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Research report

The relationship between anxiety disorders and dimensional representations of DSM-IV personality disorders: A co-twin control study

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ABSTRACT

Background: There is substantial comorbidity between personality disorders (PDs) and anxiety disorders (ADs). Sharing of familial risk factors possibly explains the co-occurrence, but direct causal relationships between the disorders may also exist.
Methods: 2801 persons from 1391 twin pairs from the Norwegian Institute of Public Health Twin Panel were assessed for all DSM-IV PDs and ADs. Bivariate Poisson-regression analyses were performed to assess whether PDs predicted ADs at three different levels: All PDs combined, PDs combined within DSM-IV-clusters and each individual PD separately. Next, bivariate co-twin control analyses were executed within monozygotic (MZ) and dizygotic (DZ) twin pairs. A similar analytic strategy was employed in multivariate models including PDs as independent variables.
Results: PDs predicted ADs at all levels of analysis in bivariate regression models. Bivariate co-twin control analyses demonstrated an increased risk of ADs in all PDs combined, all PD-clusters and in schizotypal, paranoid, borderline, antisocial, avoidant and dependent PD. In the multivariate regression model, all PD-clusters and schizotypal, borderline, avoidant and obsessive-compulsive PD predicted ADs. Only borderline and avoidant PD predicted ADs in the multivariate co-twin control analysis.
Limitations: Over-adjustment may explain the results from the multivariate analyses. The cross-sectional study design hampers causal inference.
Conclusions: Comorbidity between ADs and PDs can be largely accounted for by shared familial risk factors. However, the results are also consistent with a direct causal relationship partly explaining the co-occurrence. Our results indicate specific environmental factors for comorbidity of ADs and borderline and avoidant PDs that are not shared with other PDs.

1. Introduction

Co-occurrence beyond chance, or comorbidity, between personality disorders (PDs) and anxiety disorders (ADs) is commonly observed in both clinical and population-based studies (Grant et al., 2005; Lenzenweger et al., 2007; Shea et al., 2004). By themselves, both of these groups of disorders represent a major public health challenge as they are prevalent in both the general community setting and in clinical populations, and they are characterized by substantial morbidity and high financial costs for the society (Huang et al., 2009; Whiteford et al., 2013). In addition, results from previous studies indicate that comorbidity of PDs and ADs exerts a negative influence on treatment response and long-term prognosis in affected individuals (Ansell et al., 2011; Crawford et al., 2008; Skodol et al., 2014).

An increased understanding of the association between these disorders may inform the development of preventive, treatment, and classification efforts, and may also contribute to the understanding of etiological mechanisms (Krueger and Markon, 2006). There are several possible reasons why PDs and ADs co-occur. Alternative, but not mutually exclusive, explanations include common genetic and environmental risk factors between PDs and ADs and direct causal relationships between the disorders (Krueger and Markon, 2006; Neale and Kendler, 1995).

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It has previously been suggested that the observed co-occurrence between common psychiatric disorders could be accounted for by two broad, underlying dimensions or latent risk factors of psychopathology, usually called 'internalizing' and 'externalizing' (Kendler et al., 2003; Krueger, 1999). The corresponding groups of comorbid disorders are referred to as the 'internalizing' and 'externalizing' spectra. The first include ADs and depression, whereas the second include substance abuse and dependence and antisocial PD. Additional dimensions have been identified after inclusion of psychotic disorders and other PDs (Kotov et al., 2011a, 2011b; Markon, 2010; Roysamb et al., 2011). While the degree of comorbidity appears to be highest among psychiatric disorders within the same psychopathological spectrum, substantial cross-spectral relationships also exist, e.g. as in the case of ADs and PDs (Harford et al., 2013). Current evidence suggests that this underlying structure of psychopathology, and the observed co-occurrence patterns between individual disorders, arise primarily as a result of genetic influences (Kendler et al., 2011a).

Although it is reasonable to assume that underlying dimensions of psychopathology might explain a large part of the observed comorbidity between PDs and ADs, it is also possible that associations can be at least partly explained by direct causal relationships at the level of individual disorders, i.e. that suffering from one psychiatric disorder increases the risk of developing a second one independently of shared liability factors (Heath et al., 1993; Krueger and Markon, 2006; Neale and Kendler, 1995). Both unidirectional and bidirectional relationships may exist. The strain of suffering from a PD may heighten an individual's risk of developing ADs (Links and Eynan, 2013). Vice versa, ADs tend to have both an early age of onset and debilitating consequences (Alonso et al., 2011; Kessler et al., 2005), and these features may contribute to the development of personality pathology.

The extent to which the comorbidity between PDs and ADs is caused by common underlying genetic or environmental risk factors or by direct causal relationships can be explored in twin studies using co-twin control methodology (Carlin et al., 2005; Fagnani et al., 2014; McGue et al., 2010). By using one twin in each twin pair as a matched control for his or her co-twin, it is possible to adjust for the effect of familial risk factors (genetic effects and environmental influences shared between the co-twins) on the association between PDs and ADs. Whether a causal relationship between the disorders is unidirectional or bidirectional, or whether the association is confounded by specific environmental influences that have affected only one of the co-twins, can however not be determined with the application of this non-experimental study design alone.

In the current study, the co-twin control method was employed in a population-based sample of Norwegian twins assessed for both PDs and ADs to investigate whether the comorbidity between these disorders could be fully accounted for by the sharing of familial risk factors. We had four main aims:

1. Estimation of associations between PDs and ADs without adjustment for potential confounding variables.
2. Estimation of associations between PDs and ADs while adjusting for shared genetic and environmental risk factors.
3. Estimation of associations between PDs and ADs while adjusting for comorbid PDs.
4. Estimation of associations between PDs and ADs while adjusting for genetic and environmental risk factors and accounting for comorbid PDs.

2. Material and methods

2.1. Sample

This research report is based on analyses of data from the Norwegian Institute of Public Health Twin Panel (NIPHTP) (Nilsen et al., 2013). The twins in this database were identified through information from the National Medical Birth Registry, established January 1, 1967, which receives mandatory notification of all live- and stillbirths of at least 16 weeks gestation. NIPHTP is based on all Norwegian twins born between 1967 and 1979. 15 370 twins were born in Norway during this period. Two questionnaire studies have previously been conducted in this sample: the first one in 1992 on twins born 1967-1974 and the second one in 1998 on twins born 1967–1979. 12,698 twins (6349 pairs) received the second questionnaire, and with 8045 responders after one reminder (3334 pairs and 1377 single responders), the response rate was 63%.

Data from the current report stem from an interview-based study that was conducted between 1999 and 2004. All complete pairs from the 1998 questionnaire study in which both twins had agreed to further contact (3153 pairs) were invited, as well as 68 pairs unintentionally drawn directly from the NIPHTP. Altogether, 2801 twins (44% of those eligible) from 1391 twin pairs were assessed at personal interview for DSM-IV Axis I and Axis II disorders between 1999 and 2004. The recruitment process is shown in Fig. 1.

The twins had a mean age of 28.2 years, their mean number of years of education was 14.9 and 62% of the participants were married or living in cohabitation at the time of data collection. The sample characteristics are reported in Table 1. 2.786 participants had valid data on all phenotypes, and the sample consisted of 1.017 males and 1.769 females, 219 monozygotic male pairs (MZM), 116 dizygotic male pairs (DZM), 446 monozygotic female pairs (MZF), 261 dizygotic female pairs (DZF), 338 dizygotic opposite sex pairs (DZO) and 26 single responders. Zygosity was determined by a combination of questionnaire items and genotyping. The misclassification rate was estimated to be below 1%, and it is unlikely that this introduced any substantial bias on the results (Neale, 2003).

After a complete description of the study, written informed consent was given by all participants, and the study protocol was approved by the Regional Ethic Committee and the Norwegian Data Inspectorate.

2.2. Measures

All participants completed structured clinical interviews for DSM-IV Axis I and II disorders. ADs were assessed with a computerized version of the Composite International Diagnostic Interview (CIDI; Wittchen and Pfister, 1997), developed by the World Health Organization and used worldwide in major psychiatric surveys in recent years (Kessler et al., 2011). This instrument has been shown to have good test–retest and interrater reliability (Wittchen et al., 1998). Diagnoses were assigned without hierarchical rules in order to examine co-occurrence without exclusions.

A Norwegian version of the Structured Interview for DSM-IV Personality Disorders (SIDP-IV; Pfohl et al., 1995) was used to assess the PDs. This instrument is a comprehensive semistructured diagnostic interview for the assessment of DSM-IV Axis II diagnoses. The SIDP-IV has previously been used in a number of studies in several countries, including Norway (Kendler et al., 2008). It includes non-pejorative questions organized into topical sections to produce a natural flow in the interview. The number of criteria for each DSM-IV personality disorder varies from 7 to 9. Each of the specific criteria was rated as follows: 0=absent;