Neurodevelopmental complexity: Inflammation mediates the link between neurodivergence and chronic fatigue

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Background
Neurodivergent individuals (encompassing those with a diagnosis of Attention Deficit Hyperactivity Disorder (ADHD), and/or autism) appear to be at greater risk of developing chronic fatigue (CF). Cognitive traits that are characteristic of ADHD overlap with CF symptomatology and similar overlap is suspected to extend to autistic individuals. Neurobiological factors are proposed to contribute to such a relationship. We hypothesized that inflammatory processes implicated in CF may link the expression of neurodivergent traits to CF. We therefore investigated the developmental pathway from neurodivergent traits in childhood to chronic fatigue (CF) in adolescence.

Methods
Using a large birth-cohort, we tested if children meeting screening criteria for ADHD and/or autism at age 9 yrs had an increased risk of CF in adolescence (age 18 yrs). Odds ratios (OR) and confidence intervals (CI) for effects were computed using binary logistic regression and two separate mediation analyses were conducted to test if an inflammatory marker (Interleukin-6 level age 9 yrs) linked ADHD/autism traits to later CF (controlling for depression).

Results
Children with neurodivergent traits at age 9 yrs were around twice as likely to have CF at age 18 years. (ADHD OR=2.18, 95% CI=1.33, 3.56; autism OR = 1.78, 95% CI=1.17, 2.72). Mediation analyses showed inflammation at age 9 years mediated effects of neurodivergence on CF (significant indirect effect via IL-6 level: ADHD b=1.083, 95% CI=1.01, 1.6; autism b=1.063, 95% CI=1.02, 1.11).

Conclusion
Our results indicate that neurodivergent traits in childhood increase the likelihood of experiencing CF in adolescence. Whereas previous research focused on the symptomatic overlap between ADHD and CF, our research confirm that autistic children are also at higher risk. Our results point to a potential mechanistic neurodevelopmental pathway from neurodivergence to CF through inflammation. Importantly, increased IL-6 is not only a marker of inflammation processes underlying CF but may also be an indication of heightened biopsychosocial stress in neurodivergent children. These findings call for more mechanistic research into this relationship, and for the implementation of trans-diagnostic screening criteria to inform strategies to counteract risk early in life.