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Dysfunctional feedback processing in adolescent males with conduct disorder

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ABSTRACT

Abnormalities in neural feedback-processing systems may play a role in the development of dysfunctional behavior in individuals diagnosed with conduct disorder (CD). The present study investigated the relation between CD adolescents and feedback processing by measuring event-related potentials (ERPs) in a single outcome gambling task, which included reward valence (loss and gain) and reward magnitude (10 and 50 cents) as outcomes. N2 and P3 components have been established as effective indicators in studies of behavioral disinhibition, reward processing, and decision-making. Eighteen adolescent males (age: 13–17 years) diagnosed with CD and 19 healthy age-matched male controls were recruited. Compared to healthy controls, CD individuals exhibited reduced N2 amplitudes in response to loss condition. There was also a significant decreased P3 amplitude in all conditions. The amplitudes of P3 were negatively correlated with impulsivity scores across both groups, and the amplitudes of N2 were positively correlated with impulsivity scores across both groups. Our findings suggest that adolescents with CD may be impaired in neural sensitivity feedback and the processing of environmental cues compared to healthy controls. Moreover, N2 and P3 may be reliable indices to detect different sensitivity in reward and punishment feedback processing.

1. Introduction

Conduct disorder (CD) is a psychiatric disorder that emerges during childhood or adolescence. Affected individuals show repetitive and persistent patterns of violating the basic rights of others and difficulty in following major age-appropriate societal norms (APA, 2000). CD is accompanied by various behavioral problems, such as impulsivity, aggression, and risk-taking (Dougherty et al., 2000; Fairchild et al., 2009; Mathias et al., 2007), which represent latent externalizing traits. Previous studies have shown that individuals with CD lack empathy and compassion, and that they display impaired control over their emotions and impulses (Dougherty et al., 2000). Similar to patients with attention deficit hyperactivity disorder (ADHD), individuals with CD show deficits in tasks requiring sustained attention and cognitive function (Banaschewski et al., 2003). These characteristics are indicative of potential deficits in feedback-evaluation and self-monitoring systems (Sterzer et al., 2007).

With the ability to predict and respond to feedback cues, we learn to survive in and adapt to the environment (Flores et al., 2015). The experiences that occur in anticipation and response to feedback appear to have important implications for our interpersonal adaption and intrapsychic regulation (Cole et al., 1994). A number of studies have addressed the influences of positive and negative feedback on cognition, motivation and behavior (Schultz, 2007). In particular, anticipation of positive feedback (reward or gain) facilitates approach behavior, whereas anticipation of negative feedback (punishment or loss) facilitates avoidance behavior (Young, 1959). The Reinforcement Sensitivity model developed by Gray et al. provides one of the most cited theory for explaining reward and punishment processing (Bjork and Pardini, 2015; Byrd et al., 2014; Colder and O'Connor, 2004; Goodnight et al., 2006; Gray, 1991). Gray proposed two main systems: the behavioral inhibition system (BIS) and behavioral approach system (BAS). According to Gray, BIS serves to inhibit behavior in response to aversive stimuli or punishment, while BAS is thought to be sensitive to reward feedback or nonpunishment (Gray, 1991). Convergent findings from neurobiological studies imply that CD adolescents exhibit an aberrant difficulty in feedback-evaluation and adapting their behavior accordingly (Brazil et al., 2009, 2013; Salim et al., 2015).

Recent neuroimaging studies of individuals with CD have demonstrated structural abnormalities in various brain regions, including the bilateral temporal lobes, the orbitofrontal cortex, and the anterior

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cingulate cortex (ACC), which are brain structures associated with decision-making and reward processing (De Brito et al., 2009; Fairchild et al., 2011; Huebner et al., 2008; Jiang et al., 2015; Zhang et al., 2014). Generally, individuals benefit from these feedback-evaluations and feedback-monitoring systems to guide their decision-making and to implement optimal behavior. Impaired processing or dysfunction in these brain areas may account for the lack of empathy and self-monitoring observed in CD individuals. People with CD may find it difficult to construct a socially adaptable behavior system (Gelhorn et al., 2007; Morcillo et al., 2012; Nock et al., 2006).

Previous studies have examined electrophysiological correlates (e.g., ERPs) of feedback processing, including P2, N2 and P3 components (Franken et al., 2010; Holroyd and Coles, 2002; Pfabigan et al., 2011; Salim et al., 2015). These components are particularly sensitive to feedback valence (gain/loss), feedback magnitude (large/small), and behavioral outcome evaluations (positive/negative) (van Meel et al., 2005; Wu and Zhou, 2009). They have been proposed to encode different features of feedback evaluation and reflect motivational significance of feedback (Gentsch et al., 2013). For instance, P2 is implicated in attention selection and salience detection (Potts et al., 2006), and is related to reward system of brain (Riis et al., 2009; San Martin et al., 2010). Furthermore, the N2 and P3 components are used to examine cognitive processes that have been correlated with decision-making and feedback-evaluation processing (Baker and Holroyd, 2011; Kam et al., 2012; Kamarajan et al., 2010). Specifically, the P3 reflects a later, top-down controlled feedback evaluation process (Cui et al., 2013), whereas the N2 was thought to reflect the binary evaluation of resultant good versus bad outcomes (Holroyd et al., 2006; Kamarajan et al., 2009). These observations suggest that the two aspects underlying outcome evaluation are processed separately and rapidly in the brain (Wu and Zhou, 2009).

The N2 component of ERP has been used to study patients who exhibit traits consistent with behavioral disinhibition abnormalities. N2 is a fronto-central negative wave, occurring around 200 ms after stimulus onset, which indexes cognitive processes of stimulus evaluation, classification, decision-making and executive function, and these may be important for responding to environmental cues (Luck, 2005). Several researchers have focused on studying the behavioral disinhibitory processing in adolescents with externalizing problems using N2. The amplitude of N2 has been reported to be positively correlated with callous/unemotional temperament traits which may denote a more severe form of CD (Sumich et al., 2012). Compared to healthy controls, adolescents with comorbid ADHD + CD display significantly prolonged latency of both N2 and P3 (van Meel et al., 2005). Albrecht et al. found that the ADHD-only and oppositional defiant disorder (ODD)/CD-only groups displayed reduced Stop-N2 amplitude using a stop-task. Adolescents with comorbid ADHD + ODD/CD also showed similar or less disinhibition prominent deficits than other groups (Albrecht et al., 2005). Additionally, it has also been suggested that the N2 amplitude was reduced in the externalizing spectrum or juvenile non-psychopathic offenders compared with the control group (Anjana et al., 2010; Dikman and Allen, 2000; Kroger et al., 2014; Vila-Ballo et al., 2014).

P2, a medial frontal positive component at approximately 200 ms poststimulus is associated with the identification of task-relevant perceptual representations (Potts et al., 2006). The spatio-temporal distribution of P2 is similar with N2. P2 is elicited to error choices or responses resulting in monetary loss (Potts et al., 2006). It has been argued that amplitude of P2 is sensitive to feedback information which has a motivational value, and has been found to reflect sensitivity toward reward (Martin and Potts, 2009; Salim et al., 2015). Previous study reported that P2 amplitude in psychopathic individuals was enhanced for predicted rewards and reward omissions, but not for unpredicted feedback using a passive gambling task (Salim et al., 2015). When using an Emotional Stroop task, researchers found that individuals scoring high on psychopathic traits display reduced P2 amplitude to negative feedback compared to controls (Carolan et al., 2014). Larger P2 amplitude has also been reported in ADHD children, indicating deficiencies in early sensory processing in ADHD (Wiersema et al., 2006).

The P3 wave is a stimulus-evoked centro-parietal positivity that occurs approximately 300 to 400 ms after a stimulus. The P3 is most commonly associated with expectation violation. It has been linked to a broadly distributed neural network involving the locus-coeruleus norepinephrine system, and it is sensitive to motivationally important events (Ito and Bartholow, 2009; Wu and Zhou, 2009). Reduced P3 amplitude has been consistently linked to a spectrum of externalizing disorders, such as CD (Cappadocia et al., 2009; Iacono et al., 2002), illicit substance abuse (Iacono et al., 2002), antisocial behavior (Bauer and Hesselbrock, 2001, 2003; Costa et al., 2000) and ADHD (Iacono et al., 2002). In a comprehensive study, Iacono et al. found that reduced P3 amplitude was associated with several behavior disinhibition disorders, including ADHD, ODD, CD, antisocial personality disorder, alcoholism, as well as illicit drug abuse and dependence (Morcillo et al., 2012). In sum, these previous studies have shown that P2, N2 and P3 components are all linked to patients with impaired feedback processing which is found underlying the behavioral adaptation deficits.

However, the majority of neuropsychologic studies related to CD adolescents have rarely considered the confounding effects of comorbid psychiatric conditions (e.g. ADHD). Few studies have directly examined the feedback evaluation in adolescents with CD. It also remains unknown as to whether the symptoms of CD are associated with reward-processing abnormalities. Therefore, the present study aimed to examine whether CD adolescents have abnormalities in the evaluation of monetary reward and punishment while performing a simple outcome gambling task. This study also investigates whether the early N1, P2, later N2 and P3 components correlate with externalizing factors, such as impulsivity. Since there were distinct gender differences observed in the ERP indices of affective stimuli, the participants in the present study were designed to be male adolescents only (Criado and Ehlers, 2007). Therefore, our first hypothesis is that adolescents with CD will show decreased amplitude in both N2 and P3 components. Second, we posited that adolescents with CD will exhibit increased amplitude in P2 component. Third, we think that adolescents with CD will demonstrate higher impulsivity scores on the behavioral measures. And lastly, the decreased N2 and P3 amplitude will be correlated with increased impulsivity scores.

2. Methods

2.1. Participants

40 participants were recruited, 3 participants were excluded due to excessive artifacts in the EEG recording. Finally, CD group consisted of 18 male adolescents (age range: 13–17 years, mean: 15.4 years, standard deviation [SD]: 1.3 years), who were recruited from the outpatient clinics affiliated with the Second Xiangya Hospital of Central South University in Changsha, Hunan, China. Controls included 19 healthy age-matched male adolescents (mean age: 15.5 years, SD: 1.3 years), recruited from a school in the same city. The study was approved by the Ethics Committee of the Second Xiangya Hospital of Central South University. Written informed consent was obtained from all participants and their parents. All participants received monetary compensation upon completion of the study.

CD was diagnosed independently by two psychiatrists, according to the Structured Clinical Interview for the *DSM-IV-TR* Axis I Disorders-Patient Edition (SCID-I/P) (First et al., 2002), which has been translated into Chinese and adapted for use in both patients and healthy individuals (Cassidy et al., 2011; Shi et al., 2005). Additionally, one parent of each subject was interviewed to obtain detailed information. The psychiatrists made the final decision in the case that information obtained from the patients and parents was inconsistent.