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Genes for Well-Being, Depression, and Neuroticism: No Need to Worry—We Are Largely Responsible for our own Happiness

Philipp Koellinger, Lars Bertram, & Gert G. Wagner*

gwagner@mpib-berlin.mpg.de

An international consortium of 178 researchers from various disciplines studied anonymized genetic data from almost 300,000 people and discovered new genes associated with life satisfaction and well-being. Data from the Berlin Aging Study II (BASE-II) were included in the analysis. The study, published in *Nature Genetics*, shows diverse genetic links between well-being (life satisfaction), depression, and neuroticism (Okbay et al., 2016). The genetic effects now identified are, however, only responsible for a very small fraction of the heritability of psychological well-being and explain less than one percent of the differences in well-being in the population.

Using a genome-wide association approach, the study found three variants of the DNA sequence (single nucleotide polymorphisms or SNPs) to be linked with subjective well-being, and more than a dozen SNPs with neuroticism and depression. Although it has been known for some time that these three traits have a genetic component, very few specific genetic variants related to these traits have been identified in the research to date. What can we learn from these findings?

One important reason for the lack of statistically unambiguous results in previous studies was their use of relatively small sample sizes. When examined individually, each genetic variant explains very little about the traits of interest, implying that very large sample sizes are needed to identify such small effects reliably. This has now been achieved in the present study, where the investigators have collected data from nearly 300,000 individuals. This sample size was sufficient for the reliable detection of SNPs exerting only very small effects. However, even though these new findings can be considered as unambiguous statistically, they only explain very little of the interindividual differences in the population.

The limited explanatory power of individual genes does not contradict the often substantial heritability of personality traits. Striking similarities are often found within a family ("she's so much like her grandmother") due to the influence of thousands, if not millions, of different genetic variants that all exert only small effects when considered separately. When considered jointly, however, these small effects can add up to account for much larger shares of the observed differences across individuals. It is noteworthy that—with the exception of monozygotic twins (who are genetically ~100% identical)—the combination of genetic patterns passed on from parents to children are unique to the particular individual. Thus, heritability does not contradict the enormous individuality human beings possess.

Ultimately, psychological well-being is jointly influenced by both genes and environment. To give one illustrative example, suppose that genetic variants influenced how extraverted, or outgoing, an individual is. Furthermore, suppose that being more extraverted would help a person to make more friends, which in turn would make the person happier. In this example, changes to the intermediate environmental channel—the number of friends—could have drastic effects on the outcome of happiness. Indeed, the genetic association might not be found in environments where a person's number of friends is less strongly related to extraversion, such as in a close-knit community where people tend to know each other personally (Benjamin et al., 2016).

* Philipp Koellinger is Professor of Genoeconomics at Vrije Universiteit Amsterdam, Lars Bertram is Professor of Genome Analytics, Universität zu Lübeck, Germany, and Reader in Neurogenetics at Imperial College London. LIFE faculty Gert G. Wagner is a Max Planck Research Fellow at the MPIB and a board member of the German Institute for Economic Research (DIW Berlin), where Philipp Koellinger is a Research Fellow. Bertram and Wagner are co-principal investigators of the Berlin Aging Study II (BASE-II). Koellinger is one of the principle investigators and co-founders of the Social Science Genetic Association Consortium (SSGAC) and one of the main authors of the study cited, which also used BASE-II data.

Conversely, social circumstances can increase life satisfaction, even when the gene pool of the population does not change. For example, assume that people react negatively to social inequality. Here, it may be possible to increase the average well-being of the population through redistribution of resources like income.

Furthermore, even if the genetic effects on well-being operated entirely through non-environmental mechanisms that are difficult to modify (such as direct influences on the neurotransmitters that operate in the brain's reward pathways), powerful non-genetic interventions may still exist that, if implemented, could change the outcome of the genetic effects. Or, to use the famous example given by economist Arthur Goldberger: Even if all the variation in unaided eyesight were due to genes, these problems could be overcome by wearing glasses. Indeed, the non-genetic intervention of glasses often counteracts 100% of the genetic effects on eyesight (Goldberger, 1979).

Thus, in contrast to medical genetics, where genetic testing can predict the occurrence of some disease with great certainty (e.g., Huntington's disease or certain forms of Alzheimer's disease), genetic research into polygenic traits, such as life satisfaction or well-being cannot be expected to provide an accurate prediction of outcome. This is due to the tiny effects exerted by the individual DNA variants and their potentially complex interactions with the environment.

Nevertheless, genetic studies like the one by Okbay et al. (2016) can help to identify biological mechanisms that are relevant for mental health. Recently published findings in schizophrenia research provide a pertinent example. Using genome-wide association analyses similar to those applied in studies of subjective well-being, researchers identified over 100 genetic variants that contribute to the risk of schizophrenia, each with a small effect (Schizophrenia Working Group of the Psychiatric Genomics Consortium, 2014). Some of the identified genes appear to affect the regulation of the immune system. Follow-up research has since confirmed that specific biological mechanisms involved in the immune response do indeed contribute to the risk of schizophrenia. These mechanisms were previously unknown and may point the way toward new approaches to the diagnosis and treatment of this psychiatric condition (Sekar et al., 2016).

References

Benjamin, D., et al. (2016). *FAQs about "Genome-wide association study identifies 74 loci associated with educational attainment."* Retrieved from SSGAC website: www.thessgac.org/faqs

Goldberger, A. S. (1979). Heritability. *Economica, 46*(184), 327–347. doi: 10.2307/2553675.

Okbay, A., Baselmans, B. M. L., De Neve, J.-E., Turley, P., Meddens, S. F. W., ... Cesarini, D. (2016). Genetic variants associated with subjective well-being, depressive symptoms, and neuroticism identified through genome-wide analyses. *Nature Genetics, 48,* 624–633. doi: 10.1038/ng.3552

Schizophrenia Working Group of the Psychiatric Genomics Consortium (2014). Biological insights from 108 schizophrenia-associated genetic loci. *Nature, 511*(7510), 421–427. doi: 10.1038/nature13595

Sekar, A., Bialas, A. R., de Rivera, H., Davis, A., Hammond, T. R., Kamitaki, N., ... McCarroll, S. A. (2016). Schizophrenia risk from complex variation of complement component 4. *Nature, 530*(7589), 177–183. doi: 10.1038/nature16549.

Websites

BASE-II: www.base2.mpg.de

SSGAC: www.thessgac.org

BASE II
Berlin Aging Study II

Social Science Genetic Association Consortium