for such findings comes from an fMRI study of alcoholics tested 1–3 weeks after detoxification (Heinz et al., 2007) which found that reduced blood-oxygenation level dependent (BOLD) activation in structures associated with reward processing and response (i.e., thalamus and ventral striatum) to pleasant vs. neutral pictures predicted a higher number of drinking days over the following 6 months. In contrast, activation to alcohol-related or unpleasant pictures did not predict later alcohol consumption. Wrase et al. (2007) also found that alcoholics tested after 5–37 days abstinence showed reduced BOLD response in the ventral striatum, relative to healthy controls, during monetary reward expectation, and that lower BOLD responses in the alcoholic group (but not in controls) correlated with increased alcohol craving.

These studies all find that a blunted response to rewarding stimuli increases the likelihood of greater subsequent substance use. However, recent human and animal research suggests that this is more likely to reflect a function of being drug dependent, rather than a premorbid risk factor. For example, studies of sensitivity to

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lateral hypothalamic stimulation reward in rats after withdrawal from prolonged administration of alcohol (Schulteis, Markou, Cole, & Koob, 1995), amphetamine (Lin, Koob, & Markou, 1999), cocaine (Ahmed, Kenny, Koob, & Markou, 2002; Kenny, Polis, Koob, & Markou, 2003), nicotine (Skjei & Markou, 2003), and phencyclidine (Spielewoy & Markou, 2003) have consistently found that the magnitude and/or duration of the impairment of reward responsiveness increases with the dose and/or duration of drug administration.

According to the reward allostasis model (Koob & Le Moal, 2008), neural adaptations to chronic over-activation of reward circuitry during drug use underlie this impaired reward responsiveness. These adaptations manifest as dysphoria and anhedonia when the drug is withdrawn, motivating further substance use to "self-medicate" this reward deficit. Consistent with this model, there is evidence from human studies that anhedonia increases following the onset of substance abuse (Bovasso, 2001), predicts increased likelihood of relapse in dependent users attempting to quit (Cook, Spring, McChargue, & Doran, 2010; Leventhal, Waters, Kahler, Ray, & Sussman, 2009), and declines over time with successful abstinence in those recovering from substance dependence (Dawes, Sitharthan, Conigrave, Phung, & Weltman, 2011; Dawkins, Powell, Pickering, Powell, & West, 2009; Martinotti et al., 2011; McGregor et al., 2005; Newton, Kalechstein, Duran, Vansluis, & Ling, 2004).

Taken together, these findings suggest that impaired reward responsiveness is likely to emerge alongside the development of a substance use disorder, and may diminish with abstinence. This does not exclude the possibility that low reward responsiveness *prior* to onset of substance use could function as a premorbid risk factor, increasing vulnerability to heavy or frequent substance use later in life. However, research on adolescent risk-taking suggests that exaggerated, rather than blunted, reward responsiveness may predict initial onset of substance use and abuse. Exaggerated reactivity to reward in adolescence is widely reported (for a review, see Spear, 2011), and it has been argued that this enhanced reward reactivity may increase the likelihood of risky behaviour (including substance use) through its effects on the relative attribution of benefit vs. cost to an activity (Spear, 2011). Indeed, in a cross-sectional fMRI study of adolescents aged 13–17, Galvan, Hare, Voss, Glover, and Casey (2007) found that BOLD response in the nucleus accumbens (a key component of the reward circuit) to monetary reward correlated positively with self-reported likelihood of future engagement in risk-taking activities and anticipated positive consequences of such activities, while correlating negatively with anticipated negative consequences of such risky activities. Regarding substance use specifically, a longitudinal study (Stice, Yokum, & Burger, 2013) found that, in adolescents with no history of substance use at baseline (mean age 15.3), increased dorsal striatal response to monetary reward predicted increased likelihood of onset of substance use in the following year. Adolescents who already had a history of substance use at baseline showed lower striatal response to monetary reward than those with no substance use history, further supporting a model whereby increased reward response predicts onset of substance use but, once substance use is commenced, it causes blunting of reward response.

It is unclear whether the relationship between exaggerated reward response and substance use would also be present in adults with no prior history of substance use, or whether it is specific to adolescence. This is difficult to determine in practice because adolescence and early adulthood are associated with the highest rates of substance use onset, with few adults commencing substance use at a later age. Nevertheless, the maturation of striatal reward-related neural systems, and the associated peak in sensation-seeking in adolescence, combined with the incomplete maturation of prefrontal cortical systems (Casey & Jones, 2010; Luciana, Wahlstrom, Porter, & Collins, 2012), may mean that the relationship between reward response and risky substance use is particularly strong in adolescence. The decline in impulsivity, sensation-seeking, and reward-related behavioural activation that accompanies the transition to adulthood (Luciana et al., 2012), along with the final stages of maturation of prefrontal cortical brain structures, could be expected to dampen the relationship between reward response and risky behaviour seen in adolescents (Casey & Jones, 2010).

Prospective research exploring the relationship between adolescent reward responsiveness and substance use remains limited, particularly in terms of predicting later problematic use. To address this gap, we examined attenuation of the acoustic startle-elicited P300 component of the visual event-related potential (ERP) during viewing of pleasant and unpleasant pictures, relative to its amplitude during viewing of affectively neutral pictures, in a sample of 11–13 year-olds, when participants had either no, or extremely limited, previous use of alcohol or other drugs. The amplitude of the P300 indexes allocation of limited attentional resources to the startling stimulus. Its degree of attenuation (amplitude reduction) in the presence of an affective stimulus is thus a measure of the affective stimulus' ability to capture attention (Schupp, Cuthbert, Bradley, Birbaumer, & Lang, 1997).

Participants were assessed for alcohol use outcomes approximately 4 years later, an age at which, despite legal restrictions (the legal drinking age in Australia is 18), over 80% of this sample had at least some experience with alcohol. We were particularly interested in outcomes indicative of risk for alcohol use disorders, including frequent alcohol consumption, binge-drinking, and experience of alcohol-related problems among adolescents who had consumed alcohol. Following Spear (2011), our hypothesis was that greater responsiveness to reward stimuli, as reflected in increased P300 attenuation during viewing of pleasant pictures, would predict frequent alcohol use and alcohol-related problems later in adolescence. Response to unpleasant pictures was also subjected to exploratory analyses. While Spear (2011) suggests that reduced sensitivity to unpleasant stimuli may increase propensity towards risk-taking, there does not appear to be any empirical literature on studies of humans that suggests that it is a predictor of problematic substance use.

2. Methods

2.1. Participants

Participants were recruited from the Orygen Adolescent Emotional Development Study, a longitudinal, multi-method study of adolescents from across metropolitan Melbourne, Australia. Informed consent was obtained from participants and their parents/guardians in accordance with procedures approved by the University of Melbourne Ethics Committee. Further details about recruitment and selection of participants in this study can be found elsewhere (Whittle et al., 2008). Of 240 eligible participants, a subset of 72 (38 males, 34 females; mean age = 12.8 years, SD = .4) was randomly selected to complete baseline EEG assessment. Of these participants, 58 (26 males, 32 females; mean age 16.6, SD = .5) completed the follow-up assessment of alcohol use conducted a mean of 3.8 years (SD = .4) after baseline. There were no significant differences between those that completed the follow-up assessment and those who did not in the P300 parameters subjected to analyses ($ps > .354$), socioeconomic status ($p = .859$), or age at baseline ($p = .176$). However, those who were followed up were more likely to be female than those who were not ($\chi^2 = 7.565$, $p = .006$).

Participants were screened at baseline for current and past case level Axis I disorders by trained research assistants using the Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version-5 (K-SADS-E-5) (Orvaschel, 1995). Overall, nine participants met criteria for a current psychiatric diagnosis (attention deficit hyperactivity disorder (ADHD), $n = 3$; conduct disorder, $n = 1$; depressive disorder not otherwise specified, $n = 1$; oppositional defiant disorder (ODD), $n = 1$; separation anxiety disorder, $n = 1$; specific (blood/injection/injury) phobia $n = 1$; social phobia, $n = 2$), including one participant who met criteria for two current disorders (ADHD and conduct disorder). Of those nine participants, two met criteria for additional past disorders (one with current ADHD and past ODD, one with current ODD, past ADHD). An additional three participants met criteria only for past psychiatric diagnoses (major depressive disorder (MDD), $n = 1$; obsessive compulsive disorder, $n = 1$; specific (animal) phobia, $n = 1$). Eight of the 12 participants