Diminished Fronto-Striatal Activity during Processing of Monetary Rewards and Losses in Pathological Gambling

Supplemental Information

Supplemental Methods

Participants Continued

All participants were native English speakers and each group included one left-handed individual (demographic and self-reported measures are displayed in Table 1). Participants consisted of a community sample recruited through advertisements and flyers in the New Haven area. Pathological gambling (PG) status was assessed using the Structured Clinical Interview for Pathological Gambling – a diagnostic tool that has demonstrated clinical validity and reliability in PG samples (1). Co-occurring disorders were assessed via a Structured Clinical Interview for DSM-IV Disorders (SCID; (2)). With the exception of nicotine dependence, participants in both groups had no other current co-occurring conditions. In the PG group, four participants met past (> 3 months) criteria for alcohol abuse, one for cannabis abuse and one for alcohol dependence.

Monetary Incentive Delay Task (MIDT) fMRI Task

Participants completed two runs of the MIDT task, each consisting of 55 trials, lasting 12 seconds each (3). Each trial consisted of two anticipatory periods (A1 and A2) and one outcome phase (OC) schematically depicted in Figure 1. During the A1 phase, participants viewed a cue (duration: 1000 milliseconds) signaling the potential win or loss of a specific amount of money (either $1 or $5) and then fixated on a crosshair (variable delay of 3-5 seconds). In the A2 phase, a target appeared on the screen (variable duration) and participants pressed a button and then fixated on a crosshair (variable delay of 4-6 seconds). Finally, in the outcome phase, participants received feedback (duration: 1200 milliseconds) on the win or loss of money and also viewed their cumulative earnings on the task.

fMRI volume acquisitions were time-locked to the offset of each cue and trial types were pseudorandomly ordered within each session. Task difficulty was based on practice reaction times collected prior to the scanning session and set so that participants would experience a positive outcome on 66% of trials. All participants were informed that their compensation on the task was performance-based.

The current task has been adapted from the original MIDT (4) in several ways. First, the anticipatory phase was segregated into two periods, with A1 corresponding to the prospect of reward/loss and A2 associated with the anticipation of the reward/loss. Second, the abstract cues to signal the potential win or loss of money were replaced with the actual words (e.g. “Win $1” or “Lose $5”) in order to minimize working memory components of the task. Third, a neutral stimulus of “Win $0” or “Lose $0” was included to counterbalance conditions. Fourth, in order to separate each task phase, every period was extended by several seconds. Fifth, the motoric demands associated with pressing a button were contained in the A2 phase, while the motor preparation was contained in the A1 phase.

Image Acquisition and Analysis

Localizer images were acquired aligning the eighth slice parallel to the plane transecting the anterior and posterior commissures. Functional images were acquired with a T2*-weighed blood oxygen level dependent (BOLD) sequence with a TR of 1500 ms, TE of 27, flip angle of 60°, 64 x 64 in-plane matrix, field of view of 220 x 220 and 25 4 mm slices with 1 mm skip. High-resolution 3D MPRAGE structural images were also acquired with a TR of 2530 ms, TE of 3.34 ms, flip angle of 7°, 256 x 256 in-plane matrix, and 176 1 mm slices. Each MIDT fMRI run consisted of 486 volumes, including an initial rest period of 9 seconds for signal stability, which was subsequently removed from analyses. Statistical analyses used a robust general linear model approach and each phase of each trial type was separately modeled. Analyses combined “Win $1” and “Win $5” trials, “Lose $1” and “Lose $5” trials, and “Win $0” and “Lose $0” trials in reward, penalty and neutral conditions in order to increase power.

Experimental Procedure

Participants completed a practice version of the MIDT before entering the scanner in order to familiarize individuals with the task and minimize learning effects. Additionally, the practice session served to calibrate the computerized task so that in the scanner each individual would win on approximately 66% of trials. All participants were informed that their reimbursement would be influenced by their in-scanner performance. In the scanner, individuals completed the MIDT in two 10-minute sessions. Following each session, participants rated, on a 4-point Likert scale, specific emotions associated with each of the cue presentations (e.g. ‘Happy’ or ‘Sad’).

Supplemental Results

Main Effects

Main effects of the MIDT related to specific task phases are depicted in the control comparison (CC) group in Figure S3 and Table S1.

Affective Responses

A 2 (Group) X 6 (Affective Rating) repeated-measures analysis of variance (ANOVA) examining affective responses to the incentive value of different trial types showed a main effect of affect rating [$F(5,130) = 154.54$, $p < 0.001$]. Pairwise comparisons revealed that, in a stepwise fashion, participants reported significantly greater cue-elicited “happiness” when winning $5 than when winning $1, which in turn, was rated higher than winning $0 ($p < 0.05$). There was no significant difference in affect rating in winning $0 or losing $0 ($p > 0.05$). Compared to these former ratings, participants reported significantly greater cue-elicited “unhappiness” when losing $1 ($p < 0.05$), but even greater unhappiness when they lost $5 ($p < 0.05$). There was no significant difference in affective ratings between the PG and the CC groups [$F(1,26) = 2.31$, $p > 0.05$] and no group-by-affect interaction [$F(5,130) = 1.64$, $p > 0.05$].

In-Scanner Behavior

Multiple one-way ANOVAs examining behavioral responses in-scanner showed no significant between-groups differences in earnings [$F(1,54) = 2.22$, $p > 0.05$] $M_{PG} = 42.32$ (16.74), $M_{CC} = 35.39$ (18.02), reaction times for win trials [$F(1,54) = 2.58$, $p > 0.05$] $M_{PG} = 221.05$ (44.08), $M_{CC} = 245.33$ (66.80) or loss trials [$F(1,54) = 0.91$, $p > 0.05$] $M_{PG} = 223.01$ (45.06), $M_{CC} = 239.89$ (82.24). There were also no between-group differences in hit rates on win trials [$F(1,54) = 3.64$, $p > 0.05$] $M_{PG} = 18.18$ (2.70), $M_{CC} = 16.75$ (2.90) or on loss trials [$F(1,54) = 0.35$, $p > 0.05$] $M_{PG} = 17.43$ (2.78), $M_{CC} = 16.96$ (3.11).

Correlations Between Impulsivity and Gambling Severity

A Pearson product-moment correlation coefficient was computed to assess the relationship between self-reported impulsivity and gambling severity, as measured by the South Oaks Gambling Screen (SOGS). There were no significant correlations between SOGS scores in the PG group with Barratt Impulsivity Scale (BIS-11) total or subscale scores (all $p > 0.05$).

Ventral Striatum (VS) Activation and Impulsivity

Pearson correlations were calculated between impulsivity and VS activity, additionally collapsing across the right and left sides of this region of interest. Using this approach, and concurrent with the original analysis, we found the right VS activation correlated inversely with BIS-11 Total (r = -0.56, $p < 0.05$) and Attention subscale (r = -0.66, $p < 0.05$) scores during the A2Loss phase. There were no other significant correlations between the VS and BIS-11 scores in any other anticipatory phase.

The removal of one individual's data in the PG group with a particularly low BIS-11 score leads to a between-group difference in impulsivity [M_{PG} = 70.39 (9.03), M_{CC} = 59.13 (12.08); $F(1,24) = 7.24$, $p < 0.05$] and does not alter the correlations between the right VS activity and impulsivity scores, although the correlation between the left VS and the Motor subscale during the A2Win phase is no longer significant ($p < 0.05$).

Whole Brain Correlations with Impulsivity

Whole-brain correlational analyses examining BIS-11 scores during anticipatory phases in the PG group identified correlations with corticostriatal-limbic areas (Table S3; Figure S4).

Table S1. Main effects during MIDT trials in the Comparison Control group (*n* = 14)

MIDT Phase	Structure	BA	Left/ Right	MNI Coordinates x	y	z	k	t-value
A1 Winning	Midbrain Substantia Nigra/Anterior Cingulate/Caudate/Insula/Claustrum/ Culmen/Lentiform Nucleus/ Thalamus/Medial Frontal Gyrus/ Superior Temporal Gyrus	-	L	-9	-27	-18	10720	7.50
	Middle Temporal Gyrus/Superior Occipital Gyrus	39	L	-39	-72	18	326	5.09
	Inferior Parietal Lobule/Superior Temporal Gyrus	39	L	-39	-72	18	444	-5.86
	Inferior Frontal Gyrus/Middle Frontal Gyrus/Inferior Frontal Gyrus	45	L	-51	21	18	716	-4.76
	Middle Temporal Gyrus	22	L	-57	-42	-6	190	-3.66
A1 Losing	Midbrain Substantia Nigra/Culmen/ Precentral Gyrus/Postcentral Gyrus/ Cingulate Gyrus/Insula/Fusiform Gyrus/Caudate/Lentiform Nucleus/ Claustrum/Inferior Parietal Lobule/ Thalamus/Posterior Cingulate	-	L	-9	-30	-15	15272	7.20
	Middle Frontal Gyrus	10	R	27	48	21	154	4.08
	Middle Frontal Gyrus/Inferior Frontal Gyrus	11	L	-36	42	-21	180	-4.98
	Precuneus/Superior Temporal Gyrus	19	L	-42	-72	8	268	-4.46
A2 Winning	Cingulate Gyrus/Middle Temporal Gyrus/Thalamus/Precentral Gyrus/ Caudate/ Insula/Inferior Frontal Gyrus	24	L	-18	0	36	3931	8.19
	Cerebellum/Cuneus/Declive/ Lingual Gyrus	-	R	3	-87	-27	644	4.68
	Inferior Frontal Gyrus/Middle Frontal Gyrus/Inferior Frontal Gyrus	47	L	-45	27	-21	356	-5.59
	Precuneus/Posterior Cingulate/ Cuneus	31	L	-15	-63	18	224	-5.44
	Angular Gyrus/Superior Parietal Lobule/Superior Frontal Gyrus/ Medial Frontal Gyrus	39	L	-45	-69	33	298	-5.17
	Superior Frontal Gyrus	8	L	-27	30	51	245	-4.51
	Middle Temporal Gyrus	39	R	54	-66	24	105	-3.92
A2 Losing	Parahippocampal Gyrus/Insula/ Caudate/Claustrum/Superior Temporal Gyrus/Thalamus	30	L	-33	-51	3	1882	6.70
	Declive Inferior Occipital Gyrus/ Lingual Gyrus	-	L	-30	-93	-27	457	4.20
	Precuneus Posterior Cingulate/ Middle Temporal Gyrus/Cuneus/ Precuneus	31	L	-3	-60	30	2042	-7.93
	Middle Frontal Gyrus/Middle	8	L	-27	24	48	2246	-7.66

	Temporal Gyrus/Superior Temporal Gyrus/Medial Frontal Gyrus/Inferior Frontal Gyrus/Superior Frontal Gyrus/Precentral Gyrus							
	Parahippocampal Gyrus/Midbrain Substantia Nigra	35	L	-21	-18	-18	177	-5.85
	Postcentral Gyrus/Superior Temporal Gyrus/Middle Temporal Gyrus/ Inferior Temporal Gyrus	1	R	66	-9	30	274	-4.85
	Middle Temporal Gyrus	39	R	54	-69	24	306	-4.50
	Superior Temporal Gyrus	38	L	-54	9	-18	97	-4.42
	Precentral Gyrus/Postcentral Gyrus	4	L	-54	-9	36	106	-4.30
Winning Outcome	Parahippocampal Gyrus/Cerebellar Lingual/Insula/Superior Temporal Gyrus/Precentral Gyrus/Caudate/ Medial Frontal Gyrus/Thalamus/ Postcentral Gyrus/Culmen/Anterior Cingulate/Middle Temporal Gyrus/ Inferior Parietal Lobule	30	R	24	-48	9	10630	8.51
	Medial Frontal Gyrus/Anterior Cingulate	11	L	0	33	-15	121	3.56
	Lingual Gyrus/Fusiform Gyrus/ Superior Parietal Lobule/Inferior Temporal Gyrus/Superior Parietal Lobule/Middle Temporal Gyrus/ Cuneus/Middle Occipital Gyrus	18	R	24	-78	-9	5214	-8.65
	Inferior Frontal Gyrus/Middle Frontal Gyrus	9	L	-48	12	33	1144	-7.93
	Inferior Frontal Gyrus/Precentral Gyrus/Middle Frontal Gyrus	9	R	54	12	30	748	-5.33
Losing Outcome	Anterior Cingulate/Medial Frontal Gyrus/Superior Frontal Gyrus	32	R	9	42	6	595	6.03
	Middle Temporal Gyrus/Cingulate Gyrus/Postcentral Gyrus/Caudate/ Superior Temporal Gyrus/ Precuneus/Inferior Parietal Lobule	19	R	33	-57	15	3106	-9.64

BA, Brodmann’s area; L, left; MIDT, Monetary Incentive Delay Task; MNI, Montreal Neurological Institute; R, right.

Table S2. Pearson correlation coefficients between extracted activation from a 3 mm sphere in the ventral striatum on the left (-10, 12, -11) and the right (10, 12, -11) sides during specific anticipatory task phases and all BIS scores in the PG group (n = 14) and in the CC group (n = 13).

		A1 Win Phase		A1 Loss Phase		A2 Win Phase		A2 Loss Phase	
		r	***p***	***r***	***p***	***r***	***p***	***r***	***p***
PG GROUP									
BIS-Total	R	-0.348	0.223	-0.373	0.189	-0.006	0.985	-0.631*	0.016
	L	-.056	0.849	-0.259	0.372	-0.414	0.141	-0.433	0.122
Attention Subscale	R	-0.168	0.566	-0.158	0.588	-0.220	0.449	-0.755**	0.002
	L	0.081	0.782	0.024	0.935	-0.398	0.159	-0.494	0.072
Nonplanning Subscale	R	-0.351	0.218	-0.321	0.264	0.118	0.689	-0.445	0.111
	L	-0.222	0.445	-0.195	0.503	-0.147	0.615	-0.209	0.473
Motor Subscale	R	-0.352	0.217	-0.467	0.092	0.061	0.837	-0.427	0.128
	L	0.035	0.906	-0.488	0.076	-0.550*	0.042	-0.433	0.122
CC GROUP									
BIS-Total	R	0.048	0.876	-0.042	0.891	-0.057	0.852	-0.252	0.406
	L	-0.390	0.187	-0.490	0.089	-0.036	0.907	-0.201	0.510
Attention Subscale	R	0.126	0.681	0.097	0.751	-0.220	0.471	-0.186	0.543
	L	-0.376	0.205	-0.428	0.145	-0.231	0.448	-0.357	0.231
Nonplanning Subscale	R	-0.090	0.771	-0.216	0.478	-0.026	0.933	-0.353	0.237
	L	-0.474	0.102	-0.519	0.069	0.040	0.898	0.022	0.942
Motor Subscale	R	0.132	0.668	0.055	0.858	0.069	0.822	-0.116	0.705
	L	-0.188	0.539	-0.369	0.215	0.060	0.845	-0.274	0.366

BIS, Barratt Impulsivity Scale; CC, control comparison; L, left; PG, problem gambling; R, right.
*$p < 0.05$.
**$p < 0.01$.

Table S3. Whole-brain correlations between the BIS-11 and anticipatory phases on the MIDT in the PG group.

BIS-11 Correlation	Structure	BA	Left/ Right	MNI Coordinates x	y	z	k	r-value
A1 Winning > A1 Neutral	Subcallosal Gyrus/Inferior Frontal Gyrus	25	L	-6	18	-21	126	0.869
	Middle Frontal Gyrus/Superior Frontal Gyrus	6	L	-36	12	60	550	0.858
	Middle Temporal Gyrus/Fusiform Gyrus/Parahippocampal Gyrus/ Inferior Temporal Gyrus	21	L	-63	-33	-15	585	0.851
	Parahippocampal Gyrus/Fusiform Gyrus/Middle Temporal Gyrus	35	R	27	-18	-33	415	0.825
	Pyramis/Uvula	-	R	18	-87	-45	123	0.798
	Inferior Frontal Gyrus	47	L	-9	72	0	210	0.789
	Inferior Occipital Gyrus/Cuneus/ Declive/Middle Occipital Gyrus	18	L	-39	-96	-9	194	0.734
	Superior Frontal Gyrus/Medial Frontal Gyrus	10	L	-9	72	0	-210	-0.922
	Superior Temporal Gyrus	38	R	45	21	-27	138	-0.907
	Culmen/Middle Occipital Gyrus/ Lingual Gyrus/Transverse Temporal Gyrus/Thalamus/Precuneus/Insula/ Posterior Cingulate	-	R	6	-60	-3	2118	-0.870
	Superior Frontal Gyrus/Middle Frontal Gyrus	6	L	-18	12	54	230	-0.804
	Parahippocampal Gyrus/ Hippocampus/Thalamus	35	L	-30	-30	-9	104	-0.801
	Postcentral Gyrus/Precentral Gyrus	3	R	54	-3	45	243	-0.782
	Thalamus	-	R	9	-6	12	97	-0.712
A1 Losing > A1 Neutral	Superior Frontal Gyrus/Medial Frontal Gyrus	10	L	-15	72	3	214	-0.922
	Middle Occipital Gyrus/Posterior Cingulate/Lingual Gyrus	19	L	-30	-87	12	797	-0.865
	Middle Occipital Gyrus	19	R	36	-78	0	201	-0.830
	Thalamus/Culmen	-	R	12	-36	12	188	-0.829
	Transverse Temporal Gyrus	42	L	-63	-9	6	196	-0.824
	Lingual Gyrus	18	R	9	-63	0	97	-0.819
	Transverse Temporal Gyrus/Superior Temporal Gyrus/Insula	41	R	45	-15	6	121	-0.810
	Superior Temporal Gyrus	41	R	45	-36	9	113	-0.790
	Parahippocampal Gyrus/ Hippocampus	35	L	-30	-21	-18	104	-0.754
A2 Winning > A2 Neutral	Superior Frontal Gyrus/Precentral Gyrus	6	R	18	3	72	121	-0.796
	Anterior Cingulate/Cingulate Gyrus	24	R	3	15	24	207	-0.783
A2 Losing > A2 Neutral	Middle Frontal Gyrus	6	R	24	18	57	101	-0.784
	Anterior Cingulate	24	R	3	15	24	101	-0.762

Table lists correlations between the Barratt Impulsivity Scale Total (BIS-11) scores in the PG group during each anticipatory phase contrasted with the neutral phase on the MIDT. Data are thresholded at an uncorrected level of $p < 0.05$ two-tailed and family-wise error-corrected at $p < 0.05$ with a cluster threshold of 91.
BA, Brodmann's area; L, left; MIDT, Monetary Incentive Delay Task; MNI, Montreal Neurological Institute; PG, problem gambling; R, right.

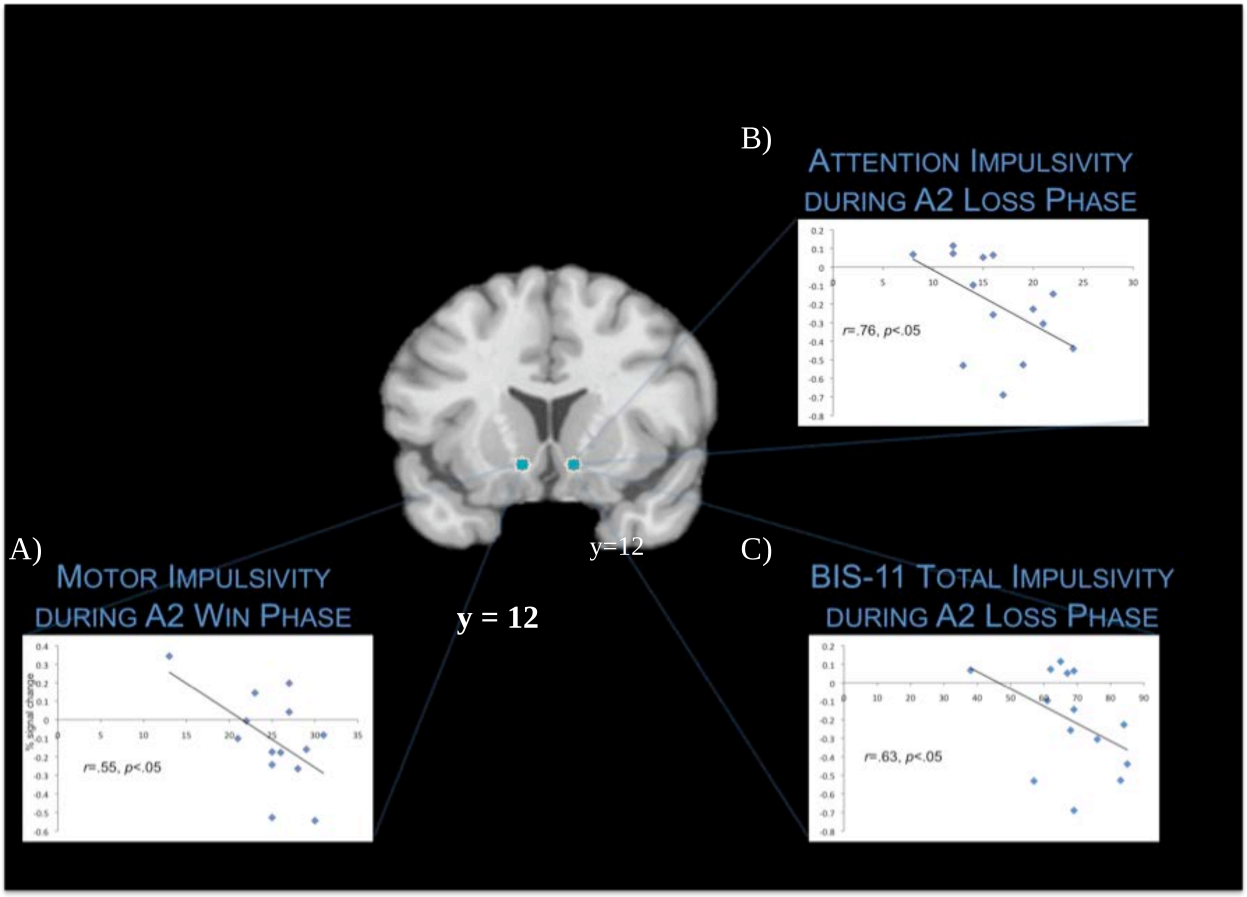

Figure S1. Coronal view of ventral striatal region of interest [±10, 12, -11]. Blue spots indicate a 3 mm sphere around the ventral striatum. a) Scatterplot demonstrating correlation between the BIS-11 Motor Subscale and % signal change during the A2 Win Phase on the MIDT in the PG group (n = 14). b) Scatterplot demonstrating the correlation between the BIS-11 Attention Subscale and % signal change during the A2 Loss Phase on the MIDT in the PG group (n = 14). c) Scatterplot depicting the correlation between the BIS-11 Total scores and % signal change during the A2 Loss Phase on the MIDT in the PG group (n = 14). BIS, Barratt Impulsivity Scale; MIDT, Monetary Incentive Delay Task; PG, problem gambling.

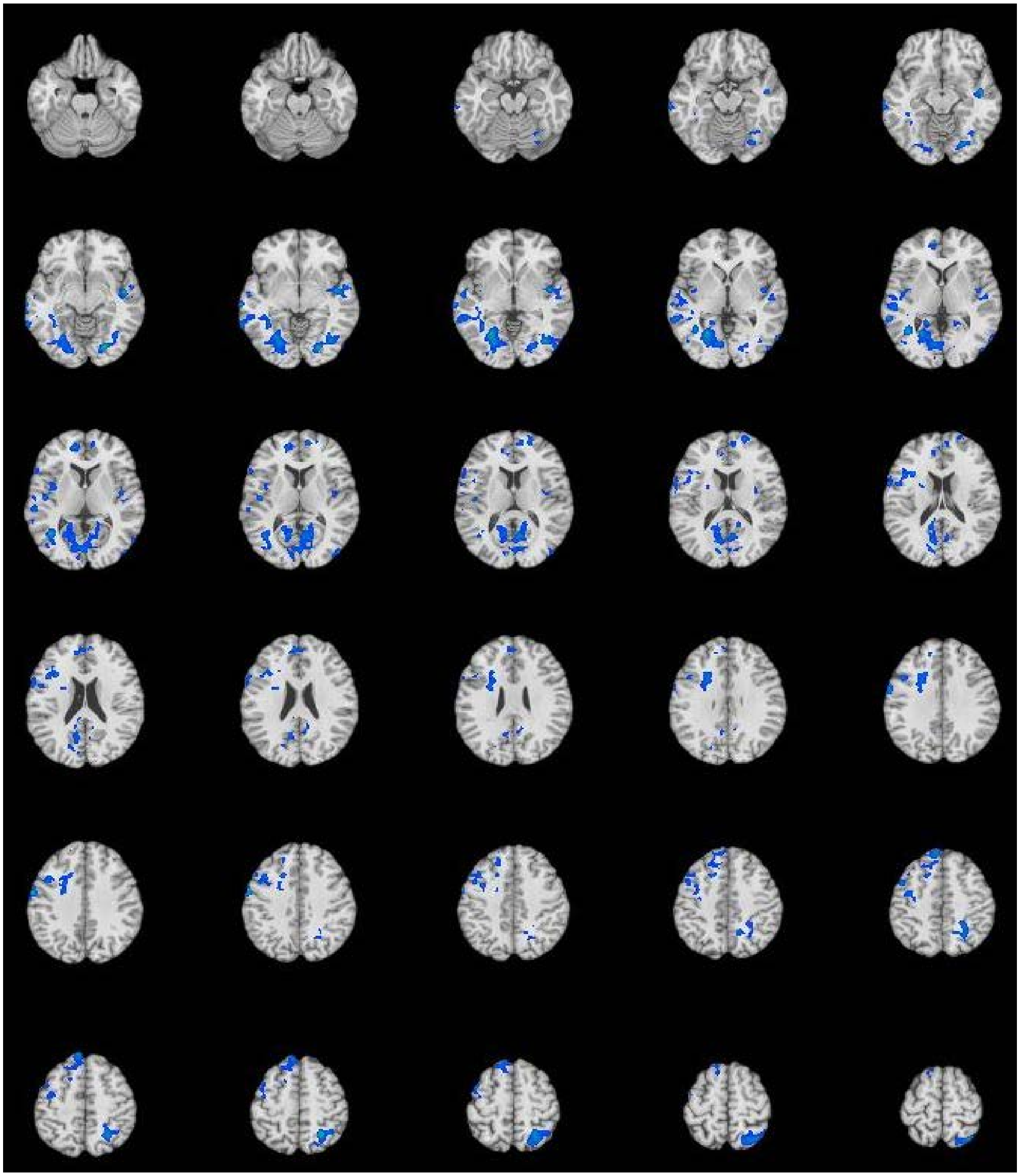

Figure S2. Group differences on the MIDT during the Outcome Loss Phase: PGvsCC. Axial view of brain activation maps demonstrate differences in the PG group contrasted with the CC group during the Outcome Loss Phase. All contrast maps are thresholded at an uncorrected level of $p < 0.05$ two-tailed and family-wise error-corrected at $p < 0.05$ with a cluster threshold of 91. Blue color demonstrates areas of significant differences between PG and CC groups where PG subjects show relatively less activation and red color indicates areas where PG subjects show relatively greater activation. The right side of the brain is on the right. Maps begin at z = -25 and increase in steps of 3 to z = 62. CC, control comparison; MIDT, Monetary Incentive Delay Task; PG, problem gambling.

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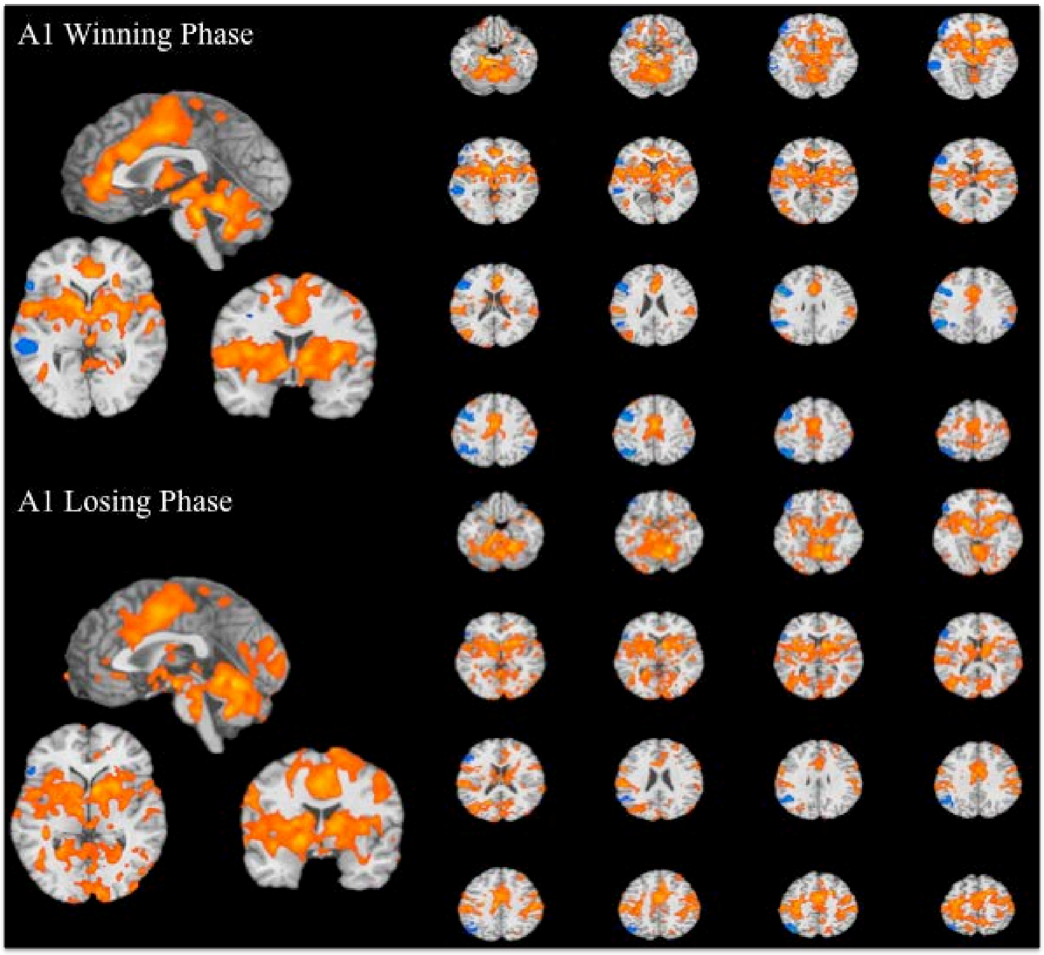

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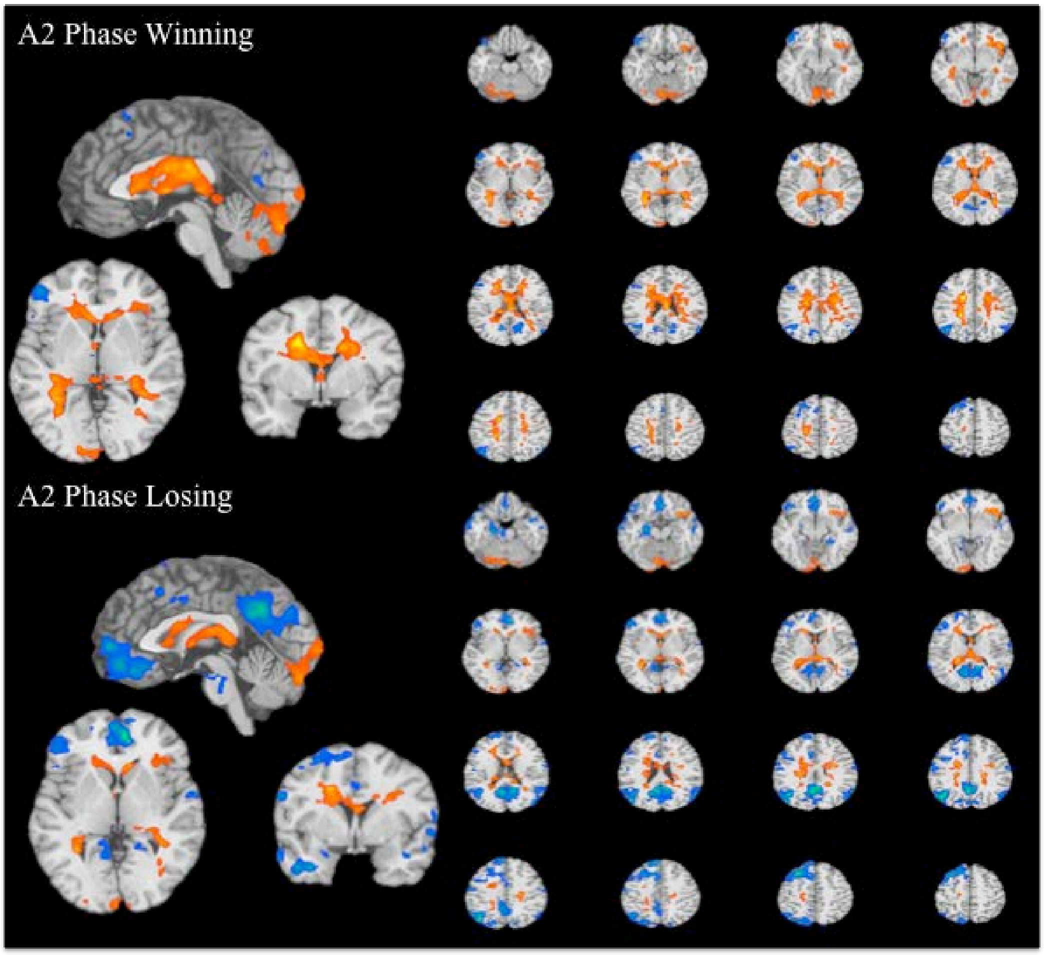

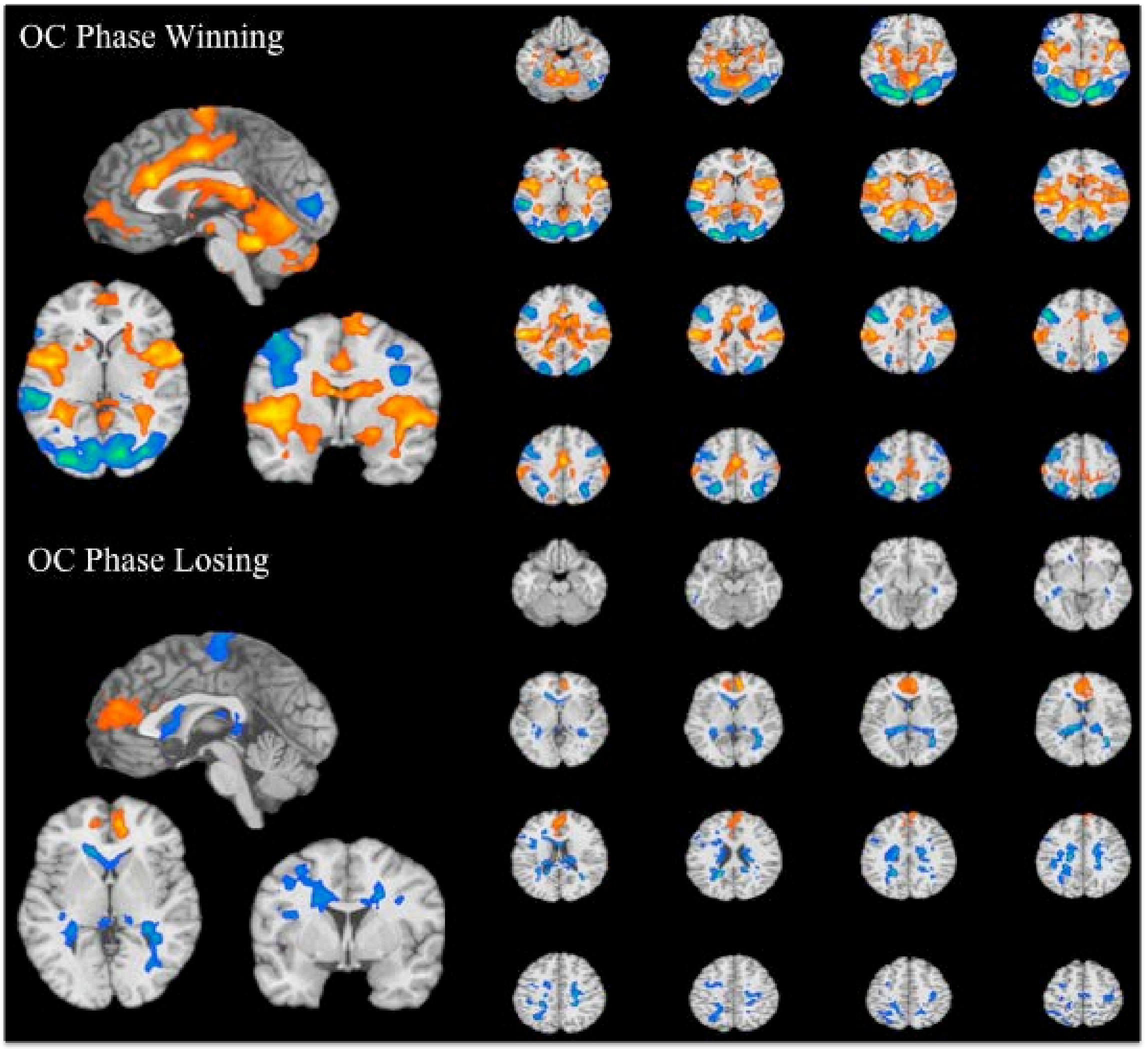

Figure S3. Main effects of the MIDT in the CC group during all 3 task phases. Brain activation maps demonstrate activity in the CC group during each phase contrasted with the neutral phase on the MIDT (n = 14). All contrast maps are thresholded at an uncorrected level of $p < 0.05$ two-tailed and family-wise error-corrected at $p < 0.05$ with a cluster threshold of 91. Blue color demonstrates areas of relatively diminished activity between the task phase and red color indicates areas with relatively greater activation when contrasted with the neutral condition. The right side of the brain is on the right. Axial maps on the left begin at z = -22 and increase in steps of 5 to z = 60. Larger maps on the left show sagittal (x = 0), coronal (y = 0) and axial views (z = 0). CC, control comparison; MIDT, Monetary Incentive Delay Task; OC, outcome.

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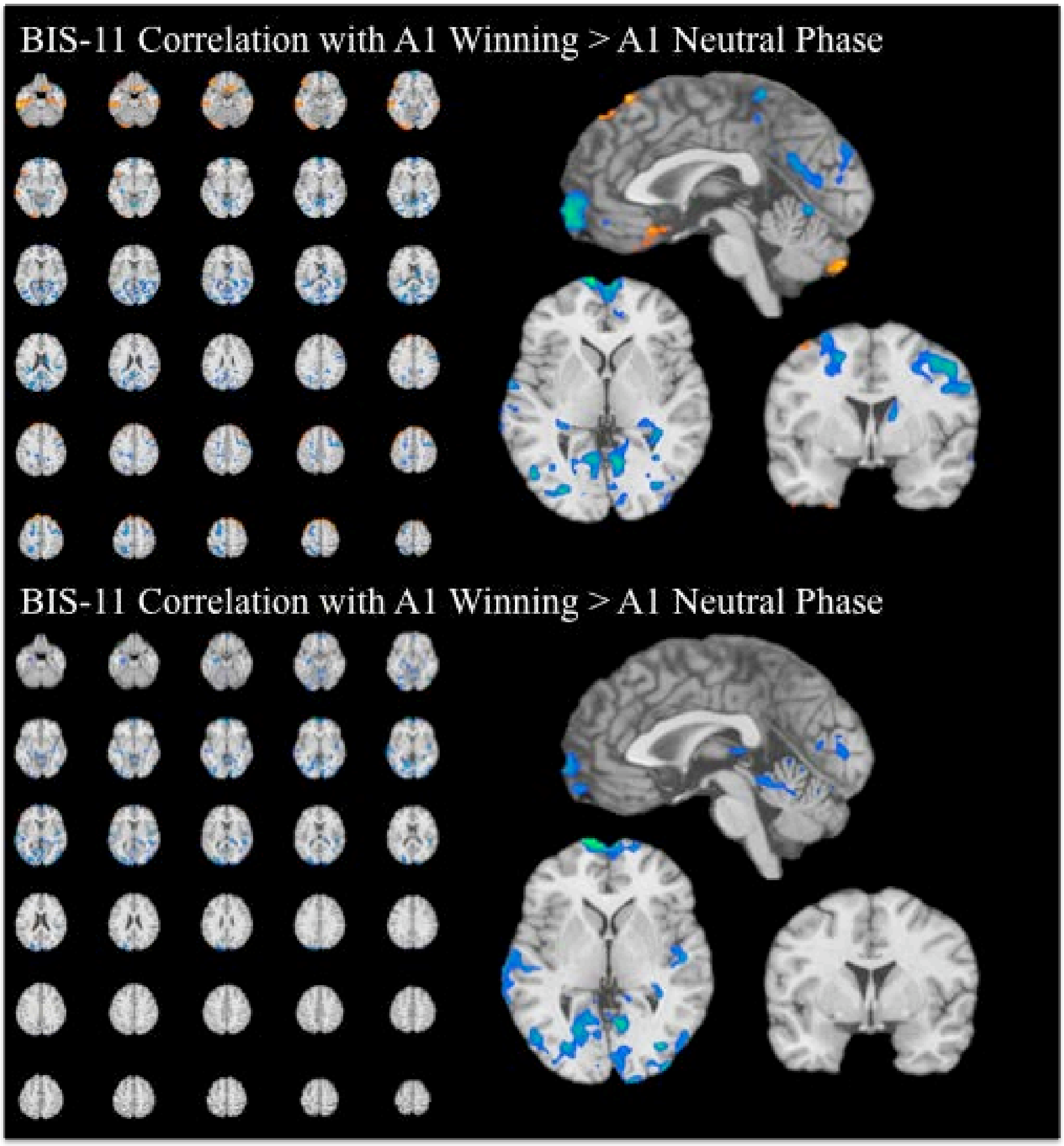

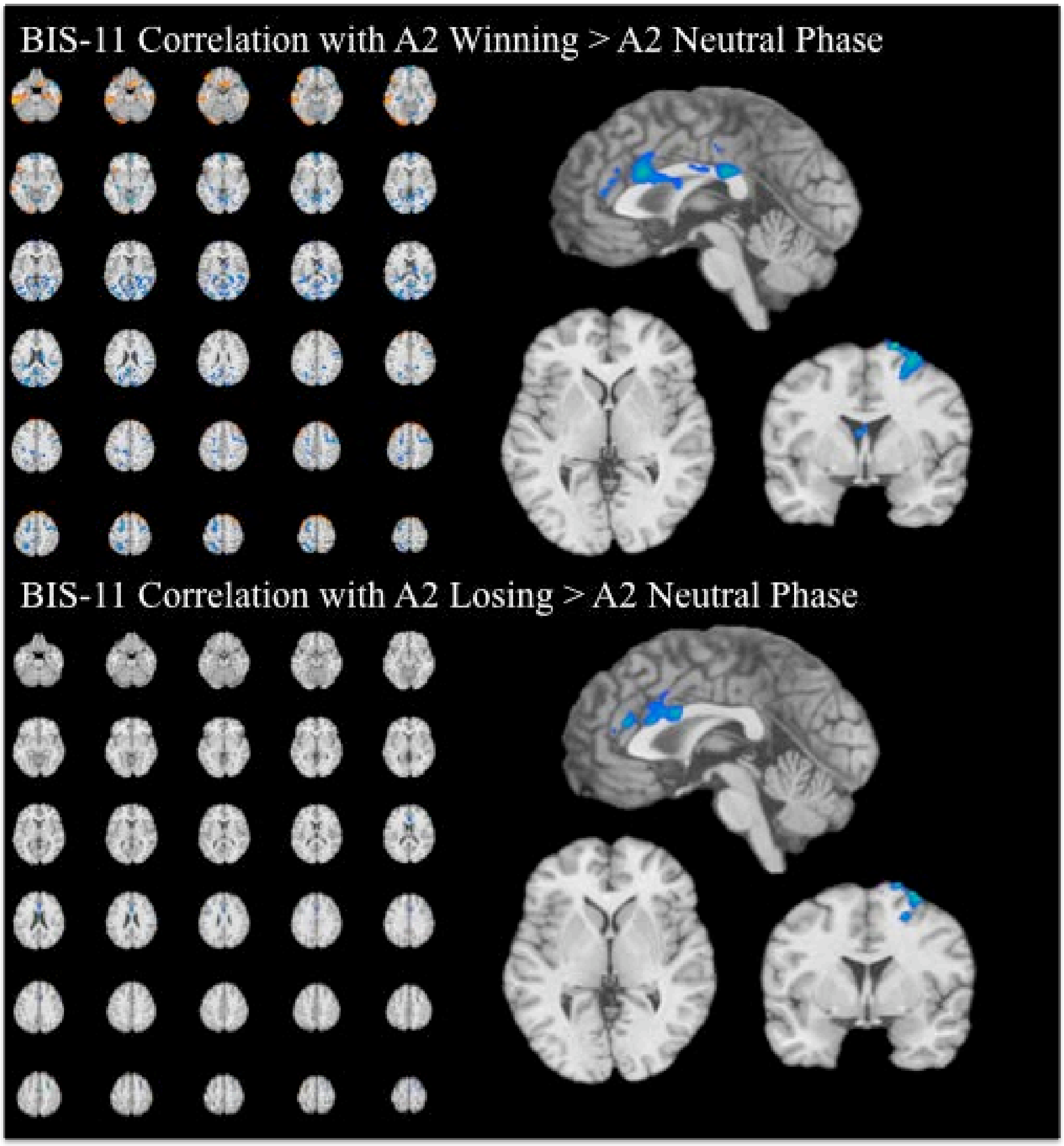

Figure S4. Correlations between the BIS-11 and Anticipatory Phases on the MIDT in the PG group. Correlational maps demonstrate relationship between BIS-11 scores in the PG group during each anticipatory phase contrasted with the neutral phase on the MIDT (*n* = 14). All contrast maps are thresholded at an uncorrected level of $p < 0.05$ two-tailed and family-wise error-corrected at $p < 0.05$ with a cluster threshold of 91. Blue color demonstrates areas with negative correlations and red color indicates areas with positive correlations. The right side of the brain is on the right. Axial correlational maps on the left begin at z = -25 and increase in steps of 3 to z = 62. Larger maps on the right show sagittal (x = 0), coronal (y = 0) and axial views (z = 0). BIS, Barratt Impulsivity Scale; MIDT, Monetary Incentive Delay Task; PG, problem gambling.

Supplemental References

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