Alcohol Affects Brain Functional Connectivity and its Coupling with Behavior: Greater Effects in Male Heavy Drinkers

(Supplementary Information)

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Supplementary Results

Between-Subject Correlations in FCD

High pairwise between-subject correlations in NM in PLC (Fig. 5a) were observed between and PFC lFCD and Calcarine gFCD ($r(22) = 0.83$, $p < 0.0001$), and between Cerebellum lFCD and Cerebellum gFCD ($r(22) = 0.88$, $p < 0.0001$). Both effects were also significant after removing the effect of other ROIs ($p < 0.0001$). In addition, there was a significant correlation between Thalamus (MDN) lFCD and Cerebellum gFCD ($r(22) = 0.64$, $p = 0.0008$) and between Thalamus (MDN) lFCD and Thalamus (VLN) lFCD ($r(22) = 0.77$, $p < 0.0001$). NM in ALC (Fig. 5c) condition showed significant correlation between Thalamus (MDN) lFCD and Thalamus (VLN) lFCD ($r(22) = 0.88$, $p < 0.0001$), which was also significant after removing the effect of other ROIs. In addition, PFC lFCD and Thalamus (VLN) gFCD were correlated ($r(22) = 0.87$, $p < 0.0001$). HD in PLC condition (Fig. 5b) showed significant correlations between Cerebellum lFCD and Cerebellum gFCD ($r(14) = 0.92$, $p < 0.0001$), and between PFC lFCD and Cerebellum gFCD ($r(14) = 0.79$, $p < 0.0001$). In ALC condition (Fig. 5d), HD showed significant Cerebellum lFCD and Cerebellum gFCD correlation ($r(14) = 0.98$, $p < 0.0001$), which was significant after removing the effect of other ROIs. Moreover, there was a significant correlation between Calcarine lFCD and Precuneus lFCD ($r(14) = 0.86$, $p < 0.0001$). Finally, similar to NM in ALC, there was a significant correlation between Thalamus (MDN) lFCD and Thalamus (VLN) lFCD ($r(22) = 0.91$, $p < 0.0001$) in HD in ALC. Average R^2 of the off-diagonal elements in the correlation matrix seemed lower in NM ($R^2 = 0.14$; Fig. 5a) relative to HD ($R^2 = 0.24$; Fig. 5b) in the PLC condition, which indicates the individual differences in FCD indices within the ROIs are more consistent in the HD relative to NM. Alcohol appeared to marginally

decrease average R^2 of between-subject correlations in NM (R^2 = 0.034, Fig. 5c) and HD (ΔR^2 = 0.013, Fig. 5d).

We assessed significant changes ($p < 0.005$) in the correlation coefficients between PLC and ALC conditions (Fig. 5e–f). In NM (Fig. 5e), alcohol decreased between-subject correlations between Calcarine lFCD and Calcarine gFCD (z = -2.84, p = 0.002), and between Calcarine lFCD and Thalamus (VLN) lFCD after removing effect of other ROIs (z = -2.61, p = 0.005). ALC relative to PLC increased partial correlations between Calcarine gFCD and Thalamus (VLN) gFCD (z = 2.95, p = 0.001), between Cerebellum lFCD and Calcarine gFCD (z = 2.60, p = 0.004), and between Calcarine lFCD and Thalamus (MDN) lFCD (z = 2.91, p = 0.002). ALC relative to PLC also increased pairwise correlation between Calcarine gFCD and Thalamus (VLN) gFCD (z = 3.62, p = 0.0001) in NM. In HD (Fig. 5f), there were significant alcohol induced decreases in the partial correlation between Cerebellum lFCD and Thalamus (VLN) gFCD (z = -2.71, p = 0.003) and between Thalamus (VLN) lFCD and Thalamus (VLN) gFCD (z = -3.43, p = 0.0003). ALC relative to PLC also decreased the pairwise correlation between Cerebellum lFCD and Thalamus (MDN) lFCD (z = -2.58, p = 0.005) in HD. Alcohol induced increases in partial correlations were seen between Precuneus lFCD and Thalamus (VLN) gFCD (z = 3.04, p = 0.001), between Thalamus (MDN) lFCD and Thalamus (VLN) gFCD (z = 3.81, $p < 0.0001$), and between Cerebellum lFCD and Cerebellum gFCD (z = 3.61, p = 0.0001).

Associations between Behavior and FCD

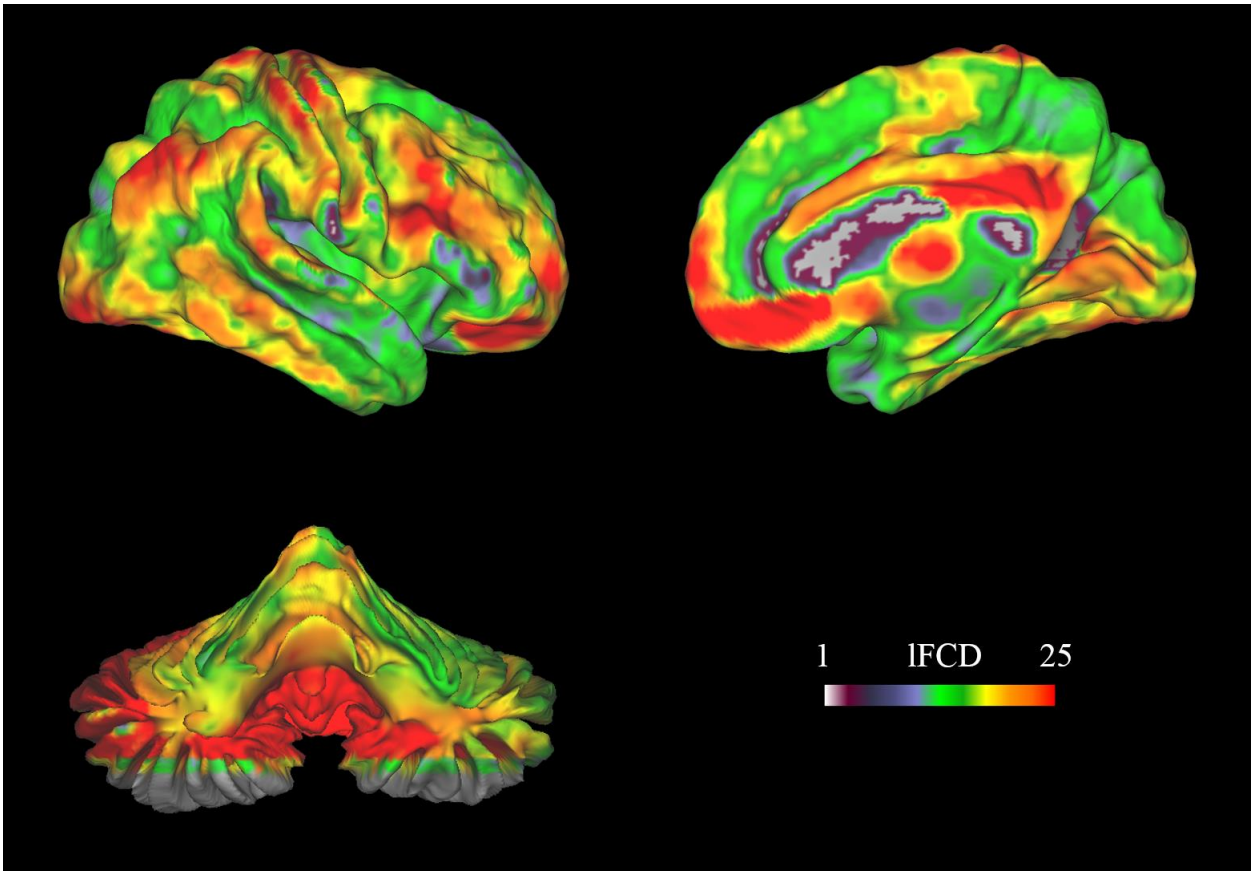
In NM in PLC condition (Supp. Table 5), there were significant correlations between Calcarine and Cerebellum ROIs' lFCD and gFCD and motor tasks ($p < 0.01$, two-tailed). In general, higher FCDs in Calcarine and Cerebellum ROIs were correlated with more errors on these ($r(21) > 0.54$, $p < 0.01$), however, Romberg time was negatively correlated with Calcarine lFCD and

gFCD ($r(21) < -0.58$, $p < 0.01$). This indicates that increased Calcarine and Cerebellum FCDs predicts a speed-accuracy trade-off for motor functions. During alcohol intoxication in NM (Supp. Table 6) the number of significant correlation was reduced (8 in PLC to 2 in ALC). Significant (and positive) correlations were observed between Posterior Cingulate and Irritability ($r(21) = 0.57$) and PFC lFCD and number of errors in the Romberg task ($r(21) = 0.58$).

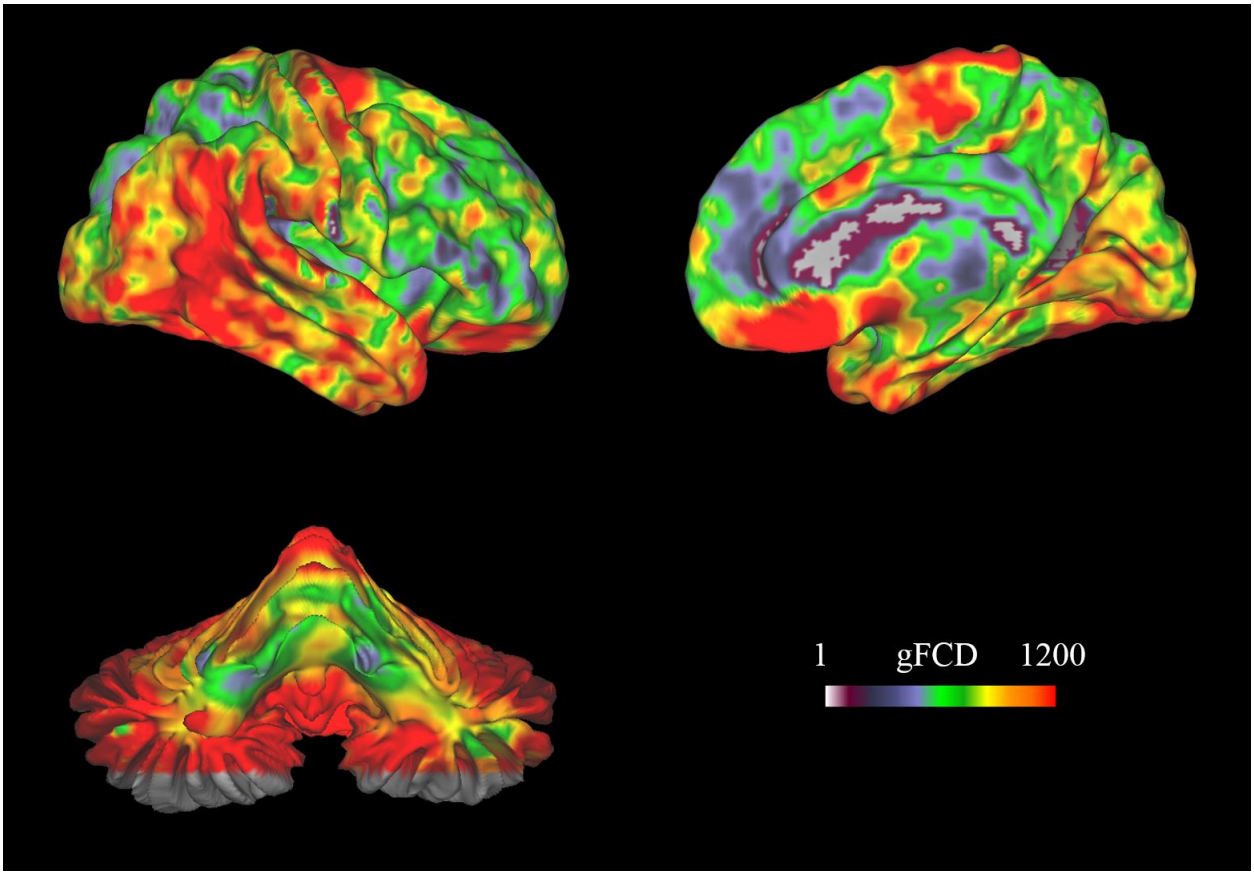
In HD in PLC (Supp. Table 7), similar to NM, more errors (e.g., One Leg task) were positively correlated with increase in Cerebellum lFCD ($r(13) = 0.86$), and higher Cerebellum FCDs as well as higher Calcarine gFCD were negatively correlated with motor time ($r(13) < -0.70$). Calcarine lFCD was positively correlated with feeling pleasant ($r(13) = 0.67$). Posterior Cingulate lFCD was correlated with performance on SDMT task ($r(13) = 0.75$). During alcohol intoxication in HD (Supp. Table 8), increase in PFC lFCD was associated with more motor errors (e.g., One Leg task, $r(13) = 0.81$). Stroop (Incongruent) task performance, however, was positively correlated with Cerebellum lFCD and gFCD ($r(13) > 0.68$), which might indicated higher Cerebellum FCDs might be as a compensatory phenomenon but only for higher cognitive abilities such as conflict resolution and inhibition, in HD under intoxication. Cerebellum gFCD also correlated with performance on Stroop Incongruent condition ($r(13) = 0.69$). Finally, higher Calcarine gFCD and Thalamus (VLN) gFCD were associated with better SDMT performance ($r(13) > 0.67$).

We also assessed the correlations between changes in behavioral measures and changes in ROI FCDs, between PLC and ALC conditions (i.e., ALC-PLC) in NM (Supp. Table 9) and HD (Supp. Table 10). In NM, Calcarine lFCD increases predicted higher sedated feelings ($r(21) = 0.81$, $p < 0.01$). Precuneus lFCD increases negatively correlated with desire for alcohol ($r(21) = -0.59$, $p < 0.01$), and Posterior Cingulate lFCD increases was associated with less Rhythm

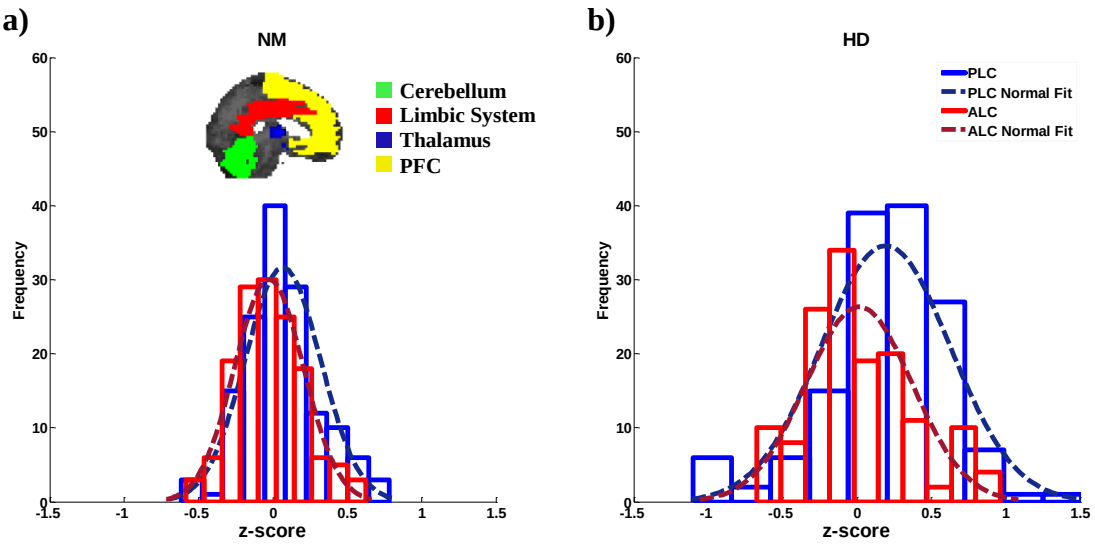
errors. In HD, increases in Cerebellum gFCD from PLC to ALC was associated with decreases in Stroop (Incongruent) scores ($r(13) = 0.81$, $p < 0.01$).



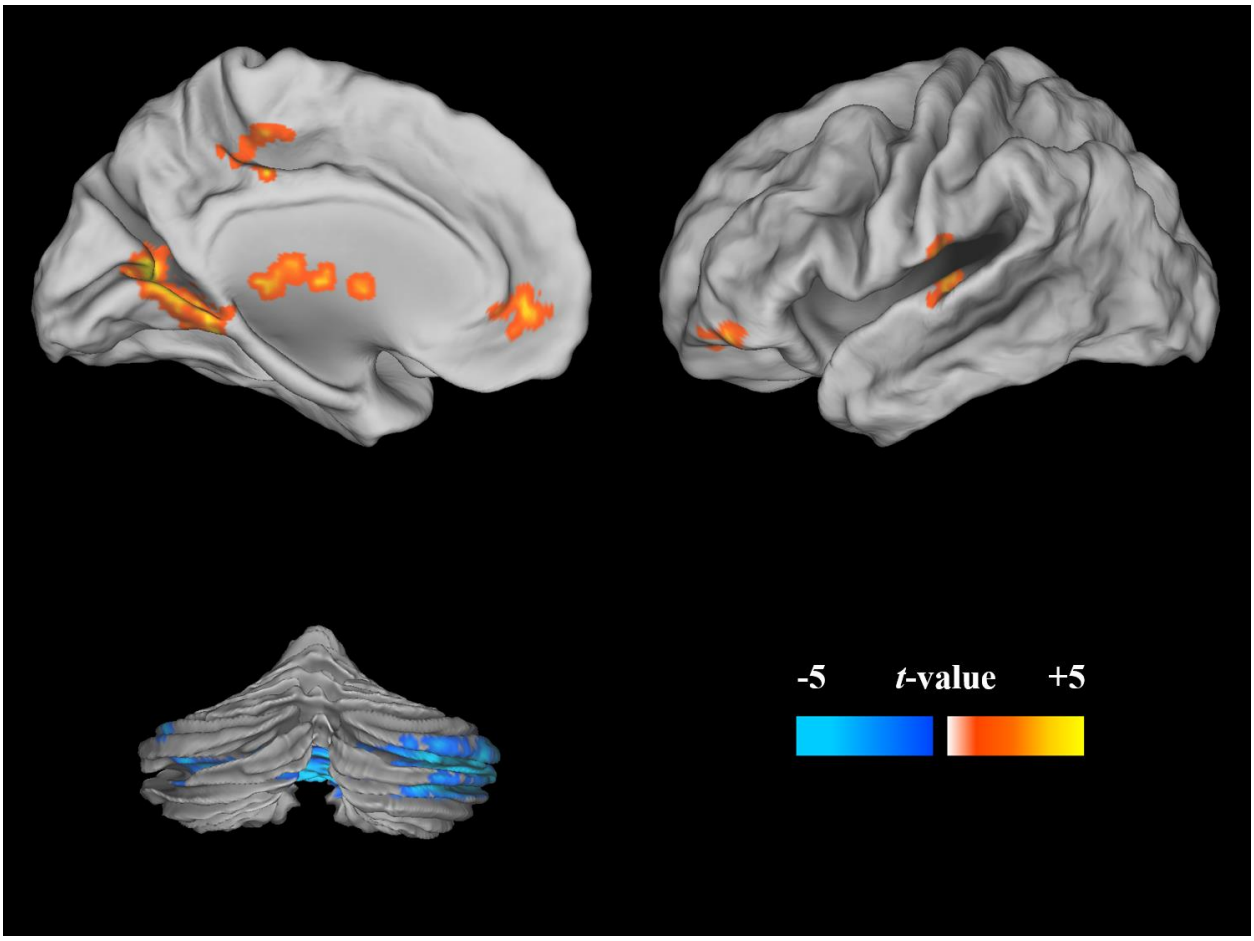
Supplementary Figure 1. Spatial distribution of the average lFCD across all the subjects in the baseline (PLC) condition with main lFCD hubs located within the posterior cingulate, ventral precuneus, inferior parietal cortex, cuneus, anterior PFC, and cerebellum.



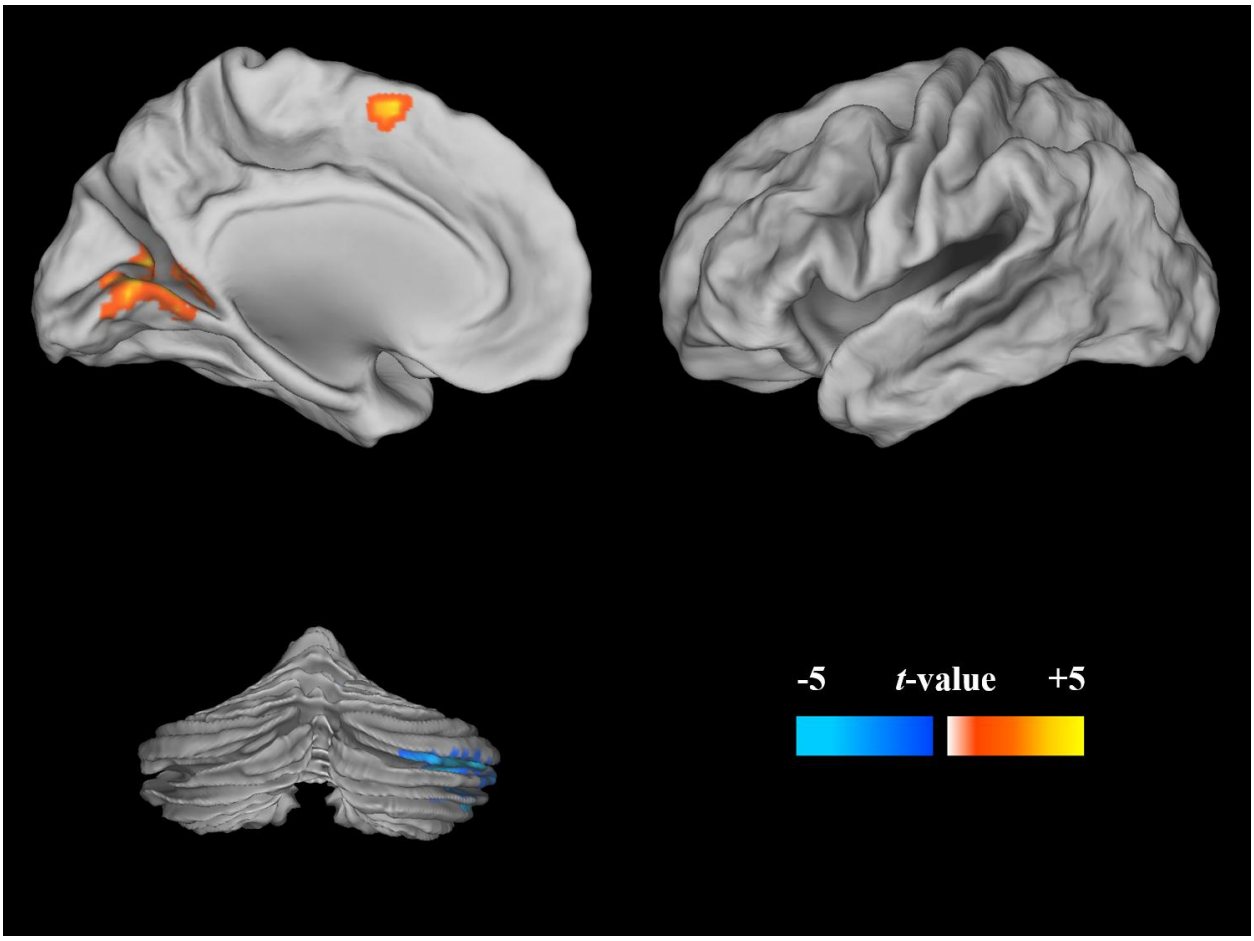
Supplementary Figure 2. Spatial distribution of the average gFCD across all the subjects in the baseline (PLC) condition with main gFCD hubs located within visual cortex, postcentral gyrus, precuneus, inferior parietal cortex, temporal lobe, and cerebellum.



Supplementary Figure 3. Neurocognitive coupling analysis with a priori ROIs. We repeated the neurocognitive coupling analysis with 4 a priori ROIs. Specifically, we used the Talairach Daemon atlas[1, 2] to create masks of cerebellum, prefrontal cortex (PFC), thalamus (and hypothalamus), and limbic system with known sensitivity to acute or chronic effects of alcohol.[3-8] Next, we extracted average local functional connectivity density (lFCD) and average global functional connectivity density (gFCD) within these masks, resulting in a total of 8 FCD values per participant. We estimated Pearson's correlation coefficients between performance on the 18 behavioral tasks with significant Group or Alcohol effects (see Supp. Tables 1–2 for list of significant behavioral measures) and the 8 FCDs (4 lFCD and 4 gFCD values obtained from the a priori ROIs), resulting in 18 × 8 correlations per group and condition. **(a)** The distribution histogram of Fisher's *z*-transformed correlations for normal controls (NM) in Placebo (PLC) and Alcohol (ALC) conditions. **(b)** The distribution histogram of Fisher's *z*-transformed correlations for heavy drinkers (HD) in Placebo (PLC) and Alcohol (ALC) conditions. A two-way repeated measures ANOVA on the Fisher's *z*-transformed correlations showed a significant main effect of Alcohol ($F(1, 143) = 32.58$; $p < 0.0001$) and a significant interaction between Alcohol and Group on the neurocognitive coupling ($F(1, 143) = 3.90$; $p = 0.05$). Additionally, there was a significant effect of Group ($F(1, 143) = 7.68$; $p = 0.006$). Similar to results obtained with functional ROIs, the a priori ROI results showed that ALC relative to PLC reduced the neurocognitive coupling in both groups ($M_{PLC} = 0.13$, $SD_{PLC} = 0.34$; $M_{ALC} = -0.01$, $SD_{ALC} = 0.29$). The interaction effect indicated that relative to PLC, the reduction in neurocognitive coupling after alcohol was more pronounced in HD ($M_{PLC} = 0.19$, $SD_{PLC} = 0.43$, $M_{ALC} = 0.01$, $SD_{ALC} = 0.36$; Fig. 6b) than in NM ($M_{PLC} = 0.07$, $SD_{PLC} = 0.25$, $M_{ALC} = -0.03$, $SD_{ALC} = 0.23$; Fig. 6a). Finally, the Group effect indicated that HD showed higher overall neurocognitive ($M = 0.13$, $SD = 0.40$) than NM ($M = 0.02$, $SD = 0.24$), indicating that between subject differences in FCD in regions closely related to alcohol effects is a stronger predictor of behavioral differences in HD than NM.



Supplementary Figure 4. Main effects of Group for local functional connectivity density (lFCD) for male participants only. Contrast involves Heavy Drinkers (HD) < Normal Controls (NM) superimposed on lateral and medial views of the cerebral surface and anterior view of the effect in the cerebellum ($p_{FWE} < 0.05$). The effects are similar to results when females were included in the NM (Fig. 3) with Calcarine, Thalamus, Prefrontal Cortex, and Precuneus, also showing higher lFCD in male NM than male HD, and Cerebellum showing higher gFCD in male HD than male NM. The Posterior Cingulate cluster was not significant here after FWE correction.



Supplementary Figure 5. Main effects of Group for global functional connectivity density (gFCD) for male participants only. Contrast involves Heavy Drinkers (HD) < Normal Controls (NM) superimposed on lateral and medial views of the cerebral surface and anterior view of the effect in the cerebellum ($p_{FWE} < 0.05$). The effects are similar to results when females were included in the NM (Fig. 3) with Calcarine showing higher gFCD in male NM than male HD, and Cerebellum showing higher gFCD in male HD than male NM. We found an additional cluster in Superior Frontal Gyrus (BA 6) showing higher gFCD in NM than HD.

Supplementary Table 1. Main effect of Group on behavioral measures. Significant effects after correction for multiple comparisons ($p_{FWE} < 0.05$, Bonferroni) are in bold and italicized (* for $p < 0.05$; ** for $p < 0.001$).

		NM		HD			
	Name of Test	***M***	**SD**	***M***	***SD***	***F*(1, 36)**	***p*-value**
Mood/Drug Effects	Stimulated	4.83	0.76	4.77	0.78	0.02	0.880
	Sedated	2.63	0.89	2.38	1.05	0.44	0.510
	Self-confident	7.35	1.51	7.43	1.08	0.00	0.961
	Social*	7.42	1.15	6.55	1.09	4.75	0.036
	Irritable	***1.50***	***0.63***	***2.58***	***1.54***	***18.35***	***0.000***
	Dizzy	2.10	1.21	2.02	1.25	0.03	0.867
	High	2.47	1.43	2.47	0.95	0.50	0.483
	Anxious	1.46	0.74	1.95	1.45	3.64	0.065
	Pleasant	5.00	1.64	5.98	1.67	3.29	0.078
	Alcohol Desire	***1.46***	***0.92***	***3.43***	***2.33***	***51.86***	***0.000***
	Control*	9.36	0.88	8.48	2.08	5.10	0.030
	Intoxicated	2.99	1.19	2.88	1.06	0.03	0.861
	Restless	***1.75***	***0.84***	***3.08***	***2.53***	***20.51***	***0.000***
Motor	Gait (time)	16.46	4.62	17.69	5.00	2.80	0.103
	Gait (errors)	1.04	0.57	0.80	0.71	0.76	0.390
	One Leg (errors)	1.23	0.96	1.20	1.61	0.05	0.831
	Romberg (time)	29.54	7.87	30.29	4.86	0.83	0.369
	Romberg (errors)	1.52	0.95	1.57	0.85	0.09	0.768
	Rhythm (time)	17.04	3.43	16.97	3.90	0.01	0.925
	Rhythm (errors)	0.85	0.79	0.65	0.65	0.43	0.516
Cognitive	***Stroop (Neutral)***	***103.13***	***10.46***	***89.70***	***19.23***	***82.36***	***0.000***
	Stroop (Congruent)	***75.99***	***9.28***	***68.10***	***15.18***	***45.61***	***0.000***
	Stroop (Incongruent)	***53.58***	***9.52***	***45.90***	***11.42***	***44.98***	***0.000***
	SDMT	***46.34***	***7.55***	***42.10***	***8.92***	***16.69***	***0.000***
	Word Association	***11.95***	***3.70***	***8.74***	***3.48***	***29.52***	***0.000***

Supplementary Table 2. Main effect of Alcohol on behavioral measures. Significant effects after correction for multiple comparisons ($p_{FWE} < 0.05$, Bonferroni) are in bold and italicized (* for $p < 0.05$; ** for $p < 0.001$).

		PLC		ALC			
	Name of Test	***M***	***SD***	***M***	***SD***	***F*(1, 36)**	***p*-value**
Mood/Drug Effects	Stimulated	4.99	1.19	4.62	1.23	1.01	0.322
	Sedated	***1.67***	***1.18***	***3.39***	***1.80***	***17.62***	***0.000***
	Self-confident	7.33	1.90	7.43	1.59	0.65	0.427
	Social	7.16	1.58	7.00	1.66	0.06	0.803
	Irritable	1.87	1.50	1.99	1.41	0.01	0.941
	Dizzy	***1.34***	***0.86***	***2.79***	***2.16***	***16.05***	***0.000***
	High	***1.28***	***0.79***	***3.66***	***2.34***	***33.31***	***0.000***
	Anxious	1.42	0.84	1.88	1.56	3.09	0.087
	Pleasant	***4.13***	***2.83***	***6.65***	***2.16***	***19.17***	***0.000***
	Alcohol Desire	1.96	1.61	2.51	2.37	2.42	0.128
	Control*	9.49	1.86	8.54	1.81	6.17	0.018
	Intoxicated	***1.17***	***0.56***	***4.72***	***2.21***	***74.90***	***0.000***
	Restless	2.17	2.08	2.38	1.89	0.23	0.633
Motor	Gait (time)*	15.71	3.93	18.17	6.09	10.07	0.003
	Gait (errors)	***0.16***	***0.35***	***1.74***	***1.18***	***47.61***	***0.000***
	One Leg (errors)	***0.25***	***0.62***	***2.18***	***2.12***	***29.22***	***0.000***
	Romberg (time)	***27.90***	***6.60***	***31.80***	***7.60***	***23.68***	***0.000***
	Romberg (errors)	***0.20***	***0.47***	***2.88***	***1.77***	***59.40***	***0.000***
	Rhythm (time)*	16.24	3.12	17.78	4.43	10.24	0.003
	Rhythm (errors)	***0.30***	***0.51***	***1.24***	***1.17***	***26.07***	***0.000***
Cognitive	***Stroop (Neutral)***	***100.00***	***16.95***	***95.25***	***15.59***	***13.77***	***0.001***
	Stroop (Congruent)	***75.50***	***14.41***	***70.30***	***10.94***	***20.40***	***0.000***
	Stroop (Incongruent)*	52.00	11.84	49.09	10.62	7.11	0.011
	SDMT	***47.24***	***9.35***	***42.10***	***8.14***	***26.73***	***0.000***
	Word Association	***12.10***	***4.53***	***9.30***	***3.87***	***21.89***	***0.000***

Supplementary Table 3. Interaction effect between Group and Alcohol factors on behavioral measures. Significant effects after correction for multiple comparisons ($p_{FWE} < 0.05$, Bonferroni) are in bold and italicized.

	Name of Test	*F*(1, 36)	*p*-value
Mood/Drug Effects	Stimulated	0.01	0.922
	Sedated	0.10	0.752
	Self-confident	1.23	0.275
	Social	0.09	0.767
	Irritable	0.28	0.603
	Dizzy	2.66	0.111
	High	0.35	0.556
	Anxious	0.09	0.768
	Pleasant	0.43	0.514
	Alcohol Desire	0.01	0.905
	Control	0.54	0.465
	Intoxicated	0.17	0.687
	Restless	1.08	0.305
Motor	Gait (time)	0.60	0.444
	Gait (errors)	1.63	0.210
	One Leg (errors)	0.54	0.468
	Romberg (time)	0.00	0.970
	Romberg (errors)	0.82	0.372
	Rhythm (time)	0.49	0.487
	Rhythm (errors)	1.74	0.196
Cognitive	Stroop (Neutral)	1.32	0.258
	Stroop (Congruent)	0.99	0.326
	Stroop (Incongruent)	0.05	0.825
	SDMT	2.97	0.093
	Word Association	1.25	0.271

Supplementary Table 4. ROI-level analysis of effects of Group and Alcohol on lFCD and gFCD while controlling for gender and smoking. The mean values are shown in Figs. 3–4.

		Group		Alcohol		Group × Alcohol	
	ROI	***F*(1,38)**	***p*-value**	***F*(1, 38)**	***p*-value**	***F*(1, 38)**	***p*-value**
lFCD	**Calcarine**	96.22	0.000	0.23	0.635	0.05	0.829
	Cerebellum	67.28	0.000	1.32	0.258	1.79	0.188
	PFC	30.30	0.000	0.15	0.705	0.02	0.885
	Posterior Cingulate	33.59	0.000	0.24	0.625	1.68	0.203
	Precuneus	52.75	0.000	4.58	0.039	0.25	0.619
	Thalamus (MDN)	51.46	0.000	8.81	0.005	1.59	0.215
	Thalamus (VLN)	16.69	0.000	22.84	0.000	2.19	0.148
	Whole Brain	0.29	0.593	0.18	0.671	1.21	0.279
gFCD	**Calcarine**	21.96	0.000	3.24	0.080	0.70	0.409
	Cerebellum	46.96	0.000	1.47	0.232	2.55	0.119
	Thalamus (VLN)	4.39	0.043	19.39	0.000	0.34	0.563
	Whole Brain	0.09	0.760	0.96	0.334	2.81	0.102

Supplementary Table 5. Correlation in PLC in 23 NM between 18 behavioral measures which showed significant effects of Group or Alcohol and 10 ROIs which showed significant effects of Group or Alcohol. Significant correlations are highlighted in green ($p < 0.01$, two-tailed).

		lFCD							gFCD		
	Name of Test	Calcarine	Cerebellum	PFC	Posterior Cingulate	Precuneus	Thalamus (MDN)	Thalamus (VLN)	Calcarine	Cerebellum	Thalamus (VLN)
Drug Effects	Sedated	0.21	0.32	0.18	0.01	0.15	0.28	-0.03	0.46	0.42	-0.01
	Irritable	0.34	0.30	-0.03	0.12	0.22	0.18	-0.10	0.54	0.27	-0.01
	Dizzy	0.37	0.44	0.56	0.08	0.13	0.24	0.09	0.01	0.33	-0.08
	High	0.39	0.06	0.13	0.07	-0.12	0.01	0.17	0.17	-0.01	-0.02
	Pleasant	-0.09	-0.20	0.39	-0.18	-0.27	0.10	0.37	-0.15	-0.06	0.31
	Alcohol Desire	-0.12	-0.08	-0.20	-0.21	-0.10	-0.16	-0.34	-0.08	-0.02	-0.18
	Intoxication	0.46	-0.08	0.07	0.05	-0.17	-0.22	-0.04	0.26	-0.14	-0.26
	Restless	0.37	0.04	-0.03	0.02	0.17	0.14	0.30	0.23	0.02	0.07
Motor	Gait (errors)	0.32	0.63	0.54	0.39	0.08	0.48	0.10	0.13	0.56	0.07
	One Leg (errors)	0.19	0.53	0.09	0.14	0.34	0.44	0.09	0.28	0.39	0.42
	Romberg (time)	-0.62	-0.47	0.00	-0.40	0.10	-0.17	0.10	-0.58	-0.43	0.17
	Romberg (errors)	0.09	0.53	0.49	0.22	-0.02	0.34	0.07	-0.09	0.42	-0.09
	Rhythm (errors)	0.56	0.07	0.18	0.28	-0.19	0.02	0.10	0.28	0.11	-0.12
Cognitive	Stroop (Neutral)	-0.20	-0.05	0.01	-0.31	-0.11	-0.03	0.11	-0.04	0.15	-0.12
	Stroop (Congruent)	-0.12	-0.10	-0.05	-0.09	-0.02	0.12	0.29	0.09	-0.01	0.07
	Stroop (Incongruent)	-0.14	-0.20	0.01	-0.14	-0.02	0.09	0.38	-0.04	-0.06	0.16
	SDMT	-0.31	-0.13	0.19	-0.35	-0.02	0.03	0.16	-0.18	0.06	0.00
	Word Association	-0.20	-0.17	-0.10	-0.42	-0.17	-0.32	-0.38	-0.23	-0.26	-0.24

Supplementary Table 6. Correlation coefficients in ALC in 23 NM between 18 behavioral measures which showed significant effects of Group or Alcohol and 10 ROIs which showed significant effects of Group or Alcohol. Significant correlations are highlighted in green ($p < 0.01$, two-tailed).

		lFCD							gFCD		
	Name of Test	Calcarine	Cerebellum	PFC	Posterior Cingulate	Precuneus	Thalamus (MDN)	Thalamus (VLN)	Calcarine	Cerebellum	Thalamus (VLN)
Drug Effects	Sedated	0.22	0.40	0.15	0.10	-0.28	0.11	0.04	-0.09	0.12	-0.19
	Irritable	0.38	-0.15	-0.08	0.57	0.32	0.11	0.00	-0.02	-0.18	0.02
	Dizzy	-0.06	-0.15	-0.01	0.14	-0.05	-0.16	-0.07	-0.28	-0.20	-0.29
	High	0.38	0.02	0.22	0.48	-0.05	0.29	0.15	-0.16	-0.09	-0.29
	Pleasant	-0.28	-0.18	-0.02	-0.35	0.01	-0.17	-0.11	-0.12	-0.32	-0.09
	Alcohol Desire	-0.19	-0.23	-0.09	-0.03	-0.12	0.02	0.01	-0.19	-0.12	-0.14
	Intoxication	0.25	0.13	0.08	0.44	-0.05	0.30	0.14	-0.19	-0.14	-0.24
	Restless	0.21	-0.30	-0.02	0.33	0.17	0.04	-0.03	-0.18	-0.36	-0.04
Motor	Gait (errors)	0.51	-0.03	0.11	0.21	-0.09	0.23	0.06	0.13	-0.05	0.04
	One Leg (errors)	-0.04	0.19	0.22	-0.28	0.07	0.16	0.30	0.02	0.17	-0.04
	Romberg (time)	-0.53	-0.26	-0.04	-0.51	0.00	-0.35	-0.06	-0.12	-0.07	-0.07
	Romberg (errors)	-0.04	0.25	0.58	-0.04	0.08	0.24	0.28	-0.06	0.27	0.00
	Rhythm (errors)	0.42	0.06	-0.07	0.09	0.26	0.45	0.24	0.34	0.15	0.34
Cognitive	Stroop (Neutral)	-0.25	0.20	0.45	-0.23	-0.14	-0.01	0.10	-0.22	0.05	-0.30
	Stroop (Congruent)	-0.11	0.07	0.05	-0.20	-0.21	-0.04	0.08	-0.13	-0.19	-0.36
	Stroop (Incongruent)	-0.02	0.19	-0.01	-0.13	-0.10	0.14	0.30	0.03	-0.06	-0.17
	SDMT	-0.39	0.17	0.03	-0.37	0.03	-0.05	0.16	-0.04	0.20	0.03
	Word Association	0.08	0.37	0.14	-0.08	-0.37	0.11	0.07	-0.12	0.12	-0.12

Supplementary Table 7. Correlation in PLC in 15 HD between 18 behavioral measures which showed significant effects of Group or Alcohol and 10 ROIs which showed significant effects of Group or Alcohol. Significant correlations are highlighted in green ($p < 0.01$, two-tailed).

		lFCD							gFCD		
	Name of Test	Calcarine	Cerebellum	PFC	Posterior Cingulate	Precuneus	Thalamus (MDN)	Thalamus (VLN)	Calcarine	Cerebellum	Thalamus (VLN)
Drug Effects	Sedated	0.30	0.36	-0.22	-0.34	-0.06	0.20	0.03	0.20	0.13	-0.08
	Irritable	0.34	0.51	0.51	0.33	0.00	0.33	-0.24	0.41	0.48	0.44
	Dizzy	-0.12	0.61	-0.28	-0.16	-0.03	0.25	0.18	0.10	0.33	-0.15
	High	0.27	0.51	-0.27	-0.01	0.14	0.39	0.16	0.13	0.37	-0.15
	Pleasant	0.67	0.13	0.09	-0.01	0.49	0.62	0.49	0.19	0.12	0.00
	Alcohol Desire	-0.62	-0.11	-0.31	-0.66	-0.43	-0.43	-0.38	-0.20	-0.18	-0.37
	Intoxication	0.29	-0.09	-0.16	0.10	0.13	0.17	0.02	-0.16	-0.05	-0.18
	Restless	-0.17	0.12	0.28	0.48	-0.21	0.02	-0.08	0.22	0.32	0.52
Motor	Gait (errors)	0.49	0.50	-0.27	-0.01	0.47	0.52	0.38	0.08	0.32	-0.23
	One Leg (errors)	0.13	0.86	-0.07	-0.08	0.04	0.39	0.14	0.44	0.64	0.06
	Romberg (time)	-0.11	-0.70	-0.29	-0.48	0.08	-0.42	-0.21	-0.70	-0.79	-0.64
	Romberg (errors)	0.05	0.02	-0.22	-0.38	-0.15	-0.08	-0.21	0.14	0.06	-0.09
	Rhythm (errors)	0.35	-0.27	0.20	-0.29	0.15	0.19	0.00	0.03	-0.29	-0.20
Cognitive	Stroop (Neutral)	0.20	0.30	0.30	0.56	0.19	0.19	0.07	0.02	0.27	0.36
	Stroop (Congruent)	0.16	0.56	0.33	0.58	0.00	0.30	0.20	0.41	0.57	0.62
	Stroop (Incongruent)	0.12	0.53	0.18	0.52	0.09	0.29	0.32	0.30	0.48	0.48
	SDMT	-0.05	0.21	0.45	0.75	0.01	0.03	-0.06	0.10	0.31	0.54
	Word Association	0.22	-0.08	0.63	0.51	0.15	0.01	-0.20	0.22	0.12	0.55

Supplementary Table 8. Correlation in ALC in 15 HD between 18 behavioral measures which showed significant effects of Group or Alcohol and 10 ROIs which showed significant effects of Group or Alcohol. Significant correlations are highlighted in green ($p < 0.01$, two-tailed).

		lFCD							gFCD		
	Name of Test	Calcarine	Cerebellum	PFC	Posterior Cingulate	Precuneus	Thalamus (MDN)	Thalamus (VLN)	Calcarine	Cerebellum	Thalamus (VLN)
Drug Effects	Sedated	-0.42	0.02	0.27	-0.09	-0.28	-0.09	-0.02	-0.55	0.00	-0.14
	Irritable	-0.37	0.04	-0.02	-0.03	-0.40	-0.26	-0.20	-0.48	0.05	-0.16
	Dizzy	-0.38	-0.17	-0.15	0.14	-0.35	0.05	0.16	-0.07	-0.12	0.29
	High	-0.09	-0.57	-0.37	0.20	-0.21	0.36	0.18	-0.40	-0.58	-0.09
	Pleasant	0.04	-0.15	-0.15	-0.01	-0.02	-0.45	-0.55	-0.10	-0.13	-0.33
	Alcohol Desire	-0.43	-0.09	-0.23	-0.34	-0.29	0.13	0.12	-0.27	-0.16	-0.02
	Intoxication	-0.16	0.26	0.42	0.10	-0.41	-0.29	-0.51	-0.30	0.20	-0.33
	Restless	-0.29	-0.02	-0.25	-0.10	-0.33	-0.27	-0.12	-0.01	0.02	0.04
Motor	Gait (errors)	0.15	0.26	0.66	0.09	0.16	-0.19	-0.26	-0.35	0.19	-0.34
	One Leg (errors)	-0.03	0.61	0.81	0.13	-0.17	-0.19	-0.31	-0.27	0.52	-0.39
	Romberg (time)	0.03	-0.34	0.20	0.11	0.00	0.21	0.06	-0.46	-0.35	-0.20
	Romberg (errors)	0.44	0.01	0.25	0.19	0.25	0.10	-0.19	-0.12	-0.05	-0.18
	Rhythm (errors)	0.04	-0.31	0.23	0.07	-0.04	0.02	-0.12	-0.28	-0.33	-0.23
Cognitive	Stroop (Neutral)	-0.02	0.32	0.06	0.18	-0.18	0.34	0.43	0.49	0.35	0.42
	Stroop (Congruent)	-0.24	0.64	0.37	-0.02	-0.31	-0.25	-0.02	0.23	0.67	0.12
	Stroop (Incongruent)	-0.15	0.68	0.36	0.00	-0.27	-0.22	-0.04	0.53	0.69	0.20
	SDMT	-0.19	0.19	-0.07	0.00	-0.38	0.32	0.39	0.67	0.28	0.75
	Word Association	0.03	-0.16	-0.17	-0.10	0.02	0.16	0.19	0.57	-0.07	0.51

Supplementary Table 9. Correlations in NM between changes in 18 behavioral measures and changes in 10 ROIs which showed significant effects of Group or Alcohol from PLC to ALC. Significant correlations are highlighted in green ($p < 0.01$, two-tailed).

		lFCD							gFCD		
	Name of Test	Calcarine	Cerebellum	PFC	Posterior Cingulate	Precuneus	Thalamus (MDN)	Thalamus (VLN)	Calcarine	Cerebellum	Thalamus (VLN)
Drug Effects	Sedated	0.56	0.22	0.16	-0.07	-0.11	0.27	0.12	0.32	0.18	-0.03
	Irritable	0.40	0.02	-0.25	0.48	0.33	0.20	0.12	0.09	-0.11	0.15
	Dizzy	0.03	-0.24	-0.10	0.29	0.11	-0.31	-0.41	-0.08	-0.39	-0.43
	High	0.05	-0.35	0.19	-0.03	-0.09	0.05	-0.17	-0.25	-0.35	-0.42
	Pleasant	-0.19	-0.03	0.34	-0.37	-0.26	-0.03	-0.04	0.10	0.18	0.15
	Alcohol Desire	-0.15	-0.10	0.12	-0.38	-0.59	-0.16	-0.39	-0.27	-0.06	-0.41
	Intoxication	-0.04	-0.20	0.15	0.00	-0.18	0.03	-0.19	-0.14	-0.31	-0.31
	Restless	-0.21	-0.03	-0.01	-0.05	0.05	-0.11	-0.10	0.05	0.07	-0.01
Motor	Gait (errors)	0.28	0.07	0.24	-0.16	-0.29	0.27	0.14	-0.11	0.16	0.01
	One Leg (errors)	0.16	0.29	0.09	-0.22	0.10	0.17	0.05	0.14	0.19	-0.32
	Romberg (time)	-0.46	0.08	0.03	0.06	-0.01	-0.05	-0.04	-0.29	0.01	-0.27
	Romberg (errors)	0.26	0.23	0.39	-0.03	0.15	0.37	0.39	0.23	0.30	0.09
	Rhythm (errors)	0.22	-0.05	0.08	-0.57	0.00	0.28	0.29	0.33	0.24	0.37
Cognitive	Stroop (Neutral)	0.31	-0.20	0.32	0.31	-0.05	0.13	0.15	0.15	-0.23	0.12
	Stroop (Congruent)	-0.11	-0.30	0.12	0.28	-0.11	-0.10	-0.24	-0.47	-0.15	-0.27
	Stroop (Incongruent)	0.14	0.08	0.11	0.04	-0.19	0.16	0.06	-0.30	0.08	-0.01
	SDMT	0.00	0.07	0.07	0.45	0.13	0.22	0.02	-0.02	0.20	0.10
	Word Association	-0.30	0.23	0.04	-0.06	-0.11	0.02	-0.09	-0.49	0.09	-0.47

Supplementary Table 10. Correlations in HD between changes in 18 behavioral measures and changes in 10 ROIs which showed significant effects of Group or Alcohol from PLC to ALC. Significant correlations are highlighted in green ($p < 0.01$, two-tailed).

		lFCD							gFCD		
	Name of Test	Calcarine	Cerebellum	PFC	Posterior Cingulate	Precuneus	Thalamus (MDN)	Thalamus (VLN)	Calcarine	Cerebellum	Thalamus (VLN)
Drug Effects	Sedated	-0.14	-0.02	0.11	-0.08	-0.31	-0.03	-0.07	-0.21	0.23	0.07
	Irritable	0.16	-0.35	-0.28	0.16	-0.03	-0.09	-0.31	-0.16	-0.11	-0.19
	Dizzy	0.06	-0.20	-0.50	-0.14	-0.15	0.20	0.14	0.29	0.10	0.38
	High	0.09	-0.36	-0.23	0.09	-0.04	0.48	0.27	0.05	0.24	0.18
	Pleasant	0.36	-0.04	-0.12	-0.26	0.48	0.06	-0.03	0.13	-0.12	-0.06
	Alcohol Desire	0.01	0.12	0.35	-0.11	-0.14	0.39	0.44	0.29	0.37	0.44
	Intoxication	-0.07	0.26	0.01	-0.17	-0.26	-0.31	-0.38	-0.39	-0.06	-0.24
	Restless	-0.07	-0.36	-0.14	0.08	0.20	-0.17	-0.19	-0.43	-0.34	-0.53
Motor	Gait (errors)	-0.36	0.13	0.09	-0.09	-0.53	-0.34	-0.30	-0.42	0.09	-0.25
	One Leg (errors)	-0.14	0.34	0.38	0.05	-0.22	-0.26	-0.26	-0.39	0.14	-0.34
	Romberg (time)	-0.05	0.06	0.34	0.13	0.05	-0.01	-0.02	-0.25	0.21	-0.13
	Romberg (errors)	0.36	0.12	0.30	0.00	-0.33	0.06	-0.19	0.13	0.26	0.08
	Rhythm (errors)	0.12	-0.19	-0.22	-0.08	0.02	0.09	0.05	0.05	-0.12	0.01
Cognitive	Stroop (Neutral)	0.54	-0.42	-0.28	0.44	0.62	0.06	-0.11	0.05	-0.57	-0.33
	Stroop (Congruent)	-0.02	-0.62	-0.31	0.45	0.18	0.01	-0.11	-0.47	-0.50	-0.27
	Stroop (Incongruent)	0.61	-0.14	-0.45	0.13	0.48	-0.18	-0.32	0.13	-0.80	-0.32
	SDMT	0.38	-0.55	-0.36	0.41	0.58	0.26	0.15	0.08	-0.60	-0.10
	Word Association	0.62	-0.30	0.30	0.34	0.52	0.22	0.06	0.39	0.02	-0.19

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