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Mortality in individuals with disruptive behavior disorders diagnosed by specialist services – A nationwide cohort study

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ABSTRACT

Disruptive behavior disorders (DBDs), inclusive of oppositional defiant disorder (ODD) and conduct disorder (CD), are associated with outcomes likely to increase risk of mortality. Using Danish National Registers, a total of 1.92 million individuals including 9495 individuals with DBDs diagnosed by specialist services were followed from their first birthday to 2013. Those with and without DBDs were compared using mortality rate ratios (MRRs) estimated using Poisson regression and adjusted for calendar period, age, sex, family history of psychiatric disorders, maternal age at time of birth, paternal age at time of birth, parental education status, and parental employment status. Over the course of follow up, which totalled 24.9 million person-years, 5580 cohort members died including 78 individuals with DBDs. The mortality rate per 10,000 person-years was 9.66 for individuals with DBDs compared to 2.22 for those with no diagnosis. This corresponded to a fully adjusted MRR of 2.57 (95% confidence interval 2.04–3.20). Comorbid substance use disorder and attention-deficit/hyperactivity disorder resulted in the highest MRR across all categories. These findings demonstrate the excess mortality associated with DBDs.

1. Introduction

Whilst many adult mental disorders have a demonstrated association with reduction in life expectancy (Hjorthoj et al., 2015; Saha et al., 2007), less is known of the increased mortality risk of mental disorders in childhood. Although childhood-onset mental disorders are not usually associated with fatal outcomes, these disorders may trigger a cascade of mental and physical comorbidity that accumulates over time and impacts upon life expectancy. For example, a nationwide cohort study of mortality associated with attention-deficit hyperactivity/disorder (ADHD) found those with ADHD and comorbid disruptive behavior disorders (DBDs; inclusive of oppositional defiant disorder [ODD] and conduct disorder [CD]) had an adjusted mortality rate ratio (MRR) of 2.17 (95% confidence intervals 1.33–3.31) (Dalsgaard et al., 2015). This was notably higher than those with ADHD only (1.50, 1.11–1.98), suggesting that DBDs are associated with an increased risk of mortality.

However, few studies have examined mortality associated with DBDs. Previous research has been restricted to special populations, e.g. offenders or inpatient samples, and/or relied on the use of symptom

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measures of DBDs rather than clinically defined disorders. For example, Neeleman and colleagues (1998) reported conduct problems at 16 years of age were associated with increased odds of suicide (odds ratio [OR]: 1.8, 1.3–2.5) and natural death (OR:1.2, 1.0–1.5) by age 50. Similarly, Zoccolillo and colleagues (1991) found that 7% of their sample of hospitalised girls with CD had died a violent death after four years compared with 0.03% of the age-matched general population. To our knowledge, no studies of mortality risk associated with DBDs have utilised a community representative sample with clinically defined diagnoses.

There are plausible reasons for these disorders to have an increased associated mortality. DBDs are associated with a greater risk of substance abuse (Messer et al., 2006), comorbid depression and anxiety disorders (Copeland et al., 2009; Erskine et al., 2016), comorbid schizophreniform psychosis (Maibing et al., 2015), psychiatric in-patient admissions (Dalsgaard et al., 2002), engagement in acts of aggression, violence, and risk taking (Nada-Raja et al., 1997), and criminal convictions (Dalsgaard et al., 2013). These health and psychosocial problems are also likely to contribute to an increased risk of accidental deaths or suicide (von Stumm et al., 2011). DBDs and ADHD overlap substantially in terms of behavior and comorbidity (Angold et al., 1999), although differ considerably in terms of the possible mechanisms behind their respective symptomologies. This has been acknowledged in the restructuring of the latest version of the Diagnostic and Statistical Manual of Mental Disorders, DSM-5 (American Psychiatric Association, 2013), where ADHD is categorised under 'Neurodevelopmental Disorders' to reflect brain developmental correlates with the disorder. DBDs, including ODD and CD, have been categorised under the new 'Disruptive, Impulse-Control, and Conduct Disorders' classification. This reflects the emotional and behavioral self-control issues seen in this group of disorders as well as unique behavioral characteristics such as violating the rights of others and engaging in significant conflict with peers and authorities (American Psychiatric Association, 2013).

ADHD is associated with considerable and heterogeneous deficits in a broad range of cognitive functions, in particular executive functions involving impulse inhibition, working memory, and planning (Willcutt et al., 2005). By contrast, evidence of cognitive dysfunction is sparse when it comes to DBD cases and available studies are inconsistent in their findings or in controlling for ADHD. It seems that in DBD, cognitive deficits are more limited. These deficits have been related to the neurological reward system and a tendency for risky decision making and slower inhibitory responses (Hobson et al., 2011). These cognitive deficits in DBDs and/or ADHD may lead to risk taking behaviours or proneness to accidents which could result in injury or death. However, given the distinctions between these disorders, it is important to examine the unique associations between the disorders and an increased risk of mortality.

We hypothesised that persons with DBDs would be at increased risk of mortality compared to those without the disorders. To the best of our knowledge, no large community representative study to date has examined mortality associated with DBDs. Utilising a nationwide cohort, we aimed to estimate excess all-cause mortality in children, adolescents, and adults with DBDs which had been diagnosed by specialist psychiatric or pediatric services. In addition, we aimed to examine the added effect of comorbid ADHD and substance use disorder (SUD) on mortality rates in individuals with DBDs.

2. Method

2.1. Study population

The Danish Civil Registration System was established in 1968 (Pedersen et al., 2006) where all people alive and living in Denmark are registered. It includes the 10-digit personal identification number (PIN) and information on sex, date and place of birth, continuously updated information on vital status, and the parents' personal identifiers. The PIN is used in all national registers, enabling accurate linkage of data between registers at the level of the individual. Our study cohort included all children born in Denmark between January 1, 1981 and December 31, 2011 who were still alive and residing in Denmark at their 1st birthday or January 1, 1995, whichever came last.

2.2. Assessment of mental illness

Data from the Danish Psychiatric Central Research Register (DPCR) (Mors et al., 2011) and the Danish National Patient Register (DNPR) were used to obtain information on mental disorders in cohort members and their parents. The DPCR was computerized in 1969 and contains data on all admissions to Danish psychiatric facilities. The DNPR was established in 1977 and contains data on all admissions to public hospitals in Denmark. In both registers, additional information on outpatient visits was included from 1995 onwards. The Danish modification of the International Classification of Diseases, 8th revision (ICD-8) was used between 1969 and 1993, and the International Classification of Diseases, 10th revision, Diagnostic Criteria for Research (ICD-10-DCR) was used from 1994 onwards. Diagnostic status of cohort members regarding DBDs was based on clinical diagnoses of ODD or CD extracted from the DPCR and the DNPR (ICD-8 code 308.03 and 308.04 and ICD-10-DCR codes F91.x and F90.1). From DPCR and DNPR, comorbid diagnoses of ADHD (ICD-8 code 308.01 and ICD-10-DCR codes F90.x or F98.8) and substance use disorder (SUD) (ICD-8 codes 291.x9, 294.39, 303.x9, 303.20, 303.28, 303.90, 304.x9 and ICD-10-DCR codes F10-F19) were obtained for all cohort members. Except for SUD, only contacts to departments of psychiatry, pediatrics, and neurology were included. Parents were classified as having a history of mental disorders if they had a contact with a public psychiatric hospital department with a psychiatric diagnosis (ICD-8 codes 290–315; ICD-10-DCR codes F00-F99). Date of onset was defined as the first day of the first contact (inpatient or outpatient) with the diagnosis in question.

2.3. Assessment of data on potential confounders

The Danish Medical Birth Register (DMBR) provided data on birth weight, gestational age, 5-min Apgar score, and congenital malformations for all cohort members. Information on maternal and paternal age at time of birth was available from the civil registration system. Statistics Denmark provided data for highest parental education (categorised as basic school grades 8–10, upper secondary school, bachelor's degree, or postgraduate degree) and highest parental employment status (categorised as outside the labour force, unemployed, enrolled in education, or employed) for the parents of all cohort members including those in the reference group.

2.4. Deaths

Information on date of death up to June 30, 2013 was available for almost 100% of all cohort members from the Danish Civil Registration System (Pedersen et al., 2006). The outcome was all cause mortality after the age of one or January 1, 1995 whichever came last. Cohort members were followed up until date of death, date of emigration from Denmark, or June 30, 2013, whichever came first.

2.5. Statistical analysis

The mortality rate ratios (MRRs) were estimated by log-linear Poisson regression using the GENMOD procedure in SAS (version 9.3) and compared the mortality rate in persons with and without DBDs. Crude MRRs were adjusted for calendar period, age, and the interaction with sex. In addition to the covariates in the crude model, the partially adjusted model adjusted for family history of psychiatric