Markers of psychological differences and social and health inequalities

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Markers of Psychological Differences and Social and Health Inequalities: Possible Genetic and Phenotypic Overlaps

René Mõttus,[1,2] Riccardo Marioni,[1] and Ian J. Deary[1]
[1]University of Edinburgh
[2]University of Tartu

Abstract

Associations between markers of ostensible psychological characteristics and social and health inequalities are pervasive but difficult to explain. In some cases, there may be causal influence flowing from social and health inequalities to psychological differences, whereas sometimes it may be the other way around. Here, we focus on the possibility that some markers that we often consider as indexing different domains of individual differences may in fact reflect at least partially overlapping genetic and/or phenotypic bases. For example, individual differences in cognitive abilities and educational attainment appear to reflect largely overlapping genetic influences, whereas cognitive abilities and health literacy may be almost identical phenomena at the phenotypic, never mind genetic, level. We make the case for employing molecular genetic data and quantitative genetic techniques to better understand the associations of psychological individual differences with social and health inequalities. We illustrate these arguments by using published findings from the Lothian Birth Cohort and the Generation Scotland studies. We also present novel findings pertaining to longitudinal stability and change in older age personality traits and some correlates of the change, molecular genetic data-based heritability estimates of Neuroticism and Extraversion, and the genetic correlations of these personality traits with markers of social and health inequalities.

As people navigate through their lives, they differ from each other in a great variety of more or less interconnected ways. In order to map this complexity, we often create different kinds of quantitative markers and refer to the classes of markers that correlate or appear similar in etiology or function as some unitary domains or traits. For example, we rank people in terms of their educational attainment, occupational prestige, income, and quality of neighborhood and refer to these markers as socioeconomic status (Hagger-Johnson, Mõttus, Craig, Starr, & Deary, 2012). Additionally, we may rank people in various aspects of health, health-related behavior, and knowledge and jointly refer to these markers as social and health inequalities. On a more psychological side, individuals can be ranked on constructs such as intelligence, personality traits of different breadth and flavor, well-being, motivation, attitudes, and the like. Each of these markers is supposed to denote a domain of people's lives, whereas the borders and interfaces between these domains are often unknown and may sometimes be arbitrary.

What we are then interested in is whether and how these different domains relate to each other and (co)develop over time. For example, social and health inequalities, which are ubiquitously interconnected (Mackenbach et al., 2008), may influence psychological differences, or the other way around. Moreover, the influence may flow in both directions at the same time (Deary & Johnson, 2010). What is more, the markers that we think of as reflecting distinct domains of individual differences may in fact have been stuck to more or less the same territory.

In particular, they may reflect the effects of at least partially overlapping samples of behaviors, skills, or life circumstances (i.e., phenotypic overlap) or, more distally, shared genetic underpinnings (i.e., genotypic overlap). For example, the rankings of people on intelligence scores and educational attainment may reflect a largely overlapping basis, of which shared genetic

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Correspondence concerning this article should be addressed to René Mõttus, Centre for Cognitive Ageing and Cognitive Epidemiology, Department of Psychology, 7 George Square, EH8 9JZ Edinburgh, UK. Email: rene.mottus@ed.ac.uk.

influences may be an important part (Marioni, Davies, et al., 2014). Highlighting the possibility that even apparently different types of markers of individual differences may reflect shared etiology, or tap the same phenomena at the phenotypic level, is an important aim of this article.

Centering mostly around the Lothian Birth Cohorts (LBC) and Generation Scotland (GS) general population cohort studies, the present article will present examples in favor of all of the above-described possibilities. We hope that this will highlight the need to consider very different interpretations of observed associations between markers of psychological differences and those of social and health inequalities. This may seem like a trivial suggestion, but it really is not. For example, as it is so tempting to interpret correlations as reflecting causal associations in one or another direction, we do have to remind ourselves that some correlations may not really refer to causal associations at all—the constructs that we are observing as being correlating may at some level and at least partly reflect the same variance. This is exactly why we are reluctant to draw clear-cut boundaries between constructs and only refer to them as *markers* of psychological differences or social inequalities, admitting that even this distinction may be arbitrary.

From among markers of psychological differences, we will mostly address what are typically referred to as cognitive traits, as these are the main focus of current LBC- and GS-based research. However, several examples will pertain to other markers, such as those typically referred to as personality traits. Social and health inequalities will be exemplified mostly by educational attainment and socioeconomic position and markers of physical and mental health, as well as health-related behaviors and knowledge. Importantly, a case will be made for genetically informed analyses, and relevant examples, based on molecular genetic data and quantitative genetic techniques, will be presented.

First, we will review the temporal stability of the markers of psychological differences and discuss the profound implications of such stability. Second, we will address the idea that social and health inequalities may contribute to psychological differences and review some apparent evidence in favor of it. Third, we will describe evidence apparently suggesting that the influence is more likely to flow the other way around—from psychological characteristics to social and health inequalities. Fourth, we offer an alternative explanation by suggesting that markers of psychological differences and social or health inequalities may often go hand in hand simply because of reflecting the same underlying "something." We will then argue that using molecular genetic data coupled with quantitative genetic techniques can be one of the ways to address this possibility. We will provide relevant examples, both already published as well as new, to demonstrate where this approach is more likely and less likely to work. Finally, we will argue that in some cases, the overlap in different markers may be phenotypic.

SUBSTANTIAL PHENOTYPIC STABILITY

At least some markers of psychological differences demonstrate high stability over several decades of life. This is an important finding, as it informs us regarding the degree to which we can expect other variables to influence the characteristics that the markers ostensibly denote (Deary, 2014). The life-course stability of a characteristic nearing unity, for example, would limit the value of any attempts to find specific factors that cause people to deviate from normative developmental trajectories in this characteristic (even though these trajectories may be influenced by both genetic factors and environmental factors the people themselves expose them to).

Phenotypic Stability of Cognitive Abilities

The unique feature of the Lothian Birth Cohorts studies (and Aberdeen Birth Cohorts studies, which we will occasionally refer to) is the possibility to study participants' cognitive abilities over up to eight decades (Deary, 2014; Deary, Whalley, & Starr, 2009). Just to give some details on the background of these studies, in 1932 and 1947, Scottish educators decided to measure the cognitive ability of all 11-year-olds going to school on a chosen day in June; these large-scale tests are known as the Scottish Mental Surveys. The resulting cognitive ability test scores were available for 87,498 and 70,805 children, respectively, in 1932 and 1947. These data were preserved, and samples of people have been followed up in their eighth and ninth decades of life from both cohorts (in fact, the surviving members of the older cohort are well over 90 now, and some are still being followed). Participants have also been retested using the same cognitive ability test that they took at age 11 (the Moray House Test No. 12; MHT).

Apparently, individual differences in cognitive ability are quite highly stable. For example, the correlations of MHT scores obtained at age 11 with various cognitive ability test scores in the eighth decade of life range in the .60s and are even higher (.70+) when corrected for restricted variance (Deary, 2014; Deary, Whalley, Lemmon, Crawford, & Starr, 2000; Deary, Whiteman, Starr, Whalley, & Fox, 2004; Gow et al., 2011). Correlations with MHT scores at age 90 were somewhat lower but still well over .50 (Deary, Pattie, & Starr, 2013). Moreover, these correlations may underestimate the actual stability in cognitive ability rankings because of less than perfect reliability of the tests.

Phenotypic Stability of Other Psychological Characteristics

The Scottish Mental Surveys did not include measurements of other markers of psychological differences, such as personality traits or well-being, and therefore the data do not allow us to investigate the lifelong stability of these. However, multiple measurements in later life have enabled us to investigate the stability of individuals' rankings in several personality traits in older age. Again, the evidence suggests substantial stability. Mõttus, Johnson, and Deary (2012) created five latent Big Five personality trait scores for 209 LBC1921 (follow-up of the 1932 survey) members for ages about 81 and 87 years. The rankings

Table 1 Correlations of FFM Scores Across Three Waves of Testing in LBC1936

	Age 70–Age 73	Age 73–Age 76	Age 70–Age 76
Emotional Stability	.84	.82	.81
Extraversion	.92	.89	.87
Intellect	.90	.88	.95
Agreeableness	.83	.84	.82
Conscientiousness	.91	.91	.85

Note. These are average ages. $N = 1{,}091$, 866, and 697 (respectively, for ages 70, 73, and 76). FFM = Five-Factor Model.

of scores correlated from .78 to .89, suggesting that whatever unique changes in health or environment had happened to the people, these did not knock them far away from the typical late-life developmental trajectories of personality traits evidenced in mean-level trends (Mõttus, Johnson, & Deary, 2012).

The third wave of data collection was recently finished in LBC1936 (follow-up of the 1947 survey), allowing us to report here for the first time the rank-order stability estimates of the Big Five traits between ages 70, 73, and 76.[1] The correlations between latent factor scores from the three testing occasions are reported in Table 1 (the scales for each factor met the criterion for full [strict] measurement invariance across the three testing occasions). The correlations were all above .80 and occasionally even above .90, exceeding the typical estimates reported by Roberts and DelVecchio (2000) for similar testing intervals. Thus, these Scottish data suggest that rankings in both types of markers of psychological differences—cognitive abilities and Big Five personality traits—are highly stable over time.

Of course, the time scale to which these personality trait stability estimates pertain is only a fraction of that spanned by our studies on the stability of cognitive abilities. Had personality traits also been measured in childhood, which rank-order stabilities could we observe? They would possibly be lower than those for cognitive abilities. For example, in a sample of more than 8,000 Britons, the stability of Conscientiousness between ages 16 and 50 was around .15 (Pluess & Bartley, 2015). Similarly, the rank-order stability estimates for the Big Five traits across about 40 years (from school age to later adulthood) have been found to range from around 0 to mostly under .30, across measures and rater perspectives (Edmonds, Goldberg, Hampson, & Barckley, 2013). In a meta-analysis, Big Five stability estimates between .31 and .47 were reported for retest intervals spanning about 25–35 years (Bazana & Stelmack, 2004). Shorter intervals yield higher stability estimates (Roberts & DelVecchio, 2000).

Mechanisms of Phenotypic Stability

Individuals' rankings in the markers of psychological differences can be stable over time because of stable genetic influences on them or because of stable environments, either self-selected, self-created, or passively exposed to in a consistent manner. For cognitive ability, follow-up samples of the Scottish Mental Surveys have provided a unique opportunity to test for the degree to which the remarkable phenotypic stability can be ascribed to genetic factors.

In particular, this has been made possible by the availability of genome-wide single nucleotide polymorphism (SNP) data and statistical methods that allow using these data to estimate genetic correlations on unrelated individuals (genome-wide complex trait analysis [GCTA]; Yang, Lee, Goddard, & Visscher, 2011; for definitions of *GCTA*, *genetic correlation*, and other genetics-related terms, see Table 2). In a combined sample of 1,940 individuals from the Lothian and Aberdeen Birth Cohorts studies, Deary and colleagues (2012) showed that the genetic correlation between MHT scores at age 11 and general cognitive ability derived from the Wechsler Adult Intelligence Scale-III (WAIS-III; Wechsler, 1997) in the seventh/eighth life decade was .62, whereas the environmental correlation was .65. The phenotypic correlation was .63 in these data. This suggests that both genetic and environmental influences contribute to the high life-course stability of cognitive ability.

Although such analyses have not been done for other markers of psychological differences using LBC or GS data, a similar argument could be made for them. For example, twin studies have made it clear that both environmental and genetic influences contribute to the rank-order stability of personality traits, although it appears to be the relative contribution of environment that becomes increasingly important over time (Briley & Tucker-Drob, 2014).

Implications of High Phenotypic Stability

Although a non-negligible proportion of the phenotypic stability of psychological characteristics appears attributable to environmental factors, the very fact that phenotypic stability is high, at least for cognitive abilities, indicates that finding the environmental markers that matter for the stability or change in these characteristics will be difficult. This is simply because limited variance in change means that there is little to relate to other variables. Furthermore, and leaving *change* aside, high phenotypic stability can guide our interpretation of the correlates of individual differences in psychological characteristics at any single point in time. Even if we find substantial correlations between some markers of people's environments and phenotypically stable psychological differences, the environmental markers are unlikely to be interpretable as reflecting causes of individual differences of the psychological characteristics—unless they reflect aspects of environments that are stable across decades too. The environmental experiences that matter for the psychological characteristics typically contribute to the stability of these characteristics (Briley & Tucker-Drob, 2014; Caspi, Roberts, & Shiner, 2005). It is then more plausible that these markers of environment are either effects of variability in the phenotypically stable psychological characteristics (and whatever underlies their stability), or the different kinds of markers simply covary because they reflect some common influences. Either way, high phenotypic stability has profound implications for

Table 2 Explanations of Genetics-Related Terms

Term	Explanation
Genetic correlation	A genetic correlation examines the association between the genetic influences on one trait with the genetic influences on another trait. Two traits having a high genetic correlation means that, largely, the same genetic variants account for individual differences in both of them. The magnitude of genetic correlation is independent from that of phenotypic correlation. For example, even in the event of a small phenotypic correlation, the genetic correlation could be close to unity. Similarly to a genetic correlation, one may calculate an environmental correlation between two variables. This reflects the degree to which environmental influences on the two variables overlap. Its magnitude is also independent of the magnitude of phenotypic correlation.
Genome-wide complex trait analysis (GCTA)	Even in a group of unrelated people, there are common genetic variants that are shared between individuals. Conceptually, GCTA can explore whether unrelated individuals who share more common genetic variants also tend to be more similar in terms of their phenotypic traits or outcomes. The method therefore estimates the proportion of phenotypic variance explained by common genetic variants. As a result, GCTA is complementary to other methods of estimating heritability, such as twin- or adoption-based designs. The method can also be used to estimate genetic correlations. The downside of GCTA is that it requires very large samples.
Additive genetic effects	In order to determine how much influence a number of genes have on a trait, one can sum their individual contributions (additive genetic model). This model assumes that genes influence the trait independently of other genes or the environment. So, additive genetic effects do not include, for example, genetic dominance and epistasis, which are referred to as nonadditive genetic influences. The GCTA-based estimates of heritability and genetic correlations reflect additive effects, as do heritability estimates based on adoption studies, for example. Twin designs, in contrast, allow for estimating both additive and nonadditive genetic effects.
Polygenic risk score	Such scores summarize the genetic "risk" for a particular trait or outcome based on the contributions from many single nucleotide polymorphisms (SNPs). The scores are calculated based on the summary output from genome-wide association studies (GWAS), which contains information on the SNPs, the "effect allele" for each SNP, the regression weight per effect allele in the prediction of the trait, and the *p*-value for the regression statistic. This information can then be used in independent samples to create a risk score for each individual. For each SNP, the number of copies of the risk allele carried by an individual will be multiplied by the regression weight from the initial GWAS. These products are summed across SNPs for each individual to give his or her total risk score. In some circumstances, the best risk score for a trait will use information from only a subset of SNPs. This can be examined by using different thresholds for the inclusion of SNPs, based on *p*-values from the initial GWAS. The threshold that produces the risk scores that most strongly predict the trait is selected.
Linkage disequilibrium	This describes nonrandom associations of alleles: Certain alleles are inherited together more frequently than expected under independence/chance. When genetic information gets passed down across generations, chunks of genetic information tend to be inherited together. Typically, SNPs that are closer together are more likely to be inherited in a single chunk than those farther apart.

attempts to link the stable psychological characteristics to other markers.

PSYCHOLOGICAL CHARACTERISTICS IN RELATION TO MARKERS OF SOCIAL AND HEALTH INEQUALITIES

Social and Health Inequalities as Contributors to Psychological Differences and Changes in These

To the extent that the stability of the rankings of phenotypic characteristics is lower than unity, however, it may make sense to (cautiously) look for potential environmental causes of the variability in them. Besides purely scientific interest, these attempts may be fueled by hopes to be able to intervene on undesirable characteristics such as low or declining cognitive ability or poor mental health. For example, many studies have linked modifiable medical conditions such as diabetes, obesity or cardiovascular disease to cognitive abilities (Nash & Fillit, 2006; Strachan, Deary, Ewing, & Frier, 1997). Especially if such studies are prospective, whereby disease onset has been measured some time before cognitive ability (e.g., Haring et al., 2013), it is hoped that a possible cause of cognitive decline has been identified. For other examples of how social inequalities may be consequential, research has linked exposure to education and multiple languages to higher cognitive ability (Falch & Sandgren Massih, 2011; Kavé, Eyal, Shorek, & Cohen-Mansfield, 2008).

Such findings are notoriously difficult to interpret, however. A contemporaneous correlation between a marker that purportedly indexes something about environment (or something nonpsychological, anyway) and a marker that purportedly indexes psychological differences could imply that either has the causal role—to the extent that there is any causality at all between the

two, of course. Moreover, given the high phenotypic stability of some psychological differences markers, considering individual differences in them as effects of environment may be unjustified, as was discussed above: The differences are often there before the environmental exposures of interest. Even if the marker of environment has been measured a fair number of years before the psychological marker, it may have been the stable level of the latter that contributed to people being exposed to the former in the first place. It is therefore preferable to have information on and control for the lifelong ("premorbid") level of the psychological marker. Put differently, this amounts to looking for the determinants of *change* in individuals' rankings in psychological characteristics—something that may be limited in magnitude, as we have argued above.

Participants of the Lothian Birth Cohorts studies sat an intelligence test at age 11. Although it is likely that many aspects of social inequalities, such as parental education or material resources, would already have influenced children by this time, they had not yet experienced at least some of the social and health inequalities that might be considered relevant for later cognitive differences, such as full educational attainment, job characteristics, or specific diseases (e.g., type 2 diabetes). This has provided a good opportunity to study the extent to which a variety of markers of social or health inequalities may contribute to the—admittedly limited—variance in cognitive ability over and above the variance in its stable baseline levels. Indeed, a number of such factors have been identified.

For example, using the data of LBC1921 and LBC1936, Ritchie, Bates, Der, Starr, and Deary (2013) were interested in the effect of educational attainment on later-life cognitive ability, controlling for age 11 ability. Indeed, it appeared that the length of educational exposure had a significant effect on later-life cognitive ability, with each additional year conferring an additional 1.42 IQ points on top of participants' childhood cognitive ability. However, the study also asked whether the association pertained to cognitive ability as an index of some presumably fundamental aspect of information-processing ability as opposed to the more specific set of skills tapped by the MHT. To this end, educational attainment was also correlated to measures of reaction and inspection time, which were assumed to tap basic information-processing speed and quality. Although more years of schooling predicted shorter reaction times and more correct recognition of stimuli at short exposure times in older age, the associations decreased substantially when age 11 ability was taken into account. It was therefore concluded that education may have a beneficial effect on complex cognitive abilities in a broad sense but not because it improves basic information-processing ability. Ritchie, Bates, and Deary (2015) also showed that the beneficial effect of education on cognitive ability does not pertain to the shared variance of different cognitive skills (*g*) but the domain-specific variance in them.

As another example, LBC1936 data were used to show that speaking one or more non-native languages correlated with several markers of later-life cognitive ability (Bak, Nissan, Allerhand, & Deary, 2014); some of these associations remained significant even when age 11 ability was controlled for. Likewise, Mõttus, Gale, Starr, and Deary (2012) found that age 70 cognitive ability correlated with self-reported quality of life in psychological, environmental, and physical domains even when age 11 cognitive ability was taken into account, suggesting that the correlations pertained to lifelong change in cognitive ability rather than its stable levels. Similarly, characteristics of work experiences, such as occupational complexity (Smart, Gow, & Deary, 2014), have been linked with cognitive abilities of LBC1936 members, as have social support, lack of loneliness (Gow, Corley, Starr, & Deary, 2013), and physical activity (Gow, Corley, Starr, & Deary, 2012).

In a similar vein, a small detrimental effect of smoking on later-life cognitive abilities of LBC1936 members—net of lower childhood cognitive ability, which predisposes people to pick up smoking—has been reported (Corley, Gow, Starr, & Deary, 2012).

Reverse Causation

Although there apparently are examples of how environmental factors may influence cognitive abilities, numerous attempts to identify them have also "failed," as we will discuss below. Given the implications of high phenotypic stability of cognitive abilities, this is, of course, not surprising. Even though a particular marker of environment or health often appears correlated with cognitive abilities in older age, the association might be substantially reduced or vanish completely once the "premorbid" cognitive ability is controlled for.

For example, numerous studies have shown that people with diabetes have lower cognitive abilities than those without the condition, and this is commonly believed to reflect the cognition-impairing effects of diabetes (Strachan, Reynolds, Marioni, & Price, 2011). Mõttus, Luciano, Starr, and Deary (2013) compared the age 70 cognitive ability of LBC1936 members with and without diabetes and found the expected difference: Those with the condition scored about a third of a standard deviation lower than those without it. However, nearly identical association was observed between diabetes status at age 70 and cognitive ability scores at age 11—the latter being far earlier than most people with diabetes would have developed the condition. This suggests that the cognitive ability difference between those with and without diabetes had existed long before diabetes emerged in those with the condition. To the extent that this finding is generalizable, it turns the diabetes–cognitive ability association on its head: It must be either low cognitive ability (and perhaps its associated lifestyle and health choices) that contributes to diabetes or they both have to reflect some common underlying influences.

As another example, Mõttus, Gale, Starr, and Deary (2012) observed an association between LBC1936 members' cognitive abilities at age 70 and the level of deprivation of their neighborhood as measured by the Scottish Index of Multiple Deprivation (SIMD; Scottish Executive, 2006). Those in more deprived neighborhoods had lower cognitive abilities. However, the

association was no longer detected once age 11 cognitive ability had been controlled for, suggesting that it was not living in a poor neighborhood—and whatever else this typically is accompanied by—that lowered cognitive abilities, but the other way around; those who had had lower long-standing cognitive abilities were more likely to be found in more deprived conditions. Likewise, it is often believed that intellectual engagement is beneficial for cognitive aging. Gow and colleagues (2012) set out to test this and observed positive correlations between a measure of social-intellectual engagement and various markers of cognitive ability at age 70. However, most of the associations were substantially attenuated and ceased to be statistically significant when age 11 cognitive ability was controlled for.

Correlates of Changes in the Big Five Traits

Finding predictors of personality change has also proven relatively difficult. This conclusion is concordant with previous suggestions that attempts to identify specific markers of environment that substantially and reliably matter for personality have yielded only modest results (Turkheimer & Waldron, 2000), although other authors may have different views (e.g., Specht et al., 2014; Specht, Egloff, & Schmukle, 2011). We present an example based on published LBC1921 data and a novel example based on LBC1936 data (reported here for the first time).

Mõttus, Johnson, Starr, and Deary (2012) used the data from 209 LBC1921 members who had completed a 50-item Big Five questionnaire twice over a period of about 6 years in their ninth decade of life to construct a latent growth curve model for each Big Five trait. Such models result in two latent traits, with one (intercept) representing the baseline trait level and the other (slope) representing change. We were interested in two questions. Was there reliable variability in the rates of change in the personality traits as would have been indicated by significant variances in the slope scores? Could this variance be predicted from what were considered markers of the most important domains of life at this age: physical fitness, cognitive ability, and level of independent functioning? Slopes of all Big Five domains showed significant variance, but we found only one significant effect on them: Higher cognitive functioning at age 79 predicted less decline in Conscientiousness in the ninth decade of life. We also found that decline in Conscientiousness was associated with decline in physical fitness, potentially reflecting either causal effects in either direction or some common influences acting on these two markers of individual differences. Given the number of associations tested for, however, these could have easily been chance findings (Mõttus, Johnson, Starr, & Deary, 2012).

Taking advantage of the fact that LBC1936 members have now provided three assessments of their Big Five traits, we also present some novel analyses. We created latent growth models for each of the traits such that both intercepts and slopes were defined by the sum scores of the appropriate traits at about ages 70, 73, and 76 years (the use of sum scores as indicators of the intercept and slope traits was justified by full [strict] measurement invariance across the three testing occasions). Although the slopes of only three of the five traits (Emotional Stability, Extraversion, and Conscientiousness) displayed significant variance, we decided to predict the slopes of all Big Five traits from the markers of the three arguably most important life domains considered in Mõttus and colleagues (2012): cognitive ability, physical fitness, and independent functioning. For each measurement occasion, cognitive ability was indexed as a principal component score of six WAIS-III subtests;[2] physical fitness was a principal component score of 6 meter walk time, grip strength, and forced expiratory volume in one second; and independent function was the score of Townsend Disability Scale (Townsend, 1962). For each Big Five trait, three bifactor latent growth models were constructed, where personality intercepts and slopes were defined as above, but additionally, a slope and an intercept for a covariate (either cognitive ability, physical fitness, or independent functioning) were defined by its scores from the three testing occasions (Figure 1). The number of observations varied slightly across models, being generally around 600 (for each analysis, data from participants with complete observations were used; see Table 3 for details). Models fit the data well, such that all comparative fit index values exceeded .95 and all root mean square error of approximation values were below 0.05.

The slope of each trait was predicted from the baseline levels of the three covariates. However, from among the 15 predictions (five traits and three covariates), only one was significant: The slope of Agreeableness was predicted by baseline physical fitness ($r = .25$, $p = .02$). Besides, we observed several correlations between personality and covariate slopes. Declining cognitive ability was tracked with declining Conscientiousness ($r = .33$, $p = .009$) and Agreeableness ($r = .42$, $p = .02$). Declining independent functioning was linked to declining Extraversion ($r = .18$, $p = .04$). Again, however, given the number of associations, it is possible that some or even all of the associations reflect chance findings.

Based on these data, there is limited evidence for changes in personality traits in older age being predictable from markers of individual differences in other arguably important domains of life. There may be somewhat stronger evidence, however, for personality change being in lockstep with changes in these other life domains. For example, declines in cognitive ability may contribute to declines in Conscientiousness-type behaviors because these require a certain level of cognitive functioning, or the other way around. Or, again, declines in Conscientiousness and cognitive ability may travel together because they both reflect a more general decline process.

GENES STEP IN

System Integrity as an Alternative Explanation

There is another explanation for the association between cognitive abilities and markers of health and social inequalities: They all may reflect some more general property of the organism.

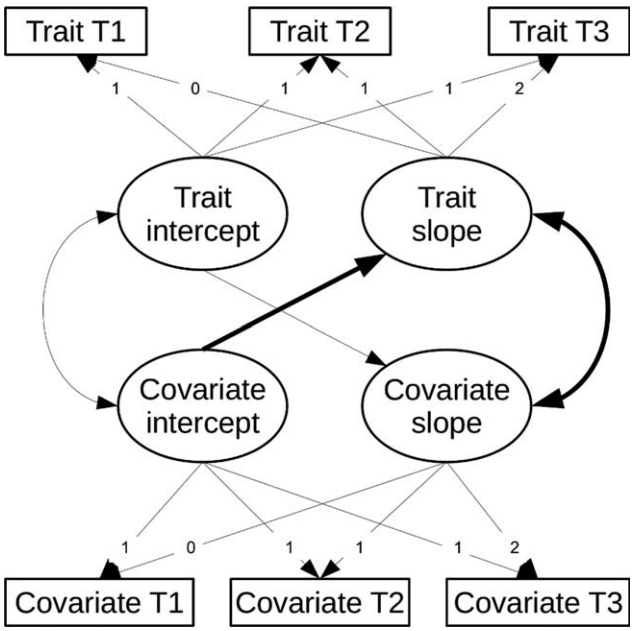

Figure 1 Bivariate latent growth model. Trait = personality trait; Covariate = either cognitive ability, physical fitness, or independent functioning; T1 = age about 70; T2 = age about 73; T3 = age about 76. Paths of interest are indicated in boldface.

Such a general property reflecting individual differences in overall build quality has been called "system integrity" (Deary, 2012). There is, as yet, no direct measure of or evidence for such a phenomenon. Instead, its plausibility has been inferred indirectly from observations that lifelong cognitive ability (measured in childhood) predicts mortality and various health conditions, controlling for possible environmental mediators or confounders such as education, occupational social class, or a wide range of health-related behaviors (Calvin et al., 2011). The childhood cognitive ability–mortality association, however, appears to be notably reduced when other and possibly closer markers of system integrity, such as basic information-processing speed, are controlled for (Deary & Der, 2005). Other evidence potentially in favor of a system integrity–type construct includes findings that psychomotor coordination in childhood correlates with seemingly very different health outcomes in later life, such as psychological distress or obesity (Gale, Batty, Cooper, & Deary, 2009), or that cognitive ability—a general marker of cognitive development—correlates with the (fluctuating) symmetry of body, which is an ostensible marker of the stability of bodily development (Banks, Batchelor, & McDaniel, 2010). Interestingly, bodily symmetry also correlates with basic information-processing speed and robustness (Hope, Bates, Dykiert, Der, & Deary, 2015), and it increases over childhood (Hope, Bates, Dykiert, Der, & Deary, 2013), as does cognitive performance. Higher cognitive abilities have also been associated with the ability of the brain to cope with systematic insults (Santarnecchi, Rossi, & Rossi, 2015).

To the extent that system integrity is a viable construct, its effects may be reflected not only in cognitive traits and markers of physical health but, perhaps eventually, also in other markers of psychological or social inequalities. For example, we might expect educational and occupational performance and their economic and social correlates, such as income or neighborhood quality, to partly reflect this general property. Even if a well-built organism provides one with only a little advantage for any given specific outcome—a skill or an aspect of health, for example—the small advantages may cumulate into a much bigger advantage over time and across its multiple manifestations.

Genes as a Tool for Testing the Effect of System Integrity

Since the biological underpinnings of system integrity are not known, it cannot be measured and thereby controlled for when markers of psychological differences are linked to each other or those of social and health inequalities. It seems plausible to assume, however, that it might, at least in part, reflect some sort of genetic variance. If so, the genetic variance should be reflected in the numerous possible manifestations of system integrity. Given this, a plausible way to study the possibility that a particular association is confounded by system integrity is to use genetic data and expect to see a genetic correlation between the phenotypically related characteristics. For example, it has been found elsewhere that having a college education has

Table 3 Correlations of Personality Slopes From Age 70 to 76 With the Baseline and Change in Cognitive Ability, Physical Fitness, and Independent Functioning (LBC1936)

	Cognitive Ability $N = 593–596$		Physical Fitness $N = 597–600$		Independent Functioning $N = 618–621$	
	Intercept	Slope	Intercept	Slope	Intercept	Slope
Emotional Stability	–.07	.08	–.05	.11	–.04	–.08
Extraversion	.10	.07	.08	.17	–.05	.18*
Intellect	.15	.21	.12	–.19	–.01	–.06
Agreeableness	.05	.42*	.25*	–.05	–.13	–.19
Conscientiousness	.05	.33**	.10	.11	–.02	–.11

Note. N = number of observations used. The estimates are standardized path coefficients.
*$p < .05$. **$p < .01$.

genetic correlations with various markers of physical and mental health (Bulik-Sullivan et al., 2015); it is possible that markers of (normal) psychological variation do as well. Of course, system integrity may not reflect only genetic influences. For example, facial symmetry was reported to be associated with parental socioeconomic status, although bodily symmetry was not (Hope, Bates, Penke, et al., 2013). Facial symmetry being a potential marker of the stability of bodily development and thereby system integrity, this finding suggests that nongenetic factors may also contribute to variance in the construct—to the extent that parental socioeconomic status is independent of children's genes, of course.

Can Other Markers of Psychological Differences Reflect System Integrity?

The concept of system integrity originates from research into cognitive abilities and was devised as one possible explanation for their associations with mortality (Deary, 2012). Its relevance for other markers of individual differences is not clear yet. It must also be borne in mind that cognitive abilities are relatively (though not completely) phenotypically uncorrelated with at least some other markers of psychological differences such as occupational interests or personality traits (Ackerman & Heggestad, 1997), which themselves tend to form a positive manifold (Van der Linden, te Nijenhuis, & Bakker, 2010).

However, a somewhat similar logic might be and has been applied to other markers of psychological differences such as personality traits. Their associations with markers of health and social inequalities might to some, or perhaps even a large, degree reflect some sort of shared genetic variance (a general genetic "pull"; Turkheimer, Pettersson, & Horn, 2014). Our above-reported findings that changes in personality traits may at least occasionally be in lockstep with changes in the markers of other major domains of later life are consistent with this possibility. Findings that early-life measures of personality predict later health, well-being, and mortality and that not all of these associations can be accounted for by known and measurable candidate mediators (Gale, Booth, Mõttus, Kuh, & Deary, 2013; Hampson, Goldberg, Vogt, & Dubanoski, 2006, 2007; Jackson, Connolly, Garrison, Leveille, & Connolly, 2015) are also consistent with this possibility (although alternative explanations such as mediation via as yet unknown pathways remain equally possible). As with cognitive abilities, the feasibility of the hypothesis that markers of personality differences reflect at least partially overlapping ground with other markers of individual differences can be tested by using genetic data.

GENERATION SCOTLAND

Using a wide range of relevant examples, we have been building an argument that at least occasionally and at least some of the observable associations between markers of psychological differences and markers of health and social inequalities may be difficult to interpret in terms of direct causality among them, especially given the apparently high phenotypic stability of psychological differences. Influences may flow in both directions, but—and this is the possibility we want to emphasize here—there may be no direct phenotype-to-phenotype causality at all. That is, a case can be made that the variables that we consider as indexing different domains of life may sometimes appear correlated simply because of reflecting shared etiology. One way to test this possibility is to make use of genetic data. A standard approach to testing and accounting for shared genetic influences has been using twin-based designs. Here, we make use of an alternative approach (GCTA; see Table 2 for details), which is based on molecular genetic data of unrelated individuals. This approach requires large samples of people with SNP data available in addition to the phenotypic markers of interest.

A useful resource for applying this approach is provided by Generation Scotland (GS). GS is a large, population-based, family-structured study from across Scotland. A total of 7,953 probands (aged between 35 and 65 years) were recruited mostly through their general medical practitioner (GP) in five regions of Scotland (Glasgow, Tayside, Ayrshire, Arran, and North-East Scotland). The probands' family members were then invited to participate in the study. A total of 24,084 individuals were recruited at the baseline wave of GS, which ran from 2006 to 2011. The age range of the sample was between 18 and 100, and up to three generations of families were sampled. Over 5,600 families participated in total, with a mean of four members per family (maximum of 37). Note that for many analyses, such as those reported in this article, only one member per family is used because the employed method (i.e., GCTA) assumes unrelated individuals. Lifestyle, health, physiological, genetic, and biomarker data were collected on participants along with data linkage to routine medical health records. Add-on studies to the initial wave will provide longitudinal clinical and biomarker data on population subsets with a particular focus on depression, cognitive ability, and mental health. Full details of the cohort have been given by Smith and colleagues (2013) and can be accessed at http://www.generationscotland.org.

Evidence for Shared Genetic Effects: Cognitive Abilities

Existing GS analyses have investigated the phenotypic and genetic associations between cognitive ability and various markers of social or health inequalities, such as education, neighborhood deprivations (SIMD, a marker of socioeconomic status), and height. All four of these are complex traits with additive genetic effects that could be detected using the univariate GCTA method (see Table 2 for a definition of additive genetic effects). The proportion of individual differences in each trait explained by the additive effects of common genetic variants was .29 (general cognitive ability; *g*), .21 (education), .18 (SIMD), and .58 (height; Marioni, Batty, et al., 2014; Marioni, Davies, et al., 2014). For *g*, education, and SIMD, family-based

heritability estimates have also been calculated and found to be higher (respectively, .54, .41, and .71; Marioni, Davies, et al., 2014).

The phenotypic correlation between cognitive ability and education was .39, whereas for cognitive ability and SIMD it was .25. This is about what one would expect based on the literature (Strenze, 2007). What we are more interested in here, of course, are genetic correlations: the proportions of variance that variables share due to common genetic causes. Genetic correlations can have any magnitude regardless of the phenotypic correlations, such that even phenotypically unrelated variables may share genetic influences or vice versa. To the extent that various markers of individual difference tap the same underlying variance—the question we are particularly interested in—they are expected to be genetically correlated.

Interestingly, the genetic correlation between *g* and education neared unity (.95, *SE* = .13), suggesting that the additive genetic effects underlying the marker of psychological differences almost completely overlapped the additive genetic variants underlying a marker of social inequalities. This is consistent with findings based on more traditional behavior genetic approaches (e.g., Calvin et al., 2012). The genetic correlation between *g* and SIMD was notably lower (.26, *SE* = .16), suggesting that although there is additive genetic variance related to where one lives, this variance is only partially overlapping with that of cognitive abilities. A somewhat smaller phenotypic correlation was observed between cognitive ability and height (.16), but there was a significant genetic correlation (.28, *SE* = .09).

In combination, these findings highlight some genetic overlap of cognitive ability with markers of social inequalities as well as such a basic anthropometric measure as height. Interestingly, all of these markers of individual differences are commonly used as predictors of health outcomes or covariates in models featuring cognitive ability. Therefore, among other implications, our results suggest that researchers need to consider the possibility of overfitting such models, given the shared genetic contributions to these characteristics.

Ongoing GS-based analyses are investigating the molecular genetic overlap between *g* and body mass index (BMI)—another common correlate of life-course health outcomes—as well as the abilities of the polygenic "risk scores" for these traits to predict across phenotypes. For example, does a polygenic risk score for BMI predict variance in *g*? The polygenic risk scores aggregate small (and mostly statistically nonsignificant) genetic effects of up to hundreds of thousands of SNPs in relation to a phenotype into a single genetic propensity prediction index. Typically, the genetic effects found for a large number of SNPs in an independent and sufficiently powerful study, regardless of their statistical significance, are used to create such risk scores (see Table 2 for additional details). For example, Luciano and colleagues (2014) aimed to see whether there was genetic overlap in cognitive ability and diabetes. For this, the authors used the effect sizes of hundreds of thousands of SNPs in relation to type 2 diabetes found in a large meta-analysis (Morris et al., 2012), created diabetes risk scores for a combined sample of about 3,000 Britons, and then used these risk scores to predict their cognitive abilities. The results of this study showed little genetic overlap. However, when a similar risk score technique was used to investigate the shared genetic basis of schizophrenia and cognitive ability (*g*), significant overlap was observed (McIntosh et al., 2013). Also, polygenic risk for autism spectrum disorders has been found to correlate with different markers of cognitive abilities (Clarke et al., in press). GS offers a rich resource for such hypotheses to be tested.

As GS includes family structures, its data have also been used in more traditional behavior genetic analyses to disentangle the associations between markers of psychological differences and markers of social and health inequalities. For example, Luciano and colleagues (2010) showed substantial genetic overlap in cognitive ability and a range of cardiovascular disease risk factors.

Evidence for Shared Genetic Effects: Other Markers of Psychological Differences

While twin studies have presented thousands of heritability estimates for personality traits and amounted to a conclusion that about 50% variance in almost whichever of them reflects genetic variance (Bleidorn, Kandler, & Caspi, 2014), GCTA-based estimates have only recently started to emerge and have been more modest in size (e.g., Verweij et al., 2012; Vinkhuyzen et al., 2012). With its large sample size, GS is a useful data set for carrying out such analyses, although participants' personality self-ratings have currently been obtained using only the Neuroticism and Extraversion scales (each operationalized using 12 items) of the brief version of Eysenck's Personality Questionnaire (Eysenck, Eysenck, & Barrett, 1985). These data are summarized in Figure 2. At this moment, therefore, the spectrum of personality traits is covered to a limited extent in GS, although there will be efforts to broaden the spectrum. Here, we report novel, previously unpublished analyses pertaining to Neuroticism and Extraversion in GS: their GCTA-based heritability estimates as well as phenotypic and genotypic correlations with education, cognitive abilities, and social class.

Univariate GCTA estimates (Yang et al., 2011) for Neuroticism and Extraversion scales were calculated in the same unrelated sample of individuals as used for previously described GS analyses. The personality scale scores were far from being normally distributed (Figure 2) and were therefore normalized by using an averaged angular transformation (Vinkhuyzen et al., 2012). Linear regression was used to control for age, sex, and population stratification (the first six multidimensional scaling components). Residuals from these models were obtained and transformed using a rank-based inverse normal transformation prior to the GCTA analyses. The GCTA estimates for Neuroticism and Extraversion were .16 (*SE* = .06, *N* = 6,349) and .11 (*SE* = .05, *N* = 6,344), which represent small but significant proportions of variance. These estimates are slightly higher than most of the few previously published estimates (Verweij et al., 2012; Vinkhuyzen et al., 2012), but still smaller than twin-based

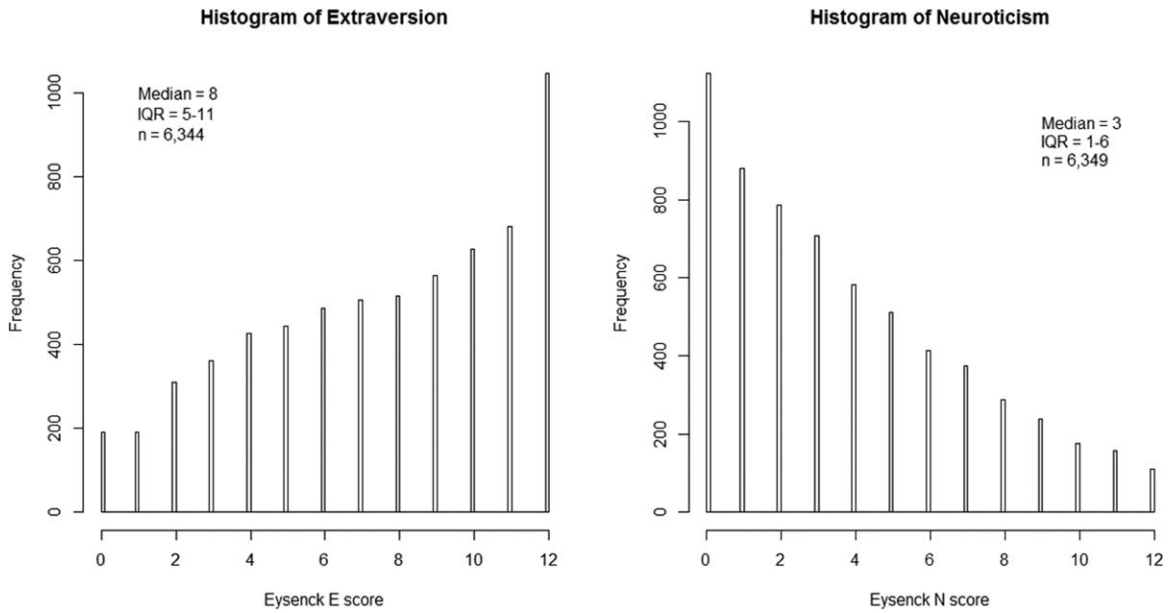

Figure 2 Distribution of Extraversion and Neuroticism scale scores in Generation Scotland.

estimates. This is an important finding, possibly suggesting that a substantial proportion of genetic variance in personality traits is nonadditive.

Prior to assessing whether the personality measures have shared genetic contributions with *g*, education, or SIMD, we first investigated their phenotypic correlations (see Table 4). The correlations were all very small, with the exception of those of Neuroticism with *g* and SIMD (–.08 and –.13, respectively). We therefore took these variables forward to the bivariate GCTA analysis (Lee, Yang, Goddard, Visscher, & Wray, 2012). SIMD and *g* were treated in a similar manner to Neuroticism: Linear regression was used to obtain age-, sex-, and stratification-adjusted residuals, which were transformed using a rank-based inverse normal transformation. Bivariate GCTA was then used to obtain their genetic correlations with Neuroticism.

We observed a large, negative genetic correlation of –.69 (*SE* = .20) between Neuroticism and *g*, which implies that 69% of the genes associated with better cognitive function are also associated with a lower Neuroticism score. This finding is especially interesting given that a much more modest phenotypic correlation is typically observed between them (Ackerman & Heggestad, 1997). The genetic correlation between Neuroticism and SIMD was –.09 (*SE* = .25), indicating no significant genetic overlap between the genetic influences on these markers.

In sum, we hope to have shown that molecular genetic data and modern quantitative genetic techniques can be used to estimate the genetic contribution to the variances and covariances of the markers of psychological differences and social and health inequalities. For example, such findings may point to situations where observed associations between markers that ostensibly index different domains of variability may in fact tap into at least partially overlapping domains (e.g., cognitive abilities and education or height). With respect to markers of psychological differences, these data and techniques may currently work better for cognitive abilities, as they yield higher GCTA-based heritability estimates and thereby contain more of the kind of signal that the approach can pick up. GCTA estimates additive genetic variance and covariance, and there seems to be less of that for personality traits. However, we still observed a large genetic correlation between Neuroticism and general cognitive ability.

A LURKING POSSIBILITY OF CONSTRUCT (OR MEASUREMENT) OVERLAP

When we find that some markers of genetic variability are related to phenotypes of interest, we want to make sure that the markers are reasonably independent in terms of not being in linkage disequilibrium with each other (see Table 2 for additional details). This is because nonrandom co-segregation of alleles could result in false signals in genetic studies. Similarly, when linking markers of phenotype to one another or to markers of genetic variability, we are well advised to consider the possibility of phenotypic construct

Table 4 Phenotypic Correlations Between Generation Scotland Variables

	g	Education	SIMD
Neuroticism	−0.08	−0.04	−0.13
Extraversion	−0.03	−0.05	−0.03

Note. *g* = general cognitive ability; SIMD = Scottish Index of Multiple Deprivation.

overlap—or at least overlap in how the underlying constructs are measured. Markers of both psychological differences and social and health inequalities reflect samples of behaviors, skills, knowledge, or (nonrandom) life circumstances, and it is possible that the samples that we regard as reflecting distinct domains may well be at least partially overlapping.

For example, considering Neuroticism and mental well-being markers of ontologically distinct domains of individual differences and explaining one broad characteristic (well-being) with another (Neuroticism) seems a possible example of such construct overlap. In addition to this, associations between these constructs may be confounded by direct measurement overlap, whereby items to measure one characteristic may be very similar to the items used to measure the other (Gale et al., 2013). It is then no surprise that the constructs also appear genetically overlapping (Weiss, Bates, & Luciano, 2008). Likewise, relating self-rated aspects of quality of life, such as satisfaction with one's physical environment or social relations, to objectively measured physical and social environment quality may entail the risk of explaining something by itself (Mõttus, Gale, Starr, & Deary, 2012). In a similar vein, when we find that a personality trait that is assessed, among other items, with questions referring to overeating predicts body weight, this may refer to something trivial (Vainik, Mõttus, Allik, Esko, & Realo, in press).

Another example of such construct/measurement overlap pertains to cognitive abilities and health literacy, a well-established marker and predictor of health inequalities that is closely tied to other markers of social inequalities (Rudd, 2010). Apparently, the concept of health literacy, or at least its most popular operationalizations, are only negligibly different from other markers of cognitive abilities that have been well established and researched for well over a century (Murray, Johnson, Wolf, & Deary, 2011; Wolf et al., 2012). Furthermore, the apparent links between health literacy and various markers of health seem to be almost fully explainable by the links between other cognitive abilities and health (Mõttus et al., 2014). Identifying such cases of construct/measurement overlap is not only important for our understanding of how psychological differences are linked to markers of social and health inequalities but also has practical implications. For example, interventions targeted at improving or dealing with the consequences of low health literacy can be informed by decades of research on other cognitive abilities.

There exist ways of mitigating measurement overlap, at least to some extent. In personality trait research, for example, self-ratings could be supplemented with ratings of knowledgeable informants (Kandler, Riemann, Spinath, & Angleitner, 2010; Mõttus, Allik, & Pullmann, 2007) or behavioral measurements (Furr, 2009), or directly overlapping items can be omitted from the analyses (Gale et al., 2013). In cognitive ability research, the influence of measurement overlap may also be reduced by employing behavioral tasks such as reaction or inspection time measurements (e.g., Ritchie et al., 2013) or tasks specific to the construct at hand (Wolf et al., 2012).

CONCLUSIONS

Associations among the markers of psychological differences and social and health inequalities are pervasive, albeit often modest in size, and likely to interact with genetic variation. The life-course-spanning research described in this article makes the case for being open to very different causal interpretations of the associations. In principle, any of these variables may serve as both predictor and outcome. And what also seems plausible in many cases is that the variables that we believe to index different domains of individual differences tap something at least partially overlapping, potentially causing spurious associations. Cognitive abilities and educational attainment constitute a good example: Whatever are the underlying processes that individual differences in them refer to, these processes seem to reflect a largely overlapping genetic basis. But the overlap does not necessarily have to be genetic, as occasionally our constructs of interest, or at least their measurement, may overlap phenotypically. The previously published findings reviewed here as well as the new analyses presented for the first time demonstrate how molecular genetic data coupled with modern quantitative genetic techniques can help to understand the network of factors surrounding psychological differences and social and health inequalities.

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Notes

1. The exact mean ages were 69.5 ($SD = 0.71$), 72.5 ($SD = 0.83$), and 76.2 ($SD = 0.68$).
2. The subtests used were Block Design, Matrix Reasoning, Symbol Search, Digit Symbol-Coding, Digit Span (backward), and Letter-Number Sequencing.

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