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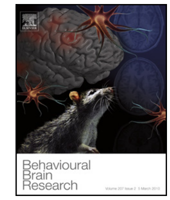

Research report

Theta-band oscillatory activity differs between gamblers and nongamblers comorbid with attention-deficit hyperactivity disorder in a probabilistic reward-learning task

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HIGHLIGHTS

- We tested whether ADHD patients and gamblers exhibit similar fronto-cortical electrical signals in a reward-learning task.
- It's the problem gambling which impairs reinforcement-driven choice adaptation in ADHD patients.
- Feedback induced theta-band power over frontal cortex was higher in ADHD gamblers versus those who were nongamblers.
- Theta and low alpha power at frontal electrodes of ADHD nongamblers matched that of control individuals.
- ADHD and problem gambling are distinct with respect to dopaminergic reward-learning.

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ABSTRACT

Problemgambling is thought to be comorbid with attention-deficit hyperactivity disorder (ADHD). We tested whether gamblers and ADHD patients exhibit similar reward-related brain activity in response to feedback in a gambling task. A series of brain electrical responses can be observed in the electroencephalogram (EEG) and the stimulus-locked event-related potentials (ERP), when participants in a gambling task are given feedback regardless of winning or losing the previous bet. Here, we used a simplified computerized version of the Iowa Gambling Task (IGT) to assess differences in reinforcement-driven choice adaptation between unmedicated ADHD patients with or without problem gambling traits and contrasted with a sex- and age-matched control group. EEG was recorded from the participants while they were engaged in the task which contained two choice options with different net payouts and win/loss probabilities. Learning trend which shows the ability to acquire and use knowledge of the reward outcomes to obtain a positive financial outcome was not observed in ADHD gamblers versus nongamblers. Induced theta-band (4–8 Hz) power over frontal cortex was significantly higher in gamblers versus nongamblers in all different high-risk/low-risk win/lose conditions. Whereas induced low alpha (9–11 Hz) power at frontal electrodes could only differentiate high-risk lose between gamblers and nongamblers but not the other three conditions between the two groups. The results indicate that ADHD nongamblers do not share with problem gamblers underlying deficits in reward learning. These pilot data highlight the need for studies of ADHD in gambling to elucidate how motivational states are represented during feedback processing.

1. Introduction

Attention-deficit hyperactivity disorder (ADHD) is the most common psychiatric disorder in children and adolescents with worldwide prevalence of 5.9–7.1% [1]. The cognitive profile of ADHD is typically characterized by developmentally extreme levels of hyperactivity-impulsivity and/or inattention-disorganization; however the manifestation of the disorder is highly heterogeneous. Evidence indicates a wide range of impairments in ADHD patients involving executive functions [2], sensory and cognitive deficits such as in perceptual encoding [3] and motor preparation [4]. Problem gambling is characterized by uncontrolled gambling despite negative consequences, and is suggested to be comorbid with ADHD [5]. The rate of co-occurrence between ADHD and problem

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gambling is variable between different studies with ranges from 1.3 to 20.0% [6], but a recent *meta*-analysis showed that the mean prevalence of ADHD in treatment-seeking problem gamblers is 9.3% [7]. This comorbidity is superficially paradoxical because ADHD is defined by an inability to maintain attentional focus, whereas problem gambling entails hyper-engagement of attention [8]. The most prominent cognitive impairments in ADHD patients are attentional deficits which the alerting and conflict-monitoring attentions are defected while the orienting attention remains intact [9]. The alerting attention plays a role in acquiring and maintaining an alert state while the orienting attention selects sensory input for specific processing. In other words, attentional selection once focused is not impaired but orienting the selection mechanism and especially the duration and vigilance of selection are impaired in ADHD [10]. The conflict-monitoring attention coordinates the resolution of the conflict that arises between competing stimuli which is a common component in any kind of gambling task.

Our hypothesis is that ADHD and problem gambling are linked by dysregulation of the neural mechanisms involved in both reward processing and attention control [11]. The prediction is that ADHD patients and gamblers would be the same on probabilistic reward-learning tasks. Dopamine is the likely neuromodulator in this system, which has broad empirical and theoretical support for a central role in signalling information about reinforcements [12], and is centrally implicated in the pathobiology of ADHD [13]. The first step in linking reward processing to attention orienting during gambling is to characterize how the brain responds when engaged in gambling. Electroencephalography (EEG) and the associated event-related potential (ERP) is one of the approaches which has been used with considerable success to investigate the electrical activity of the brain following feedback in gambling and decision-making tasks [14,15]. Several components of the EEG and ERP provide a signature of the brain processes that follow reward or loss during gambling. We have developed a simulated video-lottery terminal (VLT) game that can be played by participants in EEG experiments [11,16,17]. Although the interface resembles a simplified VLT, the underlying structure follows directly from the well-known Iowa Gambling Task (IGT). The IGT tests the ability to balance risk and reward in planning future actions [18] and problem gamblers perform poorly on this test [19].

A previous study from our group has shown that problem gamblers exhibit reward hypersensitivity in medial frontal cortex during gambling [17]. In another experiment we found that high- but not low-risk bets lead to robust but different electrical responses in medial frontal cortex depending on whether normal participants won or lost [16]. All together, these changes reflect the functioning of the frontal cortex in reward processing; however, no study has yet investigated these EEG signals in problem gamblers considering their probable comorbidity with ADHD. If ADHD and problem gambling share a common dysregulation of frontal cortical reward processing then ADHD patients without gambling problem should exhibit similar stereotypical abnormalities in feedback-related EEG relative to gamblers. If this prediction holds it will indicate that abnormalities in frontal cortical reward processing among gamblers are not due to experience with gambling but instead reflect an underlying generalized reward processing deficit which also support the theoretical link between ADHD and problem gambling. However, if ADHD players and gamblers exhibit different behavioral performance and fronto-cortical electrical signals in reward-learning tasks, then a different theory is needed to account for comorbidity between these two conditions. In a previous study [11], we showed that ADHD patients, both medicated and unmedicated, successfully learn contingencies in an IGT-like reward-learning task. Gamblers, both with and without comorbid ADHD, did not learn this task. This suggested that the two disorders are distinct with respect to dopaminergic reward-learning. In the present study we further pursued this line of evidence by comparing brain electrical responses in reward learning.

2. Materials and methods

2.1. Participants

We used a simplified computerized version of the IGT to assess differences in reinforcement-driven choice adaptation between unmedicated ADHD patients with or without problem gambling, and contrasted these data with a sex and age-matched control group. The gambler participants were screened in the problem range indicated by DSM-IV or in the lower end of the pathological range of scores on the Canadian Problem Gambling Index (CPGI) [20]. In order to assess gambling propensity as well as possible co-morbidities, participants completed the CPGI, the National Institute on Drug Abuse—modified Alcohol, Smoking and Substance Involvement Screening Test (NIDA—modified ASSIST) [21], the National Opinion Research Center DSM Screen for gambling problems (NODS) [22], and the World Health Organization Composite International Diagnostic Review (WHO CIDI) [23]. ADHD subjects were confirmed by the Conners' ADHD scale as well as the WHO Adult ADHD Self-Report Scale (ASRS—v 1.1). ADHD participants were off medication for $\geq$6 months before testing. Procedures were in accordance with the declaration of Helsinki and were approved by the University of Lethbridge Human Subjects Review Committee; all participants gave written informed consent.

2.2. Behavioral task

EEG was recorded from 20 participants (5 ADHD gamblers, 5 ADHD nongamblers, and 10 healthy controls) while they were engaged in a gambling task in which players could choose either a "small" (50 points) bet or a "large" (100 points) bet. The win/loss sequence for each bet type was randomized within runs of 20 trials with a 0.6/0.4 win/loss probability for the 50-point bet and a 0.4/0.6 win/loss probability for the 100-point bet. Thus as in the classical IGT, the optimal strategy over the long run was to choose the "small" lower-risk bet type to maximize the final score. The session was divided into four blocks of 100 trials, and participants received $5 at the end of each block if their total score was any amount equal to or greater than 100 points. If the total score for the block was less than 100, no remuneration was given. Our previous work indicates this threshold to be a reliable discriminant of non-random choice and is used to incentivize subjects to solve the task [11,16,17]. Scores were reset to 0 at the end of each block. Participants also received a fixed $20 remuneration after completion of the session, regardless of their performance on the task. Thus their financial success depended substantially but not entirely on their performance on the gambling task. Participants' bets were recorded during the course of the experiment and analyzed offline. We quantified subjects preference for the good bet over the session by subtracting the number of high-risk (large) bets from the number of low-risk (small) bets. This measure was calculated within four quartile time bins directly correspond to four blocks of the task to show subjects' learning trends over trials.

2.3. EEG recording

The EEG was recorded from 128 channels with EOG electrodes at a 500 Hz sampling rate using Ag/AgCl electrodes in a geodesic net (Electrical Geodesics Ind., Eugene, OR, USA). Impedances were maintained below 100 kΩ. The montage was initially referenced to the vertex and then digitally re-referenced to an average reference. Data were imported into the BESA software package (Megis Software, Grafelfing, Germany) for further analysis. The record