P.0035 Structural brain correlates of childhood inhibited temperament: rationale and methodology for an ENIGMA-Anxiety mega-analysis

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P.0035
Structural brain correlates of childhood inhibited temperament: rationale and methodology for an ENIGMA-Anxiety mega-analysis

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Introduction: Social anxiety disorder (SAD) is one of the most prevalent, chronic and impairing mental disorders in adolescents. As SAD is difficult to treat effectively, the personal and societal costs of SAD are substantial. Understanding the susceptibility to SAD can guide early identification of high-risk youth to advance targeted preventive interventions.

Family and twin studies have demonstrated that social anxiety has moderate heritability, indicating that genetic vulnerability is important in the pathogenesis of SAD [1]. Inhibited temperament (IT) - a stable, heritable and observable trait associated with an elevated risk for developing SAD and other anxiety disorders - may mediate the genetic risk for SAD [2]. Specifically, brain characteristics (i.e. brain structure, function, and connectivity) may provide the foundation for IT and the associated anxiety vulnerability [2,3]. Understanding of this 'neural risk signature' is still limited, as studies of the neurobiological characteristics associated with the temperamental vulnerability to SAD are scarce and

often focus on particular regions of interest. Moreover, most findings are derived from a single sample, and have not been replicated across studies [3].

Aim and hypotheses: This project aims to extend prior work by examining the neurobiological characteristics associated with childhood IT, as an early marker of risk for (social) anxiety later in life. We will use a mega-analytic approach and investigate changes in brain structure over the whole brain. Based on previous work, we expect to find IT-related alterations in brain circuits involved in processing fear, reward and emotion regulation, with small-to-medium effect sizes.

Methods: Within the framework of the ENIGMA (*E*nhancing *N*euro*I*maging *G*enetics through *M*eta-*A*nalysis)-Anxiety Working Group [4,5], we will assemble T1-weighted structural MRI-images (MRIs) of the brain, previously acquired at multiple institutes. Subsequently, we will perform mega-analyses on the largest sample related to childhood temperament available to date (data we currently have: n = 660; expected total sample size: 2300 MRI-datasets from 11 sites).

Data will be obtained from studies where subjects underwent MRI-scanning at various ages (up to age 25 years). Regardless of the age at scan, all participants will have undergone an (retrospective) assessment of childhood temperament (i.e., up to and including age 12). MRI-images will be processed using FreeSurfer software, resulting in individual estimates of regional cortical thickness, cortical surface area, and subcortical volumes. Analyses will compare participants with and without childhood IT.

Information on variables of interest (demographic variables, clinical information, questionnaire data) is also obtained to enrich the dataset and facilitate analyses of clinical outcomes and environmental influences. The study will be preregistered and analyses will start in autumn 2021.

Innovative character: This initiative is the first mega-analysis of the neurobiological characteristics associated with the innate risk for developing SAD, with the potential to detect novel IT-related brain alterations and to shed light on the mixed findings of prior work [3]. Thereby, we expect this project to increase our understanding of the pathways leading to (social) anxiety, providing new avenues to prevent the development of psychopathology in youth at risk.

Conflict of interest

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P.0036
The neural correlates of trait-anxiety in humans: a systematic review

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Background Trait-anxiety is widely conceptualized as the predisposition to appraise stimuli as threatening and respond with anxiety. Individuals with trait-anxiety are a het-