Göteborg, 2020

Restrictive eating disorders

Aetiological, epidemiological and neurodevelopmental aspects

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i sal Europa, Konferenscentrum Wallenberg, Medicinaregatan 20A, fredagen den 11 december 2020, klockan 13.00

av Lisa Dinkler

Fakultetsopponent:
Ulrike Schmidt, Professor
Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK

Avhandlingen baseras på följande delarbeten

I. Dinkler L, Taylor MJ, Råstam M, Hadjikhani N, Bulik CM, Lichtenstein P, Gillberg C, Lundström S. Association of aetiological factors across the extreme end and continuous variation in disordered eating in female Swedish twins. *Psychological Medicine*. 2019;Dec 17:1-11. E-pub ahead of print.

II. Dinkler L, Taylor MJ, Råstam M, Hadjikhani N, Bulik CM, Lichtenstein P, Gillberg C, Lundström S. Anorexia nervosa and autism: A prospective twin cohort study. *Journal of Child Psychology and Psychiatry*. 2020;Jun 4:1-11. E-pub ahead of print.

III. Dinkler L, Rydberg Dobrescu S, Råstam M, Gillberg IC, Gillberg C, Wentz, E, Hadjikhani N. Visual scanning during emotion recognition in long-term recovered anorexia nervosa: An eye-tracking study. *International Journal of Eating Disorders*. 2019;52(6):691-700.

IV. Dinkler L, Yasumitsu-Lovell K, Eitoku M, Fujieda M, Suganuma N, Hatakenaka Y, Hadjikhani N, Bryant-Waugh R, Råstam M, Gillberg C. Prevalence of Avoidant/Restrictive Food Intake Disorder (ARFID) based on DSM-5 vs. ICD-11 in a Japanese birth cohort. *Submitted*.

V. Dinkler L, Yasumitsu-Lovell K, Eitoku M, Fujieda M, Suganuma N, Hatakenaka Y, Hadjikhani N, Bryant-Waugh R, Råstam M, Gillberg C. Neurodevelopment and clinical characteristics in children screening positive for Avoidant/Restrictive Food Intake Disorder (ARFID): a Japanese birth cohort study. *Submitted*.

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR NEUROVETENSKAP OCH FYSIOLOGI

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Abstract

Restrictive Eating Disorders (EDs), including Anorexia Nervosa (AN) and Avoidant/Restrictive Food Intake Disorder (ARFID), are characterised by severely restricted food intake, commonly leading to substantial weight loss and significantly low weight, and the need for nutritional supplementation. The overarching aim of this thesis was to elucidate specific aetiological, epidemiological, and neurodevelopmental aspects of AN and ARFID, including the genetic aetiology of AN, the link between AN and autism spectrum disorder (ASD), the prevalence of ARFID, and the comorbidity of ARFID with neurodevelopmental disorders (NDDs). **Studies I and II** were based on the Child and Adolescent Twin Study in Sweden, making use of parent- and/or child-reported survey data and clinical diagnoses from the Swedish National Patient Register. Using twin modelling, **Study I** examined whether adolescent-onset EDs (excluding ARFID) can be viewed aetiologically as the extreme manifestation of continuous variation in ED traits in the population (e.g., drive for thinness). Genetic factors influencing continuous variation of ED traits were less associated with AN than with other EDs, suggesting that EDs other than AN are on an aetiological continuum with ED traits, while AN is more genetically demarcated. Considering the previously observed overrepresentation of autistic traits in individuals with AN, **Study II** prospectively examined whether autistic traits in AN are already present in childhood. Individuals later diagnosed with AN did not show elevated autistic traits at age 9. At age 18, autistic traits were elevated in girls with acute AN, but not in girls with a history of AN. Potential elevations of autistic traits in childhood might have been concealed by coping strategies and the different/less overt female ASD phenotype. Using a novel experimental design, **Study III** examined the ability and strategy to recognise facial emotional expressions—often impaired in ASD—in women recovered from AN who were part of the 30-year follow-up in a Swedish case-control study. Women recovered from AN without ASD did not have deficits in emotion recognition, suggesting that impairments might be limited to the acute AN phase and/or the ASD subgroup. **Studies IV and V** were based on a parent-reported screening tool for ARFID developed by our group, applied in a sub-cohort of 4-7-year-old children from the Japan Environment and Children's Study. **Study IV** aimed to estimate the prevalence of ARFID and found a point prevalence of ~1%. ARFID was equally common in boys and girls. Using ICD-11 diagnostic criteria resulted in a higher prevalence than using DSM-5 criteria. Taking advantage of additional parent-reported data, **Study V** found that children with ARFID had an elevated risk of a broadly atypical/delayed neurodevelopment and a 3-4 times increased likelihood of being diagnosed with NDDs. In summary, this thesis showed that AN might have a different aetiology than other adolescent-onset EDs, and that prospective studies are important to help disentangle the relationship between AN and ASD. Contrary to AN, ARFID is associated with increased risk for a range of neurodevelopmental problems/NDDs. Future studies should investigate whether ARFID in young children might be more strongly associated with NDDs than with later-onset EDs.

Keywords: Eating Disorders, Anorexia Nervosa, Avoidant/Restrictive Food Intake Disorder, Neurodevelopmental Disorders, twin study, emotion recognition, eye tracking, prevalence

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