Genetic and Environmental Stability of Neuroticism From Adolescence to Adulthood

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Longitudinal studies of neuroticism have shown that, on average, neuroticism scores decrease from adolescence to adulthood. The heritability of neuroticism is estimated between 0.30 and 0.60 and does not seem to vary greatly as a function of age. Shared environmental effects are rarely reported. Less is known about the role of genetic and environmental influences on the rank order stability of neuroticism in the period from adolescence to adulthood. We studied the stability of neuroticism in a cohort sequential (classical) twin design, from adolescence (age 14 years) to young adulthood (age 32 years). A genetic simplex model that was fitted to the longitudinal neuroticism data showed that the genetic stability of neuroticism was relatively high (genetic correlations between adjacent age bins >0.9), and increased from adolescence to adulthood. Environmental stability was appreciably lower (environmental correlations between adjacent age bins were between 0.3 and 0.6). This low stability was largely due to age-specific environmental variance, which was dominated by measurement error. This attenuated the age-to-age environmental correlations. We constructed an environmental covariance matrix corrected for this error, under the strong assumption that all age-specific environmental variance is error variance. The environmental (co)variance matrix corrected for attenuation revealed highly stable environmental influences on neuroticism (correlations between adjacent age bins were between 0.7 and 0.9). Our results indicate that both genetic and environmental influences have enduring effects on individual differences in neuroticism.

■ **Keywords:** personality, stable environmental influences, genetic correlation, simplex models

Neuroticism is included in nearly all trait theories of personality (see Digman, 1990) and has been established as a universal (i.e., not bound to any particular culture) trait in cross-cultural studies (McCrae & Costa Jr, 1997; Schmitt et al., 2007). While the term *trait* conveys the conceptualization of personality as stable, it is known that personality scores change over the lifespan (McCrae et al., 1999; Soto et al., 2011) and between cohorts (Smits et al., 2011). A meta-analysis of longitudinal studies revealed that the mean score of neuroticism decreases between age 12 and 40 years, and remains largely stable thereafter (Roberts et al., 2006). In addition, the stability of individual differences in neuroticism is characterized by an increase in rank order stability up until age 60, with a decrease in stability observed after age 60 (Roberts & DelVecchio, 2000).

Neuroticism is associated with mood and anxiety disorders (Clark et al., 1994; Enns & Cox, 1997; Kendler et al., 1993; Middeldorp et al., 2006; Roberts & Kendler, 1999). This association is partly due to pleiotropic genetic influences (Jardine et al., 1984; Kendler et al., 1993; Mackintosh et al., 2006; Middeldorp et al., 2005; 2011; Roberts & Kendler, 1999). Genetic pleiotropy also accounts for the association between neuroticism and borderline personality disorder (Distel et al., 2009). Neuroticism also has a moderate genetic correlation with somatic and neurological disorders such as migraine (Ligthart & Boomsma, 2012). The heritability of neuroticism has been estimated between 30% and 60%. There is little or no evidence for common environmental influences shared by family members, which is consistent with the lack of cultural transmission from parents to offspring (Lake et al., 2000). There is some evidence for non-additive genetic effects (Birley et al., 2006; Floderus-Myrhed et al., 1980; Keller et al., 2005; Lake et al., 2000;

Loehlin et al., 1998; Rettew et al., 2006; van den Berg et al., 2014; Vukasović & Bratko, 2015). Eaves et al. (1998) suggested that this is more likely to be attributable to epistatic interaction (i.e., interaction between alleles at different genetic loci) rather than to genetic dominance (interaction within a genetic locus).

Rettew et al. (2006) found little evidence for quantitative changes in genetic or environmental variance in neuroticism between ages 12 and 17. Wray et al. (2007; see also Birley et al., 2006) reported genetic correlations across 22 years between 0.82 and 0.95, and environmental correlations between 0.24 and 0.53. These twin studies focused on correlations in neuroticism scores between measurement occasions. However, at each measurement occasion, the participants varied appreciably in age, which introduces possible age-related heterogeneity in genetic and environmental effects. In contrast, Viken et al. (1994) collected two repeated measures of neuroticism, six years apart, in twin pairs aged between 18 and 59 years, but reordered the data as a function of chronological age at first measurement. Viken et al. (1994) reported high genetic correlations (between 0.8 and 1), and low to moderate environmental correlations (between 0.25 and 0.54) between chronological ages. Briley and Tucker-Drob (2014) recently reported a meta-analysis of genetic studies of personality, with the age of twin and sibling pairs ranging from infancy to old age. Their study included neuroticism, well-being, and measures of psychopathology, such as aggression and inattention. They found that both the genetic and environmental stability increased with age. They reported a substantially higher environmental stability when they corrected for measurement error.

In the current twin study, we analyzed repeated measures of neuroticism assessed between ages 14 and 32 years. Our aim was to further elucidate the increase in the rank stability of neuroticism from adolescence to young adulthood, a period marked by a mean decrease in neuroticism. We worked with age bins comprising two years, which provided greater resolution of the changes in genetic and environmental stability than that provided in previous work (Viken et al., 1994). In addition to estimating genetic and environmental correlations across age, we addressed the effect of measurement error on the estimation of the environmental correlations between repeated neuroticism measures. Briley and Tucker-Drob (2014) corrected the (unshared) environmental variance for measurement error by quantifying the proportion of measurement error variance $(1-\alpha)$ using Cronbach's α. Here, we accounted for measurement error by fitting a simplex (or autoregressive) model to longitudinal twin data (Boomsma & Molenaar, 1987). In this model, we distinguish between genetic and environment variance involved in the auto-regression, and occasion specific (transient) genetic and environmental variance. We assume that age specific unshared environmental variance is largely due to measurement error.

Methods

Subjects and Measures

We analyzed the data of monozygotic (MZ) and dizygotic (DZ) twins in the Netherlands Twin Register (NTR). NTR participants were initially approached via city councils and later by other means (Willemsen et al., 2013). Participants were invited, at multiple occasions, to fill out and return a set of surveys, which included a neuroticism questionnaire. Since our main interest is in the stability of neuroticism between adolescence and adulthood, we focused on data from twins aged from 14 to 32. Neuroticism was assessed in 1991, 1995, 1997, 2000, and 2002. We reordered the data from the different surveys into nine age bins, each spanning two years (i.e., 14–15, 16–17, . . . , 28–29, 30–31). The dataset comprised 15,275 observations on 6,943 twins, including 1,392 complete MZ twin pairs and 1,826 complete DZ twin pairs. Table 1 contains the number of observations in each age bin. The number of overlapping samples between adjacent age batches is substantial, but drops off with the distance between the age batches. In view of this missingness, we used full information maximum-likelihood (FIML) estimation, under the assumption that the data are missing (completely) at random. We fitted all models in Mplus 6.11 using FIML. We compared competing models on the basis of Akaike's information criterion (AIC), Bayes information criterion (BIC) and sample size adjusted Bayes information criterion (SA-BIC).

Neuroticism was assessed using the Amsterdamsche Biografische Vragenlijst (ABV; Wilde, 1970; i.e., the Amsterdam Biographic Questionnaire). The ABV neuroticism scale (ABV-N) was modeled on the Eysenck Personality Questionnaire (EPQ). The ABV-N is a 30-item instrument that contains questions like 'Do you often worry about the past?' The response options are 'yes', 'no' and '?'. Following the ABV test manual, item responses were weighted in calculating the neuroticism sum score (Wilde, 1970). Table 1 contains the ABV-N means and standard deviations by age and sex. Van den Berg et al. (2014) compared the ABV-N and other neuroticism scales and reported a large overlap in item content, and a high correlation (0.89) between the ABV-N and the IRT neuroticism scores.

Statistical Model

At each age, we modeled the neuroticism score using the Simplex model. The neuroticism score at time t was modeled as follows (discarding subject subscripts):

$$y_t = \beta_{0t} + \beta_{st}*sex + A_t + D_t + E_t + \tau_{At} + \tau_{Dt} + \tau_{Et} \tag{1}$$

In equation 1, β_{0t} is the occasions specific intercept, β_{st} is the occasion specific sex effect, and τ_{At}, τ_{Dt}, and τ_{Et} are (zero mean) occasion-specific additive genetic, dominance, and unshared environmental variables. We assume that τ_{Et} largely due to measurement error. The (zero mean) additive genetic, dominance, and unshared environmental variables

TABLE 1

Descriptives

Age bins	14–15	16–17	18–19	20–21	22–23	24–25	26–27	28–29	30–31
14–15	1,583	491	430	486	381	418	221	7	0
16–17	0.62	2,263	576	624	805	409	505	310	12
18–19	0.61	0.61	2,278	574	669	663	364	433	263
20–21	0.45	0.64	0.67	2,258	707	550	553	284	325
22–23	0.38	0.53	0.65	0.69	2,038	417	445	359	132
24–25	0.46	0.56	0.58	0.68	0.75	1,553	356	268	226
26–27	0.42	0.52	0.60	0.60	0.72	0.76	1,297	318	180
28–29	-0.23	0.45	0.53	0.56	0.65	0.76	0.76	1,050	232
30–31	NA	0.71	0.53	0.57	0.54	0.67	0.73	0.77	810
Twin correlations									
MZ correlations	0.61	0.61	0.55	0.53	0.53	0.47	0.50	0.57	0.51
DZ correlations	0.27	0.29	0.26	0.27	0.23	0.19	0.29	0.17	0.10
ABV-N mean and *SD*	Males								
Mean	50.62	49.08	46.40	46.37	43.04	42.78	41.12	40.05	37.79
SD	21.63	21.57	21.58	22.66	22.49	22.38	23.06	22.17	21.60
	Females								
Mean	58.02	58.35	58.34	55.69	53.03	53.26	50.84	49.62	49.58
SD	23.19	23.90	24.52	24.70	24.94	26.45	25.19	25.15	25.26

Note: Top: below the diagonal: phenotypic correlations between age bins (in italics) and above the diagonal available sample size for each pair of observations. Middle: the matrix the MZ and DZ twin correlations per age bin. Bottom: ABV-N scale means and standard deviations (*SD*).

A_t, D_t, and E_t are decomposed into a part due to transmission of effects from earlier ages and a part due to innovation:

$$A_t = \beta_{At} * A_{t-1} + \zeta_{At}, \quad (2)$$

$$D_t = \beta_{Dt} * D_{t-1} + \zeta_{Dt}, \quad (3)$$

$$E_t = \beta_{Et} * E_{t-1} + \zeta_{Et}. \quad (4)$$

In equation 2, β_{At} is the auto-regression coefficient, and ζ_{At} is the innovation, that is, the residual in the regression of A_t on A_{t-1} (the same interpretation applies to equations 3 and 4). Note that at $t = 1$, we set $A_1 = \zeta_{A1}$, $D_1 = \zeta_{D1}$, and $E_1 = \zeta_{E1}$. While we included sex-related mean differences at each occasion (β_{st}), we imposed a single (genetic) covariance model in the male and females twins, as large studies found no evidence for moderation of effects by gender (van den Berg et al., 2014; Vukasović & Bratko, 2015).

The equations 1–4 give rise to the following 9×9 covariance structure matrices:

$$\Sigma_A = (I - B_A)^{-1} \Psi_A (I - B_A)^{-1^t} + \Theta_A, \quad (5)$$

$$\Sigma_D = (I - B_D)^{-1} \Psi_D (I - B_D)^{-1^t} + \Theta_D, \quad (6)$$

$$\Sigma_E = (I - B_E)^{-1} \Psi_E (I - B_E)^{-1^t} + \Theta_E, \quad (7)$$

where I is the 9×9 identify matrix, B_A (9×9) contains the autoregressive coefficients β_{At} ($t = 2,9$), the diagonal co-variance matrix (9×9) Ψ_A contains the variance(A_1) ($t = 1$), and the variances var(ζ_{At}) ($t = 2,9$), and the diagonal covariance matrix (9×9) Θ_A contains the variance of τ_{At} ($t = 1,9$). Equations 6 and 7 are defined analogously. Note that the first and the last variances (e.g., in the matrix Θ_A, var[τ_{A1}] and var[τ_{A9}]) are not identified. Identification is achieved by fixing these variances to zero, or constraining them to be equal to the adjacent variances. Below we

adopted the latter constraint in the specification of Θ_A, Θ_D, and Θ_E. In MZ and DZ twin samples, the expected 18×18 partitioned covariance matrices are

$$\Sigma_{MZ} = \begin{matrix} \Sigma_A + \Sigma_D + \Sigma_E & \Sigma_A + \Sigma_D \\ \Sigma_A + \Sigma_D & \Sigma_A + \Sigma_D + \Sigma_E \end{matrix}, \quad (8)$$

$$\Sigma_{DZ} = \begin{matrix} \Sigma_A + \Sigma_D + \Sigma_E & \frac{1}{2}\Sigma_A + \frac{1}{4}\Sigma_D \\ \frac{1}{2}\Sigma_A + \frac{1}{4}\Sigma_D & \Sigma_A + \Sigma_D + \Sigma_E \end{matrix}, \quad (9)$$

where the weights 1/2 and 1/4 follow from quantitative genetic theory given a set of explicit assumptions, including random mating, which has been found to be tenable with respect to neuroticism (Eaves et al., 1998), and the absence of interaction and covariance among the genetic and environmental variables.

We expressed the unshared environmental covariance matrix corrected for attenuation due to measurement error as follows:

$$\Sigma_{E-dis} = (I - B_E)^{-1} \Psi_E (I - B_E)^{-1^t}. \quad (10)$$

This is based on the strong assumption that the variance in the matrix Θ_E is dominated by measurement error. Note that the uncorrected environmental correlation between ages t-1 and t is

$$[\beta_{Et} * var(E_{t-1})] / [\{var(E_{t-1}) + var(t_{Et-1})\}^{1/2}$$

$$\times * \{\beta_{Et}^2 * var(E_{t-1}) + var(\zeta_{Et}) + var(\tau_{Et})\}^{1/2}],$$

and the corrected correlation is

$$[\beta_{Et} * var(E_{t-1})] / [\{var(E_{t-1})\}^{1/2}$$

$$\times * \{\beta_{Et}^2 * var(E_{t-1}) + var(\zeta_{Et})\}^{1/2}].$$

TABLE 2

Model Fit Indices of the Different Models Considered

	Model	AIC	BIC	SA-BIC	Log-likelihood	Free parameters
1	AE-simplex unconstrained	125,921.89	126,323.70	126,113.99	-62,894.94	66
2	AE-simplex unconstrained Θ_d = free	125,939.32	126,395.91	126,157.61	-62,894.66	75
3	AE-simplex $\Theta_a = 0$	125,916.14	126,275.33	126,087.86	-62,899.07	59
4	AE-simplex $\Theta_a = 0$ Θ_e = equal	125,911.88	126,234.54	126,066.13	-62,902.94	53

TABLE 3

Estimates of the Genetic Variance (V_A) and Environmental Variance (V_E) for Each Age Bin

Age	14–15	16–17	18–19	20–21	22–23	24–25	26–27	28–29	30–31
V_A	282.03	282.03	286.56	286.559	300.93	299.10	288.68	309.32	285.26
V_E	215.49	222.11	262.94	278.53	284.14	336.32	299.08	302.82	323.61
h^2	0.57	0.58	0.52	0.52	0.52	0.47	0.49	0.51	0.47
e^2	0.19	0.19	0.26	0.27	0.28	0.34	0.30	0.30	0.33
error^2	0.24	0.23	0.22	0.21	0.20	0.19	0.21	0.19	0.20

Note: The table includes the standardized genetic variance component (h^2) and the standardized environmental variance components, broken down into environmental (e^2) and error components (denoted error^2). Note that the error^2 terms are equal to the standardized unshared environmental age specific components (raw variance terms in Θ_E).

Results

The phenotypic correlations between age bins are between $\sim$0.40 and $\sim$0.70 (Table 1). Females scored significantly higher at all ages (Table 1), as often reported in previous studies (Roberts et al., 2006; Soto et al., 2011). We observed a significant decrease in mean values with age $\left(\chi^2\,(16) = 301.2,\ p < .001\right)$. The twin correlations ranged from $\sim$0.61 to $\sim$0.66 in the MZ pairs, and from $\sim$0.29 to $\sim$0.10 in the DZ pairs (Table 1). The twin correlations suggested large genetic effects and the absence of shared environmental effects. The twin correlations at ages 24–25, 28–39, and 30–31 suggested dominance, as twice the DZ twin correlation is appreciably lower than the MZ twin correlation. The full ADE simplex model failed to converge (presumably due to missingness in the data) and does not feature in Table 2. We fitted a model in which only the age-specific dominance variance var(τ_{Dt}) was included (i.e., without the auto-regression terms) and this model did not fit better than the AE simplex model (see Table 2). We also considered the ADE simplex without age specific D variance, but this model did not converge, and likewise does not feature in Table 2. We observed that the estimated variances var(τ_{At}) were very small and not significant at any age. In addition, we noted that the estimated variances var(τ_{Et}) were very similar in magnitude. Constraining var(τ_{At}) to zero and var(τ_{Et}) to be equal was judged to be acceptable on the basis of the AIC, BIC, and SA-BIC (Table 2).

Table 3 contains the variance estimates and the standardized variance components, including a breakdown into environmental and error variance (i.e., occasion specific environmental). Heritability estimates showed a decreasing trend starting at 0.57 (age 14–15) and ending at 0.47 (age 30–31). The decrease in heritability was due to an increase in the environmental variance (from about $\sim$215 at age 14–16 to $\sim$323 at age 30–32). The genetic variance in neuroticism remained very similar between ages 14 and 31 (from $\sim$282 at age 14–15 to 285 at age 30–31; Table 3). The estimated genetic covariance matrix Σ_A revealed high genetic stability between the ages of 14 and 31. The genetic correlations between adjacent ages increased with age, as shown in Figure 1; for example, the correlation between consecutive ages ranged from 0.84 (age 14–15 to age 16–17) to 0.97 (age 28–29 to age 30–31). The genetic innovation variances, var(ζ_{At}), at ages 24–25, 28–29, and 30–31 were not greater than zero (p values: $p_{24–25} = .47$, $p_{28–29} = .65$ and $p_{30–31} = .26$). Dropping the innovation variances did not lead to a deterioration in model fit, $\chi^2(3) = 0.62$, $p = .88$. This suggests a nearly perfect genetic stability between ages 24 and 31.

As shown in Figure 2, the environmental covariance matrix Σ_E revealed relatively low environmental stability. The uncorrected environmental correlations between ages 14–15 and 16–17 and between ages 28–29 and 30–31 are 0.31 and 0.57, respectively. The genetic stability was appreciably greater than the environmental stability. Table 3 contains the proportion of genetic variance (h^2), and the proportions of environmental and error variance (Figure 3). Taking one minus the proportion of error as an index of reliability, the results in Table 3 implied a reliability between 0.75 and 0.81. Again, assuming the age-specific environmental effects were completely attributable to measurement error, we calculated the correlations corrected for this error variance. As expected, the environmental stability was appreciably higher: the correlation between ages 14–15 and 16–17 was 0.70, and between ages 28–29 and 30–31 was 0.93. The environmental stability increased with age because the
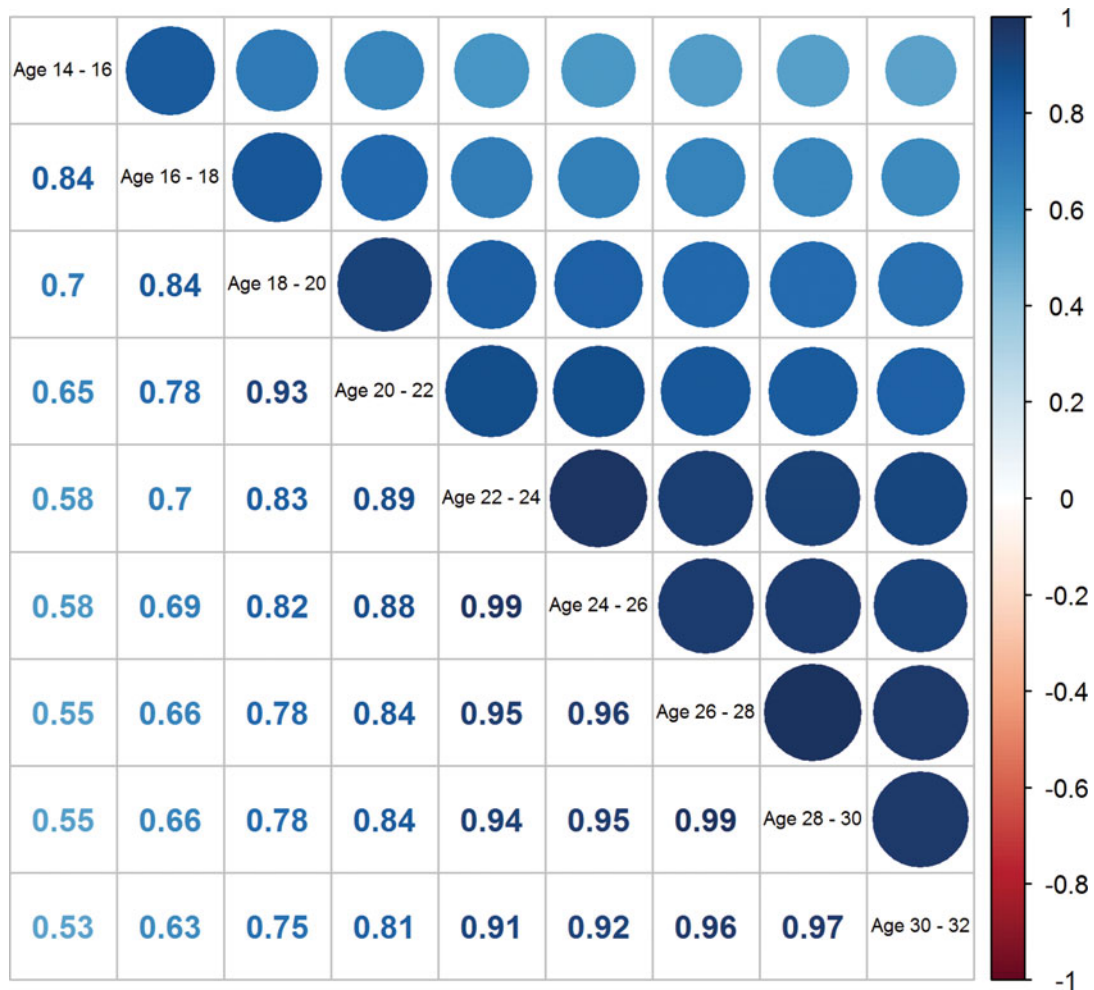
FIGURE 1

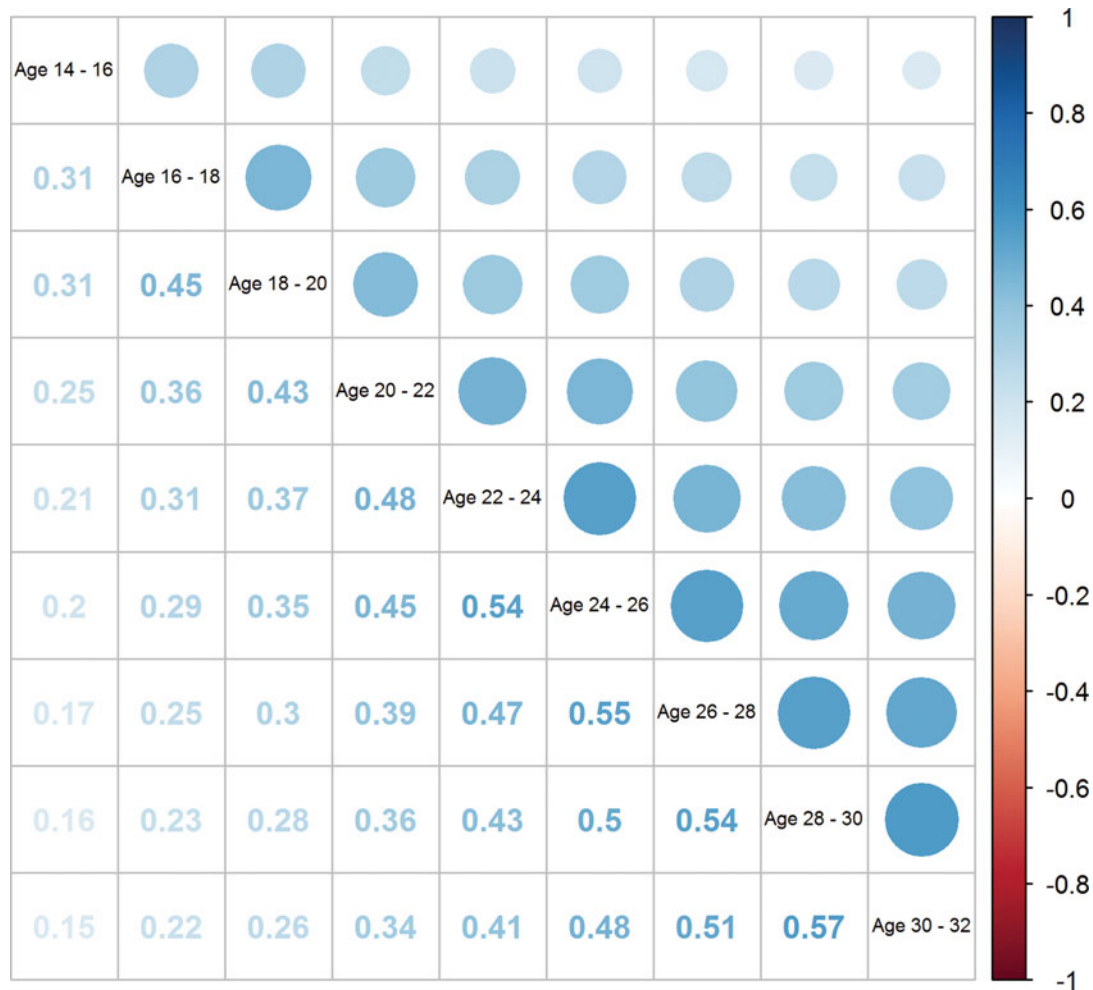(Colour online) Estimates and heat map of genetic correlations across age for neuroticism.

environmental innovation variance (ζ_{Et}) decreased with age and was no longer significant at age 30–31 (SD [ζ_{E30-32}] = 5.205, t = 1.455, p = .15).

Discussion

Using a cohort sequential twin design, we quantified the genetic and environmental stability in neuroticism. Restructuring the data from measurement occasion into age bins allowed us to estimate age-related changes in genetic and environmental stability of neuroticism in the critical period between ages 14 and 31 years, a period that is characterized by an increase in the phenotypic stability of neuroticism (Roberts & DelVecchio, 2000; Soto et al., 2011). We found evidence for increasing genetic stability resulting in nearly perfect rank stability after age 24, that is, genetic correlations approaching unity. When we corrected for measurement error, we also observed substantial environmental stability. Correcting for measurement error provides an upper bound for the environmental stability, where in the literature of-

ten the lower bound (i.e., not corrected for measurement error) is reported. It is important to note that correcting for measurement error does not guarantee a high stability as, for example, low transmission and high innovation would also result in a low stability.

The substantial environmental stability is compatible with the observation that life events have a lasting effect on mean neuroticism scores (Jeronimus et al., 2013). Other unique environmental factors that may have long-lasting effects are adverse economic circumstances, which have also been observed to have enduring effects on, for example, externalizing problems (Ramanathan et al., 2013). This result is further consistent with a meta-analysis of a more broadly defined 'personality' phenotype (Briley & Tucker-Drob, 2014). While Briley and Tucker-Drob (2014) used a different methodology to correct for measurement error, their conclusion is similar: correcting for measurement error results in substantial environmental stability and this stability increases with age. Not correcting for measurement error leads to a systematic under appreciation of the amount

FIGURE 2

(Colour online) Estimates and heat map of environmental correlations across age for neuroticism.

of environmental stability in neuroticism. This conclusion may generalize to other traits.

The high degree of genetic stability that we observed is in line with previous longitudinal studies of the genetic stability of neuroticism in adolescents and adults (Gillespie et al., 2004a; Viken et al., 1994; Wray et al., 2007). The genetic stability in neuroticism between the ages of 14 and 31 is also similar to the genetic stability reported for symptoms of anxiety and depression, two traits strongly correlated to neuroticism (Gillespie et al., 2004b; Nivard et al., 2014). The implications of the high degree of genetic stability for genome-wide association studies (GWAS) were discussed by Wray et al. (2007). Here, we add that repeated measures can be used to good effect in analyses of the association between neuroticism and polygenic scores or genetic variants such as SNPs or CNVs. Specifically, discarding repeated measures in the regression of neuroticism scores on the genotype scores or genetic variants is not advisable as this will lead to a lower statistical power compared to the regression of all repeated measures. This is comparable to discarding one of the MZ twins in a GWAS including MZ twin pairs (see Minică et al., 2014). Ideally, association between genetic variants and repeated measures of a trait would be carried out in the context of a structural equation model to account for all subtleties in the genetics of a trait across age or repeated measures. However, as computational efficiency is often an issue in genome-wide studies, and the genetic contributions to neuroticism are stable, one could also decide to aggregate repeated measures by taking the mean. Alternatively, the regression of the repeated measures on genotypes (CNVs or SNPs) and polygenic scores can be carried out using generalized estimating equations to account for the dependency among the measurement measures (e.g., see Minică et al., 2015). The inclusion of repeated measures, where available, in GWAS of neuroticism is a possible way to boost power and extend upon current gene finding efforts (de Moor et al., 2015).

Unlike other genetically informative extended pedigree studies (Eaves et al., 1998; Keller et al., 2005; Lake et al., 2000), we found no evidence for a significant contribution
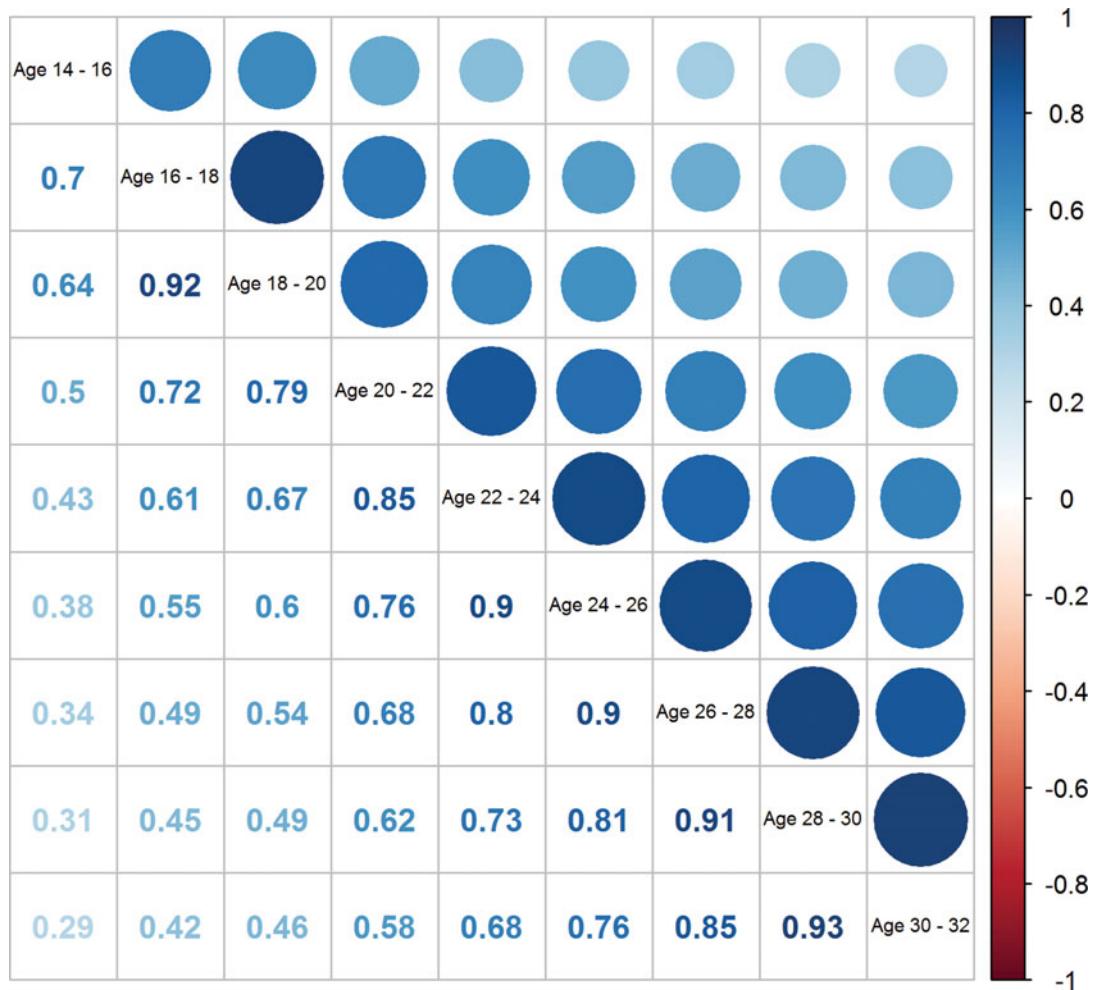
FIGURE 3

(Colour online) Estimates and heat map of environmental correlations, corrected for age-specific unshared environmental effects (measurement error), across age for neuroticism.

of non-additive genetic variation. Ordering the data into two-year age batches allowed us to estimate the changes in environmental and genetic stability with good temporal resolution. Creating smaller sub-samples per age category may have reduced the power to detect dominance variance and other non-additive effects. Future work, perhaps combining samples from multiple centers as made possible by the neuroticism score harmonization by van der Berg et al. (2014), may make it possible to concurrently estimate the effects of non-additive genetic variance and age-related effects on neuroticism. International collaboration on the genetic of neuroticism has been successful and yielded the first genome-wide significant finding for neuroticism (de Moor et al., 2015). Similar collaborations between twin and family registries could prove useful in further elucidating the genetic and environmental process underlying the development of personality across the lifespan.

Acknowledgments

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