Contribution ID: **15** Type: **Talk**

Mapping neurotransmitter receptor and transporter distributions to the connectivity and dynamics of the human neocortex

Thursday 23 September 2021 15:30 (15 minutes)

Connections and interactions among neurons manifest as patterned neural activity and adaptive behaviour. Ascending projections from the brainstem and subcortical nuclei have a modulatory effect on the electrical potential - and therefore the excitability and firing rate - of cortical neurons (Shine 2019). These modulatory influences are coordinated by overlapping and heterogeneous distributions of multiple neurotransmitter receptors at the target cells. This heterogeneous distribution of neurotransmitter receptor densities across the cortex suggests a diversity of modulatory influence, and therefore also of signal integration, neural dynamics, and whole-brain connectivity. We used two recent state-of-the-art datasets (PET and autoradiography) of neurotransmitter receptor densities across the neocortex, which include a total of 32 excitatory, inhibitory, ionotropic, and metabotropic neurotransmitter receptors, transporters, and receptor binding sites (Zilles et al., 2017). First, we mapped receptor distributions to structural and functional connectivity, thereby profiling how receptors may influence whole-brain communication. Second, we used multiple linear regression models to predict MEG-derived neural dynamics from receptor densities and find that excitatory ionotropic receptors are dominant contributors toward shaping neural dynamics. Finally, we asked how neurotransmitter receptor densities map onto meta-analytic patterns of functional activation from Neurosynth (Yarkoni et al., 2011) and disease-specific cortical thinning from the ENIGMA consortium (Thompson et al., 2020). Altogether, we uncover the neurochemical infrastructure that shapes the brain's connectivity and dynamics by comprehensively mapping receptor distributions to the structure and function of the human brain.

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Session Classification: Contributed Talks: Applications

Track Classification: Workshop Day 2 - Sep 23: Applications