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Research paper

Early adversity and risk for moderate to severe unipolar depressive disorder in adolescence and adulthood: A register-based study of 978,647 individuals

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ABSTRACT

Background: Early adversity is a known risk factor for unipolar depression. We examined the impact of 9 types of early adversity on risk for moderate to severe unipolar depression in adolescence or adulthood, and evaluated whether these effects were moderated by gender and adversity timing.

Methods: We conducted a prospective, population-based cohort study using Danish national registers. The sample included all individuals born in Denmark between 1980 and 1998 (N=978,647). Exposure to early adversity was assessed from ages 0–15. Types of adversity included parental illness, incarceration, death, disability, and psychiatric diagnosis; family disruption; out-of-home care; and childhood abuse. Individuals were followed from age 15 until first in- or outpatient depression diagnosis (ICD-10 codes F32, F33) in a psychiatric hospital, death, emigration, or December 31st, 2013, whichever came first. Hazard ratios (HRs) were calculated using Cox regressions.

Results: All adversities were significantly associated with increased risk for moderate to severe adolescent/adult depression (HR range: 1.30–2.72), although the effects were attenuated after mutual adjustment (adjusted HR range: 1.06–1.70). None of the effects were moderated by gender. The effect of family disruption was strongest between ages 0–4 (HR=1.66, 95% CI=1.61–1.71), while the effect of out-of-home care was strongest between ages 10–14 (HR=2.45, 95% CI=2.28–2.64).

Limitations: Untreated and primary-care treated depression were not measured.

Conclusions: Our results support past findings that multiple types of early adversity increase risk for moderate to severe unipolar depression in adolescence and adulthood. Certain adversities may be more harmful if they occur during specific developmental time periods.

1. Introduction

Adversity experienced early in life is known to have a significant impact on risk for depression in adolescence and adulthood. Numerous studies and meta-analyses have documented the deleterious effects of adversities such as physical, sexual and emotional abuse (Infurna et al., 2016; Li et al., 2016; Lindert et al., 2014; Mandelli et al., 2015; Maniglio, 2010), parental death or separation (Appel et al., 2013; Berg et al., 2016; Jacobs and Bovasso, 2009; Kendler et al., 2002; Otowa et al., 2014; Tyrka et al., 2008), parental incarceration (Lee et al., 2013), parental divorce or relationship instability (Donahue et al., 2010; Gilman et al., 2003), childhood out of home care (Herman, Susser, and Struening, 1994) and parental psychiatric or substance abuse (Musliner et al., 2015; Velleman and Orford, 1993; Weissman et al., 2016) on risk for unipolar depression.

Researchers have hypothesized that the association between early adversity and later depression is in part mediated by biological changes such as dysregulation of the HPA axis (Heim and Nemeroff, 2001) or changes in gene expression (Klengel et al., 2014; Weder et al., 2014). These changes, brought on by early exposure to adversity, may cause

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increased sensitivity to the depressogenic effects of stress in adolescence or adulthood (Kendler et al., 2004; Shapero et al., 2014). Numerous psycho-social explanations have also been proposed, including disruption in the ability to form close attachments (Stronach et al., 2011) or regulate emotion (Alink et al., 2009; Kim and Cicchetti, 2010), increased sensitivity to rejection (Schaan and Vogele, 2016) and associations with poor socio-economic outcomes (Font and Maguire-Jack, 2016).

Many studies in this area focused on a single type of adversity (i.e., childhood sexual abuse, parental loss). However there is substantial evidence that different types of adversities tend to co-occur (Dong et al., 2004; Green et al., 2010; Kessler and Magee, 1993; Kessler et al., 1997; Kessler et al., 2010; McLaughlin et al., 2012), and that a dose response relationship exists between the number of adversities experienced during childhood and adult depression (Anda et al., 2006; Chapman et al., 2004). As a result, the field has shifted towards evaluating the individual and cumulative impacts of many different types of adversities simultaneously. For example, Kessler and Magee (1993) evaluated the impact of 8 childhood adversities (including maternal/paternal death, parental marital problems/divorce, family violence and maternal/paternal mental illness or substance abuse) on risk for past 12-month depression in the Americans' Changing Lives (ACL) study. They found statistically significant effects (Odds Ratio [OR] range: 1.5–2.9) for parental drinking, mental illness, violence, marital problems and divorce, but no effects for parental death. Kessler et al. (1997) examined the impact of 26 types of adversity (loss events, parental psychopathology, interpersonal trauma, accidents, natural or man-made disasters, and shock/trauma) in the National Comorbidity Survey. They found that parental separation/divorce, parental depression or anxiety, molestation/rape, parental aggression, witnessing a trauma, and other PTSD events were associated with major depression or dysthymia (OR range: 1.27–2.91) in fully-adjusted models.

The vast majority of studies in this area assessed exposure to early adversity retrospectively via self-report. This form of assessment may be subject to recall and reporting bias if, as evidence suggests, individuals with past or current depression are more likely than their non-depressed counterparts to recall or report early adversities (Colman et al., 2016). An alternate method for assessing exposure to early adversity is to use register-based data. Registers are government-run, typically electronic databases which continually record, store and update information on groups of people. Not only does this approach eliminate the possibility of recall or reporting bias, but it also substantially reduces selection bias as the cohort typically contains the entire population encompassed within a catchment area, city, or in the case of Denmark, an entire country (Pedersen et al., 2006; Pedersen, 2011; Schmidt et al., 2014).

To our knowledge, one previous study has used register data to examine the impact of multiple early adversities on risk for mood disorders in adolescence and adulthood. Björkenstam et al. (2016) conducted a register-based study examining the effects of 7 types of adversity (familial death, parental psychiatric disorders, parental substance abuse disorders, parental crime, parental separation, public assistance receipt and residential instability) in a sample of 107,704 individuals from Stockholm, Sweden. They found that all adversity types were significantly associated with risk for mood disorders (unipolar and bipolar pooled) through young adulthood (ages 20–24) with hazard ratios ranging from 1.3 for familial death and residential instability to 1.9 for parental psychiatric disorder.

Our goal in this study was to examine the individual and cumulative effects of 9 different types of early adversity on risk for moderate to severe unipolar depression in adolescence and adulthood using information from Danish national registers. To our knowledge, this is the largest study conducted to date examining the effects of multiple adversity types on risk for adolescent and adult depression. Our study extends the work of Björkenstam et al. (2016) in several important ways: first, we specifically evaluated risk for unipolar depression, rather than risk for all mood disorders combined. Second, we included additional adversity types (parental disability, out-of-home placement and childhood abuse). Third, we incorporated a longer period of follow-up (up to 18 years). Fourth, we included models which adjusted for the effects of all other adversity variables. Finally, our cohort is a representative sample of the entire population of Denmark, including individuals living in rural areas. Similar to Björkenstam et al. (2016), we evaluated the extent to which the associations between adversities and adolescent/adult depression were moderated by adversity timing. We also examined gender as a potential moderating factor, as studies have suggested that the impact of early adversity on risk for depression may be different for males and females (Davis and Pfaff, 2014).

2. Methods

2.1. Study design and population

We conducted a population-based historical prospective cohort study using Danish national registers. All individuals born in Denmark are assigned a personal ID (CPR) number at birth. This number can be used to link information stored in different national registers. For this study, we included all individuals born in Denmark between January 1st, 1980 and December 31st, 1998 (N=978,647).

2.2. Measures

2.2.1. Exposures: early adversity variables

We measured 9 different types of early adversity occurring between birth and age 15. Adversity types were selected based on the information available in the Danish registers and included 1. parental somatic illness, 2. parental incarceration, 3. parental disability, 4. parental psychiatric disorders, 5. parental death by natural cause, 6. parental death by unnatural cause, 7. family disruption, 8. out-of-home care, and 9. childhood abuse. If an individual qualified for a given event at multiple points in time, we included information concerning the first occurrence of that event. The Danish Civil Registration System [DCRS] (Pedersen, 2011) links the CPR number of the individual with those of his or her mother and father. We used the parents' CPR numbers along with information contained in other registers (described below) to generate the majority of our early adversity variables. All measures of early adversity were coded as dichotomous, yes/no variables.

2.2.1.1. Parental somatic illness. Somatic illness records for parents were obtained from the Danish National Patient Register [DNPR] (Lynge et al., 2011), which includes the dates and diagnoses associated with all inpatient admissions to somatic hospitals in Denmark since 1977, and all outpatient treatment since 1995. Individuals were considered to have a history of parental somatic illness if their mother or father was diagnosed with one of the 18 somatic conditions from the Charlson Comorbidity Index (Thygesen et al., 2011). These diagnoses include: myocardial infarction, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, connective tissue disease, ulcer disease, mild liver disease, diabetes, hemiplegia, moderate to severe renal disease, tumor, leukemia, lymphoma, moderate to severe liver disease, metastatic tumor and AIDS.

2.2.1.2. Parental incarceration. Records on prison sentences were obtained from the Danish National Crime Register (Kyvsgaard, 2002), which contains the charge and decision on every offense reported to the Danish police since 1978. Individuals were considered to have a history of parental incarceration if their mother or father spent time in a Danish correctional facility. "Suspended sentences" (i.e. probation, house arrest) were not included.