Peripheral inflammation modulates the brain metastability and depressive symptoms relationship

Maria T. Wijaya[1,2], Shwu-Hua Lee [3,4], Tatia M.C. Lee[1,2,4]

[1] State Key Laboratory of Brain and Cognitive Sciences, The University of Hong Kong, Hong Kong
[2] Laboratory of Neuropsychology & Human Neuroscience, The University of Hong Kong, Hong Kong
[3] Department of Psychiatry, Linkou Chang Gung Memorial Hospital, Taoyuan County, Taiwan
[4] College of Medicine, Chang Gung University, Taoyuan County, Taiwan, 33305

Abstract

Preliminary evidence has linked changes in resting-state brain metastability to depressive symptoms, and depression is associated with peripheral inflammation. However, it is unknown whether and how inflammation and brain metastability are related and interact in the context of depression. Among all resting-state networks (RSNs), default mode network (DMN) metastability was most robustly associated with depressive symptoms. Inflammation in the body may exacerbate the consequences of heightened metastability within the DMN. This study highlights the importance of DMN and IL-6 in understanding depressive symptoms that might precede the development of clinically significant dysfunctions.

Keywords: metastability, depression, inflammation, default-mode network.

Introduction

Optimizing metastability is hypothesized to be important for emotional well-being [1]. However, only very few studies have investigated how metastability is altered in depression and the results are still inconsistent [2-4]. Furthermore, it is currently unknown how metastability are related and interact with peripheral inflammation, an important factor in the etiology of depression [5].

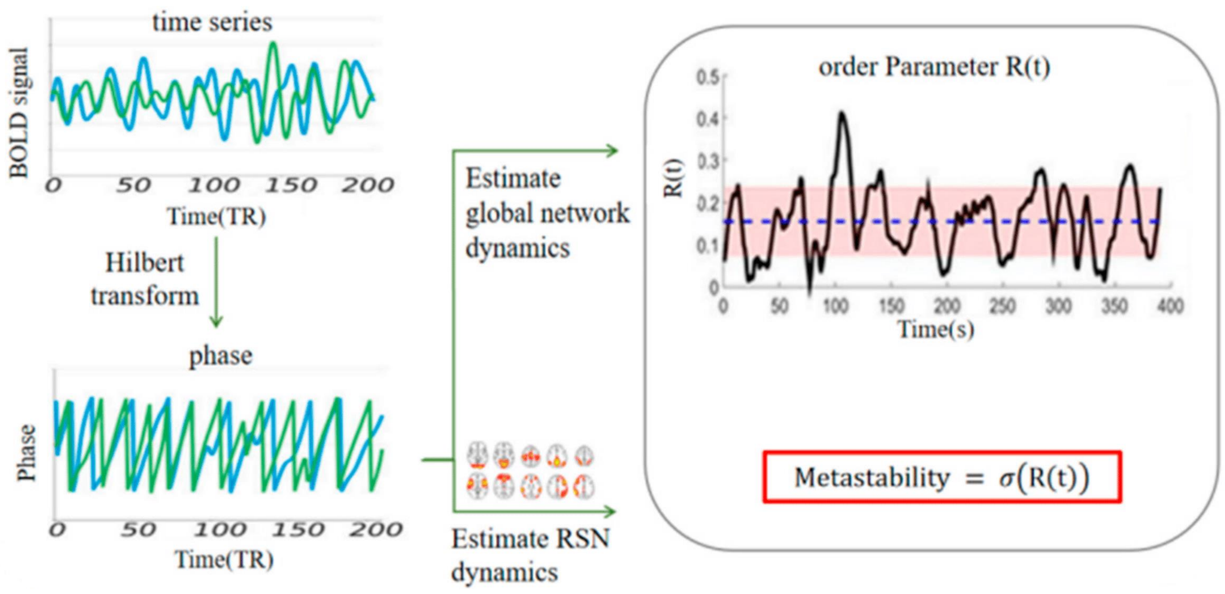


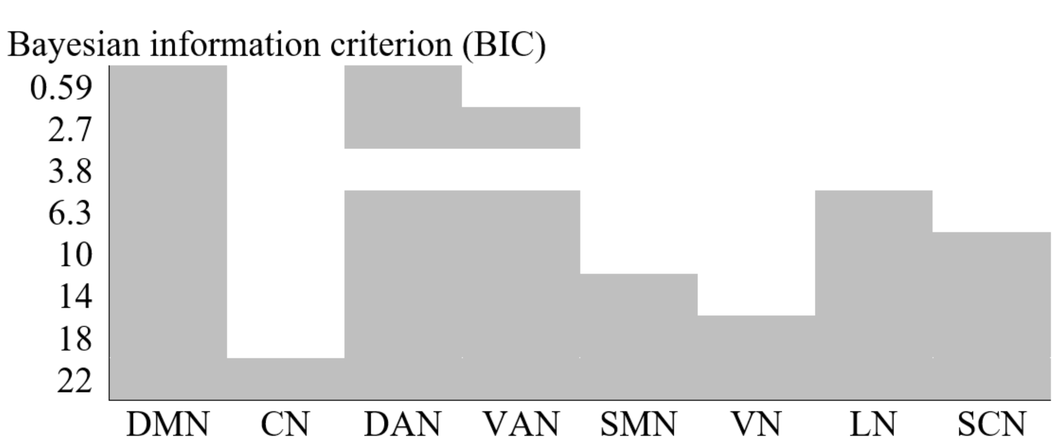
Figure adapted from [6]

Methods

We examined older adults aged 60 to 92. Metastability was measured as the standard deviation of Kuramoto order parameter, at the whole-brain level and in 8 RSNs. IL-6 and CRP were measured as peripheral inflammation markers. Depressive symptoms were measured using Hamilton depression rating scales (HAM-D).

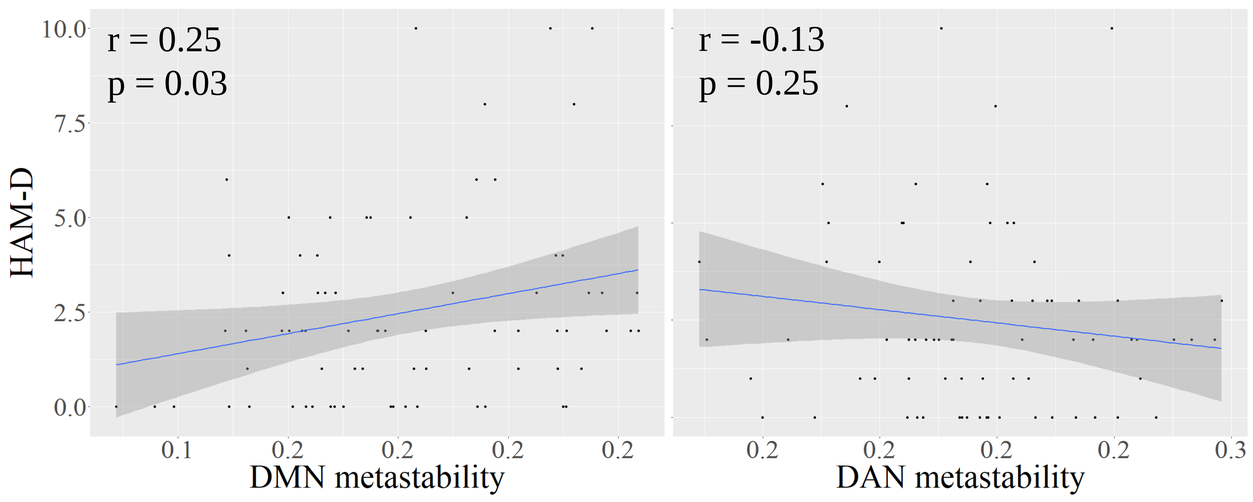
Results

Best-subset regression analysis to select the best combinations among network-level metastability measures for predicting HAM-D scores



DMN default mode network, *CN* control, *DAN* dorsal attention, *VAN* ventral attention, *SMN* somato-motor, *VN* visual, *LN* limbic, *SCN* subcortical

Correlations with best network-level predictors



Regression analysis with best network-level predictors

	B	*B* *p*-value	R^2_{adj}	*F*	*F* df	*F* *p*-value
			.22	2.90	11,63	.004
DMN	.38	.002				
DAN	-.30	.03				

Interaction between DMN metastability and IL-6

IL-6	*B*	SE	*t*	*p*-value	95% CI
-.32	.17	.12	1.45	.15	-.06 .40
-.30	.18	.11	1.65	.10	-.04 .41
.13	.53	.17	3.13	.003	.19 .86

Conclusion

This study highlights the importance of the DMN and IL-6 in understanding depressive symptoms that might precede the development of clinically significant dysfunctions. Future works may explore the relevance of DMN metastability and IL-6 for different subtypes of depressive symptomatology and establish a more mechanistic explanation of their associations using computational modelling.

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