Classical serotonergic psychedelics induce changes to functional and structural brain hierarchies

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Psychedelic intervention has garnered substantial attention in recent years for its ability to induce profound reorganisation within the human brain, both in the acute and long-term phases of its effects (Barsuglia et al. (2018), Progress in Brain Research). Understanding these aspects is important not only for a comprehensive grasp of the underlying neurobiology but also for potential therapeutic applications (Anderson et al. (2020) Lancet Psychiatry). In the brain, psychedelic effects have been hypothesised to reflect a shift in the functional hierarchy of the brain, where unimodal regions, related to sensory cortices, become less constrained from the transmodal higher-level cognitive cortices, leading to novel perceptual experiences (Carhart-Harris and Friston. (2019) Pharma.Rev.). In this work, using methods from non-equilibrium dynamics (Deco et al. (2020) Nat.Comm.Bio.), we quantify the level of hierarchy at the functional (time-shifted functional connectivity). We focus our analysis on three classical serotonergic psychedelics, namely psilocybin (Carhart-Harris et al. (2012), PNAS), LSD (Carhart-Harris et al. (2016), PNAS) and DMT (Timmermann et al. (2023), PNAS), in the acute post-intervention stage in a resting-state fMRI condition. Corroborating previous literature, we show the level of hierarchy consistently decreases for all three psychedelic drugs. This is further reflected in resting-state network analysis where we observe consistent and discriminate changes for each psychedelic drug in terms of the unimodal and transmodal separation. This is also supported by the collapse of the uni to transmodal gradient across all three drugs. In summary, our project bridges the existing knowledge gap in understanding the spatio-temporal dynamics of psychedelic effects on the brain.