Supplementary Information

Clinical, genomic, and neurophysiological correlates of lifetime suicide attempts among individuals with alcohol dependence

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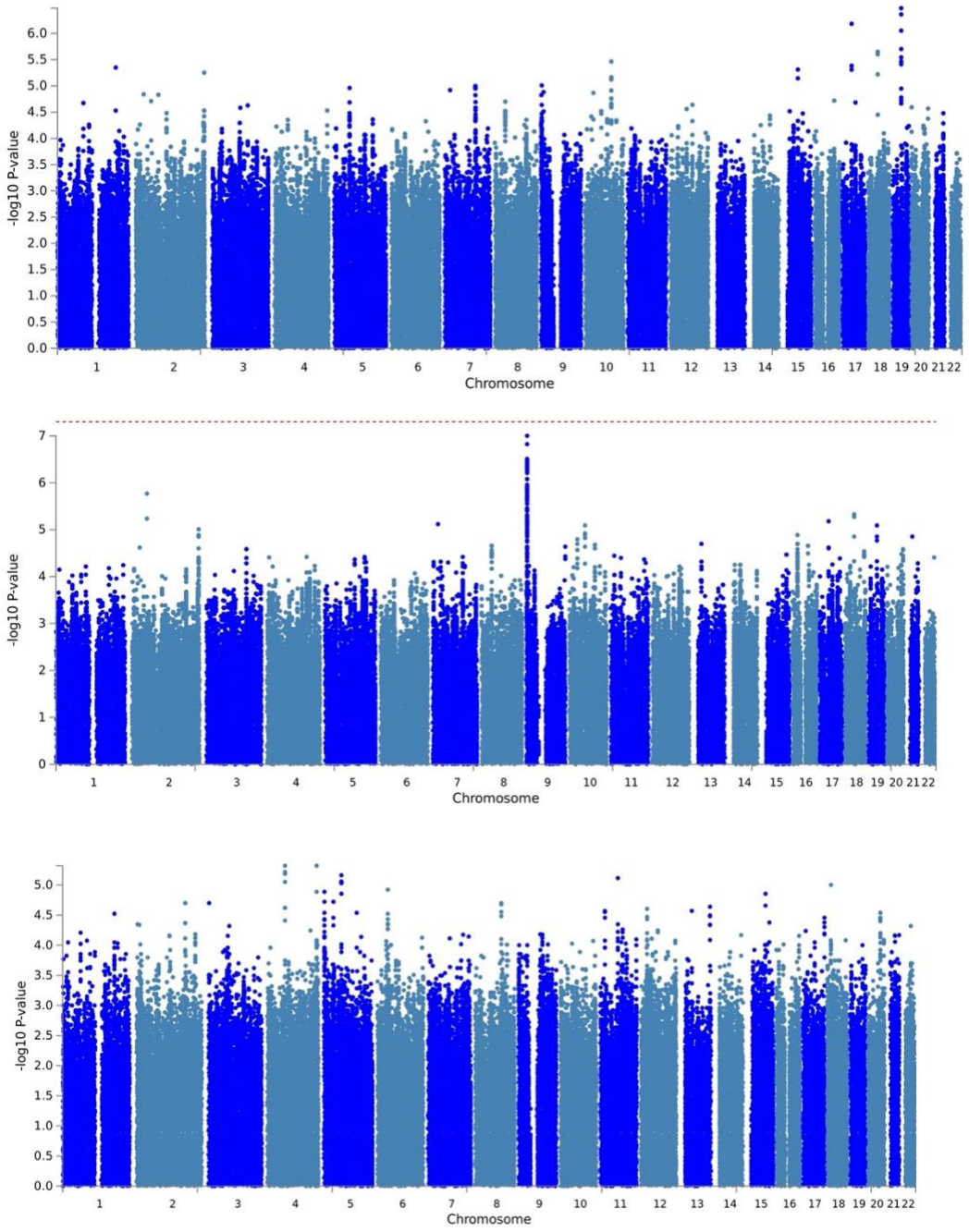
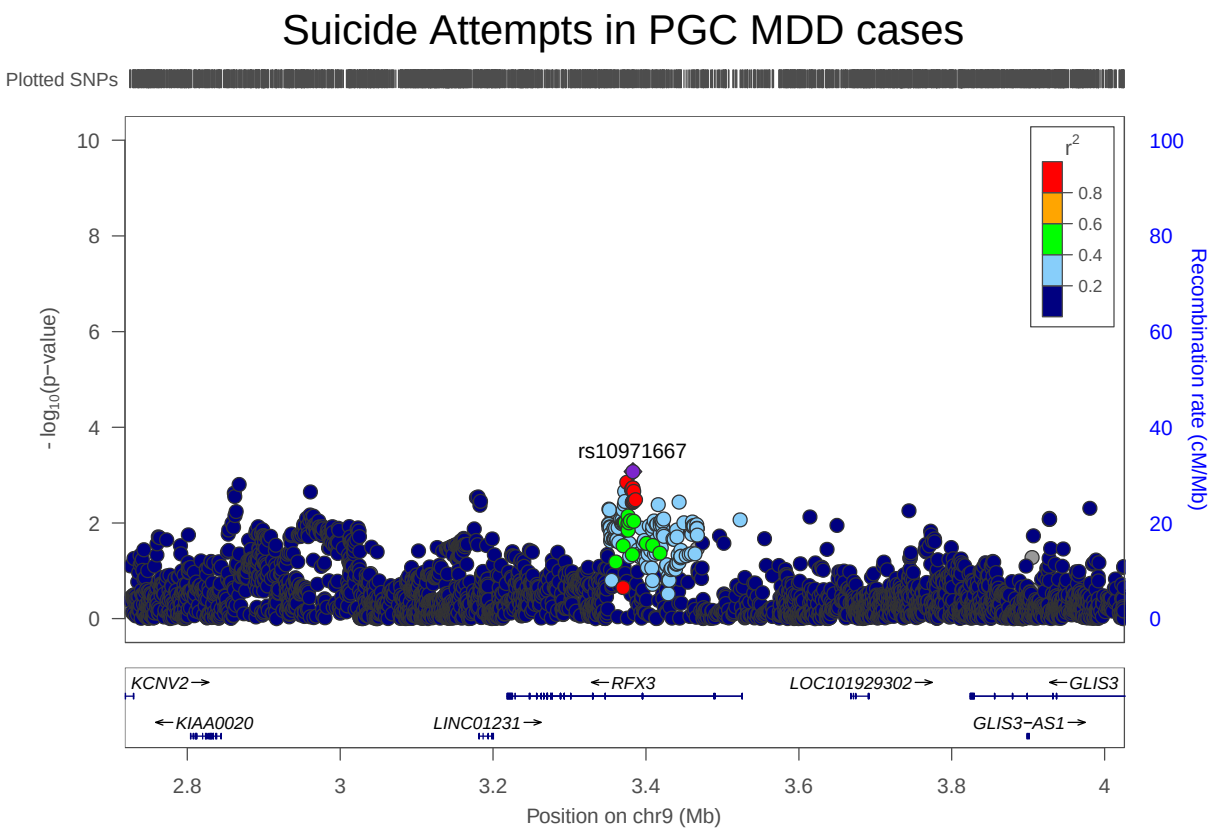
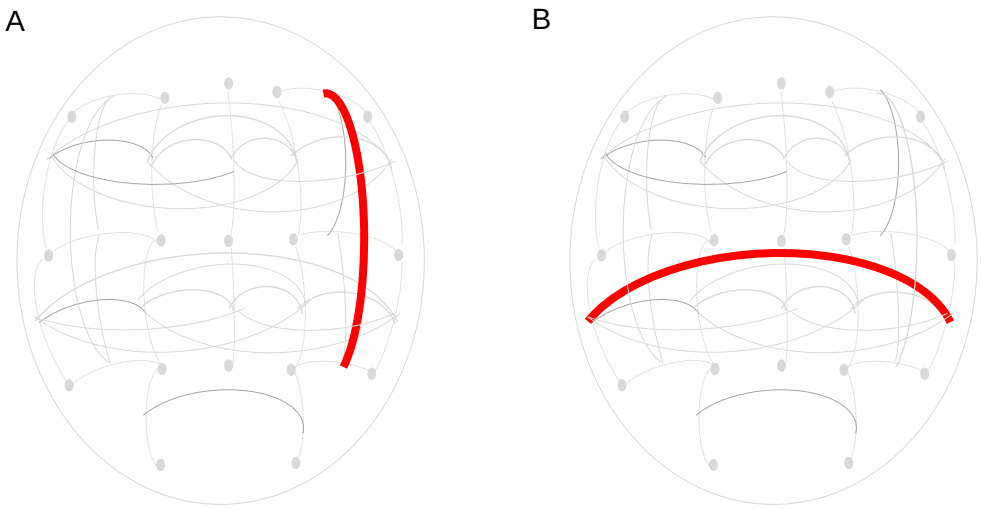


Supplemental Figure 1: Suicide GWAS Results

SNP based genome-wide association study findings comparing COGA participants with AD who have attempted suicide (N: 930) compared to those who have not attempted suicide (N: 3,138), in the (A) multi-ancestry meta-analysis, (B) European ancestries specific GWAS, and (C) African ancestries specific GWAS.



Supplemental Figure 2. Association of RFX3 in Psychiatric Genomics Consortium Major Depressive Disorder cases who attempted suicide



Supplemental Figure 1. Neurophysiological measures across those with and without a reported suicide attempt

Decreased right hemispheric frontal-parietal theta (3-7 Hz @ F8-F4--P8-P4) and decreased interhemispheric temporal-parietal (7-12 Hz @ T8-P8--T7-P7) alpha EEG resting-state coherences. A) Decreased right hemispheric frontal-parietal theta (3-7 Hz @ F8-F4--P8-P4) resting-state EEG coherence. B) Decreased interhemispheric temporal-parietal alpha (7-12 Hz @ T8-P8--T7-P7) resting-state EEG coherence

Supplemental Table 1. Sociodemographic And Clinical Indicators Of COGA Participants Without DSM-IV Alcohol Dependence Or Suicide Attempt

	AFR (N = 1,164)	EUR (N = 3,516)
Socio-Demographics		
Female (%)	61.2%	61.3%
Hispanic (%)	13.1%	1.8%
Mean Age At Last Interview (SD)	34.7 (12.6)	41.1 (15.4)
Suicide Related Behavior		
Suicidal Ideation (%)	23.6%	31.0%
Alcohol Use Disorder Indicators		
Maximum # Of AD Criteria Endorsed	0.48 (0.92)	0.66 (1.00)
Maximum # Drinks Consumed/24hrs	10.8 (13.4)	12.3 (11.7)
Mean Age Of AD Onset (SD)	NA	NA
Mean Age Of First Whole Drink (SD)	17.8 (3.0)	16.3 (2.6)
DSM-IV Psychiatric Comorbidities		
Major Depression (%)	3.3%	3.7%
Panic Disorder (%)	0.4%	1.7%
Obsessive Compulsive Disorder (%)	0.0%	0.6%
Social Phobia (%)	1.3%	2.7%
Agoraphobia (%)	0.9%	1.3%
Post-Traumatic Stress Disorder (%)	4.3%	2.0%
Anorexia Nervosa (%)	0.0%	0.4%
Bulimia (%)	1.6%	3.9%
Mania (%)	0.2%	0.3%
Attention-Deficit Hyperactive Disorder (%)	1.5%	1.9%
Conduct Disorder (%)	14.1%	9.0%
Antisocial Personality Disorder (%)	9.2%	5.8%
Nicotine Dependence (%)	15.6%	22.4%
Cannabis Dependence (%)	11.1%	8.6%
Cocaine Dependence (%)	7.5%	2.5%
Stimulant Dependence (%)	0.2%	1.8%
Sedative Dependence (%)	0.0%	0.3%
Opioid Dependence (%)	1.9%	0.2%

Supplemental Table 2. Sociodemographic and Clinical Indicators of COGA Participants with DSM-IV Alcohol Dependence by Ancestry Assignment

	AFR		EUR	
	No SA (N = 619)	SA (N = 147)	No SA (N = 2,414)	SA (N = 730)
Socio-demographics				
Female (%)	30.5%	51.7%	32.0%	53.3%
Hispanic (%)	3.2%	6.1%	6.5%	7.9%
Mean age at last interview (SD)	40.19 (10.76)	38.24 (9.45)	39.96 (12.24)	38.30 (10.84)
Suicide related behavior				
Suicidal Ideation (%)	34.2%	97.3%	50.0%	97.7%
Alcohol Use Disorder Indicators				
Maximum # of AD criteria endorsed	5.12 (1.68)	5.63 (1.60)	5.05 (1.69)	5.63 (1.66)
Maximum # drinks consumed/24hrs	30.12 (22.70)	34.92 (22.99)	28.29 (16.82)	34.69 (22.29)
Mean age of AD onset (SD)	24.98 (8.39)	22.47 (6.15)	23.93 (8.44)	22.28 (7.56)
Mean age of first whole drink (SD)	16.00 (3.14)	14.18 (2.10)	14.82 (2.12)	13.35 (2.40)
DSM-IV Psychiatric Comorbidities				
Major Depression (%)	2.2%	20.0%	12.2%	68.4%
Panic disorder (%)	0.0%	0.0%	3.8%	7.0%
Obsessive Compulsive Disorder (%)	0.0%	0.0%	1.0%	7.0%
Social phobia (%)	3.2%	5.6%	6.3%	12.9%
Agoraphobia (%)	0.8%	5.6%	4.9%	11.6%
Post-Traumatic Stress Disorder (%)	7.3%	11.1%	5.9%	21.4%
Anorexia Nervosa (%)	0.0%	0.0%	0.0%	2.8%
Bulimia (%)	4.0%	0.0%	3.4%	17.5%
Mania (%)	0.0%	0.0%	0.7%	2.8%
Attention-Deficit Hyperactive Disorder (%)	3.5%	0.0%	9.6%	6.5%
Conduct Disorder (%)	26.4%	11.1%	33.7%	38.6%
Antisocial Personality Disorder (%)	21.6%	11.1%	22.8%	38.6%
Nicotine Dependence (%)	47.5%	72.2%	57.1%	74.6%
Cannabis Dependence (%)	32.0%	23.5%	36.6%	31.0%
Cocaine Dependence (%)	39.5%	70.6%	26.0%	28.2%
Stimulant Dependence (%)	4.8%	5.6%	17.7%	20.0%
Sedative Dependence (%)	1.6%	16.7%	7.3%	14.1%
Opioid Dependence (%)	9.7%	11.1%	11.1%	14.1%

Supplemental Table 3: Logistic Regression Models for Suicide Attempt within Alcohol Dependence Cases

Ancestry (N)	Score	Beta (log OR)	SE	P	OR	95% CI (low)	95% CI (high)
EUR (N = 1,831)	AUD	0.066	0.055	2.29E-01	1.068	0.959	1.189
	MDD	0.079	0.056	1.58E-01	1.082	0.970	1.207
	SUI	0.211	0.061	5.80E-04	1.235	1.095	1.392
AFR (N = 496)	AUD	0.071	0.100	4.79E-01	1.074	0.882	1.307
	MDD	0.063	0.118	5.93E-01	1.065	0.845	1.343
	SUI	0.033	0.136	8.11E-01	1.033	0.791	1.349

* All models include cohort, sex, PC1-PC3, array, and site as covariates. SEs adjusted for familial clustering using cluster-robust standard errors.
AFR = African Ancestries, EUR = European Ancestries, AUD = alcohol use disorder polygenic score, DEP = depression polygenic score, = SUI suicide attempt polygenic score

Supplemental Table 4: Multinomial Logistic Regression Models for Suicide Attempt and Alcohol Dependence Cases*

Ancestry (N)	Score	Outcome	Beta	SE	P	OR	OR (low)	OR (high)
EUR (N = 4,892)	AUD	SA-, AD-	Ref	-	-	1.000	-	-
	AUD	SA+, AD-	0.199	0.068	3.24E-03	1.220	1.069	1.392
	AUD	SA-, AD+	0.305	0.037	1.94E-16	1.357	1.262	1.459
	AUD	SA+, AD+	0.398	0.052	3.15E-14	1.488	1.343	1.649
	DEP	SA-, AD-	Ref	-	-	1.000	-	-
	DEP	SA+, AD-	0.045	0.069	5.13E-01	1.046	0.914	1.196
	DEP	SA-, AD+	-0.027	0.036	4.57E-01	0.973	0.906	1.045
	DEP	SA+, AD+	0.051	0.053	3.40E-01	1.052	0.948	1.169
	SUI	SA-, AD-	Ref	-	-	1.000	-	-
	SUI	SA+, AD-	0.358	0.070	3.77E-07	1.431	1.246	1.643
	SUI	SA-, AD+	0.069	0.041	9.35E-02	1.072	0.988	1.162
	SUI	SA+, AD+	0.294	0.057	2.40E-07	1.342	1.200	1.501
AFR (N = 1,548)	AUD	SA-, AD-	Ref	-	-	1.000	-	-
	AUD	SA+, AD-	0.096	0.091	2.91E-01	1.101	0.921	1.317
	AUD	SA-, AD+	0.003	0.061	9.57E-01	1.003	0.890	1.131
	AUD	SA+, AD+	0.077	0.103	4.53E-01	1.080	0.883	1.320
	DEP	SA-, AD-	Ref	-	-	1.000	-	-
	DEP	SA+, AD-	0.060	0.104	5.61E-01	1.062	0.866	1.302
	DEP	SA-, AD+	0.070	0.067	2.98E-01	1.072	0.940	1.223
	DEP	SA+, AD+	0.134	0.113	2.36E-01	1.143	0.916	1.427
	SUI	SA-, AD-	Ref	-	-	1.000	-	-
	SUI	SA+, AD-	0.071	0.128	5.80E-01	1.073	0.836	1.378
	SUI	SA-, AD+	0.123	0.084	1.46E-01	1.130	0.958	1.334
	SUI	SA+, AD+	0.154	0.128	2.28E-01	1.167	0.908	1.499

* All models include cohort, sex, PC1-PC3, array, and site as covariates. SEs adjusted for familial clustering using cluster-robust standard errors.
AFR = African Ancestries, EUR = European Ancestries, AUD = alcohol use disorder polygenic score, DEP = depression polygenic score, = SUI suicide attempt polygenic score
SA- = no lifetime suicide attempt, AD- = does not meet criteria for alcohol dependence, SA+ = lifetime suicide attempt, AD+ = meets criteria for alcohol dependence

Neuropsychological tasks

In an exploratory series of analyses, we compared those with alcohol dependence (AD) who attempted suicide and those with AD who did not attempt suicide across a battery of neuropsychological measures on a subset of COGA participants (*N* = 188). Neuropsychological tasks included the Tower of London Task (TOLT) and the Visual Span Task (VST). These tasks have been detailed in previous publications [1]. Briefly, as part of the Colorado assessment tests for cognitive and neuropsychological assessment [2], the TOLT assesses planning and problem-solving ability. Participants are asked to solve a set of puzzles with graded difficulty levels by arranging the color beads one at a time from a starting position to a desired goal position in as few moves as possible. Participant performance on the TOLT was defined in the current study by the number of optimal trials achieved. The VST, also part of the Colorado assessment tests [2], requires subjects to duplicate a pattern of sequentially illuminated stimuli as well as to generate that pattern in reverse order. This test was used to assess visuospatial memory span from the forward condition and working memory from the backward condition. Participant performance on the VST was defined in the current study by the total forward and backward span (maximum sequence-length achieved).

We used multiple-group, multi-level regression models conducted in Mplus [3]. We included sex, age (at time of neuropsychological or neurophysiological assessment as appropriate), ancestry, family history of AD [4], and family relatedness as covariates. Since neuropsychological task performance was evaluated longitudinally, we used the most recent assessment from each individual (mean age = 24.2; SD = 12.3). We observed differences in neuropsychological task performance differences among alcohol dependent individuals who had attempted suicide. Those with AD who reported a lifetime suicide attempt had fewer optimal trials in the Tower of London Task (an average of 18 optimal trials among those without suicide attempts as compared with 17 optimal trials among those with suicide attempt, $p < 0.05$) and both a shorter attention span and short-term memory span in the Visual Span Task (an average of 10

words among those without suicide attempts as compared with 9 words among those with suicide attempt, $p < 0.05$). There were no significant differences between those with and without a lifetime suicide attempt in the Tower of London Task *trial time* or Visual Span Task *backward span*. These results point to some differences in cognition across suicide attempt within those with AD, but further work is necessary to determine whether these exploratory results will replicate.

References

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2. Davis HP KFR. Colorado Springs: Colorado Assessment Tests. 1998. Colorado Assessment Test manual. 1998.
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