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Shared versus distinct genetic contributions of mental wellbeing with depression and anxiety symptoms in healthy twins

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ABSTRACT

Mental wellbeing and mental illness symptoms are typically conceptualized as opposite ends of a continuum, despite only sharing about a quarter in common variance. We investigated the normative variation in measures of wellbeing and of depression and anxiety in 1486 twins who did not meet clinical criteria for an overt diagnosis. We quantified the shared versus distinct genetic and environmental variance between wellbeing and depression and anxiety symptoms. The majority of participants (93%) reported levels of depression and anxiety symptoms within the healthy range, yet only 23% reported a wellbeing score within the "flourishing" range: the remainder were within the ranges of "moderate" (67%) or "languishing" (10%). In twin models, measures of wellbeing and of depression and anxiety shared 50.09% of variance due to genetic factors and 18.27% due to environmental factors; the rest of the variance was due to unique variation impacting wellbeing or depression and anxiety symptoms. These findings suggest that an absence of clinically-significant symptoms of depression and anxiety does not necessarily indicate that an individual is flourishing. Both unique and shared genetic and environmental factors may determine why some individuals flourish in the absence of symptoms while others do not.

1. Background

Mental wellbeing and illness have traditionally been conceptualized as opposite ends of a continuum, such that the absence of mental illness is thought to indicate the presence of mental health. Such a model would imply that knowledge of one state would necessitate an understanding of the other. Yet, with the advent of the positive psychology movement, the construct of 'mental health' has been reframed in light of advanced theoretical notions of wellbeing which now include both satisfaction with life as well as positive psychological attributes such as optimism, autonomy and life mastery (Gatt et al., 2014; Keyes, 2005; Seligman and Csikszentmihalyi, 2000; Williams et al., 2009). In such models, individuals who score high on dimensions of wellbeing are said to be 'flourishing'. That is, they display high levels of both hedonic or 'subjective' wellbeing (defined by positive affect and feelings of life satisfaction), and eudaimonic or 'psychological' wellbeing (defined by a sense of life purpose, meaning and fulfilment) (Deci and Ryan, 2008), and not just the absence of illness symptoms.

Evidence from recent studies support the contention that states of mental wellbeing and mental illness symptoms are independent yet related, sharing only a small proportion of common variance (Kendler et al., 2011a, 2011b; Keyes, 2005). In Keyes (2005) study, a confirmatory factor analysis supported a two-factor dual-continua model of mental wellbeing and illness over a single factor continuum. In addition, only a quarter of the phenotypic variance between the latent factors of mental wellbeing and mental illness was shown to be shared, indicating that the two conditions were defined by separate correlated axes. Prevalence studies in the United States (US) suggest that lifetime risk for developing affective disorder ranges anywhere up to 32% (Brown and Ryan, 2003), with the remainder of the population thought to be healthy and disorder-free at any single point in time. Yet, of the total population sample in Keyes (2005) study who reported no mental illness in the previous 12 months (77%), only 21% were actually

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flourishing and functioning optimally, suggesting that even in normative samples, an absence of illness symptoms does not necessarily imply a thriving mental state. Although much higher rates of flourishing have been reported in other studies – for example, 44% in a sample of 1043 American yoga practitioners (Ross et al., 2013), and 49% in a sample of 5689 college students in the United States (Keyes et al., 2011) – this difference in flourishing rates is more likely due to the health characteristics of the specific samples (by virtue of age or health practise) rather than actual variations in flourishing rates in the general population.

Twin studies have similarly reported some evidence of shared variance between mental illness and mental wellbeing, as well as its genetic and environmental derivatives in monozygotic (MZ) and dizygotic (DZ) twin pairs. In a general population cohort, the shared genetic and environmental variance of 1386 MZ and DZ twins were compared in terms of mental wellbeing and "internalizing disorders" (previous-year prevalence of clinical levels of Major Depressive, Generalized Anxiety or Panic Disorder) and they were found to share 50% genetic variance and 5% unique environment variance (Kendler et al., 2011b). The contribution of additive genetics to the phenotypic correlation ranged from 69% at baseline to 86% across ten years (Kendler et al., 2011b), suggesting that genetics ultimately played a larger role than environment in the shared associations between wellbeing and internalizing disorders of depression and anxiety. Unique environment (e.g., birth order, differential parenting styles, peer groups, or individual personality differences) showed considerably less overlap such that most of the environmental influences on wellbeing were independent from mental illness. However, as unique environment also includes measurement error, this environmental overlap between the variables could also be confounded by this variation. Common environment (e.g., shared household rearing, parenting style and socioeconomic class) on the other hand did not contribute to these shared relationships. Together, these findings suggest that unique genetic and environmental influences specifically contribute to wellbeing and mental illness symptoms. They also suggest that the same environmental factors contribute very little to the relationship between wellbeing and mental illness such that the environments that foster wellbeing are largely unrelated to those that impact mental illness, and vice versa. Similar genetic and environmental relationships have also been reported in nonclinical twin cohorts such as the Norwegian twin study of 6326 young adults aged between 18 and 31 years (Nes et al., 2008). This study examined the genetic and environmental overlap for symptoms of depression, anxiety and wellbeing defined by a life satisfaction scale in men and women. They found the genetic and environmental relationship to be strongest between symptoms of depression and anxiety (genetic correlation, rG: 0.92 (CI, confidence intervals: 0.83–1.00) in males and females; environmental correlation (rE): 0.52 (0.42–0.61) in males, 0.60 (0.54–0.65) in females), followed by life satisfaction and depression (rG: −0.79 (−0.90 to −0.68) in males and females; rE: −0.48 (−0.56 to −0.40) in males, −0.59 (−0.64 to −0.54) in females), with the weakest relationship between life satisfaction and anxiety (rG: −0.64 (−0.78 to −0.50) in males and females; rE: −0.29 (−0.39 to −0.19) in males, −0.34 (−0.40 to −0.26) in females). However, the age range covered in this study spanned what is traditionally a period of substantial transition and development, so whether it is generalizable to a broader adult age range is unclear. Moreover, the single-item measure of "life satisfaction" is not a comprehensive assessment of mental wellbeing in that it does not measure eudaimonic aspects of wellbeing.

In this study, we examine the relationship between mental wellbeing and the normative range of anxiety and depression symptoms in healthy adult twins. We aim to derive the cross-frequency distribution of wellbeing and depression and anxiety symptoms in a healthy normative adult population, and the genetic and environmental derivatives of the shared and unique variance of wellbeing and depression and anxiety symptoms using twin modeling. The twin modeling thus allows us to examine the genetic and environmental interplay between wellbeing and depression and anxiety symptoms; that is, the degree to which genetic and environmental factors contribute in common and/or independently to both health outcomes.

2. Methods and materials

2.1. Participants

The sample comprised healthy same-sex MZ and DZ twin pairs from the TWIN-E study (the Twin study in Wellbeing using Integrative Neuroscience of Emotion) conducted at the University of Sydney, Australia (see Gatt et al., 2012, for complete study protocol). The study received approval from the Human Research Ethics Committees of the University of Sydney (03–2009/11430) and Flinders University (FCREC#08/09). All participants provided written informed consent prior to participation and after receiving a complete written description of the study.

Twins were recruited from the Australian Twin Registry. Eligible participants were healthy adult same-sex twin pairs (aged 18-62 years), with English as primary language, and of pure European ancestry. Zygosity was determined using the twins' responses to a 12-item questionnaire developed for the study (Gatt et al., 2012), using items from measures previously validated as having 95% convergence with DNA results (Eisen et al., 1989; Jackson et al., 2001; Magnus et al., 1983). For further details, see Burton et al. (2015). Ethnicity of the cohort was determined from self-report measures of the participant's parents' and grandparents' ancestry. Exclusion criteria included current or lifetime psychiatric illness, history of stroke or neurological disorder, genetic disorder, brain injury (causing loss of consciousness for more than 10 min), chronic and serious medical conditions (e.g., cancer, heart disease), blood-borne illnesses, substance abuse, or vision impairments not corrected by glasses/lenses.

A total of 2370 twins were recruited from the Australian Twin Registry for the study. 108 participants were excluded as ineligible, including 21 on the basis of past or current mental illness. This resulted in a total sample of 2262 twins, of which 1669 successfully completed Phase I baseline testing of the web-based questionnaires. 1486 participants (743 twin pairs) were included in the current analysis following the exclusion of 92 incomplete pairs (82 pairs had one twin who did not complete the web questionnaire, and another 10 pairs had indeterminate zygosity). Of the 1486 participants, 39.6% (n=588) were male. The mean age was 39.79 years (SD =12.74; range =18 to 62 years) and mean education was 14.35 years (SD =3.00). 60.3% of the total sample were monozygotic twin pairs (MZ; n=896 or 448 twin pairs), of which 45.1% were male (n=404; 202 twin pairs) and 54.9% female (n=492; 246 twin pairs). The remaining 39.7% of the sample were dizygotic twins (DZ; n=590 or 295 twin pairs), of which 31.2% were male (n=184; 92 twin pairs) and 68.8% female (n=406; 203 twin pairs).

2.2. Measures

The protocol and measures for the TWIN-E study have been previously published (Gatt et al., 2014, 2012). This study uses data derived from the first phase of the study for which participants completed the WebQ, an online test battery of self-report questionnaires (Gatt et al., 2012). Here we used total scores derived from the Depression, Anxiety and Stress Scale (DASS-42) scale