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Reward anticipation and trait anhedonia: An electrophysiological investigation in subjects with schizophrenia

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HIGHLIGHTS

- Subjects with schizophrenia are unable to integrate the incentive magnitude and reward value of future events as studied by the P3 response in event-related potentials.
- Avolition and expressive deficits are not related to P3 amplitude.
- These findings might foster the development of innovative rehabilitation treatments in schizophrenia.

ABSTRACT

Objective: Investigate impairment of reward anticipation in subjects with schizophrenia (SCZ) and its association with negative symptom dimensions and hedonic experience.
Methods: Event-related potentials (ERPs) were recorded, in thirty SCZ and twenty-three matched healthy controls (HC), during a "Monetary Incentive Delay" task in which reward and loss cues (incentive cues of positive and negative value) of different magnitude, as well as neutral cues were presented.
Assessments: anticipatory and consummatory pleasure, trait anhedonia and motivation in all subjects; avolition and expressive deficit in SCZ.
Results: SCZ had lower motivation but comparable hedonic experience with respect to HC. In HC, during reward anticipation, the early P3 was larger for large magnitude incentives, irrespective of their valence, while the late P3 was larger for large reward. In SCZ, early P3 did not discriminate the incentive magnitude and the late P3 was larger for large loss. Early P3 amplitude for large magnitude incentives was inversely related to trait social anhedonia but not to negative symptoms dimensions.
Conclusions: SCZ are unable to integrate the incentive magnitude and reward value of future events in the context of their ongoing task. P3 abnormalities are associated with trait anhedonia, but not with negative symptoms dimensions.
Significance: In line with recent studies, our findings indicate that anhedonia and avolition are partially independent constructs.

1. Introduction

1.1. Negative symptoms domains

Negative symptoms have long been recognized as a central feature of the phenomenology of schizophrenia, dating back to the early descriptions by Kraepelin (1919) and Bleuler (1950). In contrast to the positive symptoms of schizophrenia (such as delusions and hallucinations) that represent "added" phenomena, the term "negative" implies the loss of behaviors, interests, motivation and desires (Millan et al., 2014).

Negative symptoms include affective flattening or blunting (i.e., reduced intensity and range of emotional expression), alogia (i.e., reduced spontaneous speech and loss of conversational fluency), asociality (i.e., diminished interest in social drive or interest and desire for affiliation), avolition (reduced interest and motivation for productive activities, or sense of purpose) and anhedonia (i.e., reduced ability to experience or anticipate pleasure) (Kirkpatrick

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et al., 2006; Burbridge and Barch, 2007; Barch et al., 2008; Brune et al., 2008; Tremeau et al., 2008; Messinger et al., 2011). In subjects with schizophrenia, the anticipatory component of anhedonia, i.e., looking forward to a reward, recreational or other pleasurable experience (“wanting”), is more markedly and consistently impaired than the appreciation (“liking”) of the experience itself (consummatory anhedonia) (Gard et al., 2007; Foussias and Remington, 2010; Strauss et al., 2013). As a matter of fact, current research suggests that subjects with schizophrenia have intact in-the-moment hedonic experience, but show abnormalities in other facets of the motivational system (Simpson et al., 2012; Mann et al., 2013; Strauss et al., 2013).

Several factor analytic studies have shown that negative symptoms cluster in two factors: “Expressive deficit”, including reduction of facial and vocal expression, expressive gestures, quantity of speech and spontaneous elaboration, and “Avolition”, including anhedonia, asociality and avolition (Kimhy et al., 2006; Nakaya and Ohmori, 2008; Kirkpatrick et al., 2011; Strauss et al., 2012; Galderisi et al., 2013; Mucci et al., 2015a). Negative symptoms and functional outcomes have consistently been linked, with several studies reporting worse functional outcomes in individuals with more prominent negative symptoms (Milev et al., 2005; Rosenheck et al., 2006; Fulford et al., 2013).

Within negative symptoms, avolition has emerged as the most important predictor of functional impairment. It has demonstrated a significant impact on instrumental role performance, family integration, extended family functioning, and social/leisure functioning (Sayers et al., 1995; Green et al., 2012), as well as on a latent variable representing a composite measure of functioning in all the above areas (Galderisi et al., 2014). The expressive deficit subdomain of negative symptoms did not demonstrate a relationship with functional outcome in schizophrenia, particularly after accounting for the predictive role of avolition (Foussias et al., 2009; Green et al., 2012; Galderisi et al., 2013, 2014). Functional magnetic resonance imaging (fMRI) studies (Millan et al., 2014) consistently reported in subjects with schizophrenia anomalies in processes related to motivation, anticipation of reward, effort, approach behavior and goal-directed actions. In order to assess motivational impairment, many studies have focused on reward prediction in schizophrenia, with findings of striatal dysfunction (Juckel et al., 2006a,b; Schlagenhauf et al., 2008; Waltz et al., 2009; Mucci et al., 2015b). These studies have suggested that motivational deficits in schizophrenia could be related to impaired prefrontal–striatal circuits (Barch and Dowd, 2010; Mucci et al., 2015b).

Studies using fMRI have a low temporal resolution and are not able to provide the precise chronological delineation of brain activity during reward anticipation, therefore, using techniques with a high temporal resolution such as event-related potentials (ERPs), information provided by fMRI might be integrated. ERPs provide a functional measure of electrical brain activity time-locked to an internal or external event and identify discrete stages of information processing (Pfefferbaum et al., 1995).

1.2. Reward-related electrophysiological markers

Two ERP components, i.e., P3 (Johnson, 1986) and contingent negative variation (CNV) (Walter et al., 1964), have been previously studied as putative reward-related electrophysiological markers (Goldstein et al., 2006; Broyd et al., 2012; Pfabigan et al., 2014; Schevernels et al., 2014), indexing different stages of anticipatory reward processing such as the allocation of attention (Polich and Kok, 1995), motivational processes (Groom et al., 2010), along with motor and cognitive preparation (Boecker et al., 2014). The P3 is a positive-going ERP deflection peaking between 300 and 600 ms after stimulus presentation. Several studies have shown that its amplitude is related to attention spent on a task (Polich and Kok, 1995), task relevance and complexity (Isreal et al., 1980; Coles et al., 1985) and value and informative relevance of stimuli (Johnson et al., 1985; Picton, 1992).

Previous investigations have established that scalp-recorded P3 is not a unitary phenomenon, indeed the P3 component has been shown to represent a complex response, and multiple peaks in the time window of P3 are observed in relation to different experimental designs (Rushby et al., 2005; Lawrence and Barry, 2009; Barry et al., 2011, 2013), and task demands (Polich, 2007; Wronka et al., 2008). The multiple P3 peaks are generally also differentiated by their topography. In studies examining stimulus intensity effects on P3 (Rushby et al., 2005; Barry et al., 2013), only an early P3 (P3a, peaking around 300 ms) was found to be related to the intensity of the stimulus, i.e., their physical salience (Rushby et al., 2005; Rushby and Barry, 2009; Barry et al., 2011).

The CNV component is a slow negative wave that is observed between a warning and an imperative stimulus, and consists of two sub-components: an early wave (‘orienting’ O wave) related to the alerting properties of the cue, and a later component (‘expectancy’ E wave) associated with the anticipation of the target stimulus and the engagement of effortful processes associated with the required response (Broyd et al., 2012). The CNV amplitude is related to motivation (Cant and Bickford, 1967), effortful attention (Gomez et al., 2007) and anticipation of affective or motivationally salient stimuli (Baas et al., 2002).

Three studies have highlighted the role of the P3 as index of brain activity associated with anticipation of monetary reward (Broyd et al., 2012; Pfabigan et al., 2014; Schevernels et al., 2014). One study used a Monetary Incentive Delay (MID) task with monetary gain and loss conditions. The cue-P3 response was enhanced for cues anticipating monetary gain, but not for those anticipating monetary loss (Broyd et al., 2012). A second study measured P3 component in response to a modified version of the MID task with potential monetary gain or loss and found that healthy controls exhibited larger P3 components during reward versus non-reward and loss conditions (Pfabigan et al., 2014). A third study measured P3 correlates of reward anticipation during a cued visual discrimination task in which the targets were preceded by cues indicating simultaneously the level of task difficulty and the possibility of receiving a monetary reward in case of a correct and fast response and found that P3 amplitude was larger for reward cues compared to neutral cues (Schevernels et al., 2014).

Furthermore, one study has explored the neural correlates of anticipatory brain activity associated with monetary rewards of different magnitude (Goldstein et al., 2006). The authors, with a warned reaction-time paradigm in which different amounts of monetary reward (0, 1 and 45 cents) varied across blocks of trials, showed an increase of P3 amplitude to the warning stimulus as a function of reward magnitude. The amplitude of the P3 was significantly larger for the 45¢ condition than for 1¢ and 0¢ conditions. Taken together, ERP studies of reward anticipation provide evidence about sensitivity of the P3 amplitude to the anticipation of monetary reward and to reward magnitude. The amplitude of cue P3 for reward anticipation was found to correlate with fMRI BOLD signal for the contrast reward vs neutral anticipation in the ventral striatum (Pfabigan et al., 2014). No study has attempted to assess simultaneously the effects of magnitude and reward value on P3 amplitude.

Results relevant to CNV amplitude in relationship with reward or loss anticipation are somewhat mixed. Some authors observed no effect of cues anticipating monetary gain and loss on CNV amplitude (Goldstein et al., 2006; Broyd et al., 2012), while others, using only reward and neutral conditions, reported a larger CNV amplitude for the reward condition (Hughes et al., 2013; Plichta et al., 2013; Schevernels et al., 2014). Only one study found that