Default mode network resting-state functional connectivity in individuals with bipolar disorder and co-occurring alcohol dependence: Results from a 2x2 Factorial Design

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Background

- Bipolar is the psychiatric disorder most commonly associated with alcohol dependence.
- Abnormal default mode network (DMN) resting-state functional connectivity (rsFC) has been reported in both individuals with bipolar disorder (BD) and individuals with alcohol dependence (AD).
- Aberrant patterns of rsFC in DMN in individuals with AD and other classes of substance use disorders are associated with craving and relapse.
- There was found dysfunction in connectivity within DMN across studies in bipolar disorder (BD) groups when compared to health controls.
- The present study represents the first known investigation of DMN rsFC in individuals with co-occurring BD and AD (BD+AD).

Aims

The aim of this study is to investigate the rsFC within DMN using a ROI-to-ROI method in a sample of BD, AD, BD+AD and health control (HC) patients.

Methods

- Participants (*n*=104) met DSM-IV-TR diagnostic criteria for BD+AD (*n*=25), BD alone (*n*=29), AD alone (*n*=25), or no diagnosis (*n*=25).
- Participants completed a baseline assessment and returned for rs-fMRI scanning after demonstrating ≥ 1 week of abstinence from alcohol/drugs via blood serum and urine.
- Images were preprocessed and went through realignment, slice timing correction, normalization, and smoothing with CONN toolbox.
- Seed-based correlation approach between a priori regions of interest (ROIs) was performed.
- 2x2 general linear univariate models of Fisher's z-scores were tested to examine rsFC between-group differences for each pair of DMN regions (mPFC, PCC and bilateral angular gyri).
- Bivariate Pearson correlations between z-scores and symptom measures were explored within groups.

Results

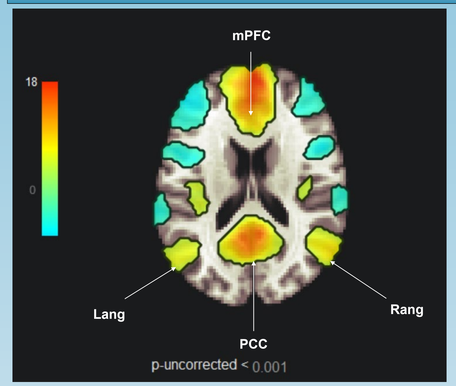

Fig. 1 DMN regions of interest: mPFC (medial prefrontal cortex), PCC (posterior cingulate cortex), Lang (left angular gyri) and Rang (Right angular gyri).

- Main effects of BD and AD and the BD x AD interaction terms were non-significant in two-by-two models.
- The directionality of PCC-mPFC connectivity and alcohol craving correlations varied between AD (r = -0.54, p = 0.005) and BD+AD groups (r = 0.52, p = 0.011).
- Connectivity across bilateral angular gyri and the PCC positively correlated with depressive symptoms in BD+AD group (r's ≥ 0.44, p-values ≤ 0.034).

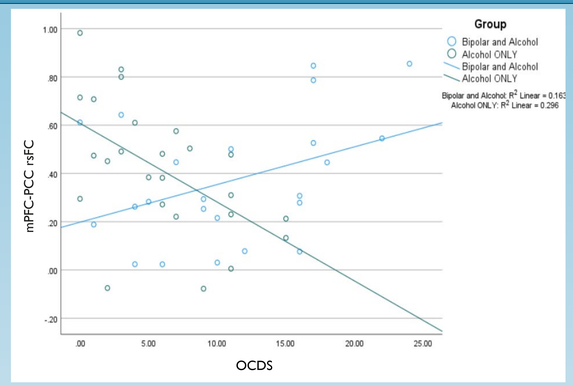

Fig. 2 Scatterplots with regression line fitting illustrating the correlation of mPFC-PCC rsFC with OCDS scores on BA+AD and AD groups.

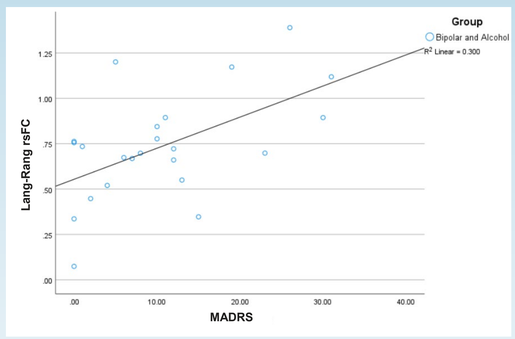

Fig. 3 Scatterplots with regression line fitting illustrating the correlation of Lang-Rang rsFC with MADRS scores on BA+AD groups.

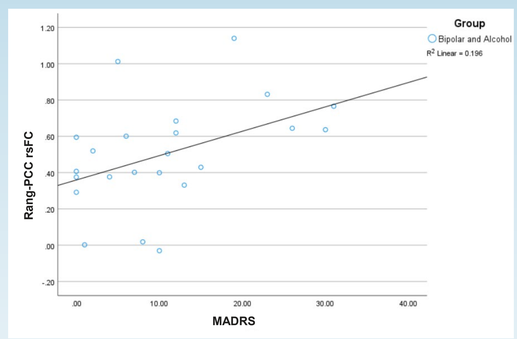

Fig. 4 Scatterplots with regression line fitting illustrating the correlation of Rang-PCC rsFC with MADRS scores on BA+AD groups.

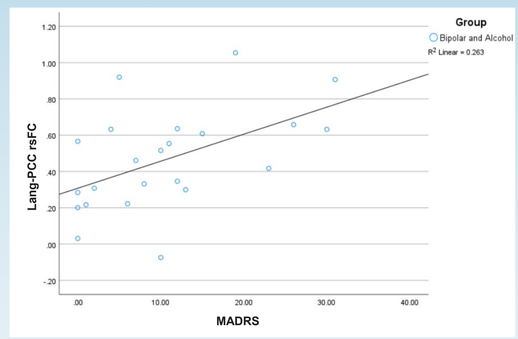

Fig. 5 Scatterplots with regression line fitting illustrating the correlation of Lang-PCC rsFC with MADRS scores on BA+AD groups.

Demographics

Table 1 *Participant characteristics and group comparison results*

	Participant group				p
	BD+AD[1] (n = 25)	BD alone[2] (n = 29)	AD alone[3] (n = 25)	HC[4] (n = 25)	
Age (in years)	35.83(10.93)	35.59(11.11)	42.12(11.91)	37.48(9.57)	0.126
Sex (% female)	43.5	55.2	32.0	52.0	0.337
Smoking status (%)	43.5	17.2	28.0	32.0	0.225
Drug dependence (%)	30.4[2,4]	0.0[1,3]	32.0[2,4]	0.0[1,3]	<0.001
Anxiety disorder (%)	69.6[3,4]	65.5[3,4]	28.0[1,2,4]	0.0[1-3]	<0.001
BD subtype (% Type-I)	68.2[3,4]	62.1[3,4]	0.0[1,2]	0.0[1,2]	<0.001
YMRS	2.13(2.83)[4]	1.82(2.72)[4]	1.44(1.69)	0.32(0.80)[1,2]	0.025
MADRS	10.65(9.57)[3,4]	7.68(6.11)[3,4]	3.52(3.99)[1,2]	0.88(1.90)[1,2]	<0.001
ADS	18.70(7.40)[2,4]	2.07(2.30)[1,3]	16.08(8.63)[2,4]	0.72(1.34)[1,3]	<0.001
OCDS	11.04(6.72) [1-4]	0.86(1.30) [1,2,4]	5.88(4.56) [1,3]	0.88(0.88) [1,3]	<0.001
% Heavy-drinking days (past 90)	35.71(19.29)[2,4]	1.25(3.55)[1,3]	40.38(20.59)[2,4]	0.96(1.84)[1,3]	0.000
% Drank w/in 2wk	57.1	32.1	25.0	36.0	0.142
Medication (%)					
Lithium	17.4[3,4]	27.6[3,4]	0.0[1,2]	0.0[1,2]	<0.001
Antipsychotic	30.4[2-4]	58.6[1,3,4]	0.0[1,2]	0.0[1,2]	<0.001
Anticonvulsant	60.9[3,4]	41.4[3,4]	0.0[1,2]	0.0[1,2]	<0.001
Antidepressant	47.8[3,4]	34.5[3,4]	0.0[1,2]	0.0[1,2]	<0.001

Conclusion

- This study extends previous research on resting-state connectivity within default mode network and contributes to mixed findings for BD and AD populations.
- Reducing angular gyrus functional connectivity may improve depressive symptoms in individuals with BD+AD as it has in prior treatment studies of major depressive disorder.
- Given associations with both depressive symptoms and alcohol craving, PCC functional connectivity may represent a putative treatment target for concurrent symptom reduction in BD+AUD.

Acknowledgements

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