Commentary: Aberrant dynamic functional connectivity of posterior cingulate cortex subregions in major depressive disorder with suicidal ideation

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Major depressive disorder (MDD) is a well-known mental disorder which influences millions of individuals worldwide (Ferrari et al., 2013). MDD not only leads to severe mental and physical disabilities but also cause a high risk for suicide (Wang et al., 2017; Dong et al., 2018). It is reported that 58% of MDD patients carry suicidal ideation (SI) and 15% of them have attempted suicide (Sokero et al., 2003). More than 50% of Chinese MDD patients have SI (Fang et al., 2018). Thus, to better understand the neural mechanisms underlying SI in MDD is of necessary and urgent significance for the progress in suicide prevention and intervention.

Recently, evidence demonstrates that changes in a wide range of brain regions and functional connectivity (FC) are associated with SI, such as the amygdala, the insula, the ventral and dorsal prefrontal cortex, the posterior cingulate cortex (PCC), the anterior cingulate cortex, the cortico-limbic-striatal FC, the orbitofrontal-thalamic FC, and the frontal-limbic FC (Du et al., 2017; Kim et al., 2017; Wei et al., 2018; Schmaal et al., 2020; Li et al., 2022b; Yang et al., 2022). Despite recent neuroimaging developments, FC abnormalities in MDD with SI are still poorly understood. Moreover, most FC studies exploring static FC on MDD with SI relied on the implicit assumption that the degree of connectivity strength among regions remains stationary over time. However, studies have indicated that our brain is not static, but rather is inherently dynamic (Allen et al., 2014; Lu et al., 2020, 2021). Till now, few studies examined the dynamic FC in MDD with SI. For example, Liao et al. showed that MDD with SI revealed increased dynamic
connectomics compared with MDD without SI and healthy controls (HCs) (Liao et al., 2018). Qiao et al. reported changed dFC between habenula and other brain regions in MDD with SI relative to MDD without SI and HCs (Qiao et al., 2020). Those studies indicated that altered dFC could help distinguish patients with SI from those without SI as compared with static FC. Hence, to understand how FC between different brain regions strengthen or weaken over time could help provide novel insight into the neural communication in MDD with SI from the view of temporal stability.

The PCC was reported to play a vital role in the neural mechanisms in MDD patients with SI. Previous studies showed abnormal structural and functional activities in PCC as well as aberrant FC between PCC and other brain regions in MDD with SI (Marchand et al., 2013; Ambrosi et al., 2019; Schmaal et al., 2020; Hong et al., 2021). Moreover, Chase et al. demonstrated disrupted static FC in PCC subregions in MDD with SI (Chase et al., 2017, 2021). However, there are no studies investigating the dFC variability of the PCC subregions in MDD with SI.

Therefore, a recent study of Li et al. (2022a) is very timely. In their study, the authors supposed that (1) MDD with SI would show aberrant dFC variability in PCC subregions as compared with MDD without SI and HCs; and (2) the anomalous dFC variability would exhibit associations with clinical variables. To test their hypotheses, resting-state functional magnetic resonance imaging (rsfMRI) data were obtained from 31 unmedicated MDD with SI (SI), 56 unmedicated MDD without SI (NSI), and 48 matched HCs. The PCC was segmented into bilateral dorsal PCC (dPCC) and bilateral ventral PCC (vPCC) according to the Human Brainnetome Atlas. Then, the whole-brain dFC analysis of each PCC subregion was performed by using a sliding-window method with a window length of 50 TR (100 s) and a step size of 1 TR (2 s), resulting in 181 consecutive windows. After that, the dFC was measured by computing the standard deviation (SD) of the z maps across the 181 windows. Subsequently, analysis of covariance (ANCOVA) was applied to examine the between-group differences in dFC maps among the three groups for each PCC subregion with age, gender, and mean FD as covariates. Next, the SI and NSI groups indicated increased dFC variability between the left vPCC and left IFG in relative to NSI group, whereas the SI and NSI groups indicated increased dFC variability between the left vPCC and left IFG in relative to NSI group. Post hoc analysis results demonstrated that SI group showed higher dFC variability between the left vPCC and left IFG in relative to NSI group, whereas the SI and NSI groups indicated increased dFC variability between the left dPCC and left fusiform gyrus, and right vPCC and left IFG among the three groups. Post hoc analysis results demonstrated that SI group showed higher dFC variability between the left dPCC and left fusiform gyrus, and right vPCC and left IFG than HCs. Further, the dFC variability between the left vPCC and left IFG was positively associated with the suicide ideation scores across all the MDD patients.

Overall, the study was the first to report aberrant dFC variability within PCC subregions in MDD with SI. Their findings revealed that the key brain regions involved in the cognition, negative self-perceptions, and negative emotion generation, as well as the default mode network and frontoparietal network were disrupted in MDD with SI, which contributes to advance our understanding of the potential neural mechanisms in MDD with SI from the perspective of dynamic FC. However, here, we want to point out several shortcomings about methodological issues. First, the educational level information was missed for the HCs. In the ANCOVA and post hoc analyses, the covariates should also include the educational level as well as the variance of FD. Second, we did not see the handedness information for participants. Thirdly, since SD will over-represent data used in the center of the run and are often dependent on the mean connectivity, we suggested that the authors could also compute the coefficient of variation (CV = SD/mean) to validate their results. Finally, in the correlation analysis, it is better to regress out the age, gender, mean FD, variance of FD, as well as the clinical information such as duration of illness, and age of onset. Another concern is that in the Figure 4, the results may be influenced by some outlier data points. In conclusion, future studies could include large sample size, more detailed demographic and clinical information, as well as more rigorous method to corroborate their findings.

Author contributions

ZH and FL conceived the idea and wrote the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

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