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Reward processing deficits and impulsivity in high-risk offspring of alcoholics: A study of event-related potentials during a monetary gambling task

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ABSTRACT

Background: Individuals at high risk to develop alcoholism often manifest neurocognitive deficits as well as increased impulsivity. The goal of the present study is to elucidate reward processing deficits, externalizing disorders, and impulsivity as elicited by electrophysiological, clinical and behavioral measures in subjects at high risk for alcoholism from families densely affected by alcoholism in the context of brain maturation across age groups and gender.

Methods: Event-related potentials (ERPs) and current source density (CSD) during a monetary gambling task (MGT) were measured in 12–25 year old offspring ($N = 1864$) of families in the Collaborative Study on the Genetics of Alcoholism (COGA) Prospective study; the high risk (HR, $N = 1569$) subjects were from families densely affected with alcoholism and the low risk (LR, $N = 295$) subjects were from community families. Externalizing disorders and impulsivity scores were also compared between LR and HR groups.

Results: HR offspring from older (16–25 years) male and younger (12–15 years) female subgroups showed lower P3 amplitude than LR subjects. The amplitude decrement was most prominent in HR males during the loss condition. Overall, P3 amplitude increase at anterior sites and decrease at posterior areas were seen in older compared to younger subjects, suggesting frontalization during brain maturation. The HR subgroups also exhibited hypofrontality manifested as weaker CSD activity during both loss and gain conditions at frontal regions. Further, the HR subjects had higher impulsivity scores and increased prevalence of externalizing disorders. P3 amplitudes during the gain condition were negatively correlated with impulsivity scores.

Conclusions: Older male and younger female HR offspring, compared to their LR counterparts, manifested reward processing deficits as indexed by lower P3 amplitude and weaker CSD activity, along with higher prevalence of externalizing disorders and higher impulsivity scores.

Significance: Reward related P3 is a valuable measure reflecting neurocognitive dysfunction in subjects at risk for alcoholism, as well as to characterize reward processing and brain maturation across gender and age group.

1. Introduction

Alcoholism is a complex disorder with multiple etiological pathways involving a host of genetic and environmental factors along with their interactions in its onset, manifestations, course, and treatment outcome. Converging evidence supports the notion that there may be a wide range of genetic, biological, neurocognitive and environmental factors involved in the causal pathways to develop alcoholism. Electrophysiological measures, such as electroencephalogram (EEG), event-related potentials (ERPs), and event-related oscillations (EROs) have played a vital role as biological markers or endophenotypes to understand neurocognitive mechanisms involved in alcohol use and related disorders (see Porjesz et al., 2005, for a review). These electrophysiological methods provide a direct measure of brain activity with high temporal sensitivity to understand neurocognitive processes, while being non-invasive and inexpensive for its applications. Specifically, ERPs can measure dynamically changing brain activity in real time during perceptual, motor, and cognitive processing while performing a task (Picton and Hillyard, 1988). ERPs have been widely and successfully used to examine neurocognitive processing during various experimental tasks in normal populations as

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well as in a range of clinical conditions including alcoholism (Porjesz and Begleiter, 1985; Begleiter and Porjesz, 1990a; Porjesz et al., 1996, 2005; Porjesz and Begleiter, 1997).

A landmark finding in the electrophysiology of human alcoholism is that individuals with alcohol dependence as well as their high risk offspring show low voltage P3(00) amplitude (for reviews, see Begleiter and Porjesz, 1990b; Porjesz and Begleiter, 1990, 1991, 1997; Polich et al., 1994; Porjesz et al., 2005). P3 is a robust, positive going ERP wave occurring around 300–700 ms following the onset of a stimulus, indicative of its context (Donchin and Coles, 1988) or importance (Sutton et al., 1978; Begleiter et al., 1983) during signal/cognitive processing. Since the first report by Begleiter et al. (1984) of low P3 amplitude in the sons of alcoholic fathers (in a study without any alcohol challenge), this finding has been replicated across many different experimental paradigms in male as well as female high risk subjects (i.e., offspring of alcoholics) in diverse samples (for reviews, see Porjesz et al., 2005; Rangaswamy and Porjesz, 2014).

It was a turning point in alcoholism research that lower P3 amplitude, observed in alcoholic individuals (Porjesz and Begleiter, 1981; Oscar-Berman, 1987; Pfefferbaum et al., 1987; Porjesz et al., 1987; Cohen et al., 1995, 1997b; Rodriguez Holguin et al., 1999a; Hada et al., 2000; Prabhu et al., 2001; Cohen et al., 2002; Suresh et al., 2003; Kamarajan et al., 2005a, 2010; Fein and Chang, 2006; Fein and Andrew, 2011), was also found in individuals with a family history of alcoholism who were considered to be genetically vulnerable but had not yet developed alcoholism (Elmasian et al., 1982; O'Connor et al., 1987; Porjesz and Begleiter, 1990; Benegal et al., 1995; Porjesz et al., 1996; Ramachandran et al., 1996; Kamarajan et al., 2005b) and had never or only rarely been exposed to alcohol (Begleiter et al., 1984, 1987; Whipple et al., 1988, 1991; Hill and Steinhauer, 1993; Steinhauer and Hill, 1993; Hill et al., 1995). However, it must be stated that P3 reduction in high risk subjects, as a phenomenon, is not consistent or ubiquitous in the literature, but often with equivocal as well as subgroup-specific findings, and has been found to be strongest in younger males (for a meta-analysis, see Polich et al., 1994). For example, some studies reported that P3 reductions were observed only in boys of alcoholic parents (e.g., Hill and Steinhauer, 1993), while other studies found the effect in both genders (e.g., Porjesz et al., 1996). Similarly, this effect has been found to be stronger in younger subjects (e.g., Begleiter et al., 1987; Polich et al., 1994) but still robust in adolescents/young adults (O'Connor et al., 1987; Porjesz and Begleiter, 1990; Porjesz et al., 1996; Ramachandran et al., 1996; Van der Stelt et al., 1998; Kamarajan et al., 2005b). Possible reasons for these inconsistent and/or subgroup specific findings may include the following: (i) the studies may differ methodologically (in terms of sample characteristics, task paradigms, ERP recording and signal processing, statistical techniques, etc.); (ii) definition of "risk" may differ across studies; and (iii) P3 reduction may in fact be a function of age, gender, and task paradigms and may be moderated by several confounding (or unmeasured) factors such as personality traits, situational/familial/sociocultural factors, and other variations due to genetic and epigenetic factors.

It is also important to note that low P3 is not unique to alcoholics and their high risk relatives, but is also found in individuals with one or more externalizing disorders or disinhibitory conditions (Carlson et al., 1999; Hill and Shen, 2002; Iacono et al., 2002, 2003; Iacono and McGue, 2006; Patrick et al., 2006; Carlson et al., 2007; Hicks et al., 2007; Iacono et al., 2008; Patrick, 2008; Gilmore et al., 2010a,b, 2012). As reported by several studies, an underlying feature among risk propensity, externalizing disorders and alcoholism is the concept of "impulsivity", which is a conglomerate of personality traits that can result in premature, unduly risky and poorly conceived actions, and is known to be closely related to disinhibitory traits and clinical vulnerability (Gorenstein and Newman, 1980; Martin et al., 1994; Olson et al., 1999; Krueger and Piasecki, 2002; Hall et al., 2007; Kamarajan et al., 2007; Crews and Boettiger, 2009; Romer et al., 2009). Interestingly, P3 amplitude has been found to be either negatively correlated with impulsivity or lower in high impulsive subjects regardless of having a diagnosis of alcoholism and/or related disorders (Justus et al., 2001; Moeller et al., 2004; Chen et al., 2007; Ruchsow et al., 2008; Kamarajan et al., 2010).

Alcoholism has often been characterized as a reward deficit disorder (Koob, 2013; Forbes et al., 2014), and several studies have successfully used ERPs to examine reward processing in healthy individuals (Homberg et al., 1980, 1981; Begleiter et al., 1983; Ivanitsky et al., 1986; Gehring and Willoughby, 2002; Yeung and Sanfey, 2004; Hajcak et al., 2005; Nieuwenhuis et al., 2005; Toyomaki and Murohashi, 2005a,b; Hajcak et al., 2006, 2007; Holroyd et al., 2006; Yu and Zhou, 2006; Kamarajan et al., 2009, 2010), as well as in alcoholic and HR offspring (Porjesz et al., 1987; Ramsey and Finn, 1997; Fein and Chang, 2008). Major ERP components studied during outcome/feedback processing during monetary gambling tasks (MGT) are the outcome-related negativity (ORN) or N2 (between 200 ms and 300 ms) and the outcome-related positivity (ORP) or P3 (between 300 ms and 600 ms) (Gehring and Willoughby, 2002; Yeung and Sanfey, 2004; Hajcak et al., 2005, 2006; Yeung et al., 2005; Holroyd et al., 2006; Cohen and Ranganath, 2007; Kamarajan et al., 2009). In our previous ERP study of reward processing using a MGT in alcoholics, we found that alcoholics showed significantly lower amplitudes of N2/ORN and P3/ORP components and decreased current density in cingulate gyrus, along with higher levels of impulsivity and risk-taking features than controls (Kamarajan et al., 2010). While FRN/N2 is another important component of feedback processing, the current study focuses solely on the P3 component for the following reasons: 1) dealing with both components (P3 and N2) in a single study with multiple factors (risk group, gender, age group) may render the study too complex; 2) with regard to alcoholism and risk, P3 is considered to be the most robust ERP component and a sensitive biomarker, and therefore the analysis of P3 has assumed its precedence in the current study; 3) FRN/N2 is a relatively subtle component and more prone to artifact distortions, rendering it more difficult to measure (especially in such a large sample of adolescents and young adults) compared to the large P3 component; and 4) implementation of a more sophisticated source localization method (e.g., sLORETA) may be essential to examine the key brain sources (e.g., anterior cingulate region) attributed to the FRN (Crowley et al., 2013). For these reasons, only the P3 component has been dealt with in the current study. As current source density (CSD), a source derivation method of electrophysiological activity, has been successfully used in several neuropsychiatric disorders including alcoholism (for a review, see Kamarajan et al., 2015), we have also compared CSD topography across the groups (see Section 2.5 for more information on the CSD method).

The overarching aim of the present study is to examine reward processing (as indexed by P3 amplitude and CSD), and externalizing features in HR offspring recruited from high density alcoholism families in comparison with LR (comparison) subjects recruited from a community sample in the COGA Prospective Study, in the context of brain maturation across age groups and gender. This is the first ERP study using a monetary gambling paradigm to study HR offspring, and has been designed to examine the following hypotheses: (1) HR offspring will show lower P3 amplitude during reward processing than low-risk (LR) individuals from the comparison families; 2) HR group will show current density differences in both magnitude and topography as compared to the LR group; and (3) HR group will have higher impulsivity scores than the LR group. As the literature regarding P3 reduction in high risk subjects, as mentioned earlier, has often been equivocal with regard to gender- and age-based subgroups, the current study also investigates the effects of age and gender on P3 amplitudes in specific subgroups. It is expected that findings of the present study may shed further light on the complex relationship among reward processing deficits (indexed by P3 amplitude and CSD), impulsivity, and externalizing disorders involved in the development of alcoholism.