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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 fulfilled 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.

Results: Fourteen reviews met inclusion criteria, comprising 16,277 cases and 77,586 controls. Psychological trauma met TRANSD criteria as a transdiagnostic factor across diferent diagnostic criteria and spectra. There was highly suggestive evidence of an association between psychological trauma at any time-point and any mental disorder (OR=2.92) and between childhood trauma and any mental disorder
(OR=2.90). Regarding specifc trauma types, convincing evidence linked physical abuse (OR=2.36) and highly suggestive evidence linked sexual abuse (OR=3.47) with a range of mental disorders, and convincing evidence linked emotional abuse to anxiety disorders (OR=3.05); there were no data for emotional abuse with other disorders.

Image:

Table 1: Application of TRANSD Criteria to assess psychological trauma as a transdiagnostic construct across mental disorders.

Domain	Subdomain	Evidence
(T) Transparent definition	Gold standard	Diagnosis according to DSM-III, DSM-III-R, DSM-IV, DSM-5 or ICD 9, 10, or 11
	Diagnostic types	Anxiety Disorders (diagnostic group comprising Generalised Anxiety Disorder, Panic Disorder and Social Anxiety Disorder), BD, BPD, OCD, MDD, Psychosis (diagnostic group comprising Psychotic Disorder, Schizophrenia, Schizoaffective Disorder), PTSD,
	Primary or secondary diagnoses	Primary diagnoses
(R) Report	Primary outcome	Psychological trauma as a risk factor for mental disorder
	Study design	Meta-analyses or Systematic reviews including case control studies
	Transdiagnostic construct	Psychological trauma
(A) Appraise the conceptual framework	Transdiagnostic type	Across diagnoses, across several spectra
(N) Numerate the diagnostic categories, spectra and non-clinical samples	Number of diagnoses	7
	Number of spectra	7
	Non-clinical sample	1 (Healthy controls without mental disorder)
(S) Show the degree of association	Diagnostic-specific Odds Ratios (ORs)	Anxiety Disorders (OR=2·66, 95% CI 2·39, 2·97) BD (OR=2·79; 95% CI: 1·98, 3·93) BPD (OR=15·66; 95% CI: 7·23, 33·95) OCD (OR=4·94; 95% CI: 3·34, 7·31) MDD (OR=2·88; 95% CI: 1·57, 5·31) Psychosis (OR=2·66; 95% CI: 1·99, 3·56) PTSD (OR=4·42; 95% CI: 2·19, 8·93)
	Transdiagnostic	Any mental disorder (OR = 2·92; CI: 2·60, 3·28) No significant difference in individual vs pooled effect size subgroup metaanalyses, except in the case of BPD (z = 4.19; p<0.001).
(D) Demonstrate the generalizability	Results replicated across at least 2 independent RCTs	Psychological trauma associated with mental disorder replicated in 78 of 106 case control studies (null hypothesis rejected).

Key: BD: Bipolar Disorder; BPD: Borderline Personality Disorder; MDD: Major Depressive Disorder; OCD: Obsessive-Compulsive Disorder; PTSD: Post-Traumatic Stress Disorder.

Image 2:

Psychological trauma in childhood is a transdiagnostic risk factor for mental disorder across diagnoses and spectra (OR = 2.92; 95% CI 2.60, 3.28)						
Diagnoses						
Anxiety Disorders (diagnostic group comprising Generalised Anxiety Disorder, Panic Disorder and Social Anxiety Disorder)	Bipolar Disorder	Major Depressive Disorder	Obsessive-Compulsive Disorder	Borderline Personality Disorder	Psychosis (diagnostic group comprising Psychotic Disorder, Schizophrenia and Schizoaffective Disorder)	Post-traumatic Stress Disorder
Spectra						
Anxiety Disorders	Bipolar Disorders	Depressive Disorders	Obsessive-Compulsive Related Disorders	Personality Disorders	Schizophrenia Spectrum Disorders	Trauma- and Stressor-Related Disorders

Conclusions: These fndings highlight the importance of preventing early traumatic events and providing trauma-informed care in early intervention and psychiatric services.

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Caregiver burden and its associated factors among family caregivers of persons with dementia in Athens, Greece: a cross sectional study

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Introduction: Studies have shown that dementia family caregivers to be significantly more burdened than non-dementia caregivers.
Objectives: The aim of the present study was to analyze factors affecting the quality of life and the burden of dementia family caregivers.
Methods: 70 dementia family caregivers who lived in the Attica Region, Greece participated in the study from February to April 2022. An anonymous questionnaire was used including 16 items regarding demographic and socio-economic factors. The 22 -item Zarit Burden scale was used to estimate the burden of dementia family caregivers. Statistical analysis was performed with SPSS 21.
Results: 1.4% of caregivers showed minimal to no burden (n = 1). 28% of caregivers (n = 20) a mild to moderate burden. 40.6% (n = 29) presented a moderate to severe burden, while 28% (n = 20) a very serious burden. According to the results of the present study, there are three main factors that affect the quality of life of caregivers. Caregivers who spend more time with the patient have an increased burden compared to caregivers who spend less time. The patient's low Mini Mental score is associated with an increase in burden. Caregivers who have attended training and management programs for the care of a patient with dementia have a lower burden than those who have not attended programs.
Conclusions: The study highlights an increased burden on caregivers. Social supports with multiple coping strategies focusing on different levels of patients with dementia and caregivers' needs should be planned to relieve the caregiver burden.

Disclosure of Interest: None Declared

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ADVANCES IN THE FIELD OF GENETICS AND DIFFICULTIES IN THE DIAGNOSIS OF DI GEORGE SYNDROME.

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Introduction: The spectacular progress of the last decade in the field of genetics is allowing a new development of medicine and the ability to make a better diagnosis. A great example of this is the