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Neural circuit mapping of waiting impulsivity and proactive inhibition with convergent evidence from fMRI and TMS

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Introduction: Waiting and stopping are essential and distinct elements of appropriate behavioral control with its dysfunction implicated in various impulsivity related mental disorders. Although rodent and human studies have investigated both phenomena, the role of preparing to stop in waiting impulsivity has rarely been investigated. Furthermore, convergent evidence from multi-modal investigation tools remains a poorly utilized approach in addressing such questions.
Objectives: Here, we conducted two separate, but hierarchical studies, using functional magnetic resonance imaging (fMRI) to map the neural circuit involved in waiting impulsivity and proactive stopping, and subsequently provide mechanistic and causal evidence of disruption of this circuit by transcranial magnetic stimulation (TMS). In the second study, based on our fMRI study data, we attempted to investigate possible causation between the LIFG and waiting impulsivity by modulating LIFG, i.e. non-invasively producing a "virtual lesion" with an inhibitory transcranial magnetic stimulation (TMS) protocol called continuous theta burst stimulation
Methods: We recruited 41 healthy volunteers who performed an adapted version (1CSRT) of the well-established 5 choice serial reaction time task to capture waiting impulsivity. We developed a novel task measuring proactive inhibition. We scanned participants while completing these two tasks. Our fMRI data showed a strong association between LIFG activity and waiting impulsivity on the 1CSRT task. We conducted a single-blind, randomized, between-subjects design of cTBS of the LIFG on a sample of 51 healthy volunteers who completed an adapted version of the 1CSRT task (2CSRT task). Our a priori hypothesis was that cTBS would transiently decrease local cortical activity of the LIFG and increase the frequency of premature responses on both fixed and delayed cue-target interval trials on the 2CSRT task.
Results: We first show a shared neural network comprising the pre-supplementary motor area and bilateral anterior insula underlying both waiting impulsivity and proactive stopping. We further demonstrate activity in dorsomedial prefrontal cortex and left inferior frontal gyrus (LIFG) negatively correlated with waiting impulsivity in trials with additional target onset delay. We demonstrate active stimulation significantly increased waiting impulsivity.
Conclusions: In these two studies, we validated a novel task measuring proactive inhibition. We further validated the significance of task structure for assessing distinct aspects of impulsivity, which is of translational interest. We further established a causal role of lIFG for waiting impulsivity thus highlighting the integrity of LIFG and related neural circuitry required in waiting impulsivity.

Disclosure of Interest: None Declared

Prevention of Mental Disorders

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Psychological trauma as a transdiagnostic risk factor for mental disorder: an umbrella meta-analysis

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Introduction: This umbrella review is the frst to systematically examine psychological trauma as a transdiagnostic risk factor across psychiatric conditions.
Objectives: This review aimed to be the frst to evaluate whether psychological trauma fulflilled criteria as a transdiagnostic risk factor cutting across various diagnostic categories and spectra. Transdiagnosticity will be assessed against the framework of the TRANSD criteria (Fusar-Poli, World Psychiatry 2019; 18 361-362). The paper additionally aimed to analyse the association of psychopathology with specifc trauma type.
Methods: We searched Pubmed, Scopus, and PsycNET databases from inception until 01/05/2021 for systematic reviews/meta-analyses evaluating the association between psychological trauma and at least one diagnosed mental disorder. We re-calculated the odds ratio (OR), then classifed the association as convincing, highly suggestive, suggestive, or weak, based on the number of cases and controls with and without psychological trauma, random-efects p value, the 95% conf- dence interval of the largest study, heterogeneity between studies, 95% prediction interval, small-study efect, and excess significance bias. Additional outcomes were the association between specifc trauma types and specific mental disorders, and a sensitivity analysis for childhood trauma. Transdiagnosticity was assessed using TRANSD criteria. The review was pre-registered in Prospero CRD42020157308 and followed PRISMA/MOOSE guidelines.