Psychological Medicine (2008), **38**, 153–156.
Printed in the United Kingdom

Correspondence

Psychological Medicine, **38** (2008)
doi:10.1017/S003329170700150X
First published online 12 September 2007

Letter to the Editor

Recently, Kendler and colleagues (2007) replicated a high genetic correlation between major depression (MD) and generalized anxiety disorder (GAD) (1.0 in females, 0.74 in males). Interestingly, they also examined the role of neuroticism (N) and found that the genetic factors indexed by N contributed around 30% to the genetic correlation between MD and GAD, substantially less than the authors had expected. Hence, they considered their results as 'somewhat disappointing'.

We like to argue that their results are not disappointing at all. As noted by the authors themselves, there was a large time lag of no less than 25 years between the assessment of N and the mental disorders. Furthermore, N was assessed only once. We think that the authors did not sufficiently take into account the time lag, probably because, apart from measurement error and random effects, they attribute the variance of N-measures (such as the N-scales from the EPQ and the NEO) mainly to stable personality traits. However, it can be argued that N-measures are best interpreted as mixed state-trait measures of psychological distress (Ormel *et al*. 2004): (1) Test–retest correlations of N-measures tend to decrease with increasing time intervals, even during adulthood (Watson & Clark, 1984; Ormel & Rijsdijk, 2000; Caspi *et al*. 2005). (2) As many have noted, the item content of N-measures is very similar to that of psychological distress inventories, with one major difference: N-measures typically lack a well-defined time frame and contain vague qualifiers of frequency, intensity and duration. (3) Longitudinal studies have found that N-measures are strongly correlated with the long-term level of psychological distress (e.g. Costa & McCrae, 1980; Duncan-Jones *et al*. 1990; Lucas & Fujita, 2000). (4) Structural equation modelling (SEM) of multi-wave N-measures covering 18 years in an adult general population sample found a 1-year autoregression of 0.967 and an estimated 25-year test–retest correlation of 0.432 (Ormel & Rijsdijk, 2000). Collectively, these findings suggest lasting change in N-scores in some individuals, perhaps as a result of steeling and sensitizing experiences.

The phenotypic correlation between N and MD and between N and GAD in Kendler *et al*.'s study is approximately 0.25 and for 75% due to the genetic correlation component (calculated from Fig. 3). This is *not* disappointingly weak but rather substantial given the fact that, attenuated for measurement error, the estimated 25-year longitudinal correlation of N with itself amounted to 0.43 in the Ormel & Rijsdijk (2000) study.

The implication for molecular genetic studies would be that individuals with MD and/or GAD and/or high N-scores can be pooled, provided multiple assessments of N that are not too far apart in time from the assessment of mental disorder. Pooling will increase the statistical power of association and linkage studies searching for the genes involved in depression and generalized anxiety.

Declaration of Interest

None.

References

Caspi A, Roberts B, Shiner R (2005). Personality development: stability and change. *Annual Review of Psychology* **56**, 453–484.

Costa Jr. PT, McCrae RR (1980). Influence of extraversion and neuroticism on subjective well-being: happy and unhappy people. *Journal of Personality and Social Psychology* **38**, 668–678.

Duncan-Jones P, Fergusson DM, Ormel J, Horwood LJ (1990). A model of stability and change in minor psychiatric symptoms: results from three longitudinal studies. *Psychological Medicine* (Monograph Supplement) **18**, 1–28.

Kendler KS, Myers J, Torgerson S, Neale MC, Reichborn-Kjennerud T (2007). The heritability of cluster A personality disorders assessed by both personal interview and questionnaire. *Psychological Medicine* **37**, 655–665.

Lucas RE, Fujita F (2000). Factors influencing the relation between extraversion and pleasant affect. *Journal of Personality and Social Psychology* **79**, 1039–1056.

Ormel J, Rijsdijk FV (2000). Continuing change in neuroticism during adulthood – structural modelling of a 16-year, 5-wave community study. *Personality and Individual Differences* **28**, 461–478.

Ormel J, Rosmalen J, Farmer A (2004). Neuroticism: a non-informative marker of vulnerability to psychopathology. *Social Psychiatry and Psychiatric Epidemiology* **39**, 906–912.

Watson D, Clark L (1984). Negative affectivity: the disposition to experience aversive emotional states. *Psychological Bulletin* **96**, 465–490.

J. ORMEL[1], F. V. RIJSDIJK[2], H. RIESE[1], H. SNIEDER[3], J. G. M. ROSMALEN[1]

[1] *Department of Psychiatry, University Medical Center Groningen, The Netherlands, University of Groningen, The Netherlands;* [2] *SGDP Centre, Institute of Psychiatry London, UK;* [3] *Unit of Genetic Epidemiology & Bioinformatics, Department of Epidemiology, University Medical Center Groningen, The Netherlands, University of Groningen, The Netherlands*

Address correspondence to:
Prof. dr. J. Ormel
Department of Psychiatry,
University Medical Center Groningen,
PO Box 30.001, 9700 RB Groningen,
The Netherlands
(Email: j.ormel@med.umcg.nl)

Psychological Medicine, **38** (2008)
doi:10.1017/S0033291707000992
First published online 20 July 2007

Research Letter

Age does not explain high rates of minor physical anomalies in schizophrenia patients

In a study of healthy individuals Lloyd *et al*. (2003) reported higher rates of minor physical anomalies (MPA) among older (>60 years) than younger subjects. Based on these results they questioned the strong association between schizophrenia and MPA and argued that age might confound this relationship. Since Lloyd *et al*.'s conclusions challenge the relevance of MPA for schizophrenia, we retested the question of whether or not age is significantly related to MPA rates in subjects with or without schizophrenia in data from four independent samples in three countries. The total samples include 298 psychosis patients and 103 controls, with good representation throughout the adult age span of both sexes. The studies of Ismail *et al*. (1998), Kelly *et al*. (2005), and Lane *et al*. (1997) have previously shown strong associations between MPA and schizophrenia, while the Nesvåg *et al*. study (unpublished observations) constitutes preliminary results from ongoing research. If Lloyd *et al*.'s conclusions are correct and generalizable, one would predict increasing MPA rates with increasing age among both patients and controls and no difference in frequencies in MPA rates in schizophrenia *versus* control subjects of the same age.

Three of the four studies comprised 271 subjects who met DSM-III-R criteria for schizophrenia. The Nesvåg *et al*. study also included 27 patients with DSM-IV other psychoses. Exclusion criteria comprised no major neurological or somatic disorder or history of head trauma. All controls were free of mental illness. More information can be obtained from the corresponding references (Lane *et al*. 1997; Ismail *et al*. 1998; Kelly *et al*. 2005) and the first author of the Nesvåg *et al*. study.

The Ismail *et al*. study included 60 patients from Malmö, Sweden and measured MPA with items from the Waldrop *et al*. study (1968), as well as additional sources. The Kelly *et al*. study included 55 subjects (28 schizophrenia patients and 27 controls from Stockholm, Sweden), all subjects being examined using the Lane Scale (Lane *et al*. 1997). The Lane *et al*. study comprised 165 patients and 76 control subjects recruited from Dublin, Ireland, MPA measured with the Lane scale. Subjects in the Nesvåg *et al*. study were part of an ongoing study in Oslo, Norway. Thus far, 45 patients (18 with schizophrenia, and the remaining with other psychoses) have been selected, and MPA were assessed using a 10-item scale.

The notable variation in the composition of the psychosis samples and the MPA scales across the studies prohibited combining the data into one common dataset. For simplification of comparison, rates of total MPA rather than specific MPA were studied. The relationship between total MPA score and age was examined using Spearman's r_s for each sample in total, for patients and controls separately, and for men and women separately. There was no evidence that the association between MPA and age was influenced by gender, so no further stratification by gender was employed. The mean and standard deviation for total MPA were calculated *per each age quartile*. The Kruskal–Wallis test was used to analyse differences for total MPA by age quartiles, and linear trends were analysed using the Jonckheere–Tepstra test. Comparison of MPA means was done by Student's *t* test.

Results and comment

None of the rank correlation between MPA score and age in each sample (or gender, patient/control status subgroups) was close to statistical significance. Table 1 presents the mean MPA score by age quartiles for patients/controls. There was no significant change in MPA scores by increasing age and no significant trend over age quartiles. In the Lane *et al*. study, mean MPA were significantly higher in patients aged >60 years (53.7 ± 10.7) than in patients aged ⩽60 years (49.5 ± 8.6) ($p = 0.040$), while no such difference was seen in corresponding control groups (33.6 ± 8.9 *v.* 33.7 ± 8.2) ($p = 0.975$). The ratio for mean MPA in patients:controls (Table 1) remained stabile (1.49, 1.47,