

Neurobiology of intelligence: Health implications?

JEREMY R. GRAY AND PAUL M. THOMPSON

Understanding the neurobiology of intelligence may, in turn, help illuminate the complex relationships between intelligence and health. There is strong evidence that the lateral prefrontal cortex and possibly other brain areas support intelligent behavior. Variations in intelligence and brain structure are heritable, but are also influenced by factors such as education, family environment, and environmental hazards. These exciting scientific advances encourage renewed responsiveness to the social and ethical dimensions of such research, including its health-relevance.

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A scientific understanding of human intelligence is more advanced and less controversial than widely realized, and permits some definitive conclusions about the biological bases to be drawn. We recently reviewed this work (Gray & Thompson, 2004), and here summarize some of the key findings. In addition, we briefly elaborate the potential relevance of intelligence to health. Research on human intelligence has progressed at three broad levels of analysis: behavior, biology, and the wider context. Understanding the health implications will require understanding these complex relationships in terms of specific causes and effects.

Childhood intelligence is significantly related to adult morbidity and mortality, although the reasons for this are not clear. More intelligent individuals may simply better avoid injury and better care for their own health.

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In addition, intelligence may act as a "cognitive reserve" or buffer against various forms of neurodegeneration (Stern, 2003). There are several variations on this theme. For example, in Vietnam veterans who were exposed to combat, those with higher intelligence subsequently had a lower incidence of Post-Traumatic Stress Disorder (McNally & Shin, 1995). Higher premorbid intelligence also appears to buffer people against schizophrenia and severe depression. Yet a high IQ is not always a good thing. People with higher IQs are not diagnosed with Alzheimer's Disease as prevalently as with the general population, perhaps because they can better compensate for cognitive difficulties. Obsessive Compulsive Disorder (a form of debilitating anxiety) is more prevalent in individuals with higher intelligence. Collectively, these findings point to the need to understand the neurobiological systems in more detail. Next, we briefly review the state of current research.

Neural Bases of Intelligence

In the late 19th century, studies of patients with brain damage implicated the frontal lobes in abstract reasoning, an ability that is strongly related to intelligence. Modern studies have both reinforced and refined these conclusions. John Duncan, of Cambridge University, and his colleagues have suggested that the frontal lobes are more involved in fluid intelligence (reasoning and solving novel problems) and goal-directed behavior, and less involved in crystallized intelligence (skills and knowledge that have been previously learned, such as vocabulary).

Brain imaging studies have consistently found a moderate relationship between intelligence and brain structure in healthy subjects. For example, we found that general intellectual function (*g*, for general intelligence) was

significantly linked with differences in frontal gray matter volumes as measured using MRI; see Figure 1A.

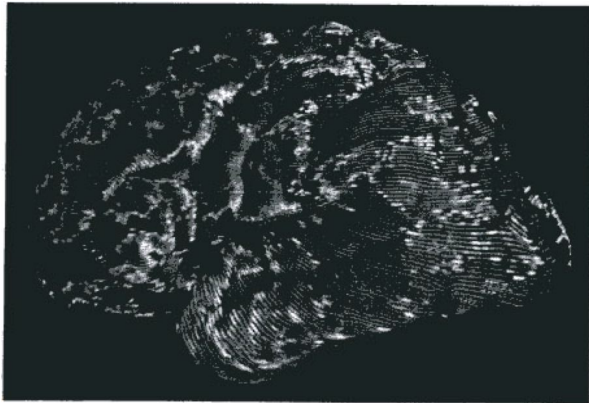
Moreover, by testing twins, we were able to determine that this relation was due primarily to genetic factors (Thompson et al., 2001). Intelligence therefore partly depends on structural differences in the brain that are under very strong genetic control. At the same time, other studies have shown that the structure of the brain is not completely determined by genes: learning a difficult perceptual motor skill (juggling) induced 3% increases in the volume of gray matter in visual attention areas. Such plasticity of brain structure in response to training has not been shown everywhere in the brain, but the juggling example does at least suggest that gray matter volume could be correlated with intelligence partly because more intelligent individuals seek out more challenging activities, exercising their mental muscles and thereby bulking up their gray matter.

MRI and PET can also be used to detect changes in blood flow that are linked to changes in neural activity. (This is *functional* neuroimaging, for revealing dynamic brain activity related to function.) Measuring brain activity in this way while participants perform an intelligence test can help identify regions that support

intelligent behavior. Duncan and colleagues (2000) predicted and found that only one region is consistently activated across three different intelligence tasks when compared to control tasks. Neural activity in several areas, as measured by a PET scan, was greater during more difficult (high-*g*) than easier (*low-g*) tasks, but the lateral prefrontal cortex was the only region consistently activated in all conditions. Conversely, other studies found widespread activity during the performance of problems from intelligence tests. This result is consistent with one of the major insights about higher brain function, that the "functional units" of higher cognition are networks of brain areas, rather than single areas. These studies have compared harder tasks against easier tasks, rather than looking at how people differ.

Frontal and parietal regions that are activated during intelligence tests are also activated during tasks of "working memory," or keeping information actively in mind and manipulating it (which people often have while solving a complex problem). The importance of working memory to intelligence was initially suggested by extensive studies on individual differences in fluid intelligence and performance on working memory tests. Research by Randy Engle and colleagues, at the Georgia Institute of Technology, suggests that the abili-

A



B

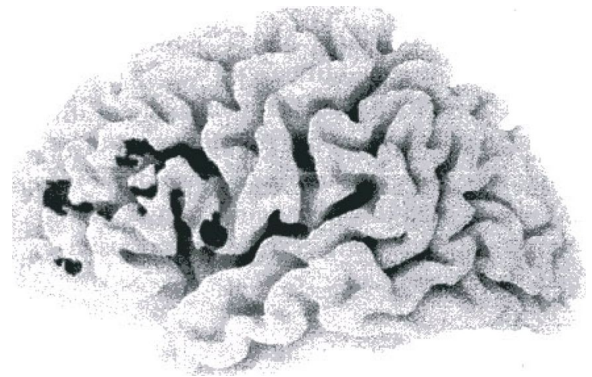


Figure 1. Different methods of assessing the relation between intelligence and the brain implicate similar brain regions (left hemisphere views shown). A, Regions in which the volume of gray matter is primarily under genetic control are shown in red and these volumes are also linked with IQ (Thompson et al., 2001). B, Individual differences in fluid intelligence are correlated with greater activity during fluid intelligence conditions of a working memory task (Gray et al., 2003).

ty to control one's attention in the face of distraction or interference is particularly important for fluid intelligence.

A complementary way to investigate the neural bases of intelligence is to examine individual differences. Such work has shown, for example, that higher intelligence is associated with how quickly and reliably neurons can carry information. In some of the first PET neuroimaging studies of intelligence by Richard Haier and colleagues at U. C. Irvine, intelligence correlated negatively with energy usage (glucose metabolism) in the brain during mental activity, suggesting a neural efficiency hypothesis. According to this hypothesis, more intelligent individuals expend fewer cognitive / metabolic resources to perform at a given level. This is an intriguing hypothesis, although other studies have sometimes found the opposite relationship, or have qualified the relationship (e.g., finding it only in males). Such complexity is to be expected, given the topic.

In the largest imaging study of individual differences in intelligence to date (Gray et al., 2003), we tested whether fluid intelligence (reasoning ability) is mediated by the neural mechanisms that support the control of attention in the face of distraction during working memory. Participants performed a task in which they had to indicate whether a current item seen on a computer screen exactly matched the item they saw three screens previously (or "3-back") while their brain activity was measured using functional MRI. Importantly, the demand for attentional control varied greatly across trials within the 3-back task due to differences in trial-to-trial interference. Not surprisingly, participants with higher fluid intelligence performed better at the task (more accurately). Critically, these participants also showed stronger neural activity in many regions across the brain, including the lateral prefrontal and parietal cortex (Figure 1B). These patterns were observed almost exclusively during the distracting, high-interference trials, suggesting that the ability to control attention in the face of distraction may be of critical importance to intelligence.

Genetic Bases of Intelligence

Genes have crucial roles in the expression of disease, and it would be extraordinary if genes had no influence on cognitive skills. Genetic influences on intelligence

can be detected by comparing test scores of related individuals using quantitative genetic techniques. In the simplest approach, a heritability statistic (h^2) reflects, loosely speaking, the extent to which intelligence test scores are explained by genetic differences ("nature") versus explained by all other factors ("nurture" or "environment" -- including nutrition, education, and health history). Heritability studies clearly show that both nature and nurture influence intelligence. Genetically identical twins raised separately following adoption show a strong correlation for intelligence; that is, one twin's intelligence strongly predicts the other's, despite their different rearing environments. Studies with adoption and extended family designs can adjust for several types of confounds in twin studies, and have confirmed that both nature and nurture are critical.

The heritability of intelligence becomes stronger with age, whereas a strictly environmental theory of intelligence would predict the opposite. If individuals select or create environments that foster their genetic propensities throughout life, genetic differences in cognition will become greatly amplified. Similar gene-environment interactions might help explain the paradox of high heritability but strong environmental effects on children's intelligence.

A common misinterpretation of heritability is that if genetic factors contribute to individual differences in intelligence, then education is pointless. This is incorrect because heritability is about 50%, i.e., nowhere near the point at which a given trait is completely determined by genes (100%). Many environmental factors can affect intelligence, and can do so favorably or adversely. Nongenetic influences on IQ include educa-

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tion, training, family environments, and -- at a more basic level -- nutrition and environmental hazards. In a massive review of 212 previous studies of intelligence,

Devlin and colleagues (1997) showed that although heritability was high (48%), the prenatal environment accounted for 20% of the correlation of intelligence between identical twins and for 5% of the correlation between non-twin siblings that shared the same womb consecutively. Maternal drug or alcohol use, and exposure to environmental toxins like lead, can also adversely affect intelligence. Duration of breast-feeding during infancy is positively associated with small but measurable gains in childhood cognitive development. Population-level gains in IQ (known as the "Flynn Effect," in honor of its discoverer) are typically attributed to environmental changes, because they have occurred over a single generation (and so genetic change in the population is improbable).

The family environment in which a child is raised affects his or her intellectual function. Growing up in the same family increases IQ similarities. An individual's IQ correlates more highly with that of an identical twin, non-twin sibling, and parent (0.86, 0.47 and 0.42, respectively) if he or she grew up with them. The strength of the correlations decreases if individuals are raised separately from these relatives (0.72, 0.24 and 0.22). Adopted children's IQs correlate with those of their adoptive siblings (0.34) and adoptive parents (0.19). So 20-35% of the observed population differences in IQ are attributable to differences between family environments. Intriguingly, the family environment's influence on IQ dissipates once children leave

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home between adult adoptive relatives, there is a correlation of IQ of -0.01, i.e., no relationship at all. Thus the lasting environmental influences on IQ are those unique experiences that an individual does not share with others.

An important recent study found that environmental factors have a much greater influence on childhood IQ in impoverished families, and relatively little influence

in families of higher socioeconomic status (Turkheimer et al., 2003). The heritability of IQ at the low end of the wealth spectrum was just 0.10. By contrast, it was 0.72 for more wealthy families, indicating that nature is more significant than nurture when socioeconomic status is high while the reverse is true when socioeconomic status is low. Such a result cautions against extrapolating heritability beyond the population and circumstances in which the data were obtained.

Although heritability implies that specific genes with a direct bearing on intelligence must exist, such genes are difficult to identify. All known behavioral traits are determined by multiple interacting genes, each having small effects (meaning that each gene will be harder to pin down, even though the overall effect, heritability, is substantial). Nonetheless, intellectual function in healthy individuals has been associated with a few specific genes that are expressed in the brain. Most such links are tentative and await replication. One example is a gene on chromosome 6, which codes for an insulin-like growth factor-2 receptor (IGF2R), and was linked with high intelligence. Another such gene codes for cathepsin D, for an acetylcholine receptor. Each gene accounted for a range of only 3-4 IQ points. The size of the *asp* gene product parallels brain size across several species. In cortical development and evolution, this gene determines whether specific cells will stop dividing and become neurons or continue dividing to form a larger brain. Some microcephaly patients also possess the *ASPM* mutation, indicating that a shortened version of the gene might lead to the development of fewer cerebral neurons and a smaller head. Gene polymorphisms also influence aspects of brain function that are potentially relevant to intelligence, including long-term memory (BDNF, brain-derived neurotrophic growth factor), short-term or working memory (COMT, catechol-O-methyltransferase), and the control of attention (DRD4, dopamine receptor D4; and MAO-A, monoamine oxidase A).

Finally, we emphasize that heritability of intelligence within a group does not imply that group differences in intelligence must be due to genetic factors. Environmental factors could completely explain between-group differences, even in a case where genetic factors completely explain within-group differences. (Imagine taking genetically identical corn kernels, and

planting some in fertile soil with adequate water and some in poor soil without adequate water. Any differences in the resulting plants are purely environmental.) For this reason, a satisfactory account of group differences in intelligence cannot appeal to within-group heritability to explain between-group differences.

Discussion

The data clearly indicate a neurobiological basis for intelligence, particularly intelligence in the sense of reasoning and novel problem-solving ability. The field is at an exciting juncture because nuanced conceptual and empirical approaches are available, and intelligence is an important human ability. Understanding the mechanisms might indicate avenues for enhancing both intelligence and health. Much remains to be discovered, of course. While neurobiological and genetic measures contribute greatly to the study of human abilities, psychometric and social psychological research is equally indispensable. The empirical successes also raise ethical issues that the science cannot resolve (Farah, 2002).

We consider a potential consequence of the claim that intelligence is a medical variable. Specifically, because ancestral geographic origin ("race") is also increasingly seen as medically relevant, research on intelligence could be on something of a collision course with race. We cannot simply ignore this possibility and hope for the best; rather, we need clear guidelines for handling datasets that include both types of data. The topic of potential race differences in intelligence has had a disproportionately large (and strongly negative) impact on public perception of intelligence research. It could be damaging to public health if the legacy of this ugly chapter (or fear of the legacy) were allowed to derail legitimate research into intelligence as a health related variable. It is widely recognized that by far most of the variance in intelligence is within racial groups not between them. Moreover, the causes of individual differences in test scores are relatively tractable with available methods, whereas the causes of racial differences in test scores are not. (Group differences in test scores exist, but are somewhat like a Rorschach "ambiguous figure" test -- a given interpretation says more about the interpreter than the way things are in the world.) In the arena of potential race differences, the imperative to investigate seems to have been placed above a bedrock

principle of research with human participants for almost 60 years: the imperative to obtain informed consent. We are of the opinion that investigating potential racial differences in intelligence is unethical if it lacks the informed consent of the target group. Note that we in no way wish to promote or legitimize such research.

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Rather, the point is that by clarifying the ethical requirements of such studies, it could help protect legitimate research.

The key dilemma is how to preserve freedom of scientific inquiry (e.g., to allow health-related investigations) while insisting on the highest ethical standards (e.g., to prevent misuse). Elsewhere, we have proposed specific guidelines intended to constrain the conduct of research so that data sets that incidentally contain information about both intelligence and race are not misused (Gray & Thompson, 2004).

To recap, research on human intelligence has advanced dramatically in the last few years, with intimations that major advances are possible in the near future. The implications of this research are exceptionally broad, and so all ethical issues must be addressed proactively. In particular, the possibility that intelligence and ancestral geographic origin are both medically relevant means that they are increasingly likely to be assessed within any given study. We advocate allowing the collection of such data (in the interests of promoting health) and advocate against allowing the secondary use of such data for purposes not explicitly approved by the participants themselves.

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