Increased Striatal Dopamine Synthesis Capacity in Gambling Addiction

Supplementary Information

Sensitivity Analyses

Atlas-based ROI results

In this analysis we estimated mean Ki values from anatomical ROIs (caudate, putamen and nucleus accumbens) based on the Hammersmith atlas (1) after normalizing whole-brain Ki images to MNI space. A repeated measures ANOVA with a Greenhouse-Geisser correction revealed a significant main effect of ROI ($F(2,52)= 77.69$, $p<0.001$), as well as a Group * ROI interaction ($F(2,52)=3.939$, $p=0.027$), but no significant main effect of Group ($F(1,26)= 2.779$, $P=0.108$). The post-hoc tests investigating the Group * ROI interaction indicated significantly higher Ki values in pathological gamblers compared with controls in the putamen ($F(1,27)= 5.538$, $p=0.026$) (Figure S1), but not in the caudate ($F(1,27)= 1.246$, $p=0.275$) or ventral striatum ($F(1,27)= 0.969$, $p=0.334$) (Figure S1).

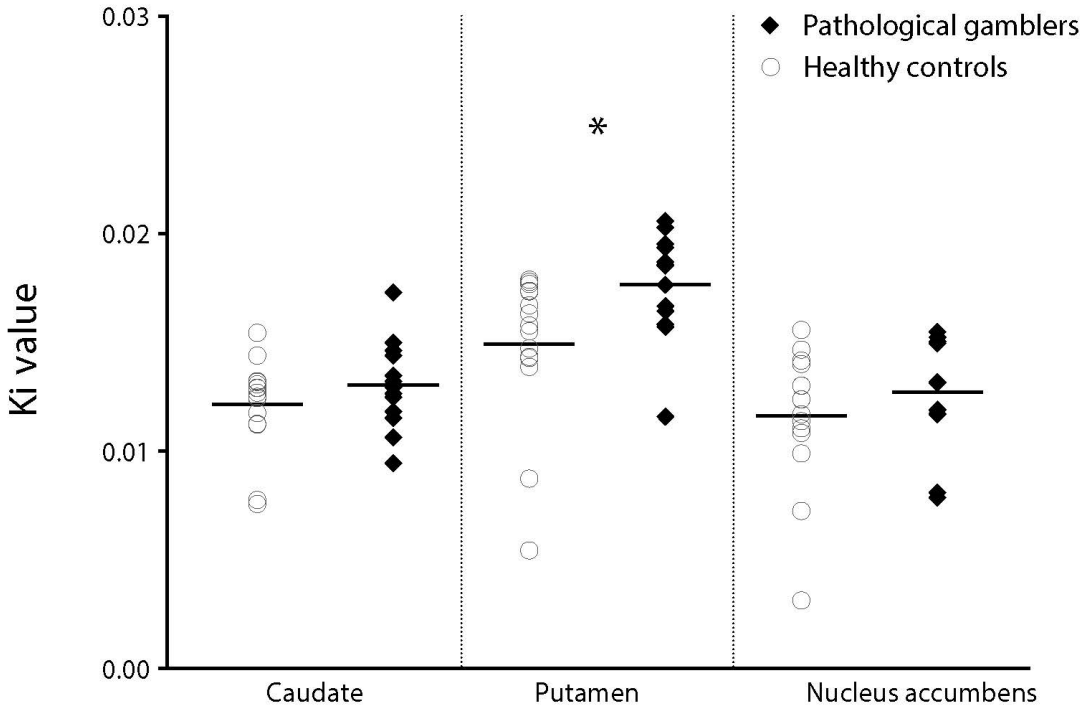

Figure S1: Scatter plot showing K_i values in anatomical ROIs in pathological gamblers and healthy controls. *p<0.05.

Results including the two pathological gamblers with comorbid cannabis dependence

Overall, including the two comorbid pathological gamblers led to similar but weaker results. Note however that the exclusion of these gamblers was precisely motivated by the known confounding effect of drug toxicity on dopaminergic functioning, and the suspicion of different dopamine-related abnormalities in drug vs gambling addiction (2).

Non partial volume corrected results. A repeated measures ANOVA with a Greenhouse-Geisser correction of Ki values within the non-PVC hand-drawn ROIs revealed a significant main effect of ROI ($F(3,84)= 131.622$, $p<0.001$) as well as a Group * ROI interaction ($F(3,84)=3.767$, $p=0.029$), but no significant main effect of Group ($F(1,28)= 2.977$, $p=0.095$). The post-hoc tests investigating the Group * ROI interaction indicated significantly higher Ki values in pathological gamblers compared with controls in the putamen ($F(1,29)= 4.593$, $p=0.041$), as well as a similar trend in the caudate body ($F(1,29)= 3.781$, $p=0.062$) and ventral striatum ($F(1,29)= 3.118$, $p=0.088$), but not in the caudate head ($F(1,29)= 0.218$, $p=0.644$) (Figure S2).

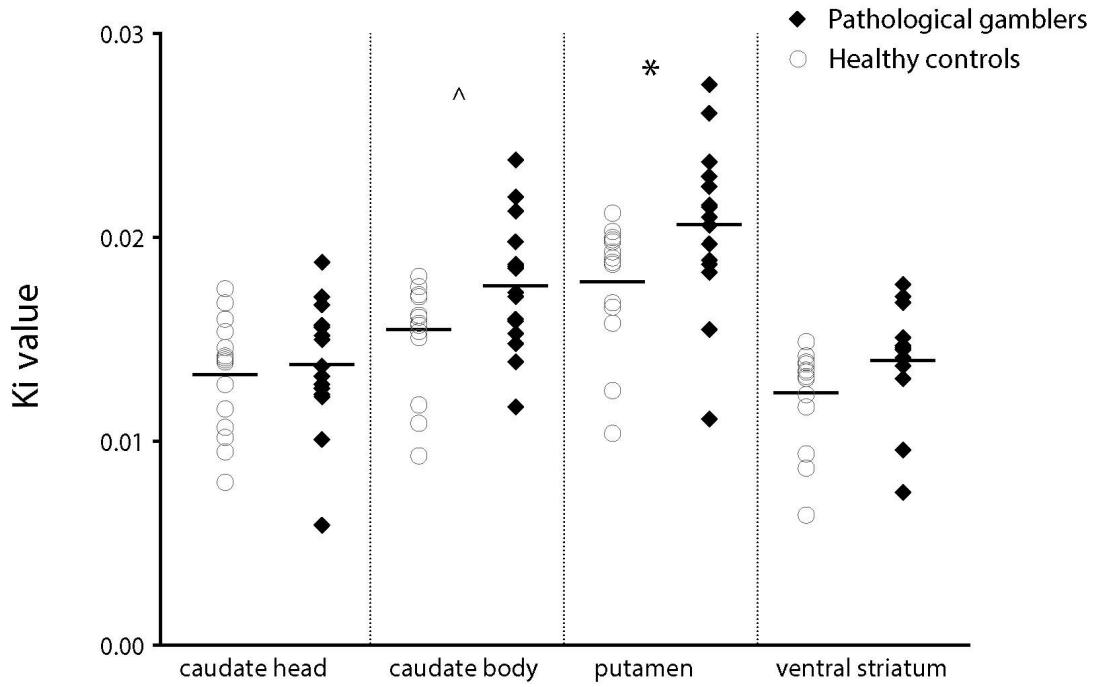

Figure S2: Scatter plot showing K_i values in non-PVC hand-drawn ROIs in pathological gamblers (including the two gamblers with comorbid cannabis dependence) and healthy controls. *$p<0.05$ ^$p<0.1$.

Partial volume corrected results. A repeated measures ANOVA with a Greenhouse-Geisser correction of Ki values within the PVC hand-drawn ROIs revealed a significant main effect of ROI ($F(3,84)= 93.589$, $p<0.001$), but no significant main effect of Group ($F(1,28)=2.304$, $p=0.140$) or a Group * ROI interaction ($F(3,84)=1.281$, $p=0.285$). The post-hoc tests investigating the Group * ROI interaction indicated significantly higher Ki values in pathological gamblers compared with controls in the putamen ($F(1,28)= 4.363$, $p=0.046$), but not in the caudate body ($F(1,28)= 0.968$, $p=0.334$), caudate head ($F(1,28)= 2.436$, $p=0.130$) or ventral striatum ($F(1,28)= 2.304$, $p=0.140$) (Figure S3).

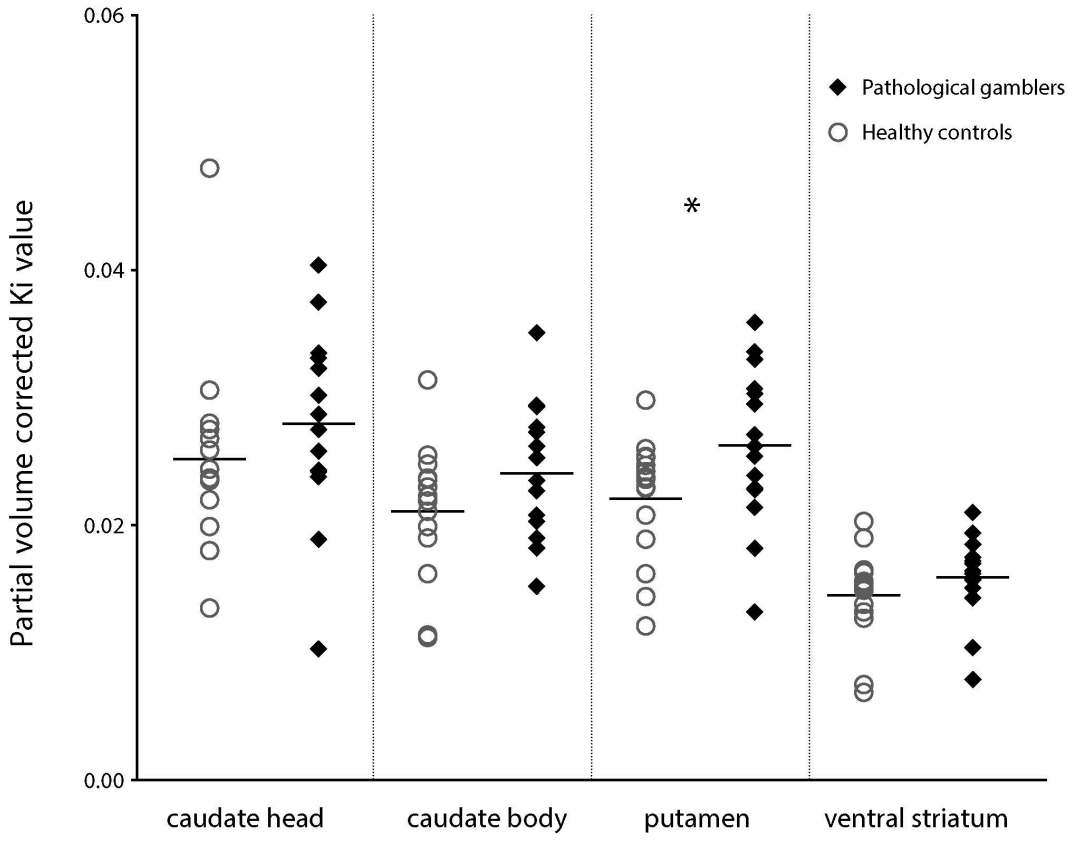

Figure S3: Scatter plot showing K_i values in PVC hand-drawn ROIs in pathological gamblers (including the two gamblers with comorbid cannabis dependence) and healthy controls. *p<0.05.

Atlas-based ROI derived results. A repeated measures ANOVA with a Greenhouse-Geisser correction of Ki values within atlas-based ROIs revealed a significant main effect of ROI ($F(2,56)= 77.367$, $p<0.001$), as well as a Group * ROI interaction ($F(2,56)=4.029$, $p=0.023$), but no significant main effect of Group ($F(1,28)= 1.250$, $p=0.273$). The post-hoc tests investigating the Group * ROI interaction indicated a trend for pathological gamblers to have higher Ki values compared with controls in the putamen ($F(1,29)= 3.398$, $p=0.076$), but not in the caudate ($F(1,29)= 0.425$, $p=0.520$) or nucleus accumbens ($F(1,29)= 0.201$, $p=0.657$) (Figure S4).

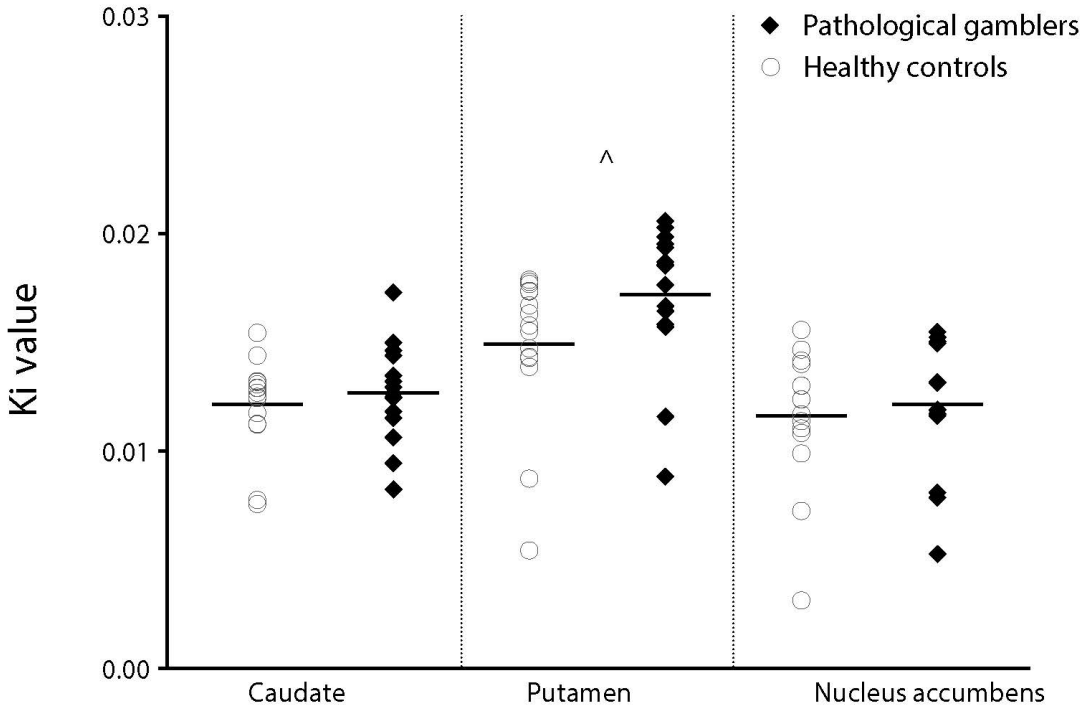

Figure S4: Scatter plot showing K_i values in anatomical ROIs in pathological gamblers (including the two gamblers with comorbid cannabis dependence) and healthy controls. ^$p<0.1$.

Correlations Between Questionnaires in Pathological Gamblers

Testing the correlations between questionnaires within the pathological gambling group did not reveal any significant relationships (BIS-11 and GBQ: $r=.471$, $p=0.117$, past-year SOGS and GBQ: $r=.001$, $p=0.998$), and past-year SOGS and BIS-11: $r=.005= p=0.877$).

Supplementary References

1. Hammers A, Allom R, Koepp MJ, Free SL, Myers R, Lemieux L, et al. No Title. Wiley Subscription Services, Inc., A Wiley Company; 2003 Aug;19(4).

2. Clark L. Disordered gambling: the evolving concept of behavioral addiction. Ann N Y Acad Sci. 2014 Oct;1327(1):46–61.