Addictive Behaviors 39 (2014) 1026–1032

Contents lists available at ScienceDirect

Addictive Behaviors

Reward-system effect (BAS rating), left hemispheric "unbalance" (alpha band oscillations) and decisional impairments in drug addiction

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HIGHLIGHTS

- Substance abuse group showed an increased left-hemisphere activity for reward choices.

ARTICLE INFO

Available online 20 February 2014

Keywords:
Drug-addition
Left lateralization effect
BAS
Reward mechanism
Alpha brain oscillations
Iowa Gambling Task

ABSTRACT

The current research explored the impact of cortical frontal asymmetry (left-lateralization effect) and Behavioral Activation System (BAS) on Substance Use Disorder (SUD) in decisional processes using the Iowa Gambling Task (IGT). Forty SUD participants and forty-two controls (CG) were tested using the IGT. Behavioral responses (gain/loss options), BIS/BAS scores and lateralized alpha band modulation (LTA) were considered. The SUD group increased the tendency to opt in favor of the immediate reward (loss strategy) more than the long-term option (win strategy) compared to the CG. Secondly, higher reward-subscale scores were observed in SUD. Thirdly, SUD showed an increase in left-hemisphere activation in response to losing (with immediate reward) choices in comparison with the CG. An imbalanced left hemispheric effect related to higher BAS trait could explain this "reward bias," because these components were found to explain (through the regression analysis) the main behavioral deficits.

1. Introduction

A vast amount of research has suggested that drug abusers might have difficulty in making advantageous decisions that opt in favor of a longer term larger reward than an immediate smaller reward (Bolla et al., 2003). Indeed, compulsive drug use can be described as a condition associated with dysfunctional brain mechanisms that subvert the ability to make decisions (Allen, Moeller, Rhoades, & Cherek, 1998; Barry & Petry, 2008; Mitchell, Fields, D'Esposito, & Boettiger, 2005). Substance abuse could arise from poor decision-making skills that lead individuals with Substance Use Disorders (SUD) to ignore long-term negative consequences in the interest of immediate gratification or relief from uncomfortable states. A tendency was observed for people with SUD, when confronted with a decision that involves a conflict between an immediate reward which has a long-term possible negative consequence (no larger reward later), to choose the immediate reward at these expense of negative consequences (Bechara, 2005; Verdejo-García & Pérez-García, 2008).

Thus, drug dependence may be related to more receptiveness to the reinforcing effect of drugs and other rewarding stimuli. Indeed, high reward sensitivity was shown to contribute to drug abuse vulnerability (Baler & Volkow, 2006; Bechara, 2005; Dawe & Loxton, 2004). Therefore, it is important to identify and clarify the neural substrates that underlie decision-making. This may elucidate mechanisms contributing to continued high-risk behaviors in drug abusers. At least two underlying types of dysfunctions have been identified where reward signals turn in favor of immediate outcomes in the case of decisions: hyperactivity in the emotional system, mediated by frontal and medial structures, such as the Orbitofrontal Cortex (OFC), Anterior Cingulate Cortex (ACC) and amygdala, which exaggerate the rewarding impact of external reinforcers; hypoactivity in the prefrontal cortex (and mainly the dorsolateral prefrontal cortex, DLPFC), which predicts the long-term consequences of a given action (Bechara & Martin, 2004). Damage or dysfunctional conditions to either of these systems can alter the normal functioning of the decisional processes. Addictive behavior seems also to be associated with specific dysfunctions in the dopaminergic mesolimbic reward system which can elicit conditioned attention allocation for dependence-associated stimuli rendering them especially salient (Adinoff, 2004). Indeed, deficient mesolimbic reward system and medial prefrontal cortex activation is reported in substance abusers

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http://dx.doi.org/10.1016/j.addbeh.2014.02.007
0306-4603/

and impulsive individuals (Scheres, Milham, Knutson, & Castellanos, 2007). It has been suggested that drug addiction is characterized by dysfunctional preference of immediate versus delayed rewards, which manifests itself as impulsivity and may contribute to early pathological onset and increased social problems (Bechara, 2005; Beck et al., 2009; Bjork, Knutson, & Hommer, 2008).

In addition, reward motivation significantly correlates with a risk-seeking profile (Knyazev, 2010). Moreover, subjects displayed significantly riskier decision-making after disruption of the right lateral PFC, choosing a larger potential reward even at a greater risk of penalty (Knoch, Schneider, Schunk, Hohmann, & Fehr, 2009). It should be hypothesized that the hemispheric "imbalance" between the left and right frontal sides would characterize the subjects' decision which shows a higher reward trait and riskier behavior, with a possible left hemisphere imbalance. Modulation of brain oscillations may be considered a valid measure of brain activation, often being applied to find distinct responsiveness in the two hemispheres for different cognitive or emotional tasks (Balconi & Mazza, 2009a,b; Sutton & Davidson, 1997). In the frontal system, reduction in a specific frequency band, that is, a reduction of alpha power (increased activity) in the left frontal brain, was found after money gains and reward trials, whereas punishment conditions induced reduction in alpha power in the right frontal brain (Buss et al., 2003; Sobotka, Davidson, & Senulis, 1992). Indeed, resting EEG studies have shown that frontal hemispheric activation asymmetry in favor of the right PFC reflects an individual predisposition to respond in terms of withdrawal-related behavior (Balconi & Bortolotti, 2012; Davidson, 2004; Harmon-Jones, 2004). One previous study used the resting alpha level to analyze the effect of stable approach/withdrawal components on decisional behavior (Schutter, de Haan, & van Honk, 2004). Another study used a wider band of frequencies (Gianotti et al., 2013). In this latter case, on the one hand, baseline cortical activity in the right hemisphere predicts individual risk-taking behavior, as the subjects with higher baseline cortical activity in this area display more risk aversion than do other subjects. On the other hand, hypoactivity in the right prefrontal cortex might serve as a dispositional marker of greater risk-taking behavior. When modulating risky decisions by means of Transcranial Magnetic Stimulation (TMS), subjects opted for significantly riskier choices after disruption of the right lateral PFC, choosing a larger potential reward even at a greater risk for penalty (Knoch, Pascual-Leone, Meyer, Treyer, & Fehr, 2006).

A strong relationship was also shown between impulsivity, drug-dependence and Behavioral Activation System (BAS) (Dawe & Loxton, 2004). Behavioral Inhibition System (BIS) and BAS measures represent a usable tool to test subjective reward-sensitivity based on neurophysiological correlates (Balconi, Brambilla, & Falbo, 2009a,b; Balconi, Falbo, & Brambilla, 2009; Balconi, Falbo, & Conte, 2012; Balconi & Mazza, 2009a,b, 2010; Carver & White, 1994; Fowles, 1980; Gray, 1981; Gray & McNaughton, 2000; Yu & Dayan, 2005). Previous findings provide support for the role of Gray's BAS in mediating approach behavior and dependence as associated with the drive to consume rewarding substances (Blum et al., 2000; Dawe & Loxton, 2004; and see for a review: Bijttebier, Beck, Claes, & Vandereycken, 2009; Smillie, Loxton, & Avery, 2011). Moreover, some other studies found significant relationships between hazardous and non-hazardous drinkers and the Iowa Gambling Task (Gullo & Stieger, 2011). A direct association between the BIS and BAS subscales (BAS Drive, Fun Seeking and Reward Responsiveness) to substance abuse has been shown (Colder & O'Connor, 2002). Indeed, it was shown that heightened BAS, and specifically BAS-reward trait related to approach reward, and drug addiction are related and the approach-reward may be considered predictive of substance abuse (Franken, Muris, & Georgieva, 2006). However it should be underlined that in some cases a negative association was found between alcohol use and BAS (Voigt et al., 2009), and a more recent study of heroin-dependent men found this subscale to differentiate between injecting and non-injecting users (Dissabandara et al., 2014). Thus, these controversial results should be considered and discussed.

BIS/BAS concerns behavior regulation mediated by emotional trait and motivated behavior (Gray, 1981). BAS was conceptualized as a motivational system that is sensitive to signals of reward and non-punishment, driving behavior toward a reward and away from a loss. Reward serves as a positive reinforcer for action (approach behavior), whereas punishment promotes negative reinforcement for avoidance (withdrawal). From the neuroanatomical point of view, the cortical correlates of BIS/BAS system are the PFC where the left PFC was shown to be implicated in approach-related motivations and emotions, whereas the right PFC was found to be involved in withdrawal-related motivations and emotions (Balconi & Mazza, 2009a; Davidson, 2004). Due to the controlateral inhibition between the hemispheres, the lateralized approach and withdrawal or punishment-reward system are mutually inhibitory. Thus, we may suppose that, based on the lateralized reward/punishment model, there are different contributions of the left and right hemispheres on decisional processes including gain and loss.

In the present work, we tried to relate the motivational system (BIS/BAS) to the hemispheric lateralization effect, that is, the contribution by the left hemisphere to the motivational components that support dysfunctional behavior in SUD. It should be plausible that the hemispheric "imbalance" between the left and right sides would characterize SUD behavior, showing a higher reward component with an imbalance in favor of the left hemisphere. The role of the reward system (BAS), on the one hand, and the frontal brain imbalance, from the other, was supposed to be able to elucidate the deficitary decisional mechanisms in SUD. In previous research, the relationship between reward-sensitivity and hemispheric imbalance was not specifically considered. Indeed, little is known about subjective differences in reward mechanisms (BAS) mediated by the left prefrontal system, and about the neural substrates of such individual differences. Only one study examined the direct link between BAS and left hemisphere activity, considering the resting state in drug-dependence (Krmpotich et al., 2013). A significant left-increased activity in SUD than control subjects was observed, and increased BAS was also revealed in SUD in concomitance with this lateralized brain activity. However, a specific relationship with dysfunctional decisional processes was not explored, taking into account the "dynamic" profile (not resting EEG) during the task execution.

To verify the relevance and the reciprocal reinforcement of these components in decisional bias, we used three distinct measures: the behavioral Iowa Gambling Task (IGT) performance (Bechara, Damasio, Damasio, & Anderson, 1994; Bechara, Damasio, Damasio, & Lee, 1999; Northoff et al., 2006) the BIS and BAS measures (Gray, 1981), and the alpha band asymmetry index. Increasing BAS-Reward and brain oscillation modulation in favor of the left frontal side was expected for SUD which may be considered predictive of increased risk-taking and dysfunctional behavior in IGT. The IGT is a sensitive measure of decision-making that simulates a real-world decision-making situation requiring evaluation of the magnitude and timing of rewards and punishments under uncertain conditions. The IGT includes a number of aspects: immediate rewards and delayed punishments, risk and uncertainty of outcomes. Generally high-risk options imply the chance of great reward but also high risk for loss. By contrast, low-risk options are often characterized by lower reward but also low risk for loss. Thus, low-risk options often entail better long-term strategies with an overall gain, despite the initial reduced short-term gain.

Insensitivity for punishment together with strong reward dependence entails a disadvantageous pattern of decision-making, and more reward-dependent subjects should make more risky, disadvantageous choices in the IGT (van Honk, Hermans, Putman, Montagne, & Schutter, 2002). Some types of patients, for example those with deficits to the ventromedial prefrontal cortex (VMPFC), appear unable to learn which deck is associated with a long-term win strategy (Damasio et al., 2000; Rogers et al., 2004; Verdejo-García & Bechara, 2009). Substance dependent patients performed more poorly than controls and their performance as a group did not differ from that of patients with