

Internalizing problems in childhood and adolescence

Predictive, etiological, and neurodevelopmental aspects

Akademisk avhandling

Som för avläggande av medicine doktorexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i sal 2119, Hus 2, Hälsovetarbacken, Arvid Wallgrens backe (Entré F), fredagen den 17 december 2021, klockan 09.00

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Avhandlingen baseras på följande delarbeten

- I. Doering S, Lichtenstein P, Gillberg C, Middeldorp CM, Bartels M, Kuja-Halkola R, Lundström S. Anxiety at age 15 predicts psychiatric diagnoses and suicidal ideation in late adolescence and young adulthood: results from two longitudinal studies. *BMC Psychiatry*. 2019 Nov 14;19(1):363.
- II. Doering S, Lichtenstein P, Gillberg C, Kuja-Halkola R, Lundström S. Internalizing and neurodevelopmental problems in young people: Educational outcomes in a large population-based cohort of twins. *Psychiatry Research*. 2021 Apr 298:113794.
- III. Doering S, Larsson H, Halldner L, Gillberg C, Kuja-Halkola R, Lundström S. Internalizing symptoms in adolescence are modestly affected by symptoms of anxiety, depression, and neurodevelopmental disorders in childhood. *Submitted*.
- IV. Doering S, Halldner L, Larsson H, Gillberg C, Kuja-Halkola R, Lichtenstein P, Lundström S. Childhood-onset versus adolescent-onset anxiety and depression: epidemiological and neurodevelopmental aspects. *Submitted*.

SAHLGRENSKA AKADEMIN
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Abstract

Internalizing problems such as anxiety and depression are common in children and adolescents. The overarching aim of the thesis is to investigate the relationship between internalizing problems and adverse outcomes in late adolescence/early adulthood, and between internalizing problems at different ages (i.e., childhood vs. adolescence), while taking various neurodevelopmental disorders (NDDs) into account. All studies are based on the Child and Adolescent Twin Study in Sweden, which uses self- and/or parent-reported survey data, clinical diagnoses from the Swedish National Patient Register, and educational data from the National School Register. **Study I** examines the relationship between anxiety at age 15 and psychiatric outcomes in late adolescence/early adulthood. The results show that adolescent anxiety predicted a variety of psychiatric outcomes, even when adjusting for NDDs. **Study II** describes the relationship between internalizing problems at age 15 and educational achievement in a genetically sensitive design. Internalizing problems were found to be negatively associated with educational achievement. Additive genetics accounted for the largest part of the covariation between internalizing problems and educational outcomes, with roughly one half of unique genetic effects being due to internalizing problems and one half due to NDDs. **Study III** assesses the extent to which internalizing symptoms at age 15 can be explained by symptoms of anxiety, depression, and NDDs at age 9. The results showed that, overall, a small proportion of internalizing symptoms in adolescence can be explained by anxiety, depression, and NDDs in childhood. **Study IV** examines different occurrences of NDDs in individuals with anxiety/depression at age 9 versus age 15. Individuals with childhood-onset anxiety/depression had a substantially higher prevalence of NDDs than did individuals with adolescent onset. Taken together, internalizing problems in adolescence can predict a plethora of psychiatric outcomes and educational underachievement, and they share etiological influences with the latter, independently of NDDs. Childhood and adolescent internalizing problems possibly represent different constructs and are differentially related to NDDs. Future studies investigating treatment approaches and the etiology of internalizing problems may benefit from taking age of onset into account.

Keywords: Internalizing disorders, Anxiety disorders, Depressive disorders, Neurodevelopmental disorders, education, twin study, age of onset, prevalence