Contribution ID: **48** Type: **Poster**

Switching patterns of cortical-subcortical interaction in the human brain

Tuesday 10 September 2024 17:30 (45 minutes)

Aims. While human neuroscience has traditionally focused on the neocortex, recent literature highlights the key role of subcortical structures in brain dynamics and cognitive processes. We investigated cortico-subcortical interactions in the human brain at rest by analyzing dynamic functional connectivity at rest in a large cohort of healthy human
participants.

Methods. We considered 1078 human participants from the Human Connectome Project, for which resting-state fMRI scans were available. We computed sliding window functional connectivity (sw-FC) on windows of 60 s (Fig. 1A). sw-FC matrices were approximated by projecting onto the leading eigenspace, vectorized, and concatenated across windows and subjects. K-means clustering was used to identify a set of recurring sw-FC patterns or dynamic functional states (DFSs) (Fig. 1B).

Results. FC fluctuations were synchronized in cortex and subcortex. Cortical regions exhibited flexible connectivity with two core subcortical 'clusters'comprising, respectively, limbic regions (hippocampus and amygdala) and subcortical nuclei (thalamus and basal ganglia). We identified two alternating DFSs: in DFS1 the hippocampus coupled positively with the default mode network and negatively with the sensorimotor network, while the thalamus showed an opposite trend; in DFS2, this pattern of subcortical-cortical connectivity was reversed (Fig. 1C). Better cognitive health was associated with a stronger segregation of cortex and basal ganglia/thalamus in DFS1, and stronger integration in DFS2., i.e., with an alternation of states with higher and lower cortico-subcortical coupling.

Conclusions. Our findings hint at a general relevance of cortico-subcortical interactions in the generation of whole-brain spontaneous FC patterns in healthy subjects.

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Session Classification: Poster Session