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## Association of ADHD polygenic risk score with ADHD and learning disorder, depression, body mass index and MCI.

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ABSTRACT: Attention deficit-hyperactivity disorder (ADHD) symptoms often persist in adulthood and resemble some symptoms of mild cognitive impairment (MCI), as well as constitute a risk factor for dementia. It is unclear if ADHD is misdiagnosed as MCI due to symptom overlap or if there is a genuine association between the two. ADHD is also more common in men than women. Subjects were 886 individual male twins from the Vietnam Era Twin Study of Aging assessed across three time points (mean ages of 56, 62, and 68). These individuals represent those in the upper and lower tertiles of an ADHD polygenic risk score (PRS) (n=443 each). Through linear mixed models controlling for twin status, age, and ethnicity, we evaluated the association of the PRS groups with ADHD itself assessed via self-report at wave 2 and other phenotypes often associated with ADHD: concurrently assessed learning disorders and body mass index [BMI], major depressive disorder assessed in their forties, as well as with MCI diagnosis at all three waves. The PRS was significantly associated with ADHD ( $p=.031$ ) and inattention ( $p=.039$ ), but not learning disorder, depression, or BMI. The ADHD PRS was significantly associated with MCI only at wave 3 ( $p=.036$ ). The association between ADHD and MCI may not simply reflect symptom overlap. Genetic liability for ADHD, validated by association with phenotypic ADHD, was also associated with the phenotypic presentation of MCI at mean age 68, but not earlier. Further research is warranted to see if this association increases as these men continue to age.

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