Young Adults at Risk for Stimulant Dependence Show Reward Dysfunction during Reinforcement-Based Decision Making

Supplemental Information

Supplemental Methods

Tables S1-S3: Group Results

Please refer to the Methods section of the main text. Tables S1-S3 report functional magnetic resonance imaging (fMRI) linear mixed effects (LME) group differences for early versus late trials.

Tables S4-S5: Robust Regressions for Substance Use

Since it was not theoretically appropriate to include lifetime stimulant and cannabis use as well as current alcohol and nicotine use as covariates in the main LME group analysis given that that occasional stimulant users (OSU) and control (CTL) groups differed significantly on these variables (1), two robust regressions (2, 3) were performed in R within OSU only (n = 161) to examine whether a priori regions (striatum, inferior frontal gyrus (IFG), insula) were associated with these measures. Each regression was subject to a bootstrapping procedure in R in order to obtain confidence limits, estimated bias coefficients, and t statistics (random sampling with replacement; n = 25 bootstraps, n = 50 maximum iterations, confidence intervals set at 95%) for each regressor. Given that LME group by decision findings revealed important group differences during late trials, the dependent variable was percent signal change during late trials. Analogous whole brain and limbic mask Alpha Sim values used for the group by decision time LME interaction were applied. The first regression examined unique variance associated with three predictors indexing lifetime use: 1) prescription stimulants, 2) cocaine, and 3) cannabis. The second regression examined unique variance associated with two predictors of current use: 1) number of cigarettes per day, and 2) number of alcohol drinks per week. All variables except weekly alcohol use

were natural log transformed + 1 due to non-normal distributions, and all variables were z-scored prior to regression entry.

Table S6: Early and Late Trials Separately

Two *t*-tests were performed in AFNI to compare OSU and CTL for early trials and late trials in the decision phase separately in order to examine differences in the processing of uncertainty (trial-and-error learning of action-outcome contingencies) apart from certainty (execution of learned contingencies). A threshold adjustment method based on Monte-Carlo simulations (AFNI's program Alpha Sim) was applied to guard against identifying false positive areas of activation (considering the whole brain voxel size and 4 mm smoothness). Alpha Sim identified a minimum cluster volume of 768 μL with a cluster significance of $p < .05$ corrected for multiple comparisons (voxel-wise probability: $p < .05$). Limbic masks were also applied to examine a priori hypotheses involving insula and dorsal striatum using a minimum cluster volume of 320 and 250 μL, respectively. For significant clusters, average percent signal change from baseline was extracted.

Table S7: Decisions during Preferred Response Selection

An exploratory analysis was performed for the decision phase in order to examine whether, regardless of early or late learning phase during decision making, OSU and CTL exhibited differential brain activation to trials in which they selected the preferred response. Each subject's behavioral performance determined three new regressors of interest: trials in which the subject selected 1) the preferred response, 2) the tied response, and 3) the worst response. A new deconvolution was performed, wherein three movement regressors (roll, pitch, and yaw), a baseline and linear drift regressor, and three behavioral regressors (preferred selection, even selection, worst selection), were convolved with a modified hemodynamic response function. The remaining fMRI preprocessing steps were analogous to those reported in the main text.

Group (OSU, CTL) and response type (preferred trials, even trials, worst trials) were subjected to a LME analysis across all voxels. Subjects were treated as random effects, whereas group and response type were modeled as fixed effects. The group by response type interaction effect was of interest to examine group differences in the response to rewarding trials. A threshold adjustment method based on Monte-Carlo simulations (AFNI's program Alpha Sim) was applied to guard against identifying false positive areas of activation (considering the whole brain voxel size and 4 mm smoothness). For the group by response type interaction, Alpha Sim identified a minimum cluster volume of 768 μL with a cluster significance of $p < .05$ corrected for multiple comparisons (voxel-wise probability: $p < .05$). Limbic masks were also applied to examine a priori hypotheses involving insula and dorsal striatum using a minimum cluster volume of 320 and 250 μL, respectively. For significant clusters, average percent signal change from baseline was extracted.

Table S8: Responses to Winning Outcomes

An exploratory analysis was performed in order to examine differential brain activation for OSU and CTL in response to wins during the outcome phase of the task only (wins, ties and losses). A separate deconvolution analysis pathway was conducted that focused on the outcome portion of each trial when win, tie, or loss feedback was presented to the subject, wherein three movement regressors (roll, pitch, and yaw), a baseline and linear drift regressor, and three behavioral regressors (wins, ties, losses), were convolved with a modified hemodynamic response function. The remaining fMRI preprocessing steps were analogous to those reported in the main text.

Group (OSU, CTL) and outcome (wins, ties, losses) were subjected to a LME analysis across all voxels. Subjects were treated as random effects, whereas group and outcome were modeled as fixed effects. The group by outcome interaction effect was of interest to examine group differences in the response to winning feedback. A threshold adjustment method based on Monte-Carlo simulations (AFNI's program Alpha Sim) was applied to guard against identifying false positive areas of activation

(considering the whole brain voxel size and 4 mm smoothness). For the group by outcome interaction, Alpha Sim identified a minimum cluster volume of 768 µL with a cluster significance of $p < .05$ corrected for multiple comparisons (voxel-wise probability: $p < .05$). Limbic masks were also applied to examine a priori hypotheses involving insula and dorsal striatum using a minimum cluster volume of 320 and 250 µL, respectively. For significant clusters, average percent signal change from baseline was extracted.

Supplemental Results

Tables S1-S3: Group Results

Please refer to the Results section of the main text.

Tables S4-S5: Robust Regressions for Substance Use

Results indicated that higher lifetime prescription stimulant use and current alcohol use were associated with lower dorsal striatum activation, whereas higher lifetime cannabis use was linked to greater dorsal striatum activation. In addition, higher current nicotine use was linked to lower insula and IFG activation (see Tables S4 and S5).

Table S6: Early and Late Trials Separately

During early trials, CTL exhibited greater medial frontal gyrus and left striatum activation than OSU when action-outcome contingencies were being established. In contrast, during late trials, OSU displayed greater anterior and posterior insula activation than CTL during the execution of learned contingencies. In addition, for early and late trials, OSU showed greater left middle frontal gyrus activation than CTL.

Table S7: Decisions during Preferred Response Selection

Results based on individual subjects' selection of the preferred, even and worst responses indicated that CTL exhibited greater dorsal striatum, IFG, anterior insula, and medial frontal gyrus activation than OSU during decision making for trials in which the preferred response was selected. OSU and CTL did not differ in activation for these regions during selection of the tied or worst response.

Table S8: Responses to Winning Outcomes

Findings for the outcome phase of the task showed that CTL displayed greater cuneus and hypothalamus activation than OSU during wins and ties. In contrast, OSU showed higher medial frontal gyrus activation than CTL for wins.

Supplemental Discussion

Tables S4-S5: Robust Regressions for Substance Use

Findings of the present study demonstrated that whereas higher lifetime cannabis use was associated with greater dorsal striatum activation during late trials, results consistent with a recent study showing that chronic cannabis users exhibited greater dorsal stratum across decision making trials during a gambling task involving reward (4). In contrast, higher lifetime prescription stimulant use and current alcohol use were linked to less dorsal striatum during the execution of learned contingencies, suggesting that use of these substances was not driving LME group differences in striatal activation in late trials. In addition, higher current nicotine use was associated with less anterior and posterior insula activation but not greater dorsal striatum activation during late trials when contingencies were being implemented, indicating that nicotine use did not appear to account for heightened insula and striatum activation during late trials.

Table S6: Early and Late Trials Separately

Group differences in early and late trials were analyzed separately in order to examine decision making processes during uncertainty (during trial-and-error learning in early trials) and certainty (in late trials when contingencies were known). In early trials when action-outcome contingencies were ambiguous, CTL exhibited greater medial frontal cortex and dorsal striatum activation than OSU during early trials. Research has shown that in healthy individuals, heightened dorsomedial prefrontal cortex and dorsal striatum activations are linked to reward prediction error as well as successful decision making in the face of uncertainty (5). The fact that OSU are under-recruiting dorsal striatum and medial frontal gyrus, regions shown to assist in initial reward learning may explain why, in late trials, these individuals are over-recruiting anterior and posterior insula during decision making, given that insula is associated with interoceptive feeling states that help to aid "gut responses" during decision making (6). Across early and late trials, OSU showed greater left middle frontal gyrus activation than CTL, suggesting that OSU need to recruit additional resources than CTL to maintain task goals and/or response sets in working memory, given prior literature the role of left middle frontal gyrus on working memory in healthy individuals (7, 8).

Table S7: Decisions during Preferred Response Selection

Results demonstrated that when CTL selected the preferred response across trials, they exhibited greater activation than OSU in dorsal striatum, anterior insula, IFG, and medial frontal cortex, findings suggesting that OSU recruits less neural resources to process reward and risk during rewarding action-outcome contingencies. Research indicates that dorsal striatum plays an important role in linking reward to optimal behavior (9) and medial frontal cortex activation during reinforcement reflects reward prediction error, or the difference between predicted and experienced reward (5). IFG is also involved in the implementation of reward prediction error as well as risk prediction error, or the difference between predicted and realized risk of a decision, the latter also implemented by the insula (5, 10). Risk prediction

error is computed when probabilities are initially unknown and the expected value of a decision needs to be learned through experience, and insula activation is thought to represent the affective experience associated with risk processing (11). Given that OSU appear to use less resources to process reward and risk during decision making in the present study, these findings may extend to everyday life situations in which positive and negative consequences of potential choices may not be fully evaluated. Promising treatments are currently being evaluated to modify substance users' neural and behavioral responses during decision making, however. For example, a recent study in methamphetamine dependent individuals demonstrated that drug treatment for stimulant addiction may improve recruitment of cognitive resources (e.g., normalized dorsal striatum, IFG and insula activation for modafinil compared to placebo) for these individuals during reward-related decision making (12).

Table S8: Responses to Winning Outcomes

OSU and CTL groups did not differ in brain activation in regions involved in reward responsivity (e.g., ventral striatum) during the outcome phase in response to wins, ties, or losses. These findings suggest that reduced neural responsivity to rewards may be a consequence of chronic or frequent drug use as opposed to occasional stimulant use.

Summary and Conclusions

Overall, results presented in the main text and findings from exploratory analyses presented here support the assertion that OSU exhibit altered brain activation during reinforcement learning in regions involved in reward and risk evaluation. First, OSU recruit excessive neural resources in dorsal striatum, IFG, and insula while making decisions wherein reward contingencies have already been learned and should not require that additional effort. Findings within late trials separately also support the over-recruitment of anterior insula by OSU to execute contingencies. Second, OSU exhibit under-recruitment of dorsal striatum, IFG and insula during decision making on trials in which the preferred behavioral

response was selected, suggesting reduced neural processing of optimal action-outcome contingencies. Finally, outcome analyses do not show these differences between OSU and CTL, suggesting that altered processing of reward outcomes may be a consequence of more chronic stimulant use rather than occasional use. Future longitudinal studies are warranted to examine whether brain activation during occasional use predicts the transition to chronic stimulus use.

Table S1. fMRI Results for the Group (OSU, CTL) by Decision Time (Early Trials, Late Trials) Interaction (n = 209).

Volume (µL)	x	y	z	L/R	Area	Early Trials	Late Trials
8960[1]	-25	-49	42	L	Precuneus	CTL > OSU	OSU > CTL
8128[1]	-49	-47	8	L	Middle Temporal Gyrus	CTL > OSU	OSU > CTL
4352[1]	-37	18	9	L	Anterior Insula/Inferior Frontal Gyrus	ns	OSU > CTL
4032[1]	44	16	17	R	Inferior Frontal Gyrus	CTL > OSU	OSU > CTL
3968[1]	37	-62	-4	R	Fusiform Gyrus	ns	OSU > CTL
2816[1]	-18	0	11	L	Lentiform Nucleus	CTL > OSU	ns
2176[1]	-41	-61	24	L	Middle Temporal Gyrus	CTL > OSU	OSU > CTL
2176[1]	21	-58	45	R	Precuneus	ns	OSU > CTL
2112[1]	-28	14	46	L	Middle Frontal Gyrus	CTL > OSU	ns
1856[1]	55	-12	9	R	Superior Temporal Gyrus	ns	OSU > CTL
1792[1]	21	4	10	R	Lentiform Nucleus	ns	OSU > CTL
1472[1]	9	-57	60	R	Precuneus	ns	OSU > CTL
1344[1]	31	-38	55	R	Inferior Parietal Lobule	CTL > OSU	OSU > CTL
1088[1]	9	-79	-5	R	Lingual Gyrus	CTL > OSU	OSU > CTL
1088[1]	46	-56	24	R	Middle Temporal Gyrus	ns	OSU > CTL
1024[1]	0	-30	4	L	Thalamus	CTL > OSU	ns
1088[2]	-36	19	5	L	Anterior Insula	ns	OSU > CTL
896[1]	58	-39	9	R	Superior Temporal Gyrus	ns	OSU > CTL
832[1]	6	39	-16	R	Medial Frontal Gyrus	CTL > OSU	OSU > CTL
512[2]	12	6	13	R	Caudate	ns	OSU > CTL

OSU, occasional stimulant users; CTL, control subjects; L, left hemisphere; R, right hemisphere; ns, non-significant at $p < .05$ corrected for multiple comparisons via AlphaSim.
Coordinates reflect center of mass.
[1] Whole brain mask.
[2] Limbic mask.

Table S2. fMRI Results for the Cannabis Group (Low MJ-OSU, High MJ-OSU, Low MJ-CTL) by Decision Time (Early Trials, Late Trials) Interaction (n = 123).

Volume (µL)	x	y	z	L/R	Area	Early Trials	Late Trials
9344[1]	-26	7	8	L	Lentiform Nucleus	Low MJ-CTL > Low MJ-OSU	High MJ-OSU > Low MJ-CTL
4224[1]	43	21	13	R	Inferior Frontal Gyrus	ns	High MJ-OSU > Low MJ-CTL
2944[1]	22	6	9	R	Lentiform Nucleus	Low MJ-CTL > Low MJ-OSU	Low MJ-OSU > Low MJ-CTL High MJ-OSU > Low MJ-CTL
1344[1]	-44	19	17	L	Inferior Frontal Gyrus	High MJ-OSU > Low MJ-OSU Low MJ-CTL > Low MJ-OSU	High MJ-OSU > Low MJ-CTL
1088[1]	40	36	12	R	Inferior Frontal Gyrus	ns	High MJ-OSU > Low MJ-CTL
832[1]	-40	36	10	L	Inferior Frontal Gyrus	High MJ-OSU > Low MJ-OSU Low MJ-CTL > Low MJ-OSU	High MJ-OSU > Low MJ-CTL
832[2]	13	11	12	R	Caudate	Low MJ-CTL > Low MJ-OSU	High MJ-OSU > Low MJ-CTL
832[2]	-11	7	12	L	Caudate	Low MJ-CTL > Low MJ-OSU	ns
576[2]	-30	-29	17	L	Anterior Insula	ns	High MJ-OSU > Low MJ-CTL
512[2]	44	-17	6	R	Posterior Insula	ns	Low MJ-OSU > Low MJ-CTL High MJ-OSU > Low MJ-CTL
320[2]	39	3	-1	R	Mid Insula	Low MJ-CTL > High MJ-OSU	High MJ-OSU > Low MJ-CTL

L, left hemisphere; R, right hemisphere; ns, non significant at $p < .05$ corrected for multiple comparisons via AlphaSim.

Low MJ-OSU = occasional stimulant users with $\leq$ 50 lifetime cannabis uses. High MJ-OSU = occasional stimulant users with $\geq$ 1000 lifetime cannabis uses. Low MJ-CTL = control subjects with $\leq$ 50 lifetime cannabis uses. Coordinates reflect center of mass.

[1] Whole brain mask.

[2] Limbic mask.

Table S3. fMRI Results for the Predominately Cocaine/Predominately Prescription Group (PCU, PPU, CTL) by Decision Time (Early Trials, Late Trials) Interaction (n = 154).

Volume (µL)	x	y	z	L/R	Area	Early Trials	Late Trials
11776[1]	-24	11	8	L	Lentiform Nucleus	ns	PCU > PPU PCU > CTL
2496[2]	-12	6	12	L	Caudate	ns	PCU > PPU PCU > CTL
1920[1]	44	19	17	R	Inferior Frontal Gyrus	ns	PCU > CTL PPU > CTL
1536[1]	-36	10	25	L	Inferior Frontal Gyrus	ns	PCU > PPU PCU > CTL
1472[2]	-35	18	5	L	Anterior Insula	ns	PCU > CTL PPU > CTL
1408[1]	24	4	9	R	Lentiform Nucleus	ns	PCU > CTL PPU > CTL
448[2]	14	17	1	R	Caudate	ns	PCU > PPU PCU > CTL
320[2]	13	9	12	R	Caudate	ns	PCU > CTL

CTL, control subjects; PPU, predominately prescription stimulant users; PCU, predominately cocaine users; L, left hemisphere; R, right hemisphere; ns, non significant at $p < .05$ corrected for multiple comparisons via AlphaSim. Coordinates reflect center of mass.

[1] Whole brain mask.

[2] Limbic mask.

Table S4. fMRI Robust Regression Results Within OSU: Lifetime Drug Use (n = 161) predicting brain activation for late trials (when contingencies are familiar).

Drug	Volume (µL)	x	y	z	L/R	Area	Correlation
Prescription Stimulants	1216	3	19	5	L	Caudate	Negative
	1088	-10	18	0	R	Caudate	Negative
	768	13	-6	17	R	Caudate	Negative
Cannabis	320	12	6	14	R	Caudate	Positive

OSU, occasional stimulant users; L, left hemisphere; R, right hemisphere.
Results above are corrected for multiple comparisons at $p < .05$ via AlphaSim using a limbic mask (no results emerged for the whole brain mask). Coordinates reflect center of mass. No effects for lifetime cocaine use emerged for the dorsal striatum. No effects of insula or inferior frontal gyrus emerged for lifetime drug use predictors.

Table S5. fMRI Robust Regression Results Within OSU (*n* = 153): Typical current patterns of substance use predicting brain activation for late trials (when contingencies are familiar).

Drug	Volume (µL)	x	y	z	L/R	Area	Correlation
Nicotine	4288[1]	26	25	7	R	Anterior Insula/Inferior Frontal Gyrus	Negative
	448[2]	40	17	4	R	Anterior Insula	Negative
	384[2]	41	-5	-2	R	Posterior Insula	Negative
Alcohol	1856[1]	-4	15	5	L	Caudate	Negative
	768[1]	17	-20	20	R	Caudate	Negative

OSU, occasional stimulant users; L, left hemisphere; R, right hemisphere.
Nicotine = typical number of cigarettes smoked per day. Alcohol = typical number of drinks consumed per week. Data was not collected on weekly alcohol use for eight stimulant users; as a result, these subjects were not included in this analysis (*n* = 153). Results are corrected for multiple comparisons at $p < .05$ via AlphaSim. Coordinates reflect center of mass.
[1] Whole brain mask.
[2] Limbic mask.

Table S6. fMRI Results for t-tests between Group (OSU, CTL) for Early Trials and Late Trials separately.

Trial Type	Volume (µL)	x	y	z	L/R	Area	Effect
Early	3648[1]	-6	29	-17	L	Medial Frontal Gyrus	CTL > OSU
	1408[1]	-36	55	0	L	Middle Frontal Gyrus	OSU > CTL
	1408[1]	2	59	18	R	Medial Frontal Gyrus	CTL > OSU
	1280[1]	-40	-24	-15	L	Parahippocampal Gyrus	CTL > OSU
	1024[1]	-19	5	-32	L	Uncus	CTL > OSU
	896[1]	-37	-24	62	L	Precentral Gyrus	CTL > OSU
	832[1]	42	-39	3	R	Superior Temporal Gyrus	OSU > CTL
	256[2]	-4	14	1	L	Caudate	CTL > OSU
Late	3648[1]	51	-39	7	R	Superior Temporal Gyrus	OSU > CTL
	2368[1]	45	-59	30	R	Angular Gyrus	OSU > CTL
	1984[1]	-43	18	8	L	Precentral Gyrus	OSU > CTL
	1856[1]	23	-68	42	R	Precuneus	OSU > CTL
	1024[1]	-52	-43	30	L	Supramarginal Gyrus	OSU > CTL
	960[1]	-35	56	2	L	Middle Frontal Gyrus	OSU > CTL
	832[2]	-39	18	5	L	Anterior Insula	OSU > CTL
	768[1]	-18	4	-32	L	Uncus	CTL > OSU
	768[1]	18	-22	-15	R	Parahippocampal Gyrus	CTL > OSU
	448[2]	40	-3	12	R	Posterior Insula	OSU > CTL
	384[2]	33	17	11	R	Anterior Insula	OSU > CTL

OSU, occasional stimulant users; L, left hemisphere; R, right hemisphere.
Results above are corrected for multiple comparisons at $p < .05$ via AlphaSim. Coordinates reflect center of mass.
[1] Whole brain mask.
[2] Limbic mask.

Table S7. fMRI Results for the Group (OSU, CTL) by Decision (Preferred, Even, Worst) Interaction (n = 209).

Volume (uL)	x	y	z	L/R	Area	Preferred	Even	Worst
14976[1]	-15	-57	24	L	Precuneus	CTL > OSU	ns	ns
3776[1]	2	-82	-3	R	Lingual Gyrus	CTL > OSU	ns	ns
2816[1]	-12	-43	42	L	Cingulate Gyrus	CTL > OSU	ns	ns
2240[1]	0	48	14	L	Medial Frontal Gyrus	CTL > OSU	ns	ns
2176[1]	32	-45	50	R	Precuneus	CTL > OSU	CTL > OSU	ns
1536[1]	0	-42	-7	L	Cerebellar Lingual	CTL > OSU	ns	ns
1536[1]	-39	-70	-7	L	Middle Occipital Gyrus	ns	ns	OSU > CTL
1472[1]	-4	-19	17	L	Thalamus	ns	ns	OSU > CTL
1344[1]	-39	-4	-17	L	Superior Temporal Gyrus	CTL > OSU	ns	ns
1344[1]	16	60	12	R	Superior Frontal Gyrus	CTL > OSU	ns	ns
1088[1]	44	-28	-13	R	Fusiform Gyrus	ns	ns	OSU > CTL
1088[2]	-1	42	13	L	Anterior Cingulate	CTL > OSU	ns	ns
1024[1]	55	-6	-17	R	Middle Temporal Gyrus	CTL > OSU	OSU > CTL	ns
960[1]	-3	5	52	L	Superior Frontal Gyrus	CTL > OSU	ns	ns
896[1]	38	32	-7	R	Inferior Frontal Gyrus	CTL > OSU	ns	ns
896[1]	-15	59	-3	L	Medial Frontal Gyrus	CTL > OSU	ns	ns
832[1]	-28	-65	-28	L	Pyramis	CTL > OSU	CTL > OSU	ns
832[1]	-41	21	10	L	Anterior Insula/Inferior Frontal Gyrus	CTL > OSU	ns	ns
832[1]	25	49	33	R	Superior Frontal Gyrus	CTL > OSU	ns	ns
768[1]	20	-45	19	R	Posterior Cingulate	ns	ns	OSU > CTL
512[2]	-9	5	17	L	Caudate	CTL > OSU	ns	ns
448[2]	45	-3	-2	R	Posterior Insula	ns	ns	CTL > OSU
384[2]	-36	21	11	L	Anterior Insula	CTL > OSU	ns	ns

OSU, occasional stimulant users; CTL, control subjects; L, left hemisphere; R, right hemisphere; ns, non significant at $p < .05$ corrected for multiple comparisons via AlphaSim.
Coordinates reflect center of mass.
[1] Whole brain mask.
[2] Limbic mask.

Table S8. fMRI Results for the Group by Outcome (Wins, Ties, Losses) Interaction (n = 209).

Volume (µL)	x	y	z	L/R	Area	Wins	Ties	Losses
7168[1]	-9	-90	-4	L	Lingual Gyrus	ns	ns	ns
1408[1]	-36	-38	7	L	Superior Temporal Gyrus	ns	ns	ns
1216[1]	12	-93	7	R	Cuneus	CTL > OSU	CTL > OSU	ns
1088[1]	3	0	55	R	Medial Frontal Gyrus	OSU > CTL	ns	ns
960[1]	-3	-13	-15	L	Mammillary Body	CTL > OSU	CTL > OSU	ns
768[1]	-2	45	43	L	Superior Frontal Gyrus	ns	ns	OSU > CTL
768[1]	37	-50	54	R	Inferior Parietal Lobule	ns	ns	ns
256[2]	9	21	3	R	Caudate	ns	ns	ns

OSU, occasional stimulant users; CTL, control subjects; L, left hemisphere; R, right hemisphere; ns, non significant at $p < .05$ corrected for multiple comparisons via AlphaSim.
Coordinates reflect center of mass.
[1] Whole brain mask.
[2] Limbic mask.

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