

## Psychiatry Mental health 2017 : Structural and functional MRI correlates of post-stroke depression - Wai Kwong Tang - The Chinese University of Hong Kong

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Depression is common following an acute stroke. Post-Stroke Depression (PSD) has notable impacts on the function recovery and quality of life of stroke survivors. Incidence decreased across time after stroke, but prevalence of PSD tend to be stable. Many studies have explored the association between lesion location and the incidence of PSD. For example, lesions in frontal lobe, basal ganglia and deep white matter have been related with PSD. Furthermore, cerebral microbleeds and functional changes in brain networks have also been implicated in the development of PSD. In this presentation, evidences of such association between the above structural and functional brain changes and PSD will be reviewed. One in three survivors of stroke experience poststroke depression (PSD). PSD has been linked with poorer recovery of function and cognition, yet our understanding of potential mechanisms is currently limited. Alterations in resting-state functional MRI have been investigated to a limited extent. Fluctuations in low frequency signal are reported, but it is unknown if interactions are present between the level of depressive symptom score and intrinsic brain activity in varying brain regions. A cross-sectional analysis of 63 stroke survivors who were assessed at 3 months poststroke for depression, using the Montgomery-Åsberg Depression Rating Scale (MÅDRS-SIGMA), and for brain activity using fMRI. A MÅDRS-SIGMA score of  $>8$  was classified as high depressive symptoms. Fractional amplitude of frequency fluctuations (fALFF) data across three frequency bands (broadband, i.e.,  $\sim 0.01-0.08$ ; subbands, i.e., slow-5:  $\sim 0.01-0.027$  Hz, slow-4:  $0.027-0.07$ ) was examined. Of the 63 stroke survivors, 38 were classified as “low-depressive symptoms” and 25 as “high depressive symptoms.” Six had a past history of depression. We found interaction effects across frequency bands in several brain regions that differentiated the two groups. The broadband analysis revealed interaction effects in the left insula and the left superior temporal lobe. The subband analysis showed contrasting fALFF response between the two groups in the left thalamus, right caudate, and left cerebellum. Across the three frequency bands, we found contrasting fALFF response in areas within the fronto-limbic-thalamic network and cerebellum. Post

stroke, patients frequently experience motor, sensory, cognitive, and behavioural changes, all of which may impact recovery. Changes to a stroke survivor's mood are also common, with depression as the most frequently reported psychiatric disorder following ischaemic stroke. Poststroke depression (PSD) is estimated to affect approximately one-third of survivors, compared to about one-sixth of the nonstroke population. PSD is associated with poorer recovery prospects, including increased disability, worse cognitive outcomes, decreased quality of life, and increased risk of mortality. In particular, PSD negatively impacts response to rehabilitation in acute and subacute phases of recovery. However, our understanding of the potential mechanisms underlying the negative impact of depressive symptoms on recovery and rehabilitation is currently limited. Determining factors that may assist in the identification of those “at risk” of developing poststroke depression may aide in the recovery process and/or prediction of response to rehabilitation. The value of biomarkers of stroke recovery that focus on brain structure and function has recently been highlighted in consensus-based recommendations. Neuroimaging markers of depression may be used to provide new insight into neural mechanisms underlying depression, to predict the likelihood of future depressive symptoms, and/or to predict readiness to engage in treatment or treatment response. All are important reasons to identify stroke survivors with underlying vulnerabilities that may be “at risk” of developing depression.

One approach has been to investigate the relationship between lesion location and depression; however, despite a large number of studies, findings are equivocal. These findings suggest that lesion location alone is unlikely to be an informative biomarker associated with PSD. A meta-analysis of behavioural, biochemical, and neuroimaging markers of PSD found associations with reduced cerebral blood flow and regional volume reductions. In the broader literature of clinical depression, the disorder is not considered to be caused by independent, localised changes within specific brain regions but is thought to be partially due to disruption of communication between areas. Several

meta-analyses of fMRI cohort studies of clinical depression have found changes in brain activation and connectivity. Findings highlight alteration of brain regions consistent with the current system-level models of depression. It may therefore be useful to examine biomarkers of PSD using resting-state methods that focus on intrinsic brain activity and whole brain. Resting-state fMRI methods focus on low frequency fluctuations (LFF) present within the blood oxygen level-dependent (BOLD) signal (0.01 to ~0.1 Hz) which in part reflect intrinsic neuronal activity. Several methods have been developed that evaluate different aspects of the signal. For example, local or regional correlations between BOLD time series are able to be examined, collectively known as functional connectivity. These functional connectivity analyses focus on temporal correlations of the BOLD signal. The spectral (frequency) characteristics of signal within individual voxels during resting-state can also be examined, typically by taking the sum amplitude of low frequency fluctuations (ALFF) or a ratio of LFF over the entire estimated spectra (fractional ALFF, fALFF). Of these two methods, fALFF has been shown to be robust against physiological artefacts and vascular effects, which are common poststroke given changes to neurovasculature post-stroke. While methods typically focus on the full LFF range, spectral measures allow the exploration of subbands, which have been suggested to be important for a scope of physiological and function processes within the brain. Wang et al. used fALFF to examine LFF and subbands of slow-5 (0.01–0.027 Hz) and slow-4 (0.027–0.07) in medication of naive participants with major depressive disorder over two studies. Both studies found similar changes in LFF measures when depressed participants were compared to controls. Wang et al. also found areas that displayed an interaction effect between controls and those with depression and subband signal changes. Their results showed that the areas of the left ventromedial prefrontal cortex, left inferior frontal gyrus, and bilateral precuneus showed changes in amplitude in the slow-5

band, but not slow-4. This suggests that examination of subbands may be useful in identifying regions that are associated with depressive symptoms. It also highlights the value of investigating for an interaction effect in brain regions. To date, PSD studies of resting-state changes have not been widely employed, have focused on functional connectivity from specific regions, e.g., within the default mode network (DMN) and anterior cingulate, and have included participants of varying times post stroke. Results from these studies have been inconsistent. For example, Lassalle-Lagadec et al. found correlations at 10 days post stroke between the depression score and the left middle temporal cortex and precuneus and at 3 months with the neostriatum. Vicentini et al. found an association with the posterior cingulate cortex and depression score at approximately 1-month poststroke, while Liu et al. failed to find any regional correlations of the posterior cingulate with a depression score in a cohort of chronic stroke survivors. More recently, Balaev et al. explored changes in the default mode network and found changes post treatment. Only one study, by Egorova et al., used voxelwise spectral analysis of fALFF and found mean differences between depressed and nondepressed stroke survivors in the frontal and insular regions.

#### **Biography:**

Wai Kwong Tang was appointed as a Professor in the Department of Psychiatry, the Chinese University of Hong Kong in 2011. His main research areas are addictions and neuropsychiatry in stroke. He has published over 100 papers in renowned journals and has also contributed to the peer review of 40 journals. He has secured over 20 major competitive research grants. He has served the Editorial Boards of five scientific journals. He was also a recipient of the Young Researcher Award in 2007, awarded by the Chinese University of Hong Kong.

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