Comparison of two Major Depression (MD) phenotypes: Primary Major Depression and Alcohol Induced Major Depression

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Introduction and objective

The differentiation between primary depressive episodes and those induced by substance use is one of the difficulties in the diagnosis of depressive symptoms when there is co-occurrence with substance use.

The objective of the present study is to investigate clinical and genetic differences in among Primary Major Depression (PMD) and Alcohol Induced Major Depression (AI-MD) using genome-wide association study (GWAS).

Methods

Comparative study of a total of 81 patients divided in two groups: 48 patients with PMD and 33 with AI-MD (diagnosis made according DSM-V criteria using PRISM interview). Socio-demographic data, and also clinical data related to depression, anxiety, personality and life events of participants were collected. A blood test was conducted to make a GWAS analysis.

Results

Results showed significant differences between PMD and AI-MD mainly in: medical comorbidity (29.8% vs 54.5%, p<0.026), family history of depression, alcohol use disorder and substance use disorder (79.5% vs 56.7%, p<0.042; 28.3% vs 53.3%, p<0.033 and 8.7% vs 31.1%, p<0.016) and traumatic life events scale (9,30 ±7,381vs 14,21 ±11,352, p<0.021). There were no significant differences between groups of patients in sociodemographic data, depression and anxiety symptoms scores or suicide behaviour. Table 1 and 2 show the sociodemographic and clinical results.

Table 1: Sociodemographic results

Variables	All participants N = 80 (%)	PMD N = 47 (%)	AI-MD N = 33 (%)	p[a]
Age (Mean ± SD)	50.09 ± 10.33	49.87 ± 11.32	50.39 ± 8.89	0.140[b]
Gender				
Men	39 (48.8)	22 (46.8)	17 (51.5)	
Women	41 (51.2)	25 (53.2)	16 (48.5)	0.678
Civil status				
Single	24 (30)	15 (31.9)	9 (27.3)	0.292
Married	29 (36.3)	20 (42.6)	9 (27.3)	
Divorced	23 (28.7)	10 (21.3)	13 (39.4)	
Widow	4 (5)	2 (4.3)	2 (6.1)	
Education level				
Primary studies	19 (24.1)	11 (23.4)	8 (25)	0.071
Secondary studies	22 (27.8)	9 (19.1)	13 (40.6)	
Higher education	38 (48.1)	27 (57.4)	11 (34.4)	
Employment situation				
Employed	22 (27.8)	16 (34)	6 (18.8)	0.271
Unemployed	1 (1.3)	1 (2.1)	0	
Disability	52 (65.8)	27 (57.4)	25 (78.1)	
Retired	4 (5.1)	3 (6.4)	1 (3.1)	
Medical history				
Serious illness (SI)	32 (40)	14 (29.8)	18 (54.5)	**0.026***
Hospitalization due to SI[c]	31 (96.9)	14 (100)	17 (94.4)	0.370
Current medication[d]				
Treatment history				
Psychiatric treatment	64 (80)	36 (76.6)	28 (84.8)	0.364
Family history				
Depression[e]		35 (79.5)	17 (56.7)	**0.042***
Alcohol use disorder[f]		13 (28.3)	16 (53.3)	**0.033***
Substance use disorder[g]		4 (8.7)	10 (31.3)	**0.016***

[a]Chi-Square, [b]Student's T-Test *Significance (p<.05) [c]n=32 [d]n=76 [e]n=74 [f]n=76 [g]n=78

Table 2: Clinical results

Variables	PMD N=47 (Mean ± SD)	AI-MD N=33 (Mean ± SD)	P[a]
Age of onset of depression	37.64 (13.53)	39.18 (11.26)	0.593
HAM-D	15.64 ±10.34	11.88 ±7.54	0.79
BDI	22.37 ±14.65	23.41 ±11.59	0.739
SSI	11.68 ±8.12	12.36 ±8.48	0.156
HAM-A	25.22 ±14.32	25.67 ±12	0.884
STAI			
State	28.17± 13.82	27.44 ±13.78	0.817
Trait	30.00 ±13.16	32.28 ±11.17	0.425
LSC-R	9.30 (7.38)	14.21 (11.35)	**0.021***
Personality Dimensions			
Temperament			
Novelty seeking (NS)	47.38±11.07	50.84±9.89	0.172
Harm avoidance (HA)	54.60±11.82	60.87±11.61	0.415
Reward dependence (RD)	43.57±9.65	45.68±10.66	0.381
Persistence (PS)	44.45±9.92	47.55±11.62	0.224
Character			
Self-directedness (SD)	42.33±11.92	39.61±11.12	0.325
Cooperativeness (CO)	45.14±11.42	45±12.22	0.959
Self-transcendence (ST)	48.74±10.57	50.35±11.53	0.536

[a]Student's T-Test, *Significance (p<.05)

HAM-D Hamilton Depression Rating Scale, *BDI* Beck Depression Inventory, *SSI* Suicidal Ideation Scale, *HAM-A* Hamilton Anxiety rating Scale, *STAI* State- Trait Anxiety Inventory, *LSC-R* Life Stressor Checklist-Revised

In the GWAS analysis, for each single variant, among the 341,946 common variants for genotyping data, 3 different tests were performed separately: **i)** basic allelic chi-square, **ii)** Fisher's exact test and **iii)** logistic regression. A Manhattan plot resulted from each test (Figure 1). In overall, none of the variants reaches significance beyond multiple testing. Interestingly, variants rs3130531, rs7772901, rs73115241, rs386580033 and rs529060937 rs529060937 are among the top 20 variants for all the 3 different applied association tests showed a tendency to differentiate both phenotypes.

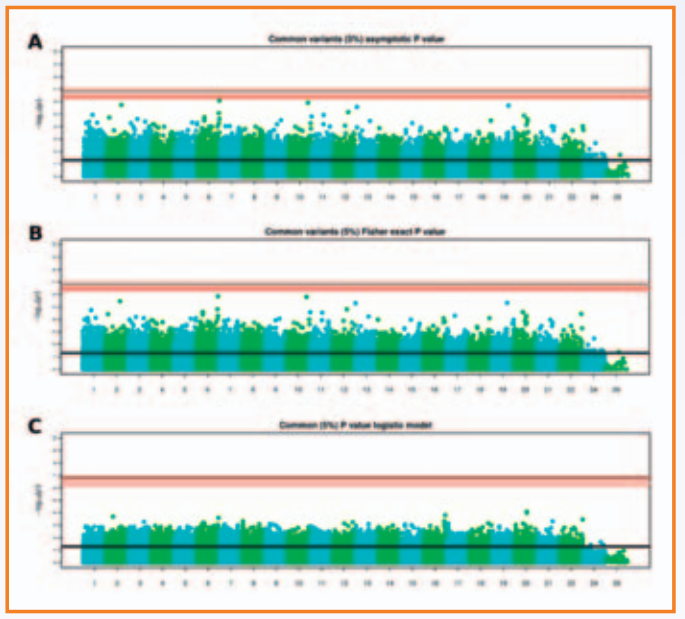

Figure 1: GWAS results. Manhattan plots indicating the negative base 10 logarithm of the P-values obtained performing: basic allele chi-square test (A) and Fisher's exact test (B) and logistic regression model (C).

Conclusions

Although this study has some limitations, this is the first study investigating biomarkers in AI-MD compared to PMD. The findings from this study may help clinicians to make an accurate diagnosis of these two depression phenotypes.

References:

Magidson, J. F., Wang, S., Lejuez, C. W., Iza, M., & Blanco, C. (2013). Prospective study of substance-induced and independent major depressive disorder among individuals with substance use disorders in a nationally representative sample. Depression and Anxiety, 30(6), 538–545. https://doi.org/10.1002/da.22122.

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