

Frequent Sub-Threshold Gamblers Display Unique Pattern of Brain Activation during Investment Decision-Making Task

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Abstract

Gambling is a popular social activity, but can become pathological, which might reflect changes in specific brain regions. Gambling disordered individuals have therefore been the focus of many imaging studies, and deactivation in regions such as the ventromedial prefrontal cortex and striatum have been consistently found. In contrast, the neurobiology of frequent gamblers, but whose gambling is not severe enough to meet current diagnostic criteria for Gambling Disorder ("Sub-threshold" gamblers), has been relatively poorly studied. It may be beneficial to study Sub-threshold gamblers since they may provide insights into developmental and/or protective factors related to Gambling Disorder. In the present study we utilize an existing investment task, carried out while subjects underwent functional magnetic resonance imaging (fMRI), to examine differences between Sub-threshold gamblers (n=16) and Non-gamblers (n=23) during a financial decision-making task. While we found differences in overall reward recruitment in the thalamus and insula, we did not find any significant differences between the groups in any brain regions during the decision-making phases of the task. We also found that this group of gamblers, in contrast to findings from previous studies in individuals with a Gambling Disorder, did not have the same patterns of regional deactivation. Interestingly, we also found that Sub-threshold gamblers made more rational decisions when given poorer advice, suggesting that some propensity towards gambling may be beneficial to investors in the face of wayward advice. From our results we hypothesize that the difference between remaining a sub-threshold non-distressed gambler, instead of a pathological distressed gambler, may be linked to several specific brain regions including the ventromedial prefrontal cortex (vmPFC) and ventral striatum. This is because these regions remained functionally intact in sub-threshold gamblers in the present study in contrast to previous findings in pathological gamblers. Further studies directly comparing these two groups are required to validate this hypothesis.

Introduction

Gambling has become a widespread and very popular recreational activity, often involving very significant sums of money being gambled across a wide variety of populations [1]. While for most, gambling represents an enjoyable social activity with no associated problems, for perhaps as many as 5% of the population, gambling-related problems can develop [2]. When these problems reach clinical significance they are termed "Gambling disorder" [3]. Generally, research has been carried out in those who have the clinical condition of gambling disorder, and usually with individuals whose gambling occurs in casinos, bingo halls, horse racing, sports betting, or using electronic video-lottery machines [1]. However, one example of gambling behavior has frequently been overlooked in research, in part as it isn't always considered as gambling, namely investing by individuals in the stock market. Nonetheless, it has been repeatedly suggested that investing in the stock market has many obvious parallels to gambling [4,5]: both involve making decisions under conditions of uncertainty and both can have major financial consequences. While there are many studies of gambling behavior, understanding gambling *via* research utilizing a stock market investment perspective is relatively unusual. Furthermore, although most research has been carried out on those who meet clinical criteria for a gambling disorder, subclinical gamblers are relatively poorly studied.

Neurobiological studies of gambling behavior have reported findings similar to those from other addictions such as substance abuse [6]. A common theme has emerged in much of the literature: diminished activation in the ventromedial prefrontal cortex (vmPFC)/orbitofrontal

cortex (OFC) during gambling and exposure to gambling cues [2]. Other areas of interest include the ventral striatum [7,8], insula [8-10], dorsal anterior cingulate cortex (ACC) [11], ventrolateral prefrontal cortex (vlPFC) [12], and thalamus [11]. In the current study, we wished to examine if any of these differences also appear with subclinical gamblers, or if they have their own unique neurobiological effects.

Taking both economics and theories of the neurobiology of addictions and gambling into account, the present study compares sub clinical gamblers to non-gamblers in an investment task during functional magnetic resonance imaging scanning (fMRI).

In the current study, we wished to examine if the differences consistently found in pathological gamblers also appear with subclinical gamblers, or if there are unique neurobiological effects. Based on the previous literature we had several hypotheses:

1. We predicted that subclinical "Gamblers" would differ from "Controls" on the overall task and overall feedback phases of the task. We anticipated regional differences in the vmPFC and the striatum (reward pathway regions).
2. We hypothesized that "Gamblers" would perform poorly on the task compared to "Controls", as indicated by lower financial outcome in the task. This would be similar to previous studies which have found dysfunctional decision-making patterns made by pathological gamblers. Additionally, we expected "Gamblers" not to be as obedient/affected by the advice presented during the task compared to "Controls", and to follow "expert" advice less frequently

3. Since we do not expect “Gamblers” to follow the advice provided by the “expert”, we hypothesized that there would be no differences in brain activation when comparing Advice trials to No Advice trials for the group of “Gamblers”, but that differences would emerge when comparing “Gamblers” to “Controls”. Regions of hypothesized differences were the ACC and prefrontal cortex.

Materials and Methods

Ethics statement

This study was approved by the Ethics review board of the University of Alberta. All participants signed an informed consent form. As a standard for ethical research the Ethics review board requires that individuals are not paid substantially more than the minimum wage, to prevent inappropriate incentives for research. For this reason, the possible financial incentives available to individuals were at least \$45 (representing \$15 per hour for their time, including screening and actually taking part in the task). Nonetheless, it was accepted as ethically appropriate to have an additional monetary award available that would make participation more realistic, and after discussion with the Ethics committee the maximum additional amount any individual could theoretically obtain was limited to an additional \$60, although the expectation was that it would be much less in almost all cases.

Recruitment and study process

Participants were recruited from the University of Alberta Campus and surrounding area *via* online advertising. A total of 39 individuals entered the study (mean age 26.13 ± 6.23 years, range: 28 years) of which 74.4% were male. Based on the scores on the Problem Gambling Severity Index (PGSI), there were 23 individuals in the Control group and 16 individuals in the “Gambler” group.

Prior to participation all participants were screened for any potential metal in their body, since this is an MRI exclusion factor. Other exclusion criteria included a history of Axis I psychiatric disorders, following interview to determine a history of any disorder meeting DSM-IV-TR criteria [13], including substance abuse or any Axis 1 or Axis 2 mental health disorder. After screening, participants were asked to attend the NMR Centre for a 2-hour session in which the scanning was completed. Participants were compensated for their time (min \$45) with the opportunity to earn additional money (\$45-\$105) depending on task performance (the more money earned in the task the more the participants would receive).

Gamblers

Participants gambling behavior was assessed using the Problem Gambling Severity Index (PGSI) [14]. Participants were asked to think about the last 12 months and answer nine questions (e.g. Have you bet more than you could really afford to lose?), scoring from 0 (never) to 3 (almost always). Responses for all questions were summed for a total scale score of problem gambling. Total scores of 3-7 indicate a moderate level of problems due to gambling, leading to some negative consequences. It should be noted that a recent study on the validity of the PGSI found that the differences between low and moderate-risk categories on the PGSI was not statistically significant across all tested dimensions and that a suggestion to combine the two groups to improve discrimination did emerge [15]. However, the study did conclude that this group did differ significantly from problem gamblers and thus we are confident that our cut-off scores were appropriate.

Investment task

Prior to participation in the fMRI scan, participants were trained on the study investment task (Figure 1), which we have utilized in previous

research [16]. Participants were informed that the investigators were interested in investment decision-making. Participants were shown a series of stocks, each presented individually. These showed the probability that the stock would win a specified amount of money, but also provided the risk that each stock could also lose a specified amount of money.

At the initiation of the fMRI study, all participants began with a nominal amount of \$100. This was chosen to be realistic in context of what they were receiving for their time, and that any changes would be relevant and realistic compared to this sum (\$45). They were instructed to indicate, *via* one buttons in each of their hands, whether they would like to “Buy” or “Not Buy” the stock. If a stock were bought, the participant would receive immediate feedback on whether or not that decision yielded a win, or a loss, and their total would be adjusted accordingly. If the stock were not bought, the participant would not receive feedback, and their total would remain unchanged. In order to earn a higher payout post task (ranging from \$45-\$105), participants were required to earn as much money as possible throughout the task. Each participant was allowed a practice run of the task that was equivalent in length to the first run that they would complete in the MRI scanner. During the practice run of 19 trials, seven were “No Advice” trials while the remaining 12 were all “Good Advice” trials.

Participants were told that in order to simulate real-world investing, advice was going to be presented with some of the trials. All participants were told that the advice came from an outside financial expert, with over 20 years of experience in the financial field, who had been asked to indicate what advice he would give to his clients for each stock in the task. In reality, the advice was manipulated throughout the entire task, as was the outcome of each trial, with each result based on its expected value. Thus, the “advice” was helpful, or “correct” if there was a greater chance of the expected value being positive. For example, if the information shown was a 30% chance of losing \$50 (which would be \$15) was less than the expected value of 70% chance of winning \$30 (which could be \$21) then the “correct” advice would be to “buy” (Figure 1). If the subject followed the advice then they would have made the appropriate decision and the



Figure 1: Investment task-a: Fixation Point (6-10s): Participants were instructed to attend to the fixation point b: Trial (7s): Participants are presented with a stock and must decide to either “Buy” or “Not Buy”. Advice to “Buy” is rational as the expected value of buying the stock ($0.7 \times 30=21$) outweighs the expected value of not buying the stock ($0.3 \times -50=-15$). c: Feedback (1s): Participants are presented with feedback based on their decision (in this case the participant chose to obey the advice and “Buy” thus the trial resulted in a win) and their total is adjusted accordingly.

amount they had would increase by the total amount available (in this case \$30). However, the advice was gradually changed during the course of the task, starting initially where all advice was correct but by the end all the advice was incorrect. Thus, during the first trials the advice would be correct in all cases, and would correctly prompt participants to “Buy” stocks that would yield wins and increase their money. Similarly, during all of the early trials any advice to a participant to “Not Buy” stocks would prevent them losing money. Thus, if the participant followed the advice on all occasions during the first part of the study task then their money would increase, and they would not lose any. However, and unknown to the participants, after 1/3 of the tasks had been completed the advice changed to having an equal mix of either corrector being given incorrect advice. Therefore, should individuals follow the advice in the first 1/3 of tasks they would make money, and during the next 1/3 of tasks they would neither win nor lose overall. However, in the final 1/3 of the tasks, again with no indication of a change to the participants, the advice changed so that it was always incorrect. Thus, if individuals followed the advice during the final 1/3 of the task they would always lose money (Table 1).

Image acquisition

Scanning took place at the University of Alberta’s Peter S. Allen MR Research Centre using the 1.5T Siemens MRI system with an 8-channel head coil. Thirty-two axial slices (3 × 3 × 4 mm voxels) were acquired in a descending interleaves order. Functional images were acquired using a gradient echo EPI sequence (TR=2000 ms, TE=40 ms, FOV=256 mm, flip angle=90°). Structural images were acquired with a T1-weighted pulse sequence (MPRAGE, TR=1670 ms, TE=3.82 ms, TI=1100 ms, flip angle=15°, FOV=256, 1 mm thick). Images were pre-processed and analyzed using SPM8. Pre-processing steps included 6-parameter rigid body motion correction, slice-timing correction, and co-registration to each participant’s anatomical image to their functional scans. Structural scans were normalized to the Montreal Neurological Institute (MNI) template, and functional images were normalized to the new anatomical image. Lastly, we performed smoothing using a three-dimensional Gaussian filter (8-mm FWHM). Five participants (four from the “Control” group; one from the “Gambler” group) were excluded from further analyses due to significant movement artifacts that occurred during the scans (pitch, roll or yaw translation greater than 8mm).

Statistical analysis

Behavioral data on the investment task was analyzed using SPSS 21. An ANOVA and independent samples two-tailed *t*-test were performed to determine differences between the groups in terms of age and gender. To test differences in obedience between the groups Hotellings T² test

was performed on the three dependent variables: percent obedience in Runs 1/2 (first 1/3 of trials), Runs 3/4 (second 1/3 of trials), and Runs 5/6 (final 1/3 of trials). All the study runs were grouped based on type of advice presented), with Group (“Gambler” or “Control”) as the independent variable.

fMRI data were analyzed using the General Linear Model. Trials were classified by type of advice (No Advice, Good Advice, Bad Advice), type of buy (Good Buy resulting in a win, Bad Buy resulting in a loss), decision (Buy, Did Not Buy), and feedback (Win, Lose) during model specification. Nuisance predictors included run offsets and six motion parameters. We included the trials from all runs in a single GLM, grouping together run 1 with run 2, run 3 with run 4, and run 5 with run 6, as per the type of advice (Good, Bad or both) provided. GLM parameters were estimated using linear least-squares error fitting. We computed the following first-level statistical contrasts separately for each participant: Buy-Did Not Buy, Did Not Buy-Buy, Advice-No Advice, No Advice-Advice, Obedient-Not Obedient, Not Obedient-Obedient. (Obedient and Not Obedient trials, respectively, were defined as those in which the participant’s choice matched/did not match the advice), Win-Lose and Lose-Win. We performed three second level analyses on the amplitudes of each contrast: within group *t*-test across all participants in the “Control” group to detect significant contrast amplitude, within-group *t*-test across all participants in the “Gamblers” group, and between-groups *t*-test comparison. For all analysis, we used a voxelwise statistical threshold of $t(37)=2.0262$ ($p<0.05$ uncorrected) and a cluster size threshold of $k=201$ voxels, yielding $p<0.05$ corrected for multiple comparisons across both the voxel population as well as the statistical tests. Cluster size threshold level was computed using Monte Carlo simulation. Post-hoc analysis of reaction-time data was conducted using SPSS 21.

Results

Behavioral results

There were no statistically significant differences in age or gender between the two groups; however, as required by the design, gamblers scored significantly higher on the PGSI ($t(37) = -8.160, p<0.0001$).

The assumption of equality of covariance matrices was satisfied for our two-group MANOVA (Box’s $M=6.44, p=0.44$). There was a statistically significant difference between the groups (Gamblers and Non Gamblers) on the combined dependent variable (Run), ($Hotellings T^2=11.25, F(3/35)=3.549, p=0.024$; Note. $T^2=Trace coefficient \times (sample size-number of groups)=0.304 \times (39-2)=11.25$). Post-hoc univariate ANOVAs were conducted to determine the effect of group on each of the Runs (Figure 2). A significant difference between the groups only appeared in Runs 5/6 ($F(1,37)=5.416, p=0.026$). Both runs 1/2 ($F(1,37)=0.63, p=0.43$) and 3/4 ($F(1,37)=0.144, p=0.71$) failed to reach statistical significance.

Task performance: Total monetary score at the end of the task determined task performance with higher performance indicated by a higher total score. There were no statistically significant differences between the groups in terms of task performance ($t(37) = -1.872, p=0.069$, Cohen’s $d = -0.625$).

Reaction times: Reaction time analyses revealed no statistically significant differences in overall reaction times throughout the task between groups.

Significant reaction time ANOVAs:

2(Group; Non-Gambler, Gambler) × 2(Obedience; Obedient, Not Obedient) ANOVA

A main effect for Obedience emerged ($F(1,72)=8.124, p=0.006$) with Not Obedient ($M=3.574$ seconds, $SD=0.757$ seconds) decisions taking longer than Obedient decisions ($M=3.135$ seconds, $SD=0.596$ seconds). There was no main effect of group or interaction effect.

Trials	Duration of Run	Type of Advice	Type of Buy	Number of Trials
First 1/3 of trials Runs 1 and 2	5 min 30 sec	No Advice	Good Buy	8
			Bad Buy	6
		Good Advice	Good Buy	12
			Bad Buy	12
Second 1/3of trials Runs 3 and 4	9 min	Good Advice	Good Buy	18
			Bad Buy	16
		Bad Advice	Good Buy	16
			Bad Buy	16
Last 1/3of trials Runs 5 and 6	5 min 30 sec	No Advice	Good Buy	8
			Bad Buy	6
		Bad Advice	Good Buy	12
			Bad Buy	12

Table 1: Investment task conditions

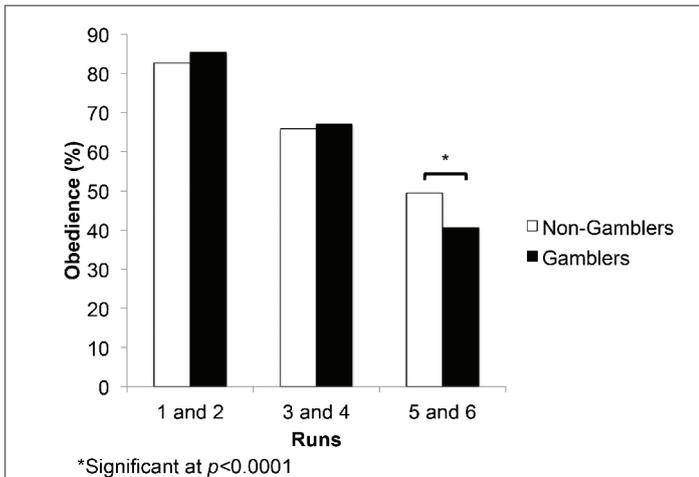


Figure 2: Comparison between Non-Gamblers and Gamblers in obedient decisions—Significant differences in number of obedient decisions in the final two runs of the study ($F(1,40)=16.254, p<0.0001$). The “Expert” group was significantly more obedient to the advice in the last two runs than the “Peer” group.

2(Group; Non-Gambler, Gambler) × 2(Good Advice Obedience; Good Advice Obedient, Good Advice Not Obedient) ANOVA

A main effect emerged for Good Advice Obedience ($F(1,72)=14.776, p<0.0001$) with Not Obedient ($M=3.717, SD=0.828$) decisions being slower than Obedient ($M=3.073, SD=0.605$) decisions when the advice presented was good.

2(Group; Non-Gambler, Gambler) × 2(Advice; Good Advice, Bad Advice) ANOVA

A main effect approached significance for group ($F(1,72)=3.178, p=0.079$) with Gamblers ($M=3.509$ seconds, $SD=0.117$ seconds) being slower than Non-Gamblers ($M=3.236$ seconds, $SD=0.099$ seconds). There was no main effect of Advice or interaction effect.

Neuroimaging results

Overall task: There were no group differences when comparing overall task activation during all presentation/decision phases of the task. Differences in activation did emerge when comparing the two groups during the feedback phase of the task. Thus, “Gamblers” displayed greater activation in bilateral insula, thalamus and dorsal-medial prefrontal cortex compared to non-gamblers (Figure 3).

Obedient vs Not Obedient: Statistically significant differences emerged when comparing Obedient to Not Obedient trials in the middle runs, 3 and 4 (when subjects received a mix of good advice and bad advice). During these study runs there was significant activation compared to baseline for Obedient compared to Not Obedient trials in “Gamblers” in the left inferior parietal lobule, insula, medial frontal gyrus and the ventral anterior cingulate cortex compared to “Non-Gamblers” (Figure 4). There was significant activation compared to baseline for Not Obedient compared to obedient trials in “Non-gamblers” in both the dorsal and ventral anterior cingulate cortex compared to “Gamblers”. In contrast, no statistically significant differences between the groups emerged when comparing the first two runs (1/2) (all advice correct) and the final two runs (5/6) (all advice incorrect).

Advice vs No Advice: Differences emerged between “Gamblers” and “Non-gamblers” when comparing Advice to No Advice trials, with “Gamblers” displaying significant activation in the superior frontal gyrus and the anterior cingulate gyrus compared to baseline during Advice trials

(Figure 5). At the within-groups level, differences between Advice and No Advice trials did emerge in “Gamblers” with Advice trials recruiting the occipital lobe and No Advice trials recruiting the left putamen and left precentral gyrus (Figure 6).

Good Advice vs Bad Advice: No significant differences emerged between groups when comparing Good Advice trials to Bad Advice trials. No significant difference emerged between Good and Bad Advice trials when combining the groups together.

Buy vs Did Not Buy: Differences emerged when comparing Buy to Did Not Buy trials. “Gamblers” displayed significantly greater activation in the bilateral precuneus while “Non-gamblers” displayed significant deactivation in the posterior cingulate cortex and right inferior parietal lobule in Buy compared to Did Not Buy trials. “Non-gamblers” showed significantly greater activation compared to baseline in the posterior cingulate gyrus in Did Not Buy compared to Buy trials.

Win vs Lose: Significant differences emerged when comparing Win feedback and Lose feedback. “Non-gamblers” showed significant activation while “Gamblers” showed significant deactivation compared to baseline in the right inferior frontal gyrus, bilateral medial frontal gyrus and right insula when receiving Win feedback. There was significant deactivation compared to baseline in the right thalamus and right superior frontal gyrus in “Gamblers” while “Non-gamblers” displayed significant activation in the left insula and right dorsal medial prefrontal cortex compared to baseline when receiving Win feedback.

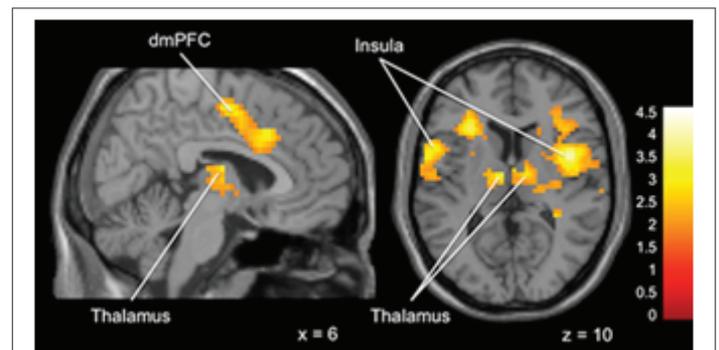


Figure 3: Brain activation for statistical contrast maps Overall Task Feedback Phase –“Gamblers” show increased activation in bilateral insula, thalamus and dorsal-medial prefrontal cortex. “x” and “z” coordinate provided at bottom right corners in MNI space. All results voxelwise statistical threshold at $t=2.0211$ ($p<0.05$) and a cluster threshold level of $k=201, p<0.05$ corrected for multiple comparisons.

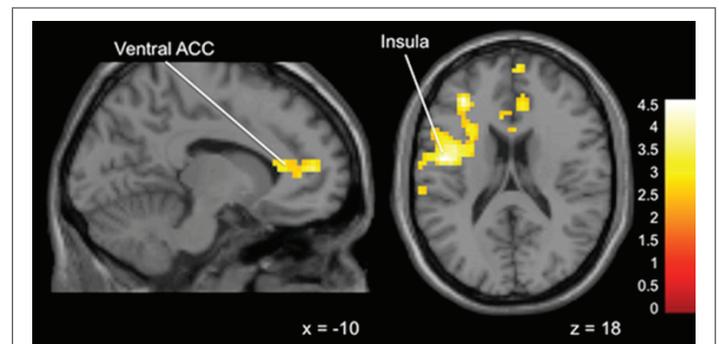


Figure 4: Brain activation for statistical contrast maps OBEDIENT–NOT OBEDIENT in Sub-threshold Gamblers–“Gamblers” display greater activation in the ventral ACC and insula. “x” and “z” coordinate provided at bottom right corners in MNI space. All results voxelwise statistical threshold at $t=2.0211$ ($p<0.05$) and a cluster threshold level of $k=201, p<0.05$ corrected for multiple comparisons.

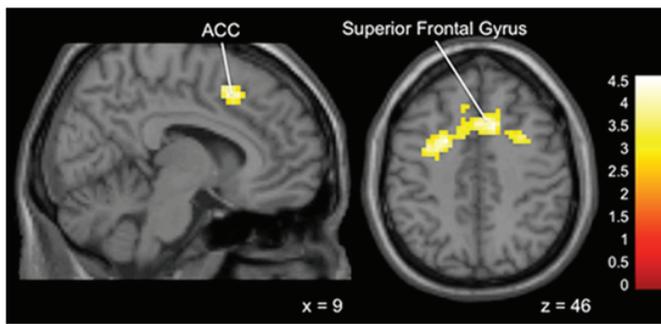


Figure 5: Brain activation for statistical contrast map ADVICE-NO ADVICE in Gamblers-“Gamblers” show greater activation in the superior frontal gyrus and anterior cingulate gyrus compared to non-Gamblers. “x” and “z” coordinate provided at bottom right corners in MNI space. All results voxelwise statistical threshold at $t=2.0211$ ($p<0.05$) and a cluster threshold level of $k=201$, $p<0.05$ corrected for multiple comparisons.

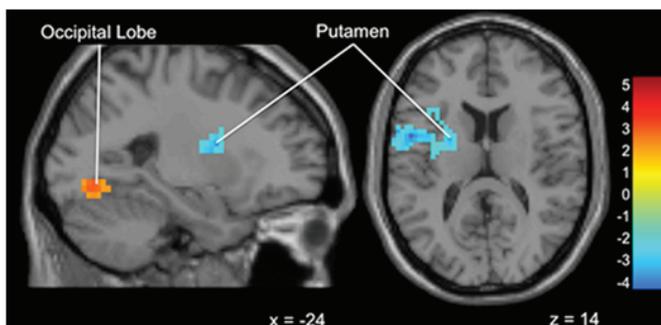


Figure 6: Brain activation for statistical contrast map ADVICE-NO ADVICE (Within groups sub-threshold gamblers)-At the within groups level, “Gamblers” show activation in the occipital lobe during Advice trials and greater activation in the putamen in No Advice trials. “x” and “z” coordinate provided at bottom right corners in MNI space. All results voxelwise statistical threshold at $t=2.0211$ ($p<0.05$) and a cluster threshold level of $k=201$, $p<0.05$ corrected for multiple comparisons.

Discussion

Overall decision-making

In the present study we were interested in examining how sub-threshold gamblers respond during our investment task and how this manifests itself neurobiologically. Based on previous research it has been established that pathological gamblers frequently show deactivation in the vmPFC during gambling tasks. Interestingly, however, this pattern of activation was not found in the present study in the group who had sub-threshold gambling, and also there no statistically significant differences in the overall decision-making phases of the task between controls and those with sub-threshold gambling.

In a previous fMRI study, a decrease in the ventral striatal and ventromedial prefrontal cortex (vmPFC) activation during receipt of monetary rewards was found in pathological gamblers compared to healthy controls [7]. Additionally, the authors found that there was a negative correlation between the severity of gambling problems and activation in the ventral striatum [7]. These results support the hypothesis that gamblers may have a decreased reward sensitivity compared to non-gamblers. Similarly, one group found that pathological gamblers performed poorly compared to nicotine dependent men and healthy controls during an affective switching task [12]. In this other study, participants were asked to respond to one of two stimuli presented at each trial and were then given either positive or negative feedback (8:2 ratio)

and pathological gamblers performed the worst, followed by nicotine dependent men, with healthy controls performing the best [12]. Given these findings, it would have been anticipated that the sub-threshold gambling group in the present study would have been similar to previous findings from studies in problem gamblers, but in fact this is not what we found.

Similarly, cue reactivity has been associated with cravings and attentional bias to addiction-related stimuli, and is also a central characteristic of pathological gambling [17-19]. Potenza et al. [20] were the first to conduct an fMRI study on gambling urges. They tasked their participants with viewing a tape designed to evoke emotional and motivational cues to gambling. The pathological gambling group exhibited less activation, compared to healthy controls, in the cingulate gyrus, OFC, caudate, basal ganglia and thalamic areas [20]. Another group, utilizing a similar gambling movie paradigm, found an increased BOLD signal in the right dlPFC, right inferior frontal gyrus, medial frontal gyrus, left parahippocampal region and left occipital cortex when pathological gamblers are presented with gambling-related cues [21]. Again, given these findings, it would have been anticipated that in the present study the group of sub-threshold gamblers would have had similar brain changes during this paradigm, but it is not what we observed.

It can be seen that previous research with pathological gamblers suggests that gamblers display dysfunctional brain activation in several regions during decision-making including the ACC, OFC, vlPFC, NAcc and amygdala [22-25]; however, these patterns were not replicated with sub-threshold gamblers. Thus from our findings it is possible that these areas, typically dysfunctionally recruited in pathological gamblers, may represent regions associated with the severity of gambling behavior.

In contrast, when the task was analyzed to compare “Buy” with “Did Not Buy” decisions, statistically significant differences did emerge. Thus, Sub-threshold gamblers displayed activation in the precuneus during “Buy” trials compared to non-gamblers. The precuneus has been linked to episodic memory [26], and it is therefore possible that in this group of sub-threshold gamblers decisions to “Buy” may conceivably be triggered by context-related (gambling) memories. Furthermore, deactivation in the posterior cingulate cortex may signify a lack of emotional salience associated with choosing to gamble/buy a stock in non-gamblers, since as this region has been linked to memory of emotional stimuli [27]. A suppression of activation in this region suggests that the decision to buy a stock in this task does not present strong positive or negative emotional valence in non-gamblers compared to sub-threshold gamblers. One, potentially speculative explanation, would be that decisions to gamble are not as strongly encoded in memory for non-gamblers. Another possibility could be that, in this stock market investment task, bounded rationality may have impacted an individual’s decisions. Bounded rationality refers to the use of cognitive shortcuts in decision-making when uncertainty is present, and where the cost of gathering information and solving a problem exactly are far greater than the value of such an exact solution [28,29]. It can therefore be seen that studying sub-threshold gamblers, and not just those with gambling disorder, may open potential new approaches to consider regarding the mechanisms for underlying changes that occur in those with a gambling disorder.

Our overall task analysis yielded differences between the two groups (gamblers and non-gamblers) during the feedback phase, partially supporting our first hypothesis, indicating that some of the reward pathways (insula and thalamus) may be affected in those who gamble but do not meet the criteria for Gambling Disorder, at least when compared to those who do not gamble. This suggests that it is conceivable that sub-threshold gamblers may have dysfunctional reward pathways compared to non-gamblers, at least in regards to financial decision-making. This could potentially comprise part of the mechanism that leads to continued and

increased levels of gambling. Interestingly, when comparing Win feedback to Lose feedback, several differences emerged between the groups. The inferior frontal gyrus has been implicated in GO/NO-GO tasks, and is believed to be involved in response inhibition [30-32]. Thus, a dampening of activation in this area would be consistent with the possibility that after sub-threshold gamblers are presented with winning feedback, they may be less likely to 'stop while they are ahead', whereas a win may signal when it is time to quit in non-gamblers. Such a suggestion is also compatible with some findings from previous studies. For example diminished activation in gamblers compared to controls in response to reward has been suggested [7,8], and our results support this finding with regard to the insula. Our findings also suggest that one of the key elements separating sub-threshold gamblers and pathological gamblers may be the addition of decreased activity in both the vmPFC and ventral striatal area [7,8]. This in turn could lead to greater reward processing dysfunction, followed by increased likelihood of development of Gambling Disorder.

Performance and obedience

Our second hypothesis was that sub-threshold gamblers would perform poorly compared to controls, but this was not supported by our findings. This would imply that in sub-threshold gamblers decision-making is not significantly impaired. In marked contrast, previous work has suggested that pathological gamblers perform significantly worse, often by taking higher risk options, on a variety of tasks including the Iowa Gambling Task (IGT) [33-36], Game of Dice task (GDT) [37,38], and the Wisconsin Card Sorting Test (WCST). Additionally, one study determined that the nucleus accumbens (NAcc) tracks price bubbles in stock markets as well as level of aggressiveness in trading [5]. The authors found that this aggressive (based on NAcc signals) trading earned less overall, with more successful traders having an "early warning system" signal from the anterior insular cortex when stock prices reach a peak, leading these traders to sell their stocks prior to a crash. It is suggested that examining the signals from the NAcc might demonstrate an individual's "irrational exuberance" and that such methods could be applied to gamblers as well [5].

Our results suggest that this harmful decision-making pattern is not significantly present in our gambling group (who were sub-threshold). This finding is in keeping with the lack of significant findings in brain activation in the overall task, as with this lack of significant neurobiological difference we may not see any significant behavioral differences.

However, part of our second hypothesis was supported, namely that we expected "Gamblers" not to be as obedient/affected by the advice presented during the task compared to "Controls". Thus, we found that obedience to the presented advice did differ between the groups, with "Non-gamblers" making more obedient decisions than "Gamblers" on the overall task. When examining the task during each successive run, we found that the groups differed significantly in the final 1/3 of the task, when the advice being given was always incorrect. It is of great interest that our results imply that the gamblers were, in fact, making more rational decisions than the controls, and that their decision-making was superior to that of the non-gambling control group. Nonetheless, this more rational decision-making during the final 1/3 of the task was not enough to significantly improve final performance/financial outcome, as neither group outperformed the other. These findings provides some evidence that not all gambling behavior leads to irrational decision-making, and that it is conceivable that a moderate degree of gambling propensity could potentially shield investors from following poor advice, and in the long run result in more profitable decisions. However, such a suggestion is speculative at present, even though differences in obedient decisions between the two groups continued to grow larger throughout the task.

Another reason for caution was that statistically significant differences in BOLD signal between the two groups were only found during the middle 1/3 of the task, which is at variance with the behavioral results. However one way to explain both these findings is that it is conceivable that in the middle 1/3 of trials, when the advice was equally mixed between correct and incorrect advice, the sub-threshold gambling group was learning not to trust the advice, so that for the final 1/3 of the task they were no longer concerned with the poor advice at all, negating any large obedience or disobedience effects. Consistent with this suggestion was our finding that the sub-threshold gambling group recruited the insula and ventral ACC during obedient trials, while the non-gamblers recruited the dorsal ACC when making non-obedient decisions. In choosing to not follow the advice of the "expert" our non-gamblers displayed activation in an area linked to error detection [39,40] as well as violation of expectancy [41]. Meanwhile, in sub-threshold gamblers obedient trials recruited activation in regions associated with interception [42], risk-avoidance [43,44] and sensitivity to social and emotional evaluation [41]. The activation of the ventral ACC may signify a desire of the sub-threshold gamblers to appear likeable when following advice that, based on the insula recruitment, may no longer seem sound.

Our third *a priori* hypothesis was that there would be no differences in brain activation when comparing Advice trials to No Advice trials for the "Gamblers", but that differences will emerge when comparing "Gamblers" to "Controls". We further hypothesized that regions in which we would see differences would be the ACC and prefrontal cortex. However, contrary to this hypothesis, differences did emerge in Gamblers when comparing Advice to No Advice trials. No Advice trials produced activation in the putamen, which may suggest that sub-threshold gamblers associated No Advice trials with having a greater risk, since increased risk-taking has been associated with greater activation in the striatum [45]. However, when comparing our two groups, greater activation in the ACC [39,40] and superior frontal gyrus [46], during Advice trials in the gambling group may suggest that this group was less affected by the advice. If the advice were influencing decision-making, we would expect that in the presence of advice there would be a decrease of cognitive effort. That this pattern of activation was not found in the sub-threshold gamblers might suggest that the non-gamblers made better use of the advice to a greater extent than the sub-threshold gamblers.

Interestingly, neither group displayed differential activation between corrector incorrect advices. This suggests that neither group really differentiated between the two types of advice, since if this had been the case we would have anticipated that Bad Advice trials would have elicited greater frontal lobe activation related to a greater effort in decision-making.

Reaction times

Post-hoc analysis of reaction times indicated that throughout the overall task there were no significant differences between the "Gamblers" and "Controls". There were also no differences in reaction times when comparing Good and Bad Advice trials, which was consistent with the fMRI findings.

Overall, choosing not to follow the presented advice took longer than choosing to follow it for both groups, suggesting that both were taking the advice into account to some degree as this took greater cognitive processing. However, this finding would also provide support for the idea that sub-threshold gamblers were not completely ignoring the advice. When looking at only Good Advice trials, this pattern of disobedient decisions taking longer than obedient decisions was repeated; yet, interestingly, this same effect was not seen when comparing on Bad Advice trials, suggesting that when the advice was not correct participants were able to decide not to follow it more easily.

Consistent with our fMRI results, the reaction times of sub-threshold gamblers were slightly longer than non-gamblers during Advice trials (i.e. they were slower) and this difference approached statistical significance. It may suggest that in the presence of advice non-gamblers were quicker to make their decisions, possibly due to the use of the advice as a cognitive shortcut in their decision-making process, whereas the sub-threshold gamblers did not make as great a use of the advice, thus requiring more cognitive processing time before deciding what action to take.

Comparison to other recent imaging study findings

Recent fMRI studies have been somewhat supportive of the findings described. Thus, while previous research suggested gamblers may have dysfunctional changes in amygdala functioning [22-25], we did not find this with sub-threshold gamblers. However, another group found that amygdala activity varied depending upon individual differences in appetite regarding loss aversion [47], with which may account for differences in our findings from those of previous studies. Another group examined brain activity in ventral striatal reward networks during decisions that weight the utility of possible gains against possible losses. They found that pathological gamblers had a dysregulated U-shaped response profile, reflecting hypersensitivity to the most appetitive and aversive bets [48]. The finding that the network is dysfunctional, particularly for extreme bets with large potential consequences, could be consistent with the findings from the present study that sub-threshold gamblers associated “No Advice” trials with having a greater risk, since increased risk-taking has been associated with greater activation in the striatum [45]. Similarly, another group found that ventral striatal connectivity is positively correlated with gambling severity [49] and this group also reported that their findings corroborated the ‘non-categorical’ nature of reward processing in gambling, where both near-misses and full-misses are processed differently.

Finally, in terms of possible baseline differences, one group has suggested that there are multiple differences in functional changes in the resting state of individuals with internet gaming disorder, and that there were several similarities to changes seen in those with alcohol use disorder [50]. Such suggestions may suggest that there could be resting-state changes also in sub-threshold gamblers that may link them on a continuum of changes with other addictions. Further research is required to determine the accuracy of such assumptions.

Conclusion

It is important to note that while the sub-threshold gamblers did not meet the requirements for gambling disorder, which was an *a priori* requirement, they still reported high levels of frequent gambling and thus this group should still be considered regular and experienced gamblers. We suggest that, based on the DSM-5 criteria of significant distress for diagnosis, this *lack* of distress leading to overall *unimpaired* decision-making of sub-threshold gamblers may have neurobiological underpinnings that differ from both non-gamblers but also from pathological gamblers. While overall decision-making brain region recruitment does not differ significantly between non-gamblers and sub-threshold gamblers, the reward pathways do. It is certainly conceivable that the vmPFC, in particular, plays an important role in the development of Gambling Disorder, as frequent gamblers who do not meet the criteria fail to show the pattern of deactivation so robustly found [2] in this area. However, to understand possible differences it is suggested that future research contain groups of healthy controls, sub-threshold gamblers, and those with gambling disorder in order to examine differences between these groups. Our results suggest that the inclusion of frequent gamblers, who are sub-threshold for gambling disorder, may help greater understanding of some of brain changes that lead to the huge societal and individual issues caused by pathological gambling.

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