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Developmental Population Neuroscience

发展人口神经科学（个体认知与智能水平）

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National Basic Science Data Center  
Chinese Data-sharing Warehouse for In-vivo Imaging Brain

# 伤仲永



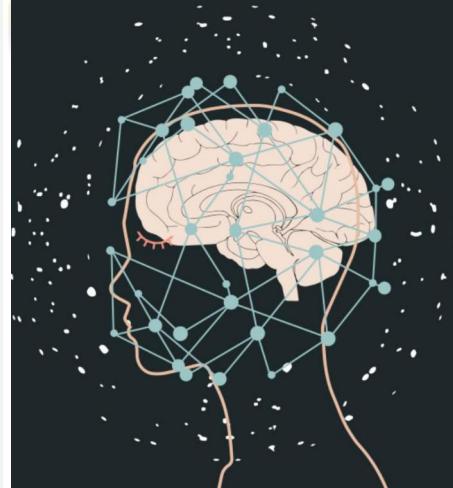
# Intelligence

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## SUMMARY POINTS

1. Intelligence differences continue to be a focus for lively research in psychology and also of considerable interest to nonspecialist psychologists, academics in other fields, and the public.
2. The past decade produced many books on intelligence, from introductory accounts to specialist discussions of specific issues. There are also historical accounts and books challenging the measurement and study of intelligence differences.
3. There is new research on the psychometric structure of intelligence. The  $g$  factor from different test batteries ranks people in the same way. There is still debate about the number of levels at which the variations in intelligence is best described. There is still little empirical support for an account of intelligence differences that does not include  $g$ .
4. There has been progress in establishing that sensory discrimination, inspection time, and reaction time are all associated with intelligence and achieving estimates of the population effect sizes. However, they now attract less attention as possible ways to understand intelligence differences, although sensory discrimination does attract attention as part of the common cause account of aging and intelligence.
5. The biology of intelligence is the subject of much research. Behavior genetics research continues to refine what we know about environmental and genetic contributions to intelligence, such as moderating effects of age and social circumstances, and the shared genetic influences of intelligence with, for example, brain size, processing speed, and birth weight. Molecular genetic research on intelligence has had a dry time with candidate gene studies and is now poised to take on sufficiently powered genome-wide association studies. Brain imaging studies of intelligence are providing more replicated findings that are cohering around an account of a defined but distributed network in the brain that works more efficiently in people with higher intelligence scores.
6. New work on education and social mobility and social position as the outcomes of intelligence differences has plotted people's life courses from impressive longitudinal studies. Health outcomes are a new and burgeoning outcome for intelligence differences, and it is only in the past decade that the new field of cognitive epidemiology has emerged.
7. Aging is another expanding focus for intelligence research, with new findings. Also, this field increasingly takes a life-course view and is becoming more integrated with the study of intelligence differences in younger adulthood and in child development.
8. Controversial issues continue to be studied in intelligence. One such issue is the changing twin-singleton intelligence difference. Also, sex differences in intelligence continue to attract new research, with studies of both mean and variance differences.



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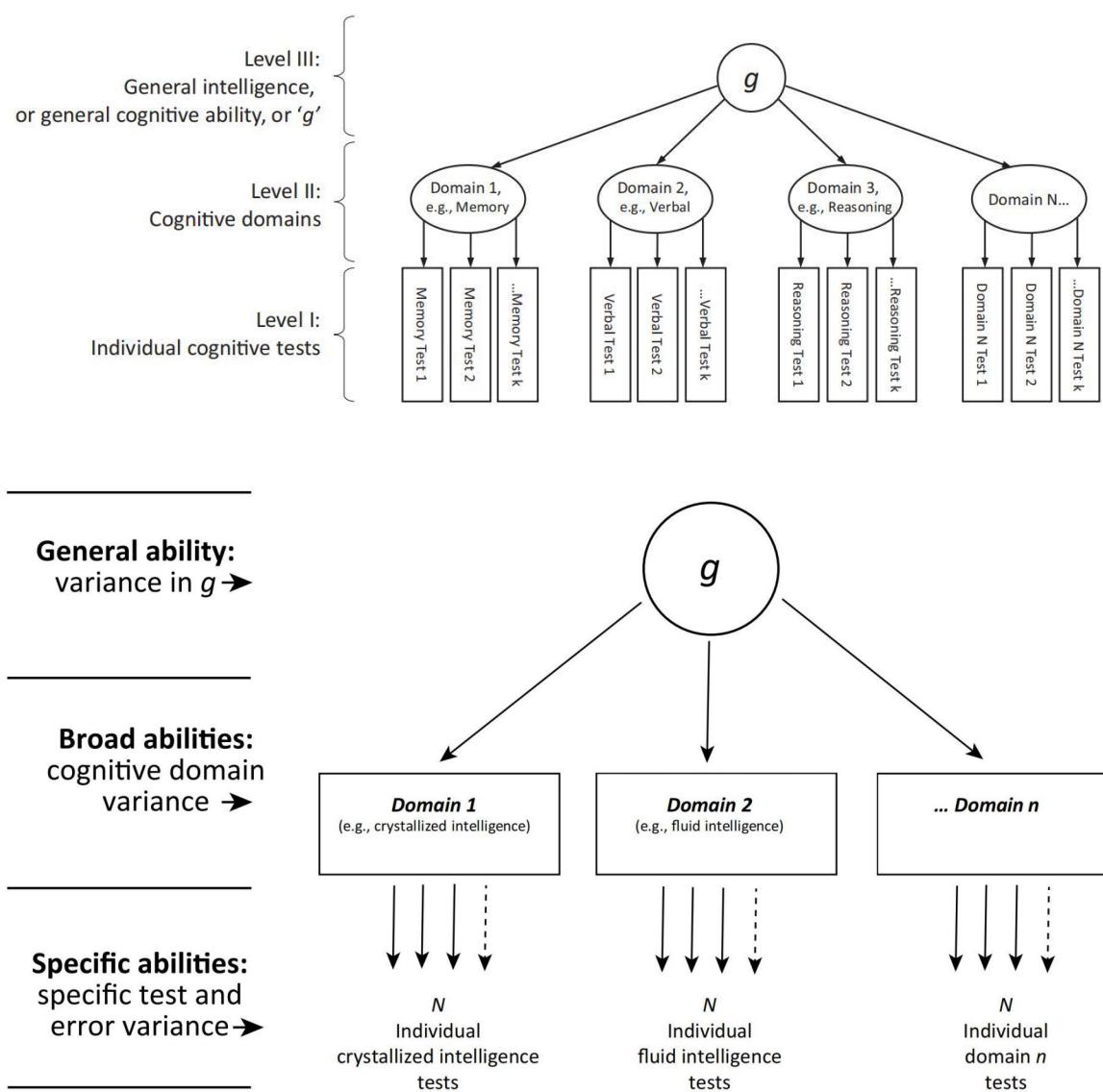
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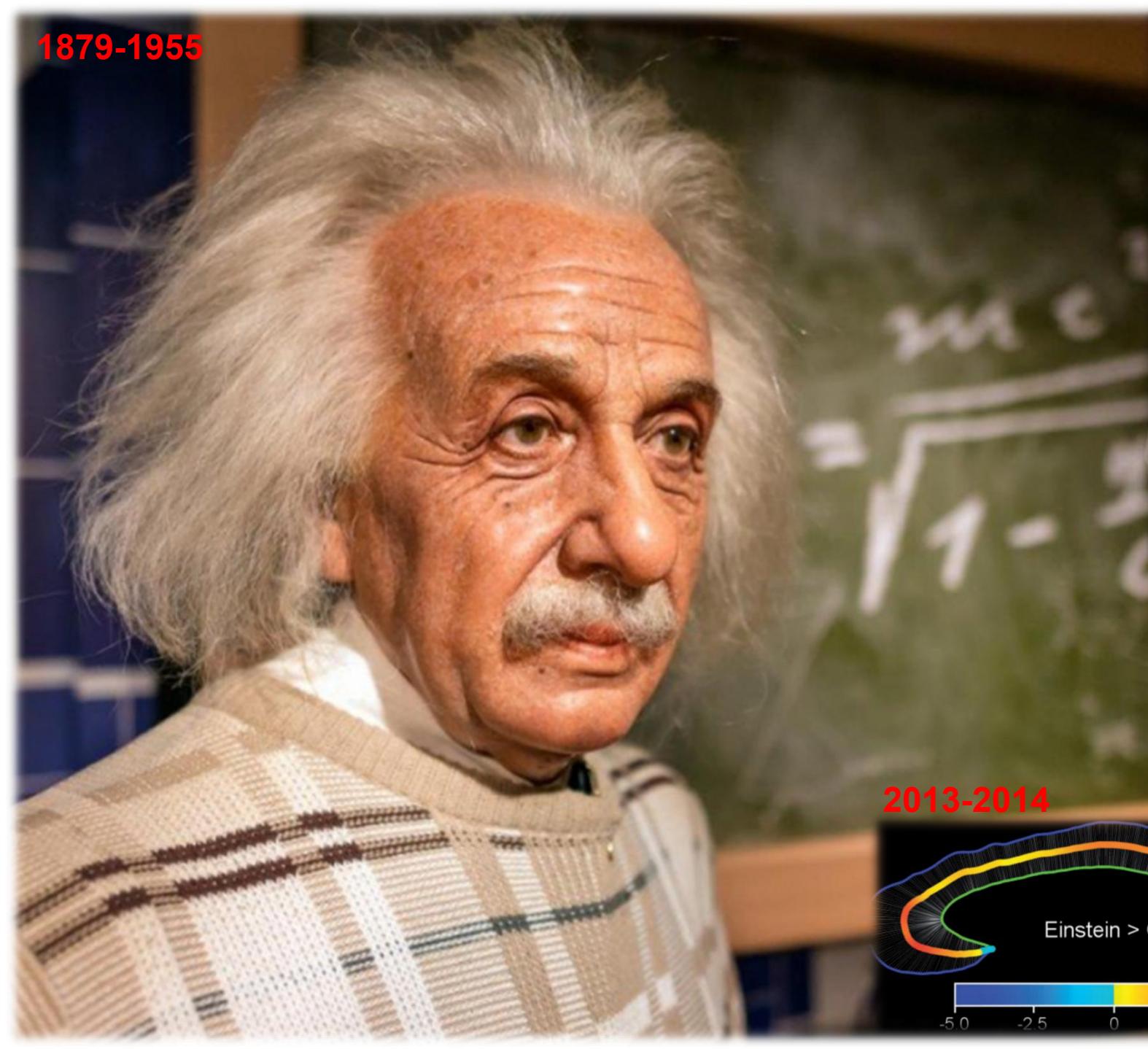
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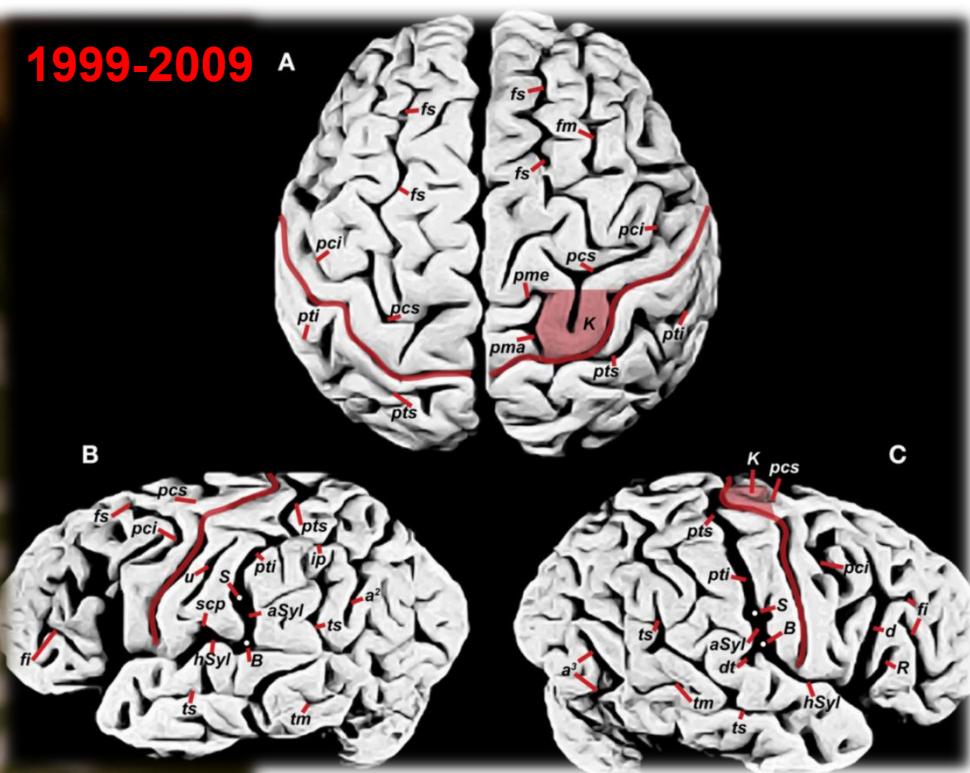
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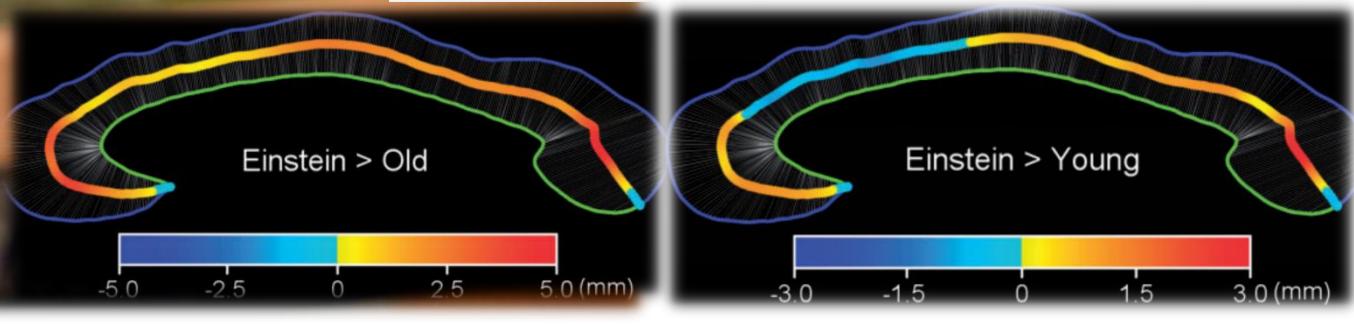
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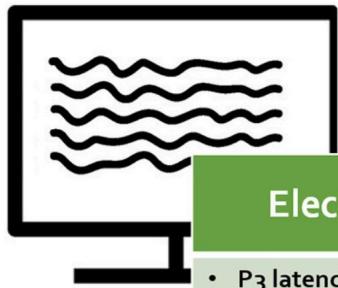
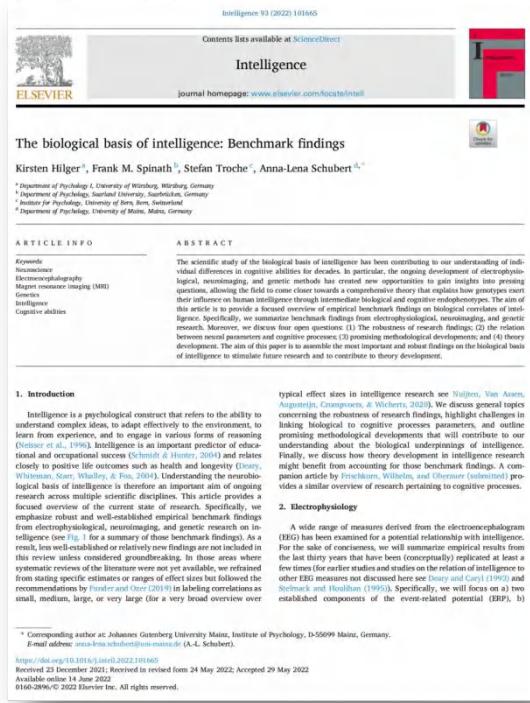


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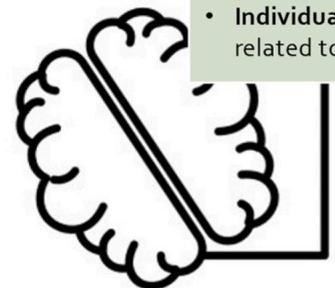
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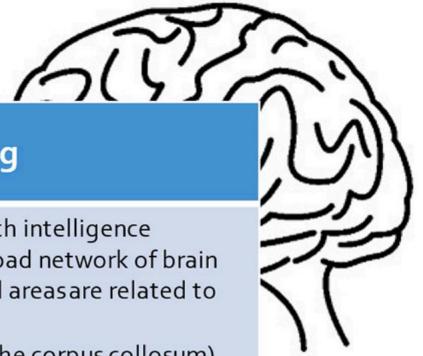
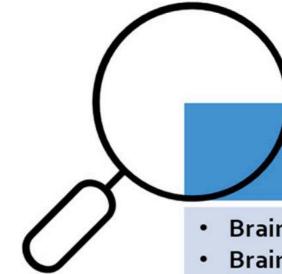
## Electroencephalography

- **P3 latency** correlates negatively with intelligence
- **MMN amplitude** correlates negatively with intelligence
- Modifying conditions of these relationships are unclear
- **Event-related desynchronization (ERD) of alpha power** is negatively associated with intelligence when the subjective task-difficulty is moderate
- **Individual alpha frequency** is not consistently related to intelligence



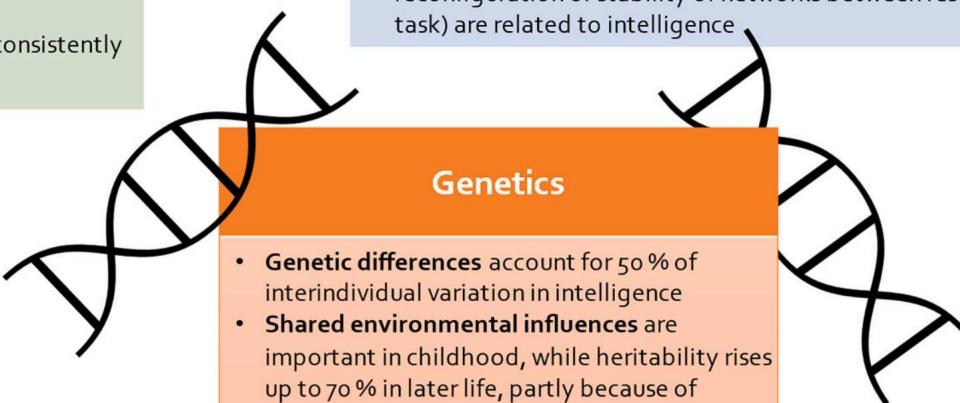
## Neuroimaging

- **Brain size** is positively correlated with intelligence
- **Brain structure and function** in a broad network of brain regions including frontal and parietal areas are related to intelligence
- **Structural brain connections** (e.g., the corpus callosum) and **functional brain connections** are related to intelligence and can even predict individual test scores
- **Global efficiency** of functional brain connections is not consistently related to intelligence
- **Dynamic properties of brain networks** (e.g., the reconfiguration or stability of networks between rest and task) are related to intelligence



## Genetics

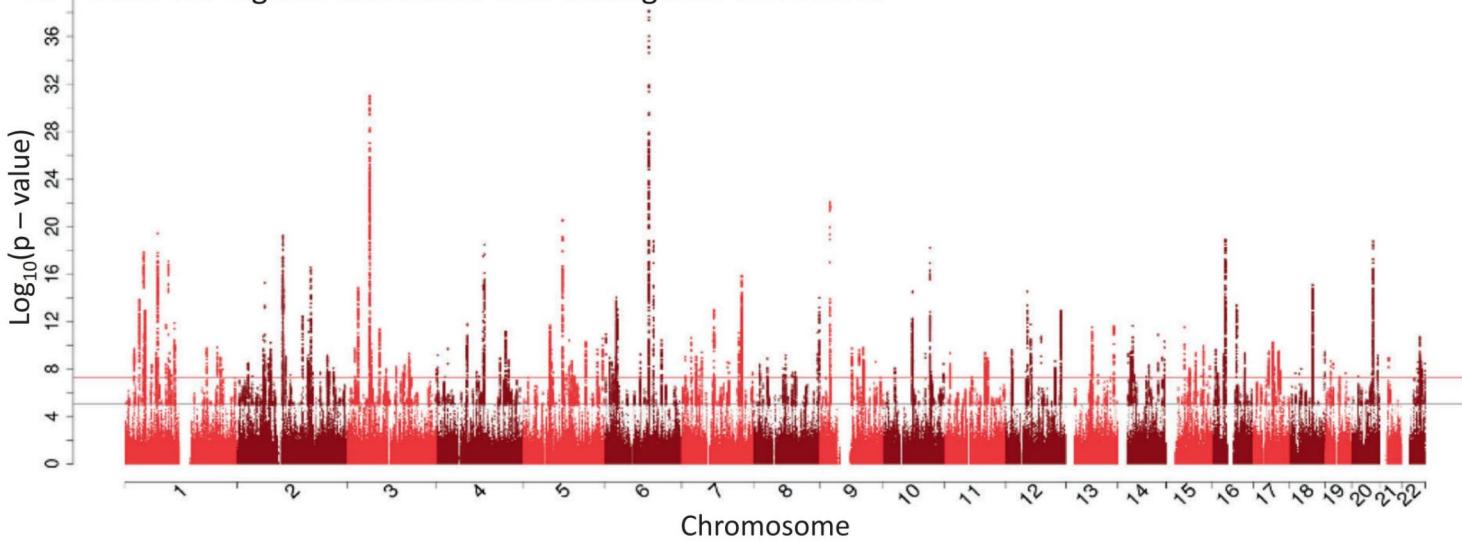
- **Genetic differences** account for 50 % of interindividual variation in intelligence
- **Shared environmental influences** are important in childhood, while heritability rises up to 70 % in later life, partly because of active gene-environment correlation
- **Genomewide polygenic scores (PGS)** from GWAS on intelligence and years of education explain up to 10 % of variance in intelligence



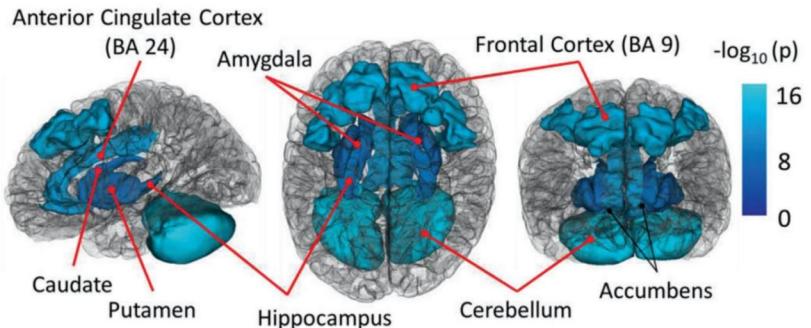
# 人类智力的生物基础



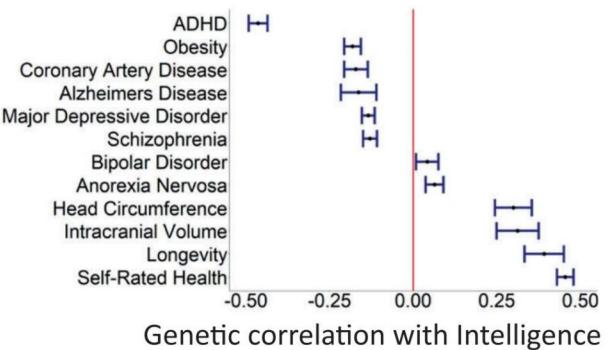
### A. Genomic regions associated with intelligence test scores



B.



C.



### Genetic variation, brain, and intelligence differences

Ian J. Deary<sup>1</sup> · Simon R. Cox<sup>1</sup> · W. David Hill<sup>1</sup>

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#### Abstract

Individual differences in human intelligence, as assessed using cognitive test scores, have a well-replicated, hierarchical phenotypic covariance structure. They are substantially stable across the life course, and are predictive of educational, social, and health outcomes. From this solid phenotypic foundation and importance for life, comes an interest in the environmental, social, and genetic aetiologies of intelligence, and in the foundations of intelligence differences in brain structure and functioning. Here, we summarise and critique the last 10 years or so of molecular genetic (DNA-based) research on intelligence, including the discovery of genetic loci associated with intelligence, DNA-based heritability, and intelligence's genetic correlations with other traits. We summarise new brain imaging-intelligence findings, including whole-brain associations and grey and white matter associations. We summarise regional brain imaging associations with intelligence and interpret these with respect to theoretical accounts. We address research that combines genetics and brain imaging in studying intelligence differences. There are new, though modest, associations in all these areas, and mechanistic accounts are lacking. We attempt to identify growing points that might contribute toward a more integrated 'systems biology' account of some of the between-individual differences in intelligence.

#### Individual differences in human intelligence

#### Describing the phenotype of intelligence

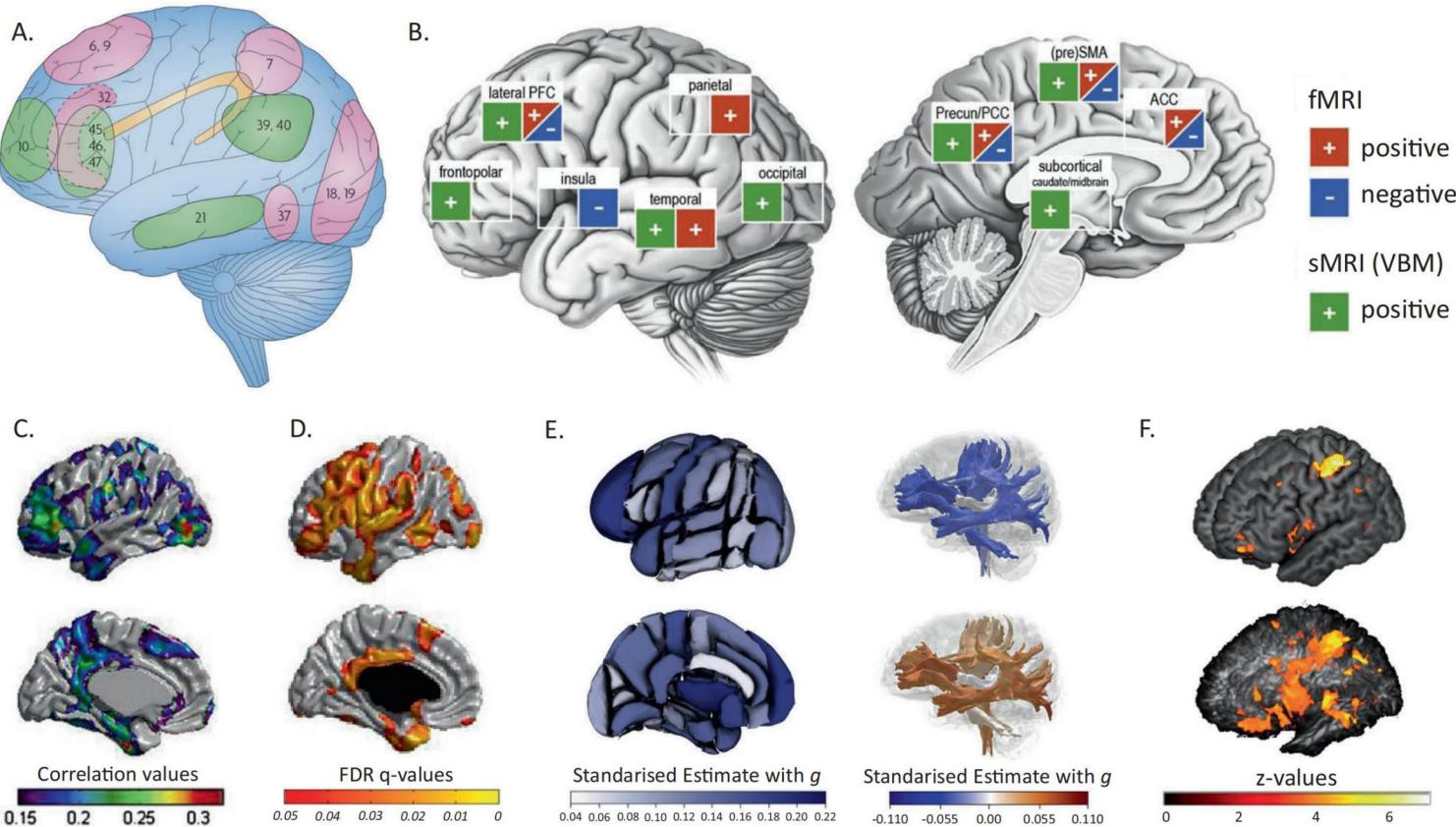
This article is about some new contributions toward understanding the aetiology of individual differences in human intelligence. The focus is on genetic variation and brain imaging-derived differences, including where those two sources overlap. For more than a century, the field of research that studies intelligence differences has had some controversies (Box 1). Notwithstanding these, research findings on intelligence have much consensus, based on robust findings. The first part of this article summarises some of the findings from which reductionist approaches—including brain imaging and genetics—to intelligence differences proceed.

These authors contributed equally: Ian J. Deary, Simon R. Cox, W. David Hill

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We should make it clear to the reader that 'intelligence' is just one of the terms that are used to describe humans' differences in thinking skills; others, sometimes used as near-synonyms, include cognitive ability, cognitive performance, cognitive functioning, and mental ability. Sometimes IQ (intelligence quotient) is used, although that has a specific meaning within the field of psychometrics. Intelligence (or the other terms listed in the previous sentence), as a human phenotype, is measured using cognitive tests, of which there are thousands. This hands the cynic a weapon that, to the ignorant, can glibly dismiss the field of research because, as Boring [1] famously wrote in 1923, "...intelligence as a measurable capacity must at the start be defined as the capacity to do well in an intelligence test. Intelligence is what the tests test." That much-quoted last short sentence was not Boring's opinion; rather, it was his saying that that is what one would think if one did not know the research findings. His next sentence starts, "This is a narrow definition, but it is the only point of departure for a rigorous discussion of the tests". We shall have that rigorous discussion here. Before that, we offer another, much-cited definition: "Intelligence is a very general mental capability that, among other things, involves the ability to reason,



## Genetic variation, brain, and intelligence differences

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Review

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# Cognition through the lifespan: mechanisms of change

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**Cognitive abilities rise steeply from infancy to young adulthood and then are either maintained or decline to old age, depending on the specific ability. This pattern suggests corresponding continuities of mechanism and process, but it is striking that the fields of cognitive development and cognitive aging make little contact with each other's methods and theories. In this review we examine reasons for this cultural separation, and show how recent findings from both areas fit a framework couched in terms of cognitive representation and control. These two broad factors have very different lifespan trajectories; consideration of their relative growth and decline makes it clear that cognitive aging is not simply 'development in reverse'. This framework is offered in light of recent interest in finding greater continuity throughout the lifespan and creating a more comprehensive explanation of cognitive function and cognitive change.**

## Introduction

There is symmetry to our physical lives: we are independent and robust in youth and middle age, but dependent and frail in infancy and old age. On the surface, cognition appears to follow the same general pattern of building up and wearing down. In the brain, too, the consolidation of networks in infancy and early childhood is mirrored by the reduction of connectivity and structural atrophy in older age (Box 1). In all these cases, there is a vulnerability in youth and old age that is not present in the middle of life. However, the conclusion that cognitive aging is 'development in reverse' is an oversimplification of a dynamic that unfolds over the lifespan, fuelling the changes that are reflected in distinct types of cognitive ability at different times of life. In the brain, for example, similar behaviors in older and younger adults are often mediated by different neural circuits [1,2]. Our purpose in this article is to propose a framework for examining changes in cognition over the lifespan and consider the implications of that framework for conceptions of cognition and the factors responsible for its change.

There are remarkably few integrated accounts of lifelong changes in cognitive ability, making the exceptions particularly noteworthy. For example, in a dynamic view of lifespan development, Baltes and his colleagues

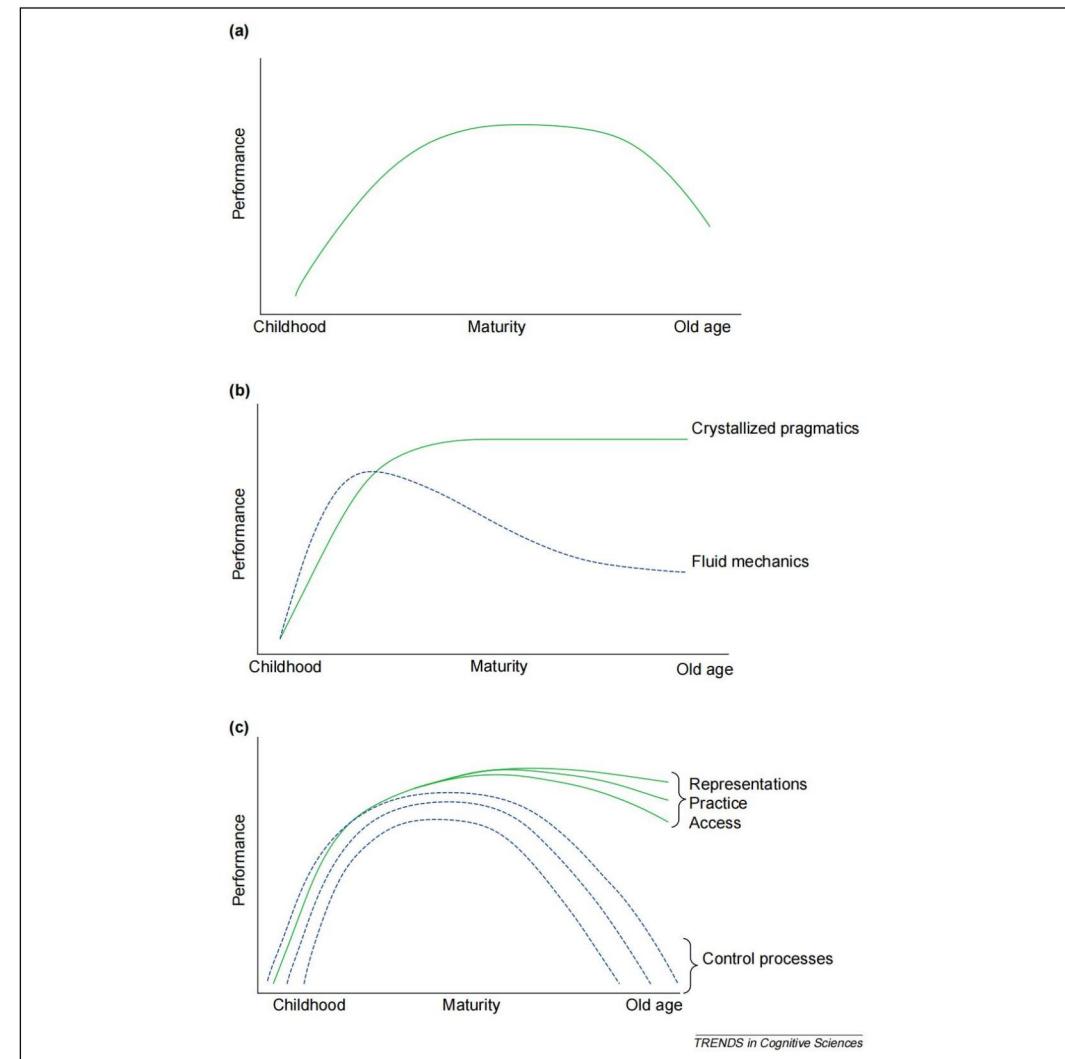
[3,4] have stressed that change can occur at any time, that development depends on interactions among genetic, environmental and social factors, that all processes of development entail both gains and losses, and that the relative mixture of biological and social-cultural factors change with age. From a different perspective, Salthouse [5,6] has shown that processing speed increases from infancy to young adulthood and then declines from the twenties to old age; he has argued that this general slowing is the primary cause of age-related declines in cognitive performance. Aside from these exceptions, the fields of cognitive development and cognitive aging have shown little contact.

An integration of the processes of cognitive change in development and aging is essential to the construction of a comprehensive account of the structure of cognition and the factors that influence cognitive performance. The details of cognitive change at each end of the lifespan are now sufficiently known that a broader perspective can be applied. However, a lifespan description of cognitive change requires more than a simple blending of the two fields. Taking language as an example, vocabulary and grammar develop through childhood with only small age-related losses from age 70 on [7]. But aging brings problems of access to stored information, even if there is no decrease in knowledge. The most common memory complaint of older adults is their difficulty in recalling names and words that are specific labels [8]. This information has not been lost from memory, as it can be retrieved later either spontaneously or with better cues. Therefore, although knowledge deficiencies are associated with both development and aging, the limitation in children is due to incomplete acquisition whereas the limitation in old age is associated with difficulties of access. Such asymmetries need to be explained.

## Representation and control in lifespan cognition

Our proposal for a more comprehensive explanation of cognitive change is that processes concerned with representation, control, and their interaction evolve across the lifespan and determine cognitive ability. *Representations* are the set of crystallized schemas that are the basis for memory and knowledge of the world; *control* is the set of fluid operations that enable intentional processing and adaptive cognitive performance (Box 2). These systems are interactive: representations of the world are not constructed randomly but are selected on

# 人类认知毕生发展模型



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LETTERS

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ARTICLES

<https://doi.org/10.1038/s41593-022-01042-4>



## On the growth and form of cortical convolutions

Tuomas Tallinen<sup>1\*</sup>, Jun Young Chung<sup>2,3†</sup>, François Rousseau<sup>4</sup>, Nadine Girard<sup>5,6</sup>, Julien Lefèvre<sup>7,8</sup> and L. Mahadevan<sup>2,3,9,10\*</sup>

## Genetic variants associated with longitudinal changes in brain structure across the lifespan

物理  
基因  
生物  
化学

**BIOPHYSICS**

## A new wrinkle on the brain

The folded structure of the human brain is a hallmark of our intelligence — an optimized packing of neurons into a confined space. Similar wrinkling in brain-on-a-chip experiments provides a way of understanding the physics of how this occurs.

Larry A. Taber

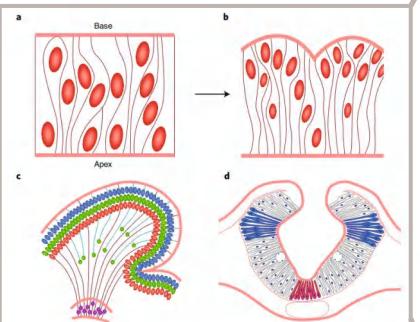
During development, the human brain evolves from a relatively simple, smooth-walled tube into a complex organ with a highly convoluted surface. Abnormal folding is associated with many developmental disorders, including retardation, epilepsy, autism and schizophrenia. But understanding the physical mechanisms that drive this transformation has been hindered by a lack of biological models amenable to controlled manipulation. Now, writing in *Nature Physics*, Eyal Karzbrun and co-workers have used human embryonic stem cells to create organoids that fold via an analogous mechanism.

Stem cells can differentiate into a myriad of cell types with specialized functions. Karzbrun et al. used neural progenitor cells — future neurons and their supporting cells — like those in the brain tube of a month-old human embryo. And yet they found that these cells form surface wrinkles or folds like those created in the cerebral cortex during the third trimester, with the inner region of each brain organoid constraining the expanding outer region, causing the surface to buckle.

When cultured in media containing appropriate ingredients, the cells self-organize into a one-cell-thick layer of column (or cell sheet) surrounding a fluid-filled cavity, much like the cylindrical brain tube. These organoids, however, are relatively spherical shells, about a millimetre in diameter, compressed into a disk for fluorescence imaging. With this technique, development in living brain tissue can be followed for several weeks.

As in the brain tube, cells in the organoid extend radially across the neuroepithelium and are narrower than their nuclei.

To maintain cell-cell connections at the apical (inner) and (outer) surfaces of the neuroepithelia, the nuclei move back and forth between the cell apex and base during the cell cycle, a process known as interkinetic nuclear migration<sup>1</sup>. Prior to cell division, nuclei divide at the apex, then move outwards toward the base before returning to the apex to divide again.

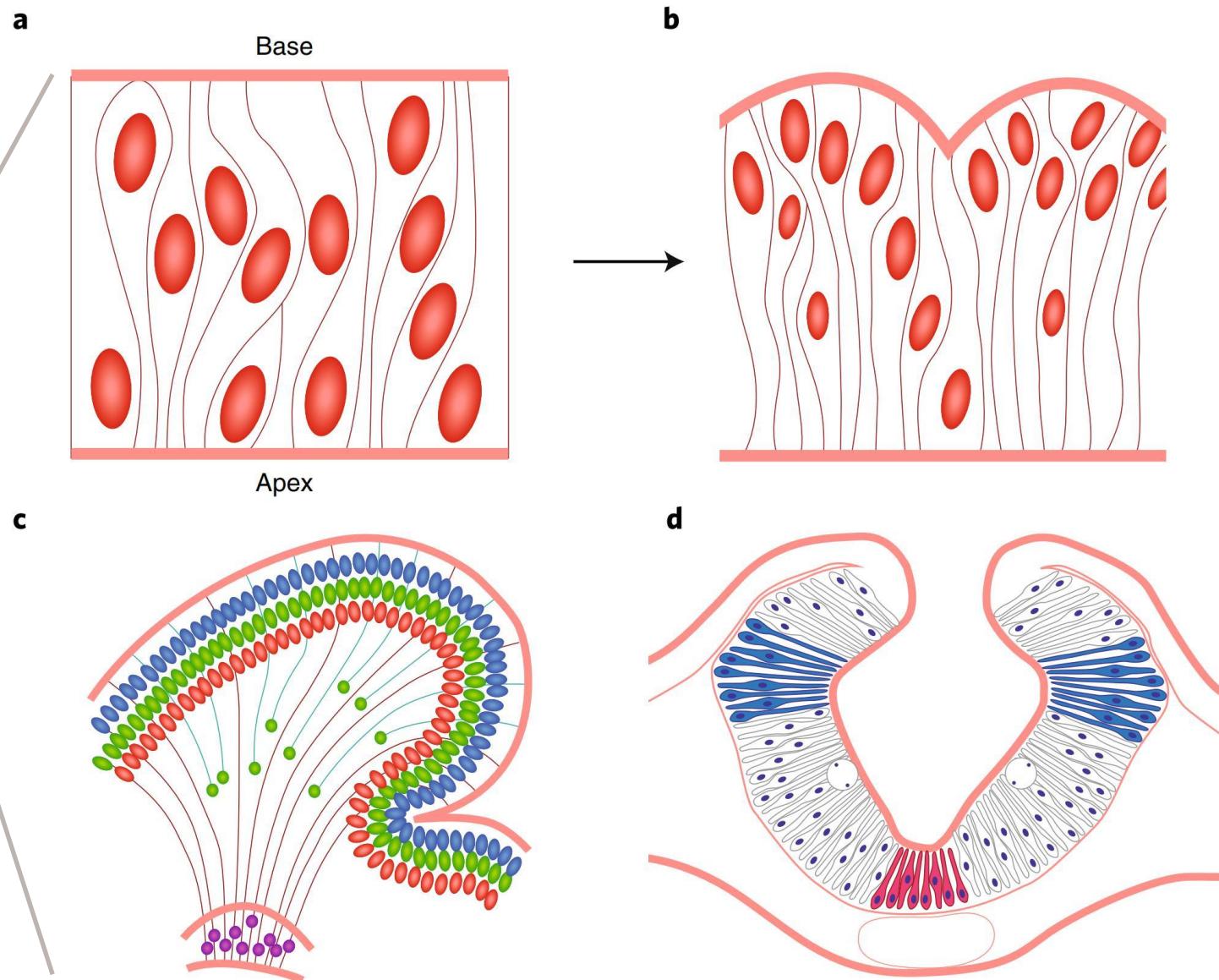


**Fig. 1 | Neural morphogenesis in organoids and embryo.** **a**, Before wrinkling, nuclei are staggered across the wall of the organoid. **b**, Nuclei later migrate and accumulate near basal surface, causing compression and buckling into wrinkles. **c**, The folding of the cerebral cortex is driven by growth-induced compression of neural tissue near the outer surface of the brain. **d**, Cell nuclei accumulate near the basal surface of the neural plate, creating local hinge points (blue and red) that help bend the plate into the neural tube. Credit: adapted from ref. <sup>3</sup>, Springer (**a**); ref. <sup>1</sup>, Macmillan Publishers Ltd (**b**); ref. <sup>2</sup>, OUP (**c**); and ref. <sup>4</sup>, Wiley (**d**).

After about a week of incubation, the surfaces of the organoids begin to form wrinkles that strongly resemble the folds that develop in the cerebral cortex, a thin outer layer of brain cells<sup>2</sup> (Fig. 1b,c). This wrinkling is surprising for two main reasons. First, the only wrinkles that form in the brain tube of the early embryo are local constrictions that develop in the absence of widespread folding of the cortex occurs much later. Second, the organoids wrinkle despite being an order of magnitude smaller in diameter than the adult mouse brain, which has a relatively smooth surface. In fact, significant folding generally occurs only in mammals as large or larger than a ferret.

Karzbrun et al. spent considerable effort examining the physics of folding in their organoids. As the nuclei move radially outward during interkinetic nuclear migration, they increase in size, slow down and become more numerous near the outer surface. Wrinkling begins when the nuclei reach a critical density. Moreover, the nuclei gradually elongate radially until wrinkling begins and they become more circular. Taken together, these observations suggest that the outer nuclei become compressed circumferentially, causing the surface to buckle.

Although there are some important differences, this mechanism is analogous to current thinking on the physics of cortical folding<sup>3,4</sup>. Like the organoid nuclei, neural progenitor cells divide at the inner surface of the brain and migrate outward toward the cortex. Unlike the nuclei, however, these cells



### Cortical Evolution: Judge the Brain by Its Cover

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<sup>2</sup>Department of Neurobiology and Kavli Institute, Yale University, New Haven CT, 06520, USA

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To understand the emergence of human higher cognition, we must understand its biological substrate—the cerebral cortex, which considers itself the crowning achievement of evolution. Here, we discuss how advances in developmental neurobiology, combined with those in genomics, including genome evolution via gene duplications and the emergence of novel regulatory elements, can provide insights into the evolutionary mechanisms culminating in the human cerebrum. Given that the massive expansion of the cortical surface and elaboration of its connections in humans originates from developmental events, understanding the genetic regulation of cell number, neuronal migration to proper layers, columns, and regions, and ultimately their differentiation into specific phenotypes, is critical. The pre- and postnatal environment also influences the brain's growth trajectory, yielding a cortex that is refined via selection and elimination of synaptic connections, a process that is prolonged in humans. This knowledge provides essential insight into the pathogenesis of human-specific neuropsychiatric disorders.

Since the time of Darwin's *The Origin of Species* about 200 years ago, there has been little disagreement among scientists that the brain, and more specifically its covering cerebral cortex, is the organ that enables human extraordinary cognitive capacity that includes abstract thought, language, and complex higher cognitive functions. Thus, it is surprising that relatively little attention has been given to the study of how the human brain has evolved and become different from that of other primates and non-primate mammals (Cowan et al., 2010). Yet, the study of human brain evolution is essential for understanding causes and to possibly develop cures for diseases in which some of the purely human behaviors may be involved. These disorders include autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), schizophrenia, as well as a number of human-specific neurodegenerative conditions, including Alzheimer's disease (e.g., Catts et al., 2009; Jia et al., 2009; Jia and Kotilinek, 2009; Kotilinek and Carlson, 2009; Kotilinek and Younkin, 2009; Kotilinek and Carlson, 2010; Miller et al., 2010; Preuss et al., 2009; Xu et al., 2010).

Traditionally, a major area of research that has informed our understanding of how our brain may have changed over the last 200 million years of mammalian evolution (Kauf, 2010; Preuss, 1995). These studies left no doubt that the human cerebral cortex has expanded significantly relative to other hominids, including the great apes, and that this expansion involved temporal lobes in humans (Dobrza, 1993; Fazl et al., 2012; Preuss, 1995; Rakic, 2008; Trifunovic and Serendipity, 2013). It also became evident that although the basic principles of brain development are conserved across species, the timing of these developmental events during evolution produce not only quantitative but qualitative changes as well (Table 1).

Due to the limits of space, we cannot provide a comprehensive review of the literature on this topic. Instead, we will focus on the expansion and elaboration of the human cerebral neocortex and provide our own personal perspective on some of the key advances in this area, including the high promise, as

well as enormous challenges ahead. We organize our thoughts into two major areas—the phenotype-driven and genome-driven approaches, which, unfortunately, only rarely meet in the middle.

Our hope is that in the near future, it will be possible to connect some of the known human genetic adaptations to the developmental and maturational features that underlie uniquely human cognitive abilities.

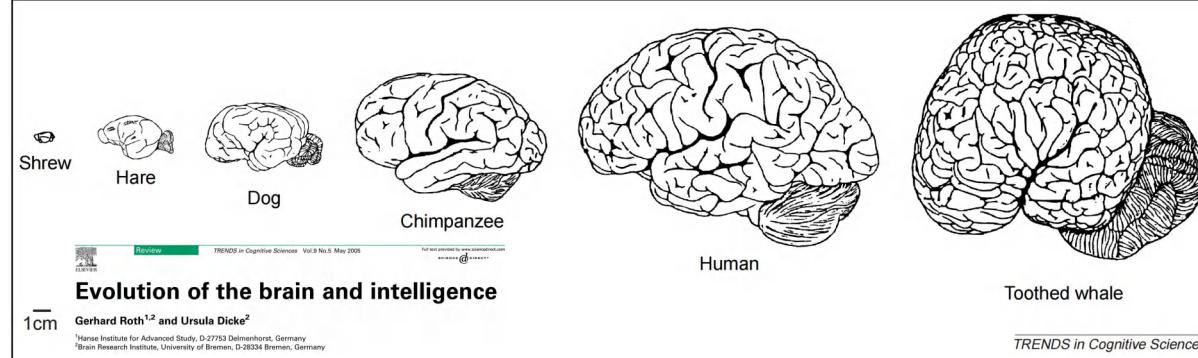
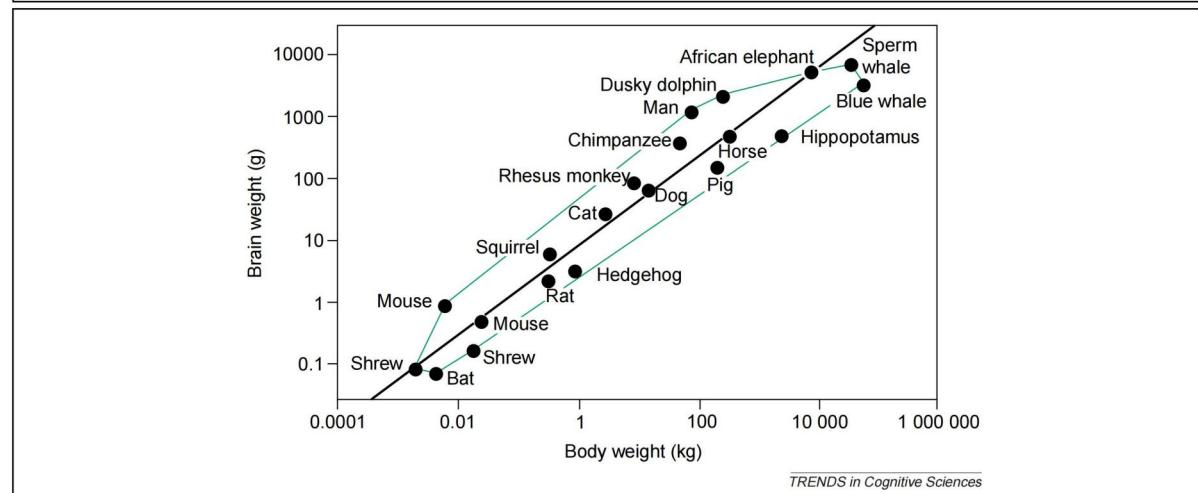
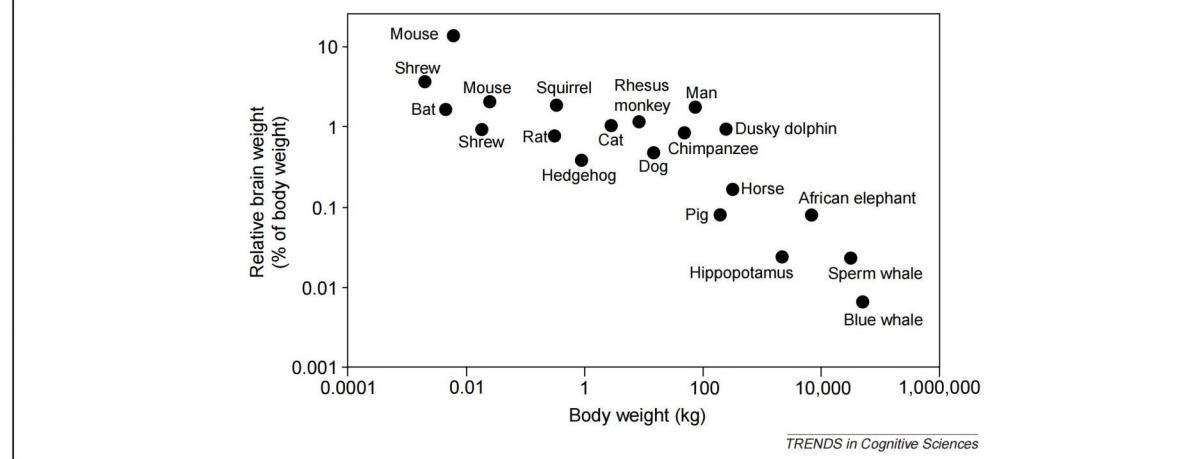
#### The Phenotype-Based Approach

**Cortical Expansion**

It is well established that the expansion of the cortex occurs primarily in surface areas greater than 1 mm<sup>2</sup>. This is true for non-human primates, including humans, in which the neocortex comprises up to 80% of the brain mass. We have also known for a long time that the neocortex is subdivided into distinct cytoarchitectonic areas with neurons organized in horizontal layers, and that these areas undergo dramatic changes during cortical evolution (Mountcastle, 1950; Goldman-Rakic, 1987). Of course, brain size is not merely a matter of cell number; some changes in brain arrangement are due to connectivity (Herculano-Houzel et al., 2009), which is relevant here, as the distance between cell bodies in the cerebral cortex, especially prefrontal regions of humans, is greater than in other primates (Rakic, 2008). In addition, the increase in brain size is not the sole factor for the changes in cerebral size over mammalian evolution; large changes in cell number, morphology, and composition.

However, it is not sufficient to enlarge the entire brain, as Neumann (1995) has shown that the number of neurons in the cortex may differ by 2-fold among individuals. From this perspective, many genes that modify cell cycle can increase or decrease brain size but not necessarily in a manner that is relevant to cerebral cortex expansion. This is why we have focused on a more sophisticated analysis of the function of BAF-170 in mouse brain development (Tusco et al., 2013). This study shows that BAF-170 controls cortical neurogenesis via modulating the

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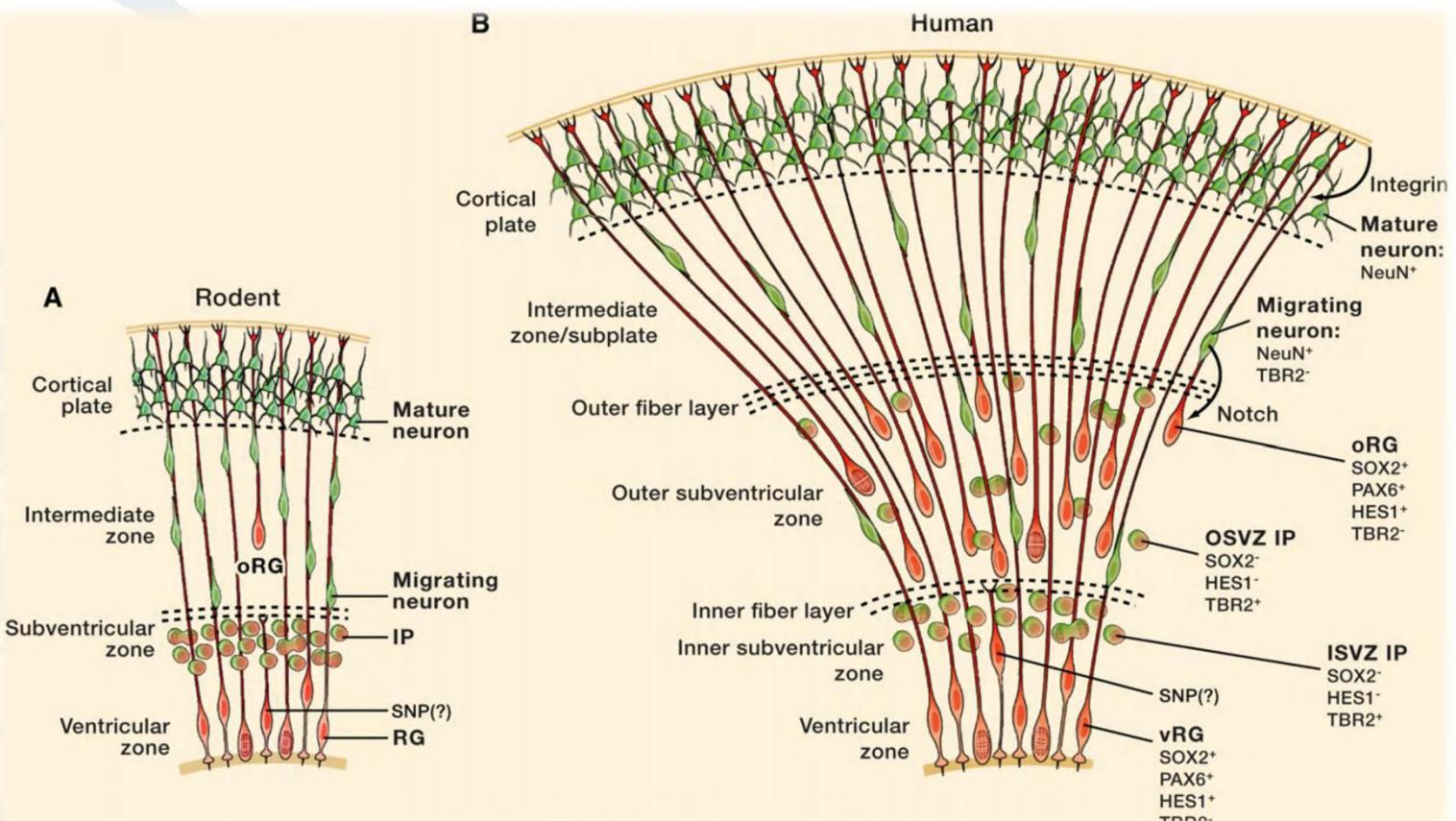
### Quantitative Differences\*

- Number of neurons and surface area ~1000 x larger
- Number or ontogenetic (radial) columns ~ 1000x higher
- Length of cell cycle length (~ 3- 4 x longer)
- Duration of cortical neurogenesis ~ 20 x longer
- Subplate Zone occupies several-fold larger portion of the embryonic cerebral wall
- Configuration gyrencephalic rather than lissencephalic
- Birth occurs during later stages of cortical development
- Lower density of neurons, larger neuropil, higher dendritic and axonal branching
- Tempo of cortical maturation in relation to onset of reproduction very different
- Very prolonged neoteny with cortical maturation surpassing puberty and adolescence

# 人鼠皮层对比

### Qualitative Differences

- Introduction of new genes, gene variants, regulatory elements, and expression patterns
- Introduction of new neuronal types (e.g. Predecessors, VEN-Spindle cells; ISN)
- Distinct upper stratum of the outer subventricular zone (OSVZ)
- Subset of GABAergic interneurons originate from the dorsal VZ/SVZ
- Neuronal migration to thalamus from the GE absent in all examined mammals (CGT)
- Transient Subpial Granular Layer (SGL, absent in rodents and carnivores)
- Distinct Radial Glial Cells (early GFAP+ and differentiated and genetically distinct)
- Modification of common cytoarchitectonic areas (e.g. layer IV in A17)
- Introduction of new cytoarchitectonic areas (e.g. A22, 28, 44, 45, 46)
- Absence of neuronal turnover and resistance to regeneration



## Development and Evolution of the Human Neocortex

Jan H. Lui,<sup>1,2,3</sup> David V. Hansen,<sup>1,2,4</sup> and Arnold R. Kriegstein<sup>1,2,\*</sup>

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The size and surface area of the mammalian brain are thought to be critical determinants of intellectual ability. Recent studies show that development of the gyrate human neocortex involves a lineage of neural stem and transit-amplifying cells that forms the outer subventricular zone (OSVZ), a proliferative region outside the ventricular epithelium. We discuss how proliferation of cells within the OSVZ expands the neocortex by increasing neuron number and modifying the trajectory of migrating neurons. Relating these features to other mammalian species and known molecular regulators of the mouse neocortex suggests how this developmental process could have emerged in evolution.

### Introduction

Evolution of the neocortex in mammals is considered to be a key advance that enabled higher cognitive function. However, neocortices of different mammalian species vary widely in shape, size, and neuron number (reviewed by Herculano-Houzel, 2009). These differences are presumably reflected in the organization and behavior of neural progenitor cells during embryonic development. Recent models of neocortical development have largely been based on cellular and molecular studies of the mouse and rat, whose neocortex exhibits many of the key features general to all mammals, including a six-layered organization and regionalization into sensory, motor, and association areas. However, because the rodent neocortex is small and nonfolded (lissencephalic), its ability to model or illuminate the developmental mechanisms of larger and highly folded (gyrencephalic) neocortex, such as that of *Homo sapiens*, is inherently limited.

Because the fossil record for soft tissues such as the brain is severely restricted, efforts to understand the evolution of the neocortex at a cellular level have been limited to comparisons of living species—an approach known as *ex-dico* (Gould, 1977). This approach assumes that related biological systems share inherent functional modularity, such that a small number of evolutionary changes to key regulators of these modules, if heritable and beneficial, can be positively selected and have major consequences for the species. Observed differences in the mechanisms of brain development across species may therefore be evolutionary variations of the same ancestral mechanisms.

Although our understanding of mouse development exceeds that of other species, recent observations of the developing neocortex in humans, nonhuman primates, carnivores, and

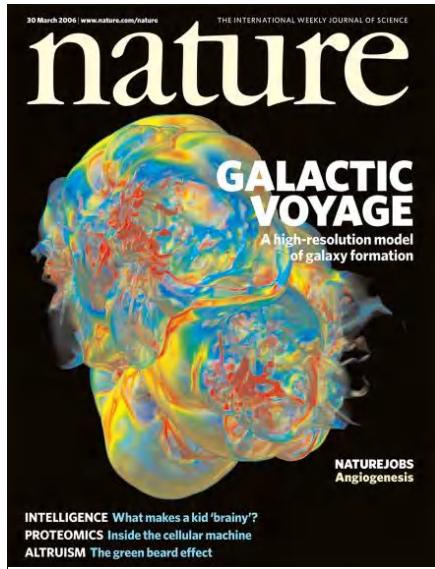
marsupials begin to reveal how differences in neural progenitor cell populations can result in neocortices of variable size and shape. Increases in neocortical volume and surface area, particularly in the human, are related to the expansion of progenitor cells in the outer subventricular zone (OSVZ) during development (Smart et al., 2002; Hansen et al., 2010; Fietz et al., 2010). Therefore, it is of increasing importance to place these developmental mechanisms in the broader context of neocortical evolution and explore how features of human neocortical development could be explained by changes to known molecular regulators of the developing rodent neocortex.

Following an introduction to previous models of neocortical expansion, this Review will focus on how the observed proliferation of stem and transit-amplifying cells in the OSVZ functions to increase neuronal number and surface area of the neocortex. We hypothesize that OSVZ proliferation is contingent on evolutionary changes that permit the generation and maintenance of neural progenitor cells outside of the ventricular epithelium and look toward molecular studies of the rodent to understand how the intracellular signaling states of neural progenitor cells could be recapitulated in the OSVZ. Finally, we will compare OSVZ proliferation in different species and explore how the degree of OSVZ proliferation may be tuned to give rise to diversity in brain size and shape.

### Historical Perspective

An appreciation that the structure and organization of the mature neocortex depends on proliferation of cells lining the ventricle of the neural tube began with the work of Wilhelm His, who from observations of the developing human neocortex, asserted several key principles: (1) that germinal cells divide rapidly in

# 脑智关联的队列研究三十年 (1989-)



Intellectual ability and cortical development in children and adolescents



2000



NIH-PD



NICH  
60

YEARS OF  
INNOVATION

PNC  
EBDS

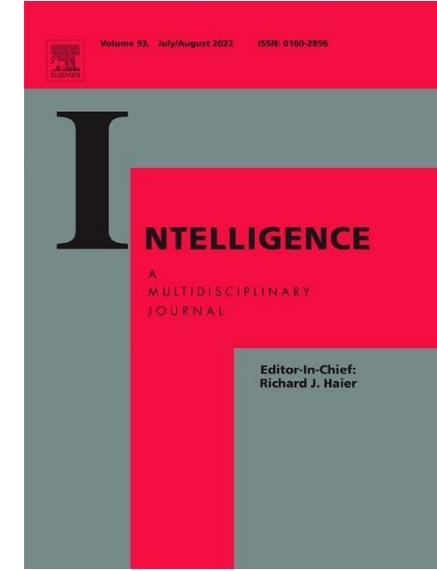
early brain development study



Adolescent Brain Cognitive Development®  
Teen Brains. Today's Science. Brighter Future.



The  
Developing Human Connectome  
Project



The biological basis of intelligence



2013

2015

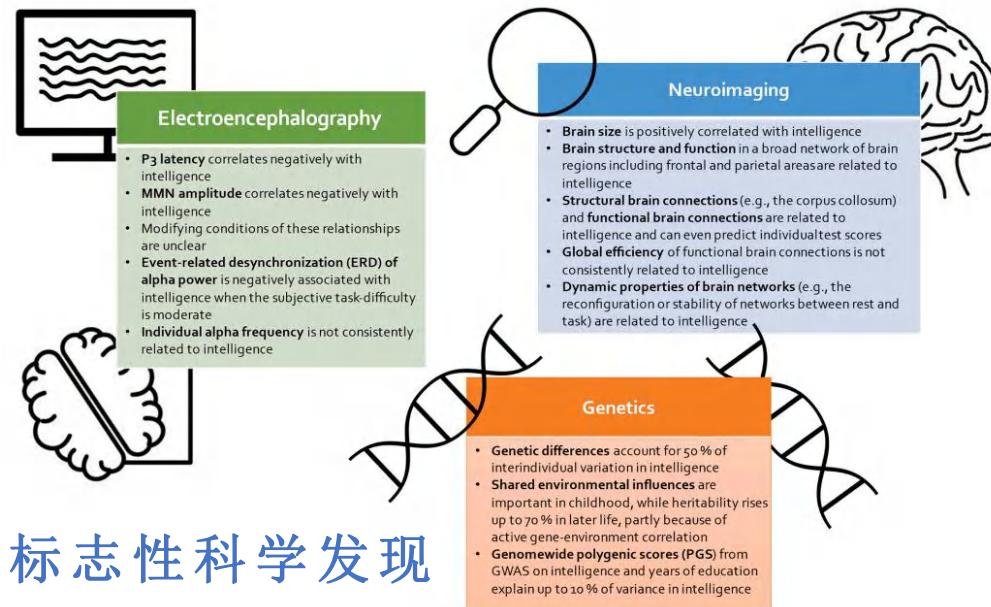
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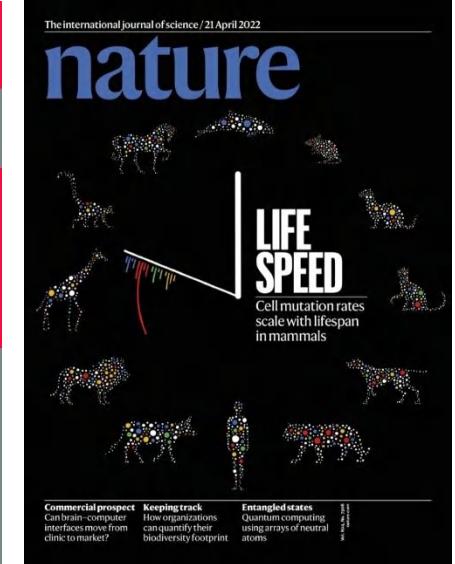
VETSA  
VIETNAM ERA TWIN STUDY OF AGING



The HEALthy Brain and Child Development Study  
Understanding long-term effects of opioids, other exposures on early childhood development



标志性科学发现



Brain charts for the human lifespan

# NIMH-CPB加速纵向队列 (1989)

nature  
Vol 440(30 March 2006) doi:10.1038/nature04513

## LETTERS

### Intellectual ability and cortical development in children and adolescents

P. Shaw<sup>1</sup>, D. Greenstein<sup>1</sup>, J. Lerch<sup>2</sup>, L. Clasen<sup>1</sup>, R. Lenroot<sup>1</sup>, N. Gogtay<sup>1</sup>, A. Evans<sup>2</sup>, J. Rapoport<sup>1</sup> & J. Giedd<sup>1</sup>

Children who are adept at any one of the three academic 'R's (reading, writing and arithmetic) tend to be good at the others, and grow into adults who are similarly skilled at diverse intellectually demanding activities<sup>1–3</sup>. Determining the neuroanatomical correlates of this relatively stable individual trait of general intelligence has proved difficult, particularly in the rapidly developing brains of children and adolescents. Here we demonstrate that the trajectory of change in the thickness of the cerebral cortex, rather than cortical thickness itself, is most closely related to level of intelligence. Using a longitudinal design, we find a marked developmental shift from a predominantly negative correlation between intelligence and cortical thickness in early childhood to a positive correlation in late childhood and beyond. Additionally, level of intelligence is associated with the trajectory of cortical development, primarily in frontal regions implicated in the maturation of intelligent activity<sup>4–6</sup>. More intelligent children demonstrate a particularly plastic cortex, with an initial accelerated and prolonged phase of cortical increase, which yields to equally vigorous cortical thinning by early adolescence. This study indicates that the neuroanatomical expression of intelligence in children is dynamic.

Structural neuroimaging studies generally report a modest correlation ( $r = 0.3$ ) between psychometric measures of intelligence and total brain volume<sup>7</sup>. Links between intelligence and specific regions of the brain may vary according to developmental stage: the anterior cingulate in children<sup>8</sup>, the orbitofrontal and medial prefrontal cortex in adolescents<sup>9</sup>, and the lateral prefrontal cortex in older adults<sup>10</sup>. Most previous studies infer developmental processes from purely cross-sectional data, an endeavour fraught with methodological complications<sup>11</sup>. Only one longitudinal study has linked cortical development with cognitive variation, demonstrating greater cortical thinning in the left dorsal frontal and parietal regions among children who gained more in a measure of verbal intelligence<sup>12</sup>. However, this study was limited by its small sample size ( $n = 45$ ), narrow age range (5–11 yr), and consideration of only linear cortical change, whereas brain development generally follows more complex growth patterns<sup>13</sup>.

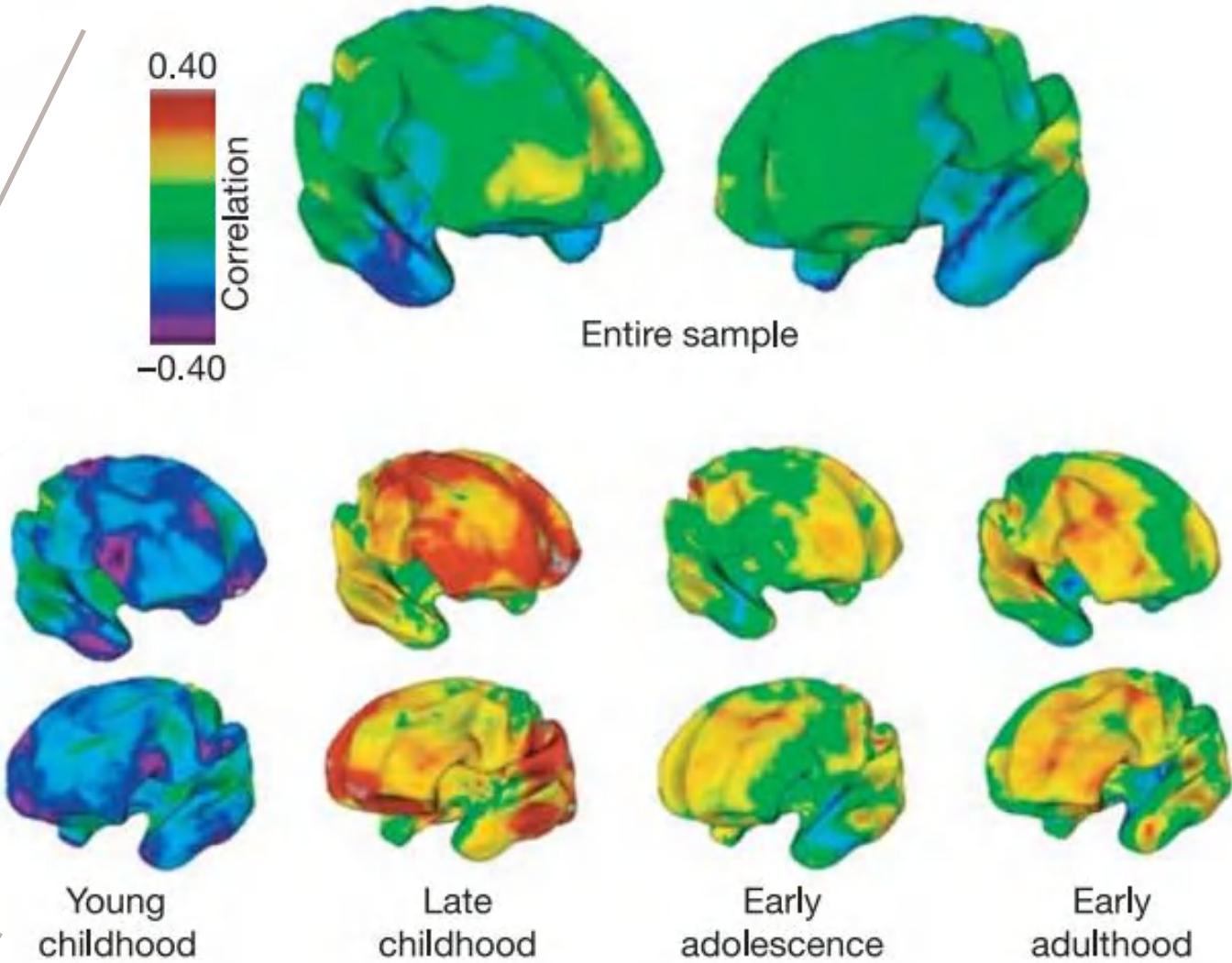
We characterized brain development from childhood to adulthood in a large group of typically developing subjects ( $n = 307$ ), the majority of whom had prospectively acquired repeated neuroanatomic scans (see the Methods). Subjects were stratified on the basis of Wechsler intelligence scales, which give a standardized 'intelligence quotient' (IQ) based on subtests assessing verbal and non-verbal knowledge and reasoning<sup>14</sup>. We examined the thickness of the cortex throughout the entire cerebrum, as it is a sensitive index of normal brain development<sup>15,16</sup>, using a fully automated technique, and have validated these measurements by expert manual determination of cortical thickness and population simulations<sup>14,17</sup>. We reasoned that the trajectory of cortical development in children stratified on the

basis of IQ would differ primarily in the prefrontal cortex, which has both structural and functional correlations with intelligence. The institutional review board of the National Institutes of Mental Health approved the research protocol, and written informed consent and assent were obtained from parents and children, respectively.

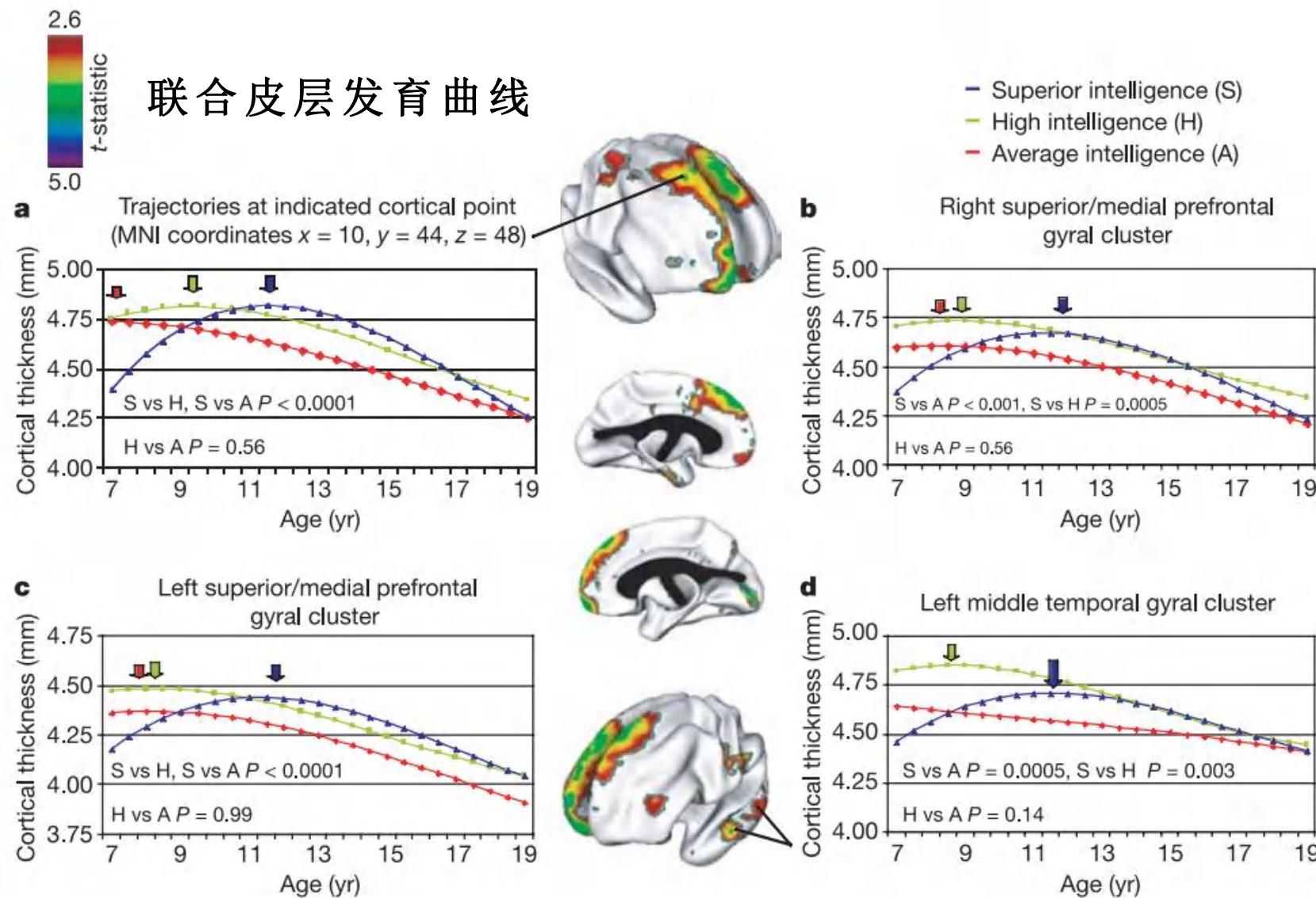
We estimated Pearson's correlations for all subjects (each subject contributing one scan), and found modest positive correlations throughout most of the frontal, parietal and occipital cortex, and similarly modest negative correlations in the anterior temporal cortex (Fig. 1 and Supplementary Table 1). Throughout most of the cerebral cortex, the correlations were not significant at an unadjusted  $P < 0.05$ .

Dividing the sample into different age groups, however, revealed notable age-related changes. A predominantly negative correlation between IQ and cortical thickness in the early childhood group contrasted with later positive correlations, which peaked in late childhood, but were present in an attenuated form in the adolescent and early adult groups. The change in the valence of the correlation between IQ and cortical thickness was significant between the young and late childhood groups throughout the prefrontal cortex, and the

**Figure 1 Correlations between IQ and cortical thickness.** a. Pearson's correlations for all 307 subjects were generally positive and modest ( $P > 0.05$ ), with  $r$  between 0 and 0.10 (green/yellow), except in the anterior temporal cortex, which showed a negative correlation, with  $r$  between 0 and -0.1; (purple/blue). b. Correlations in different age groups showed that negative correlations were present in the youngest group, indicating that higher IQ was associated with a thinner cortex particularly in frontal and temporal regions. The relationship reverses in late childhood, with most of the cerebral cortex correlating positively with IQ.

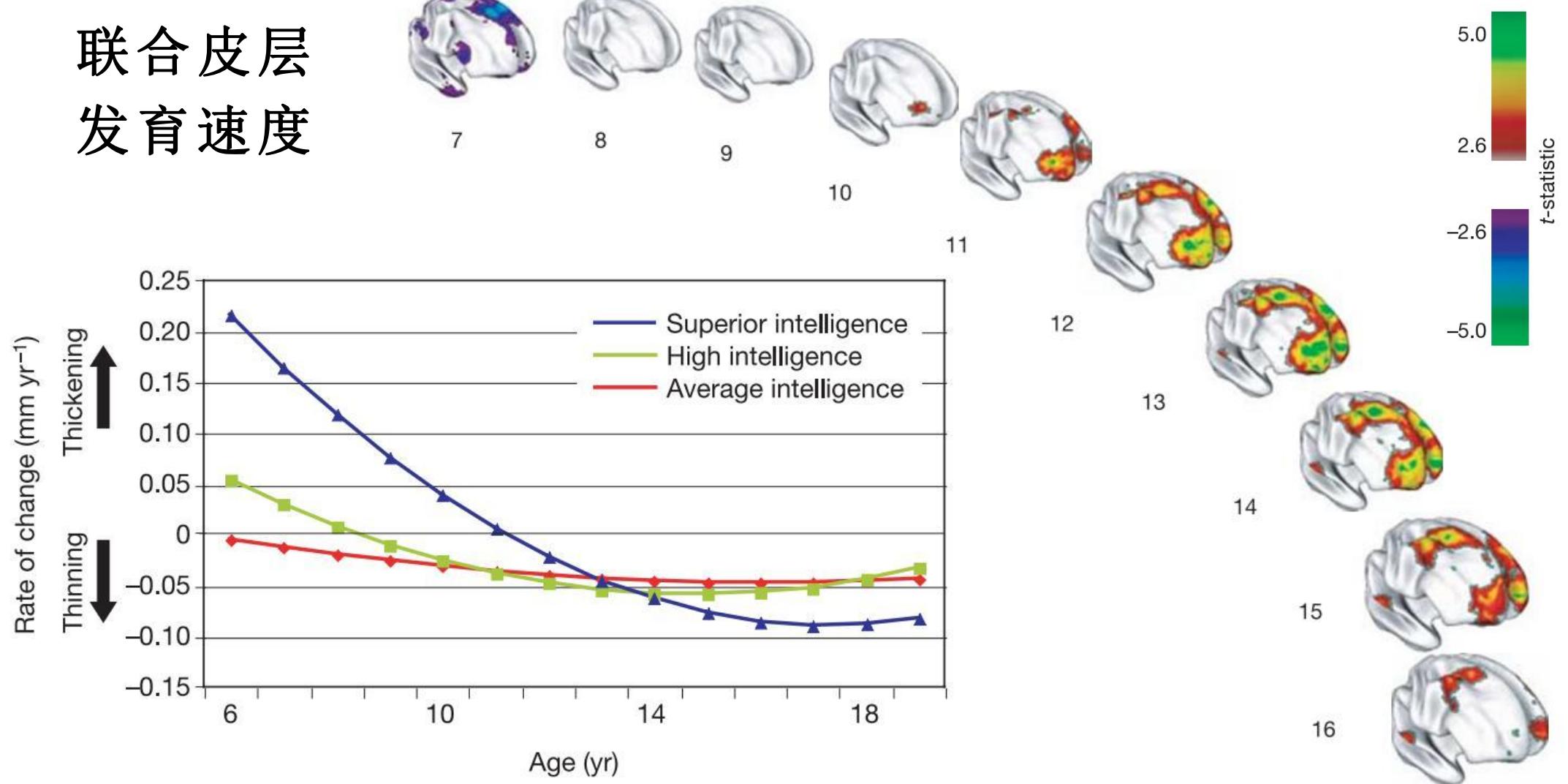


# NIMH-CPB加速纵向队列 (1989)

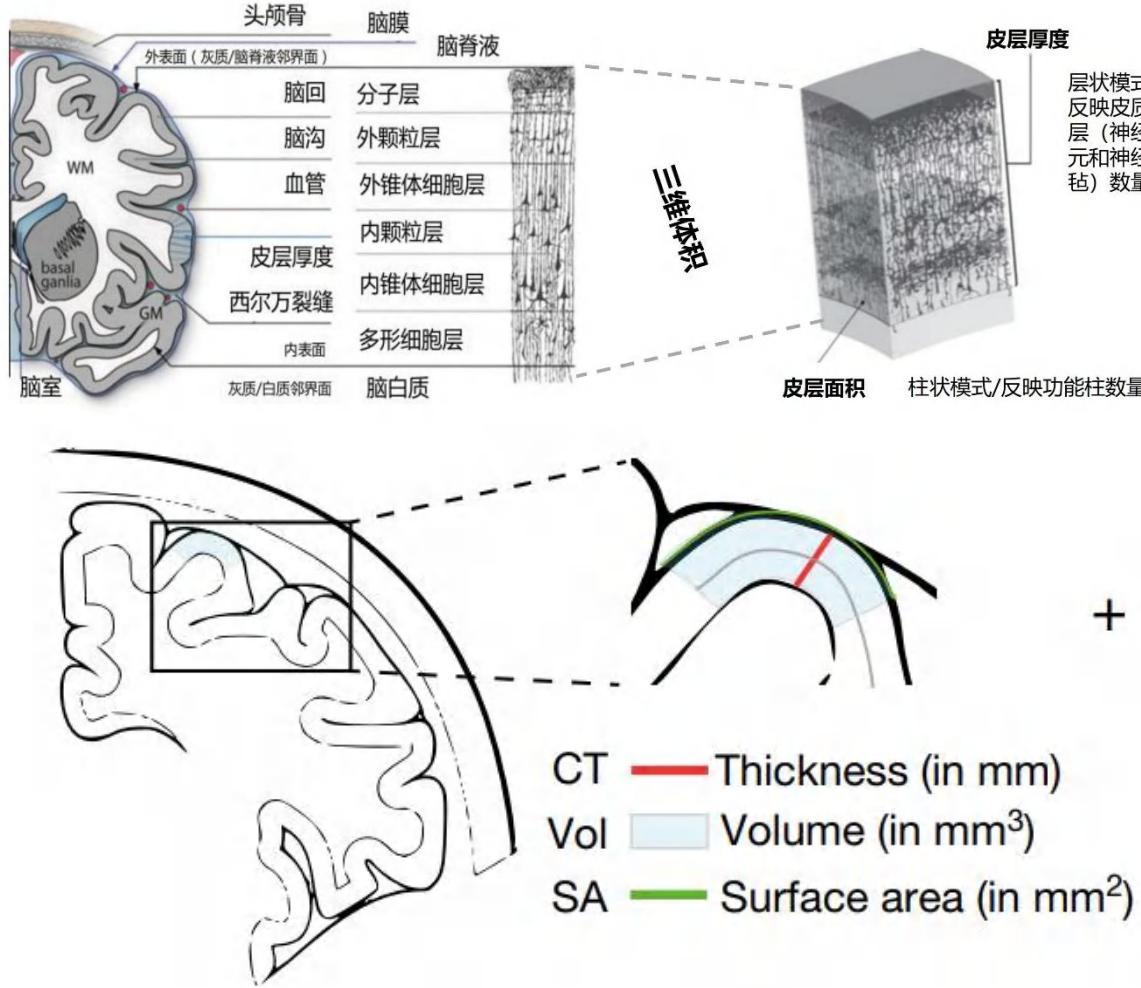


# NIMH-CPB加速纵向队列 (1989)

联合皮层  
发育速度



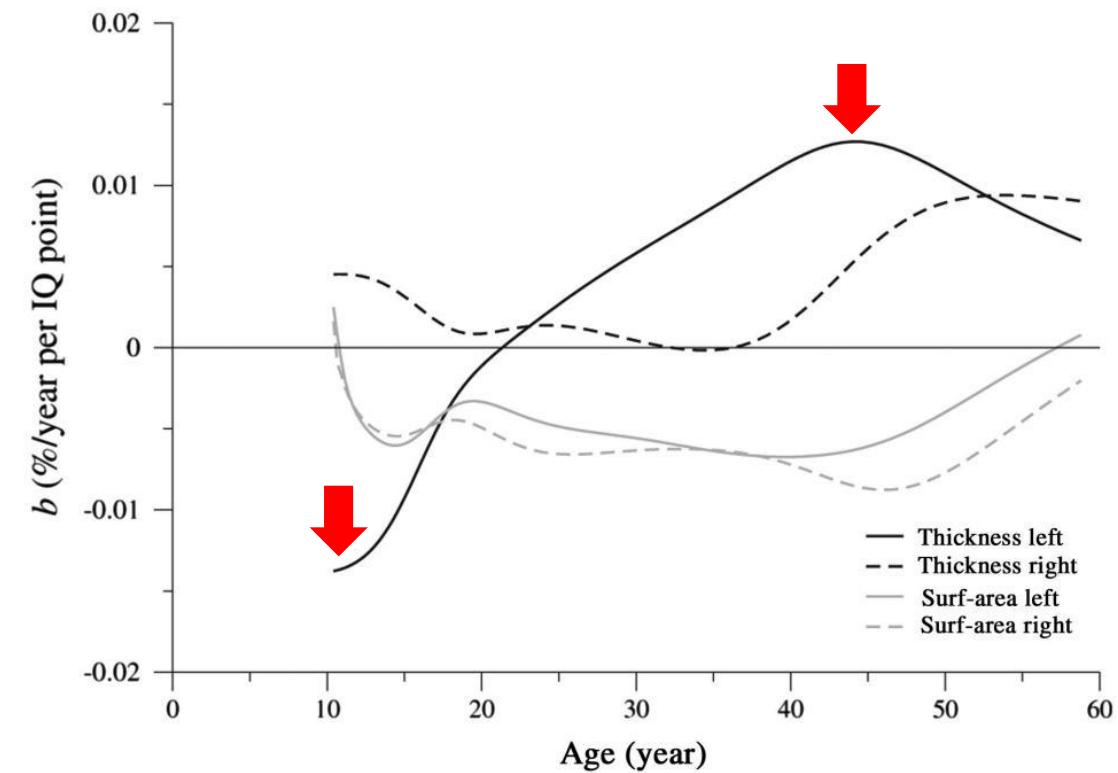
# UMC-Utrecht纵向加速队列 (2006)



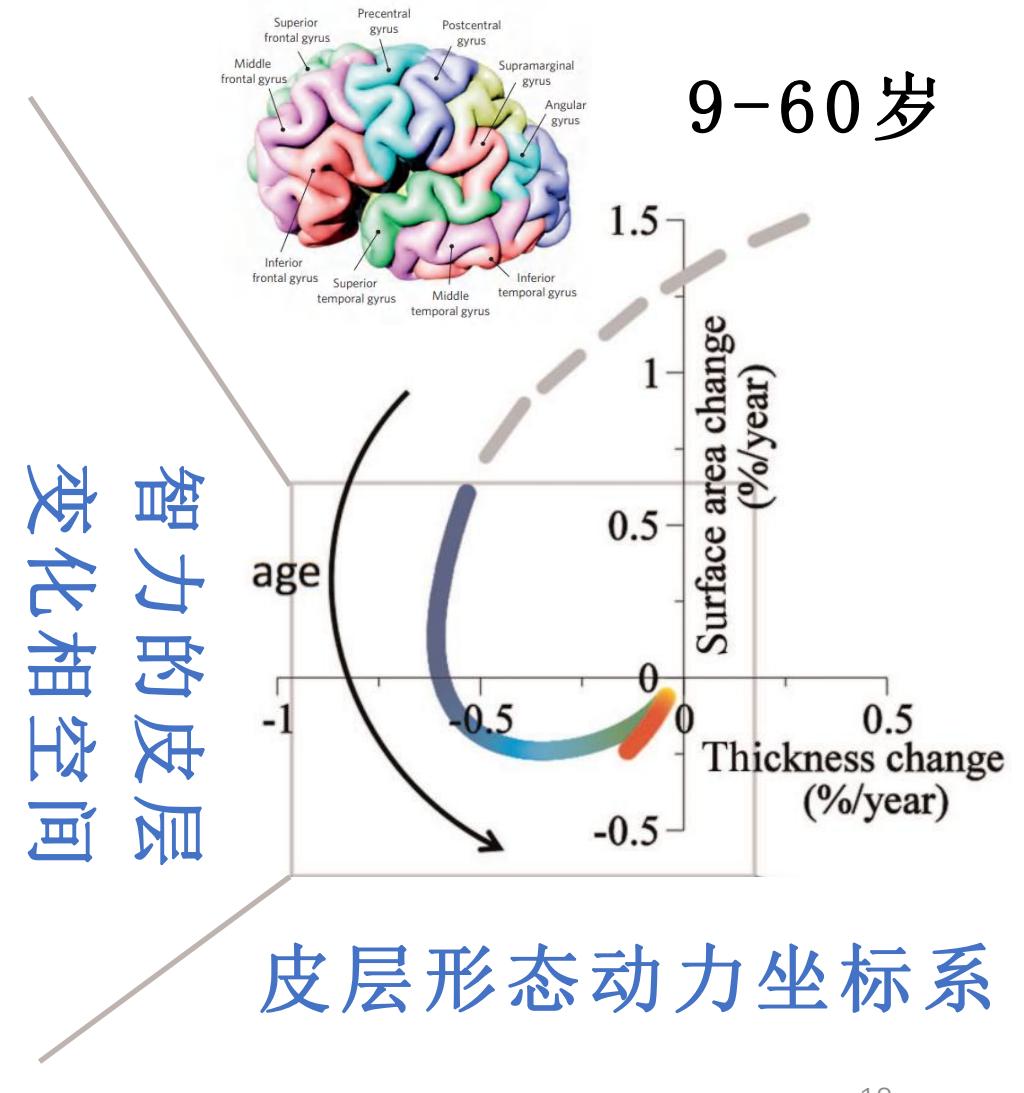
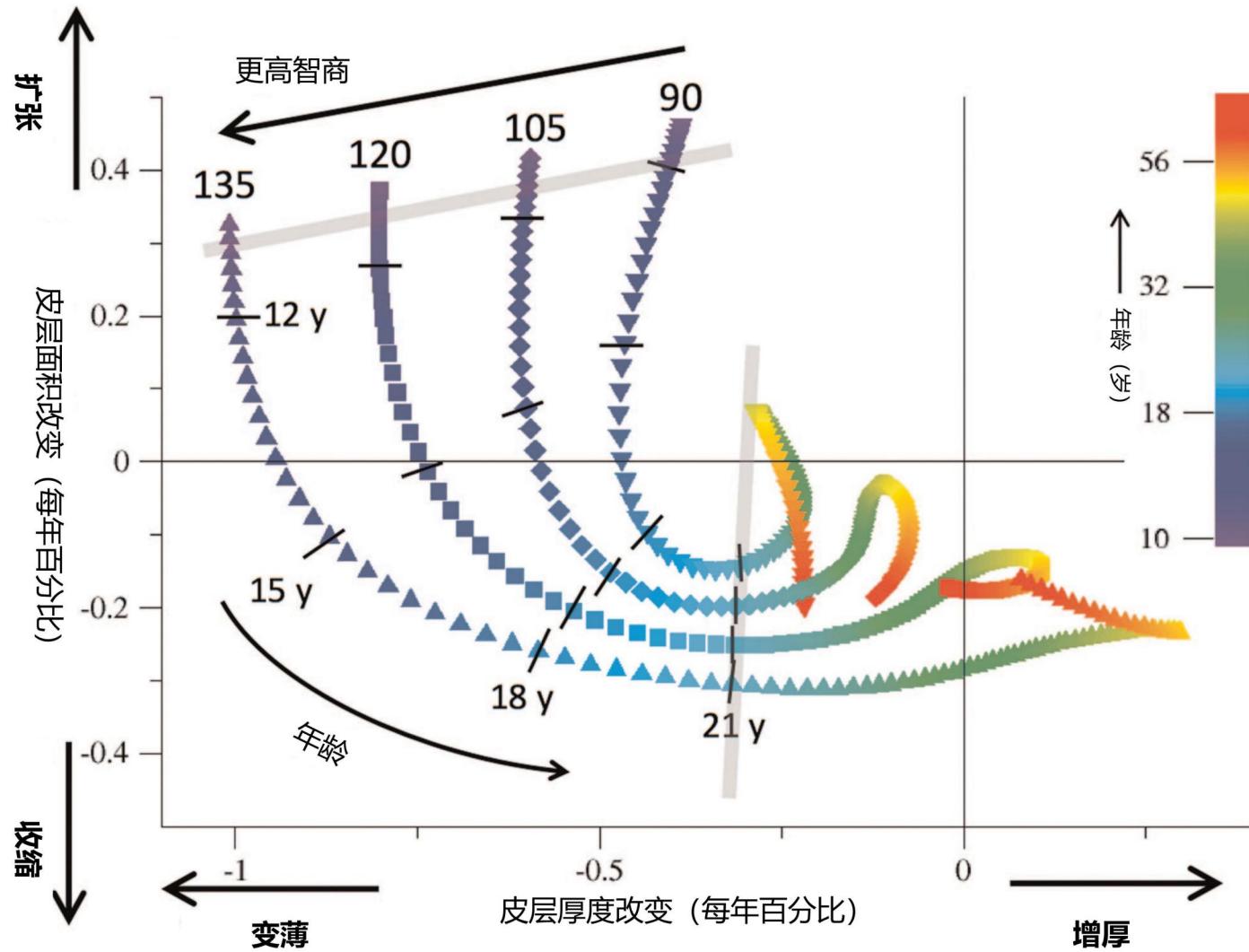
Cerebral Cortex June 2015;25:1608–1617  
doi:10.1093/cercor/bht357  
Advance Access publication January 9, 2014

## Changes in Thickness and Surface Area of the Human Cortex and Their Relationship with Intelligence

Hugo G. Schnack<sup>1</sup>, Neeltje E.M. van Haren<sup>1</sup>, Rachel M. Brouwer<sup>1</sup>, Alan Evans<sup>2</sup>, Sarah Durston<sup>1</sup>, Dorret I. Boomsma<sup>3</sup>, René S. Kahn<sup>1</sup> and Hilleke E. Hulshoff Pol<sup>1</sup>



# UMC-Utrecht纵向加速队列 (2006)



# NIH-ABCD纵向队列 (2013)

## 横断设计的挑战

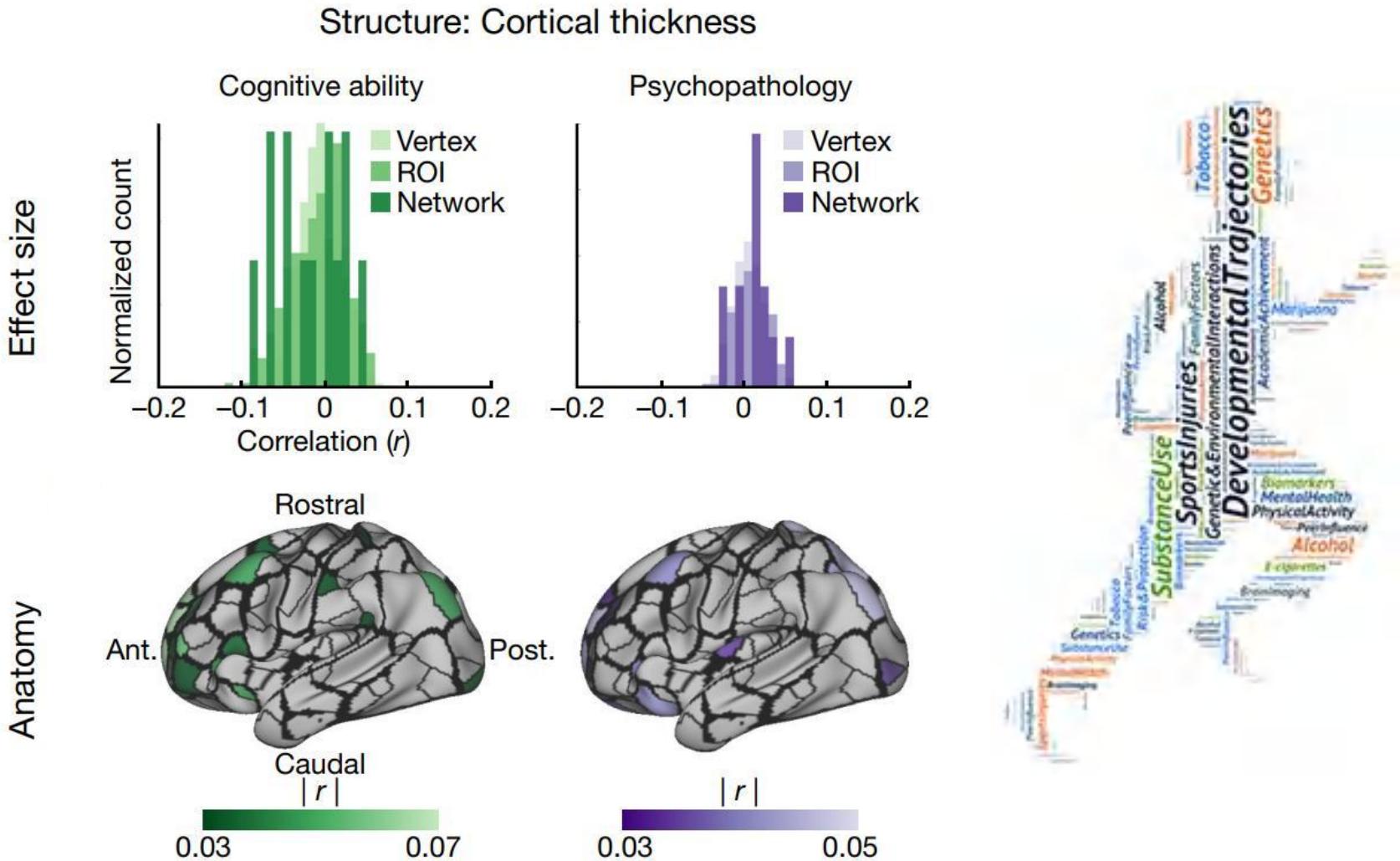
### Article Reproducible brain-wide association studies require thousands of individuals

https://doi.org/10.1038/nature222-022-04492-9  
Received: 19 May 2021  
Accepted: 31 January 2022  
Published online: 16 March 2022  
Open access  
Check for updates

9-1  
Magnetic resonance imaging (MRI) has transformed our understanding of the human brain through well-replicated mappings of abilities to specific structures (for example, lesion studies) and functions (for example, task functional MRI (fMRI)). Mental health research and care have yet to realize similar advances from MRI. A primary challenge has been replicating associations between inter-individual differences in brain structure or function and complex cognitive or mental health phenotypes (brain-wide association studies (BWAS)). Such BWAS have typically relied on sample sizes appropriate for classical brain mapping<sup>1</sup> (the median neuroimaging study sample size is about 25), but potentially too small for capturing reproducible brain-behavioural phenotype associations<sup>2</sup>. Here we used three of the largest neuroimaging datasets currently available – with a total sample size of around 50,000 individuals – to quantify BWAS effect sizes and reproducibility as a function of sample size. BWAS associations were smaller than previously thought, resulting in statistically underpowered studies, inflated effect sizes and replication failures at typical sample size. As sample size grew into the thousands, replication rates began to improve and effect size inflation decreased. More robust BWAS effects were detected for functional MRI (versus structural), cognitive tests (versus mental health questionnaires) and multivariate methods (versus univariate). Smaller than expected brain–phenotype associations and variability across population subsamples can explain widespread BWAS replication failures. In contrast to non-BWAS approaches with larger effects (for example, lesions, interventions and within-person), BWAS reproducibility requires samples with thousands of individuals.

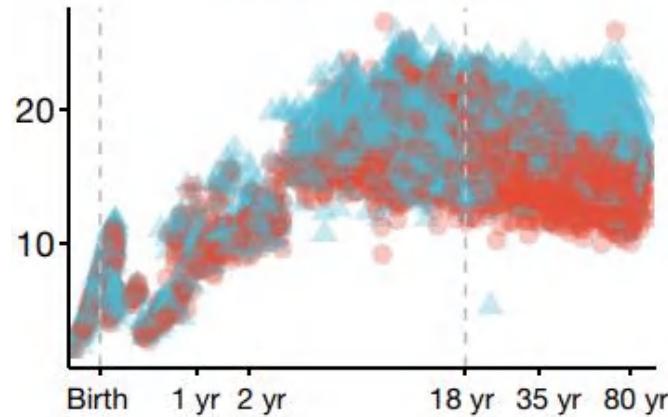
MRI data (such as cortical thickness or resting-state functional connectivity (RSFC)) is increasingly being used to address the task of relating individual differences in brain structure and function to complex cognitive and psychological phenotypes (for example, cognitive ability and psychopathology). To clearly distinguish such BWAS from other neuroimaging research, we formally define them as studies of the associations between inter-individual variability in cognitive and psychological traits and corresponding brain structure or function. BWAS are typically univariate. BWAS have recently been becoming more powerful, but more difficult to interpret multivariate prediction techniques (for example, support vector regression (SVR) and canonical correlation analysis (CCA)). BWAS hold great promise for predicting and reducing psychiatric disease burden and advancing our understanding of the cognitive abilities that underlie complex real-world tasks. However, obtaining large and diverse samples is expensive (requiring up to 100 per participant), resulting in small sample BWAS findings that have not been replicated<sup>3–5</sup>.

Factors that have contributed to poor reproducibility of population-based research in psychology<sup>6</sup>, genomics<sup>7,8</sup> and medicine<sup>9</sup>, such as methodological variability<sup>9</sup>, data mining for significance<sup>10</sup>, lack of power<sup>11</sup> and statistical overfitting<sup>12,13</sup>, and inadequate statistical power<sup>14</sup> probably also affect BWAS. Researchers are starting to address replication failures by standardizing analyses, pre-registering hypotheses, publishing null results and sharing data and code<sup>15</sup>. Nevertheless, there have been concerns that reliance on

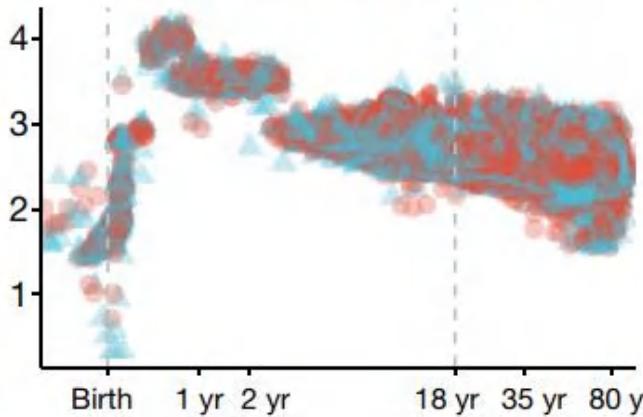


# IBC国际脑图表联盟 (2022)

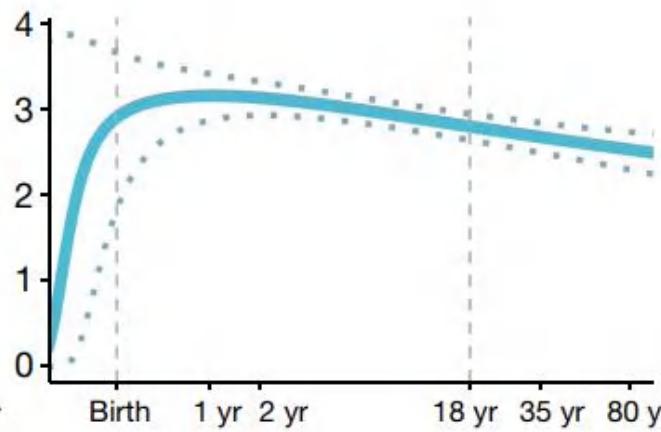
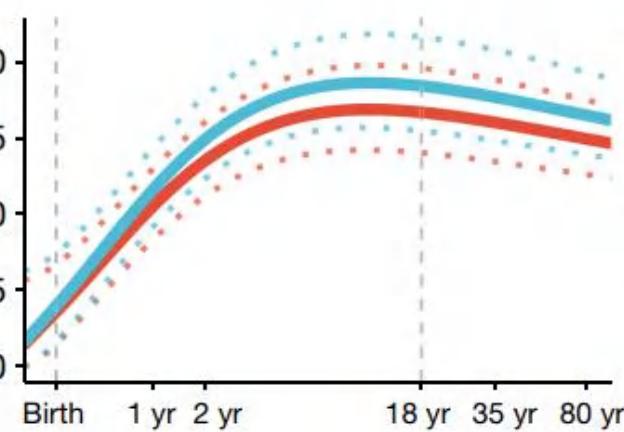
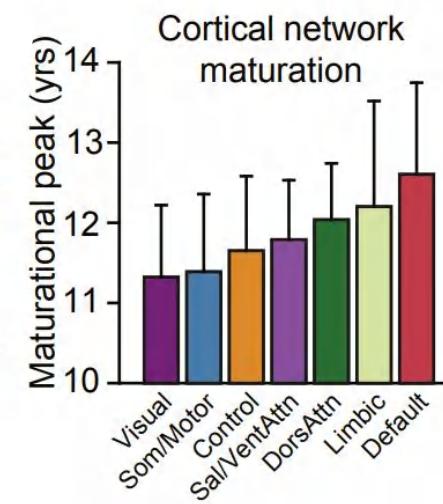
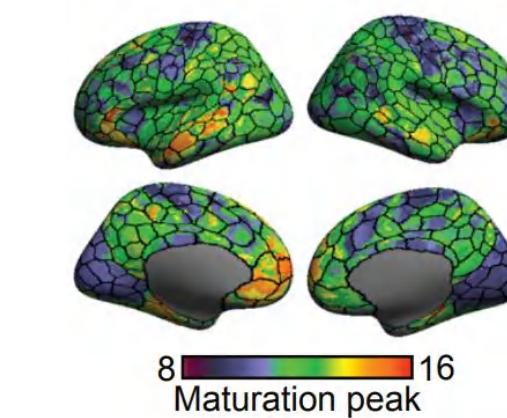
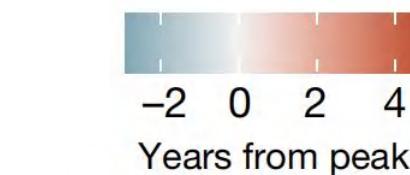
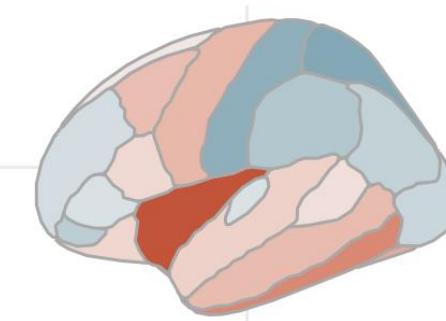
Total surface area



Mean cortical thickness

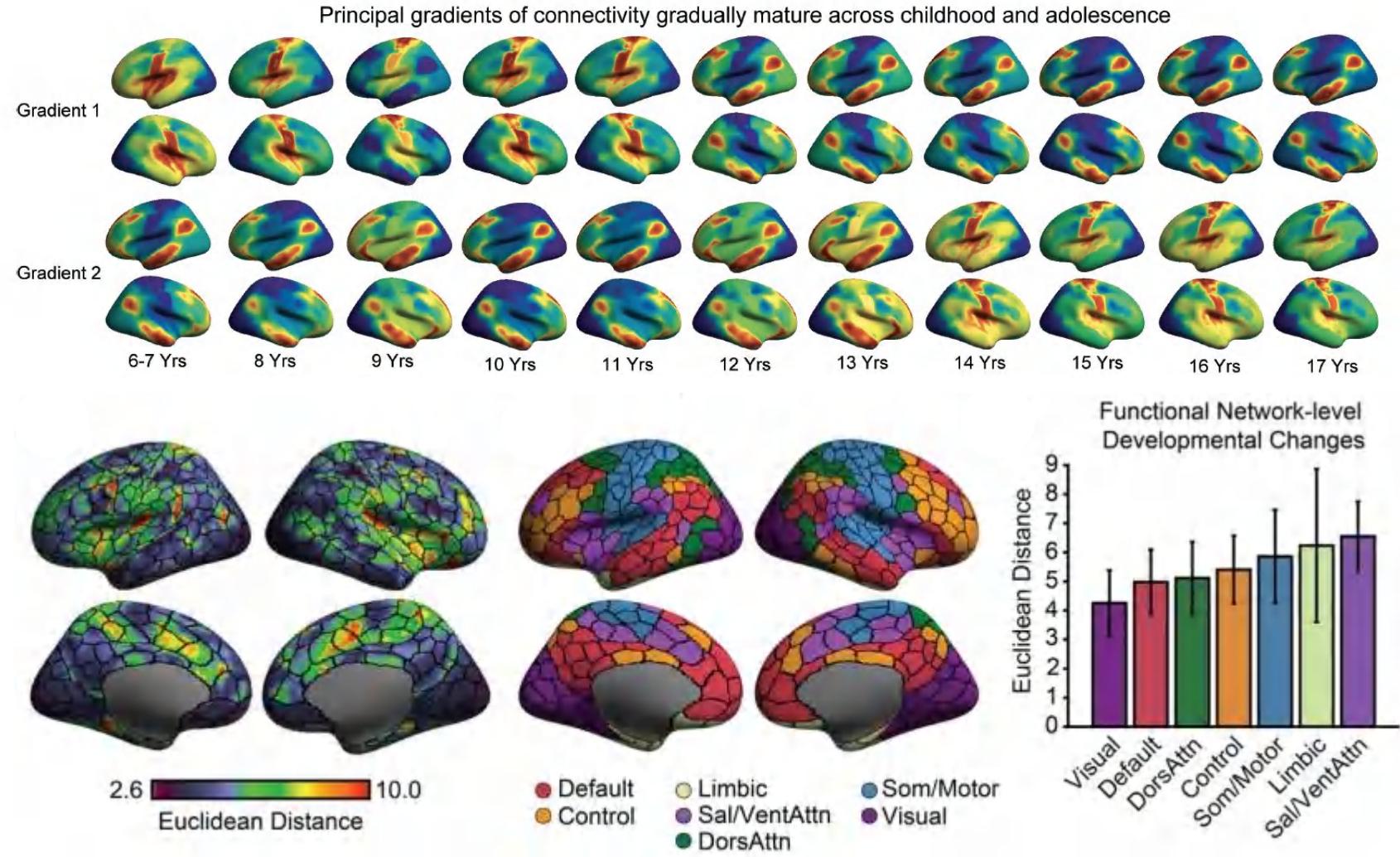
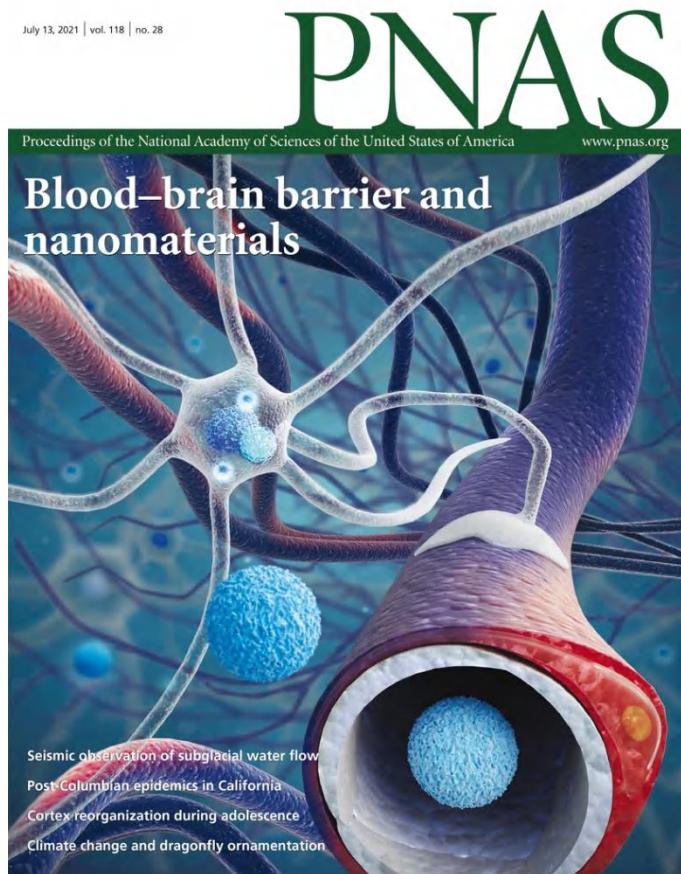


皮层成熟图谱



# devCCNP加速纵向队列 (2013)

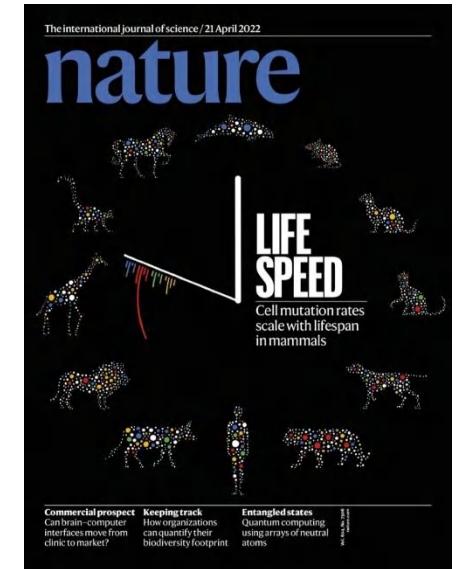
July 13, 2021 | vol. 118 | no. 28



# IBC国际脑图表联盟-开放式大规模脑智研究范式

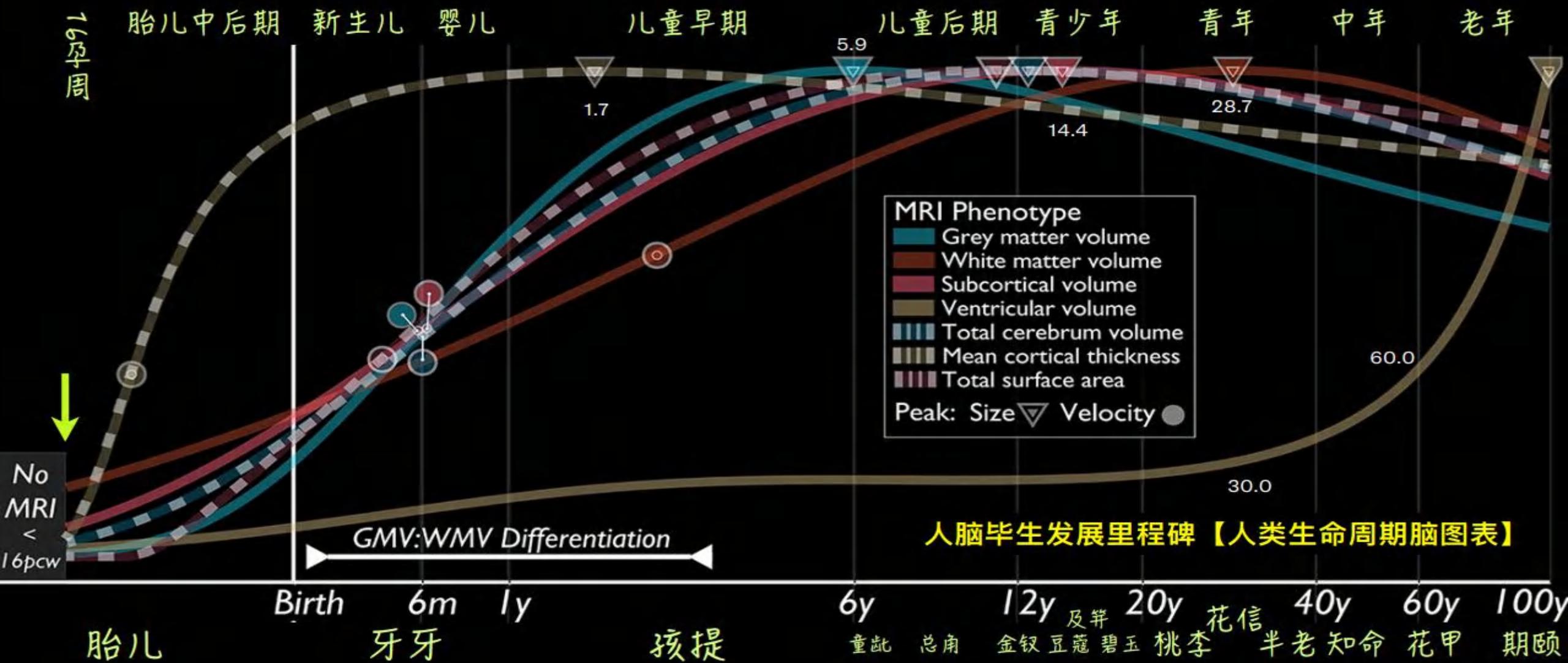


- > 100 datasets
- > 100k participants
- > 120k samples
- Ages: 115 days - 100 years
- Team work
- Open science
- Reproducibility



# 人类生命周期脑图表草图揭示脑智发展里程碑

详细内容解读请参见 <http://deepneuro.bnu.edu.cn/?p=625>



# Brain-Mind Development across The Human Lifespan

科学通报 2015年 第60卷 第11期: 966 ~ 975

专题: 心理学与大数据

评述

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评述

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## 神经影像大数据与心脑关联: 方法学框架与应用

杨志\*, 左西年\*

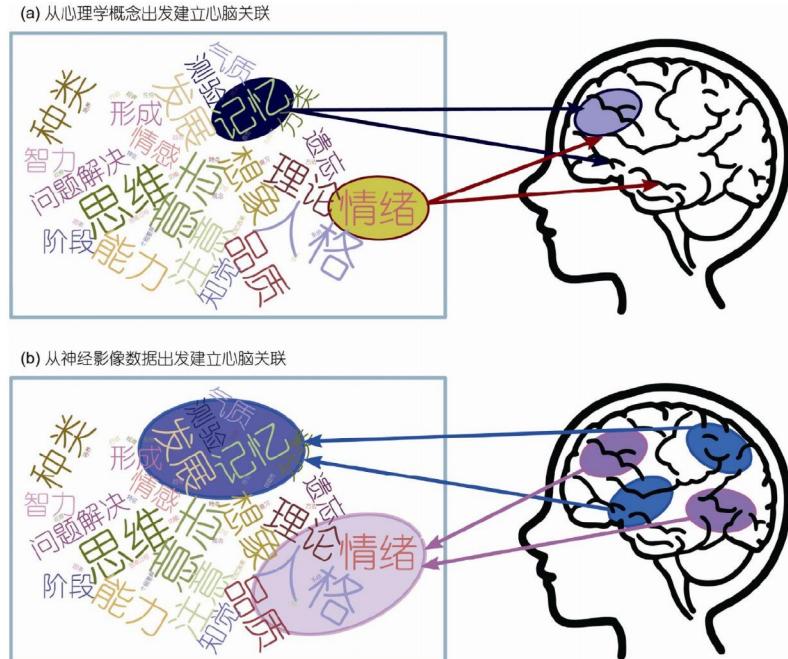


图1 两种心脑关联的研究策略. (a) 传统的心脑关联研究策略: 从现有心理学概念出发, 检验与心理学概念关联的脑活动特征; (b) 以脑为中心的心脑关联研究策略: 从脑功能网络出发, 检验与脑功能网路关联的心智、行为特征集合

## 发展认知神经科学: 人脑毕生发展的功能连接组学时代

颜志雄<sup>①②</sup>, 刘勋<sup>①</sup>, 谭淑平<sup>③</sup>, 谭云龙<sup>③</sup>, 魏高峰<sup>①</sup>, 杨志<sup>①④</sup>, 左西年<sup>①②\*</sup>

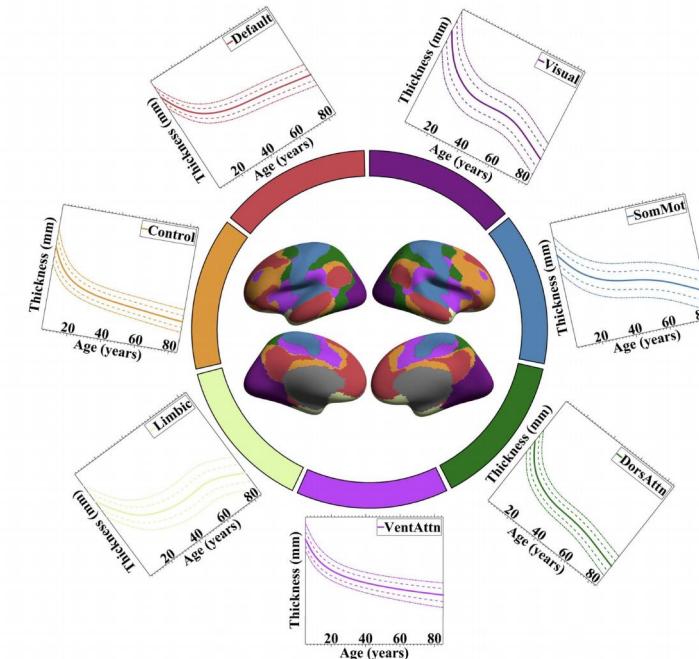
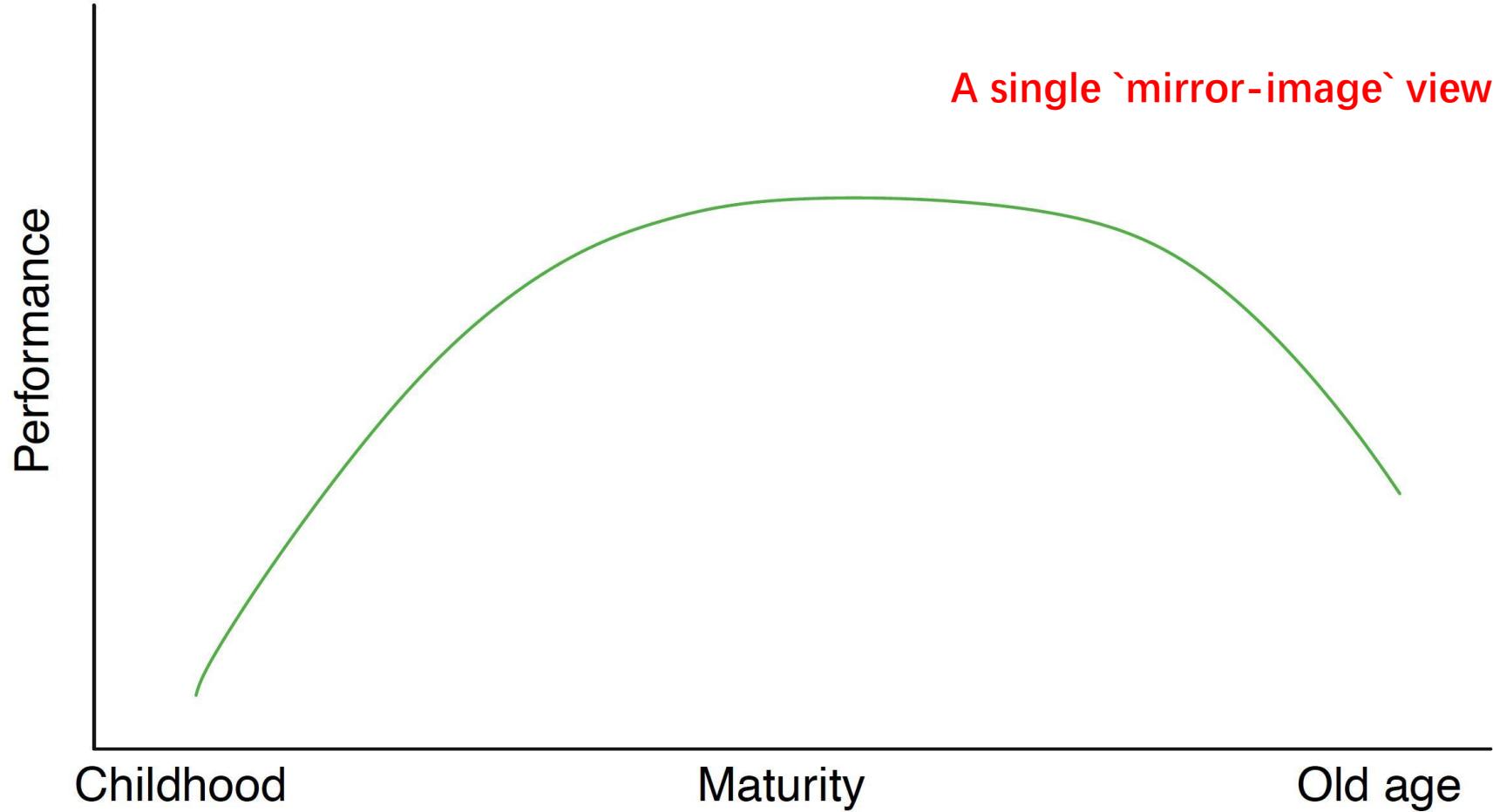


图1 人脑功能网络皮层厚度毕生发展轨迹(摘自文献[57]). 人脑七大皮层功能网络分别为: 视觉网络(Visual)、体感运动网络(SomMot)、边缘网络(Limbic)、默认网络(Default)、控制网络(Control)、背侧注意网络(DorsAttn)和腹侧注意网络(VentAttn). 圆图的中央部分表示这七大功能网络在皮层上的空间分布(上部分: 外侧面; 下半部分: 内侧面; 左半部分: 左半球; 右半部分: 右半球). 圆环部分表示各网络空间分布和发展轨迹的色彩, 外周部分表示七大功能网络皮层厚度的毕生发展轨迹, 各网络内的曲线分别表示其皮层厚度的百分位数在: 10%, 25%, 50%, 75%, 90%以上的分布(年龄分布范围5~90岁)

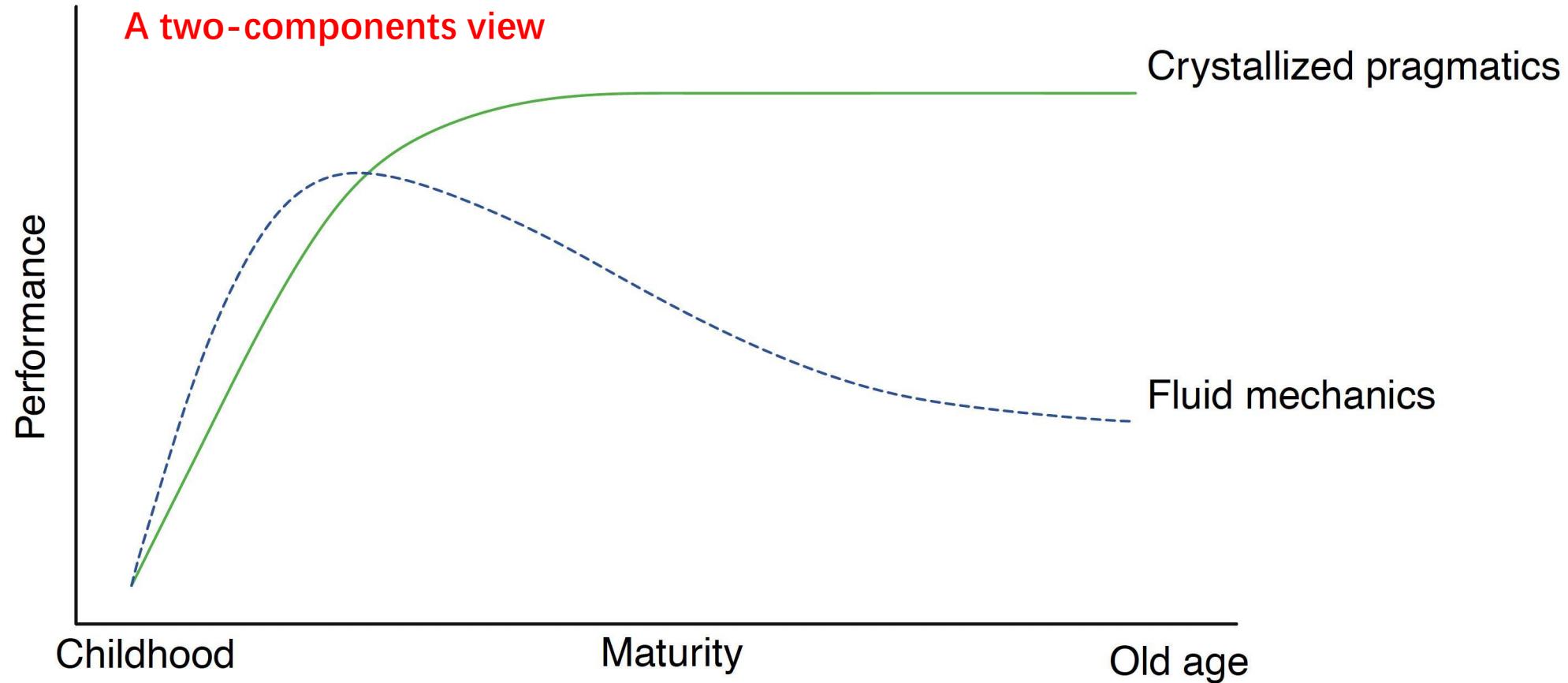
# Brain-Mind Development across The Human Lifespan

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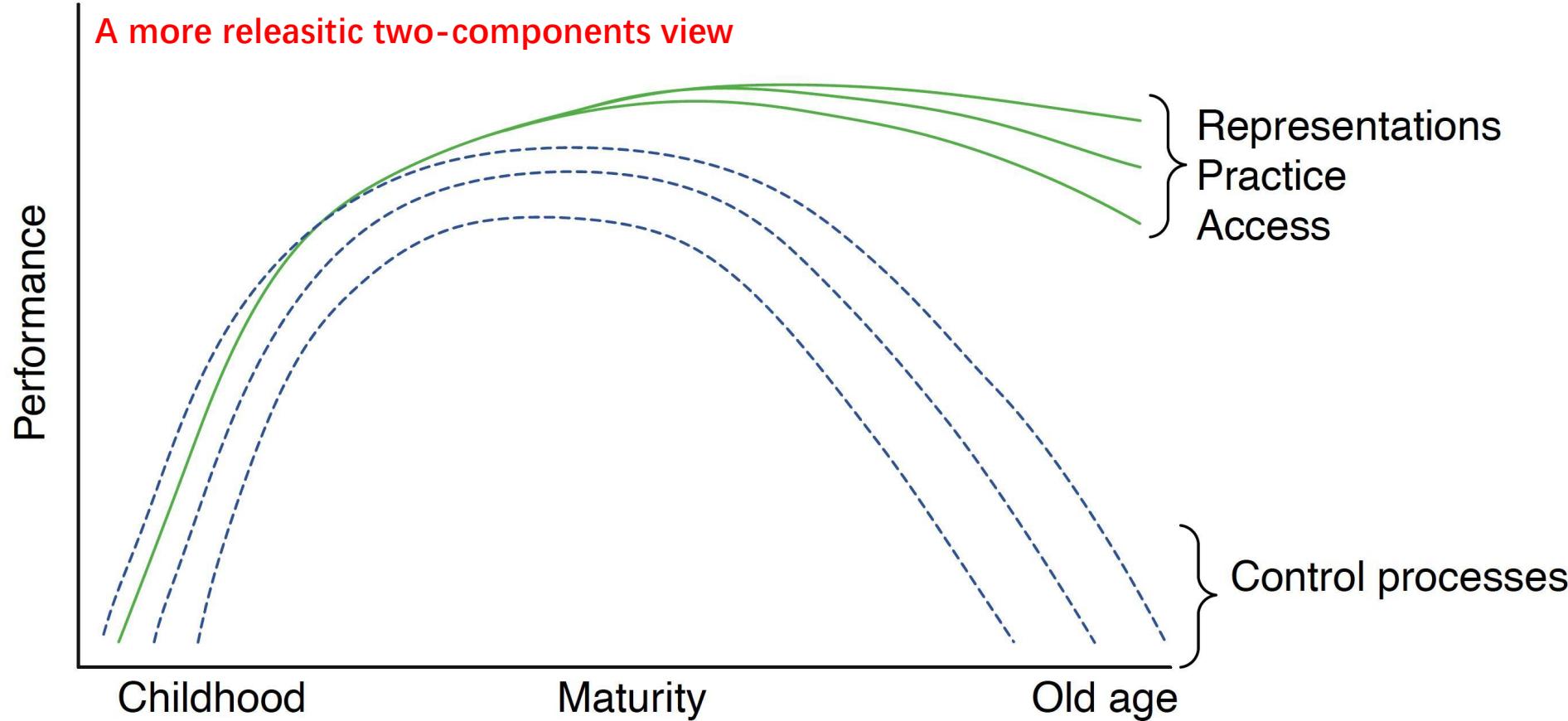
# Brain-Mind Development across The Human Lifespan

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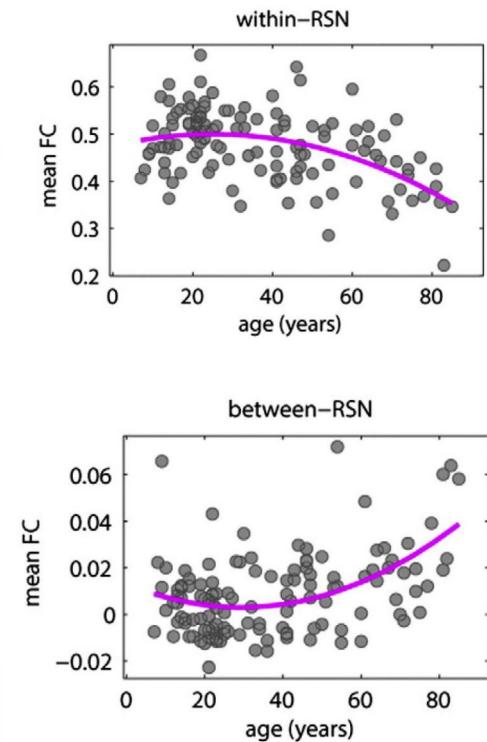
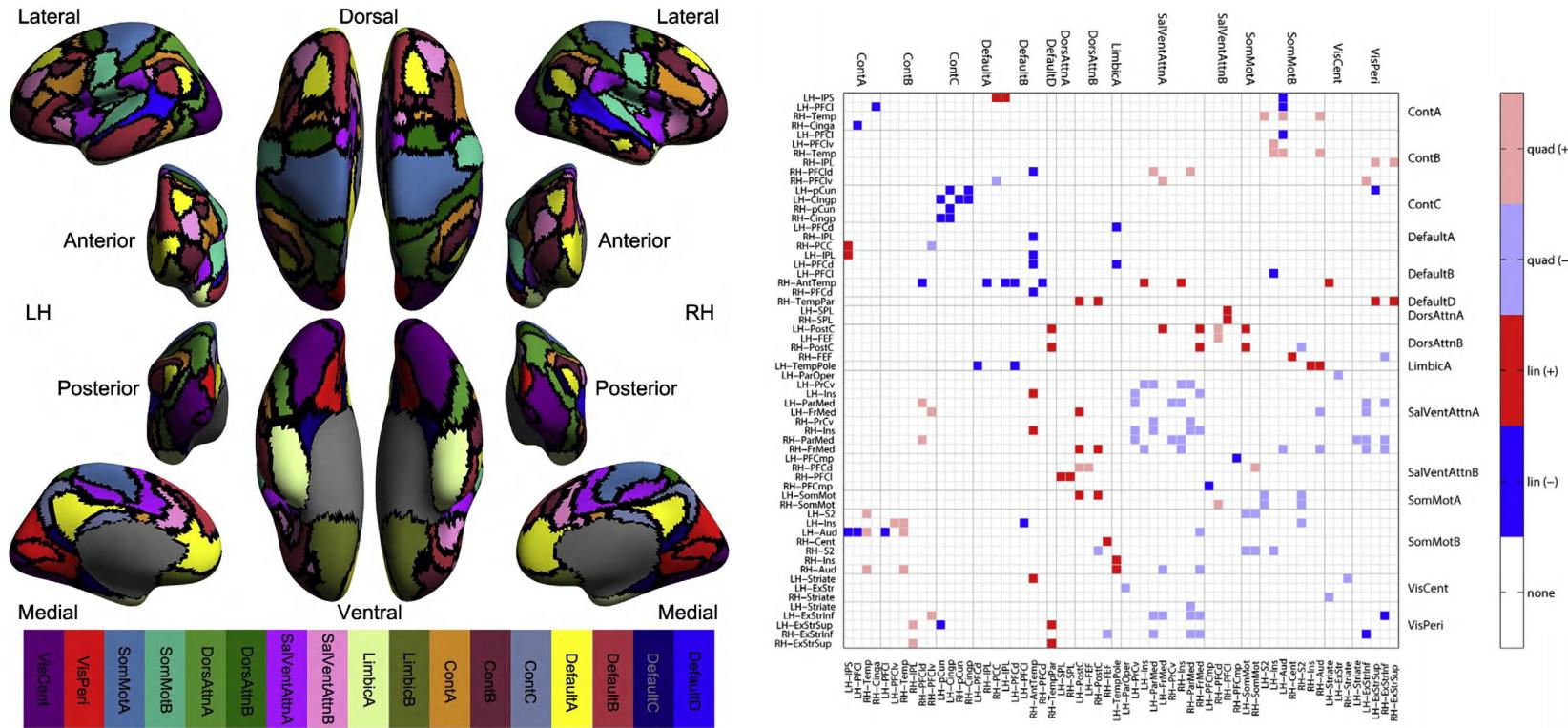


# Brain-Mind Development across The Human Lifespan

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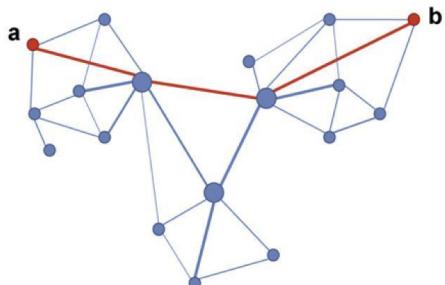
# Brain-Mind Development across The Human Lifespan



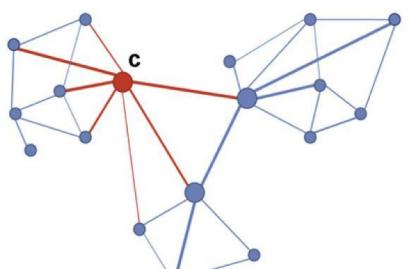
# Brain-Mind Development across The Human Lifespan

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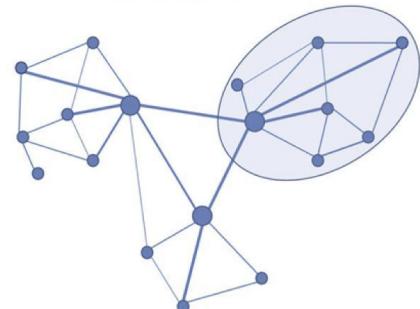
A. Characteristic path length



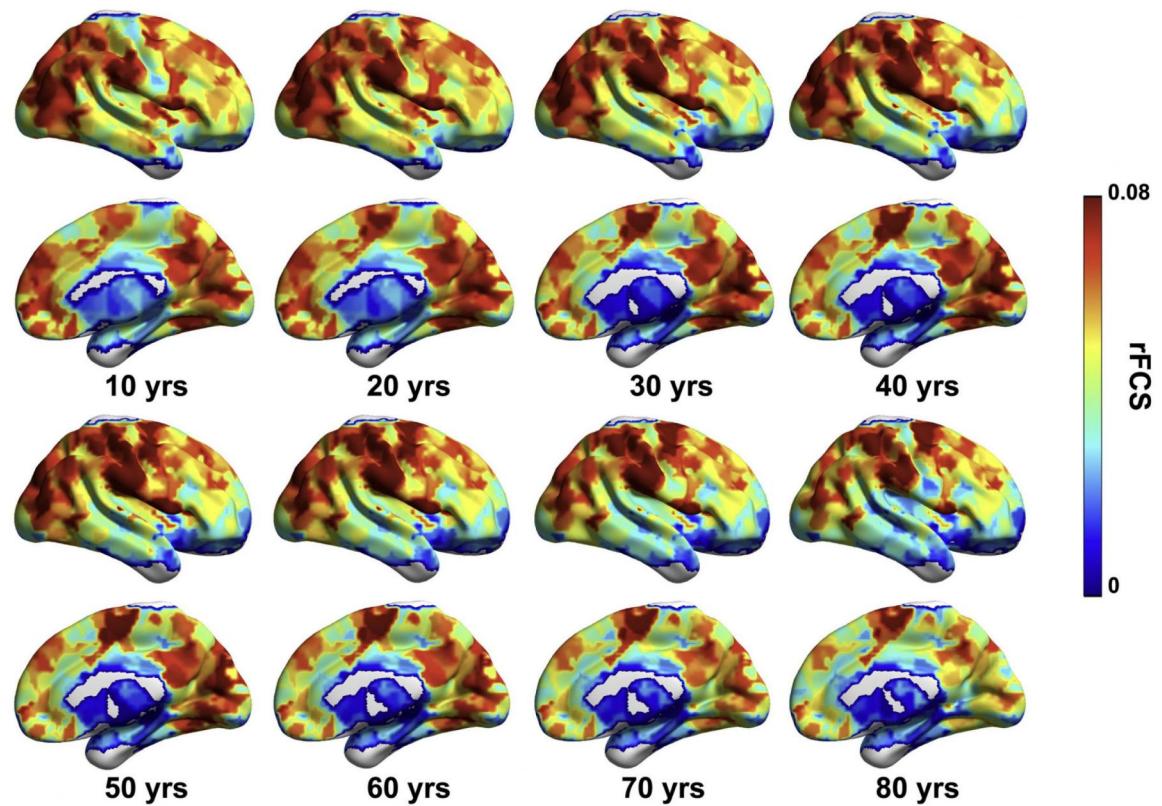
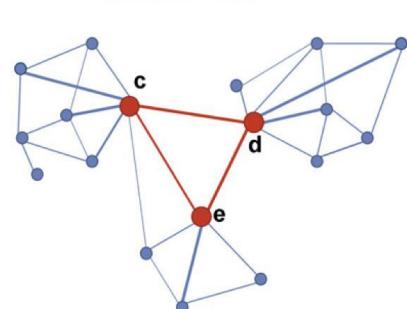
B. Strength



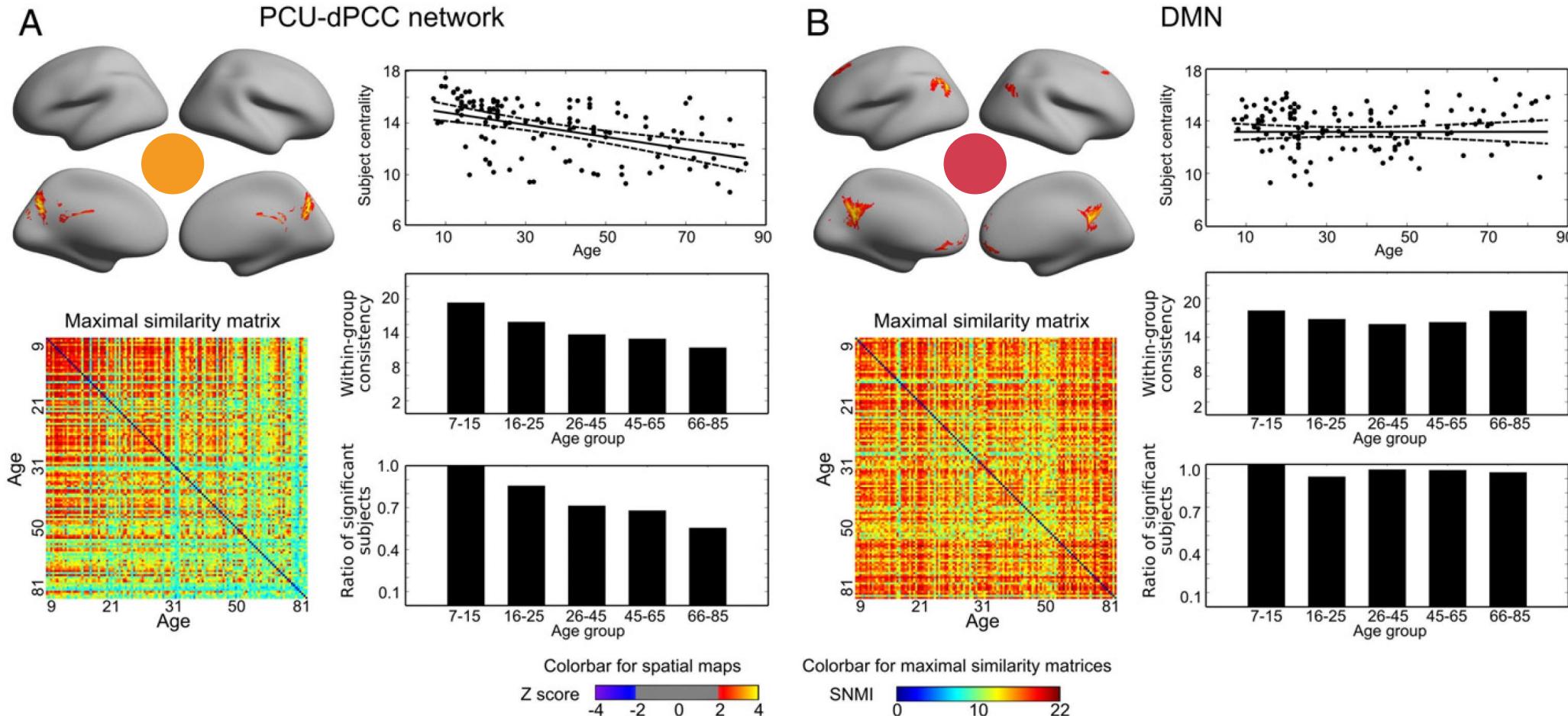
C. Module



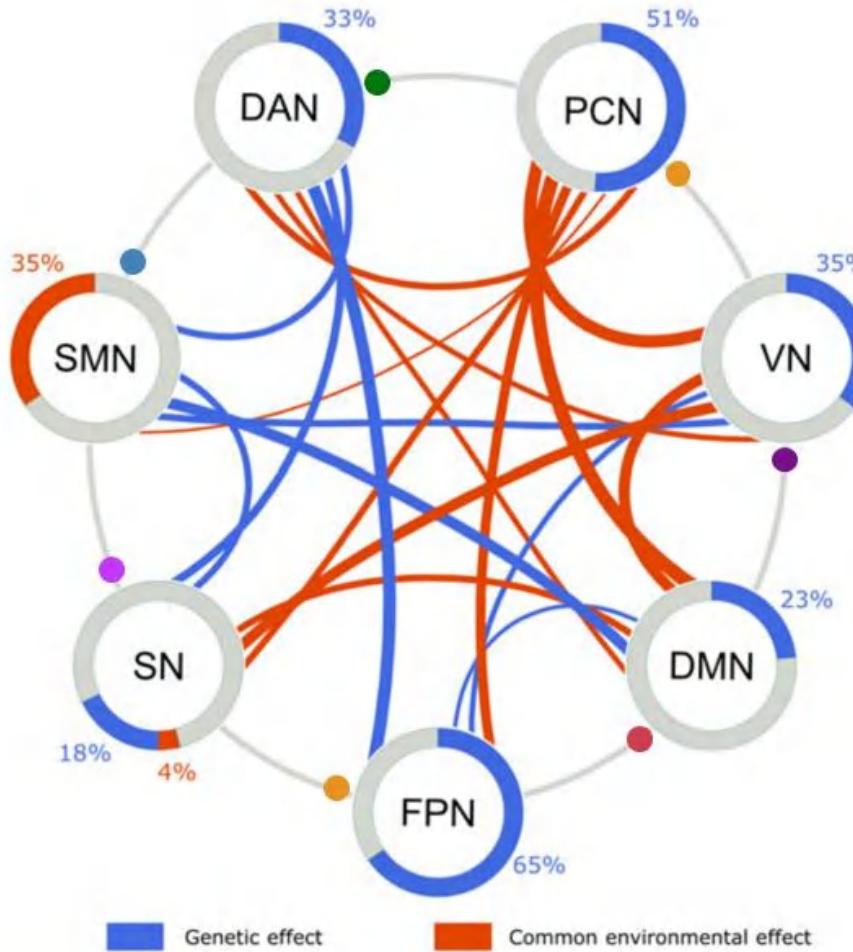
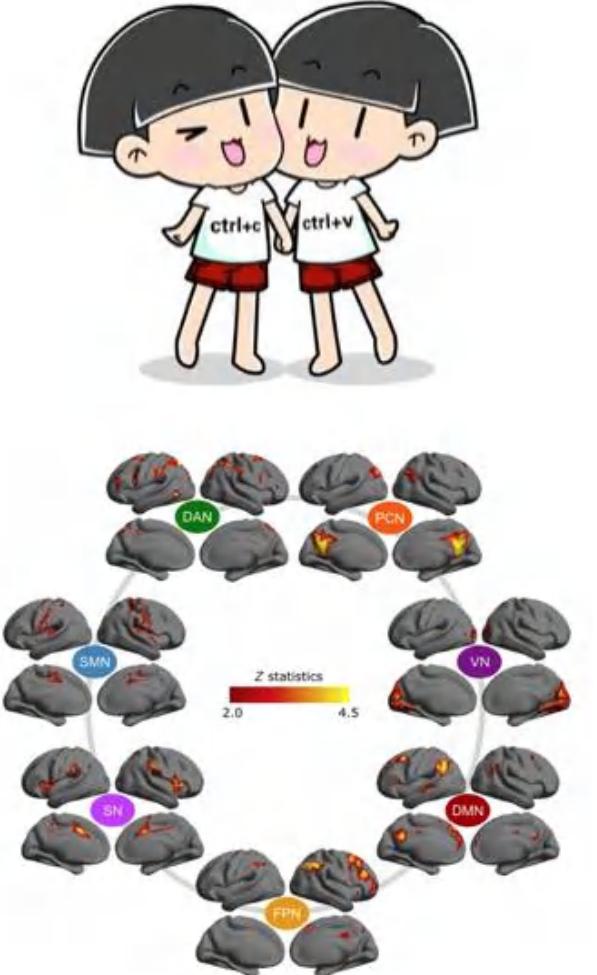
D. Rich club



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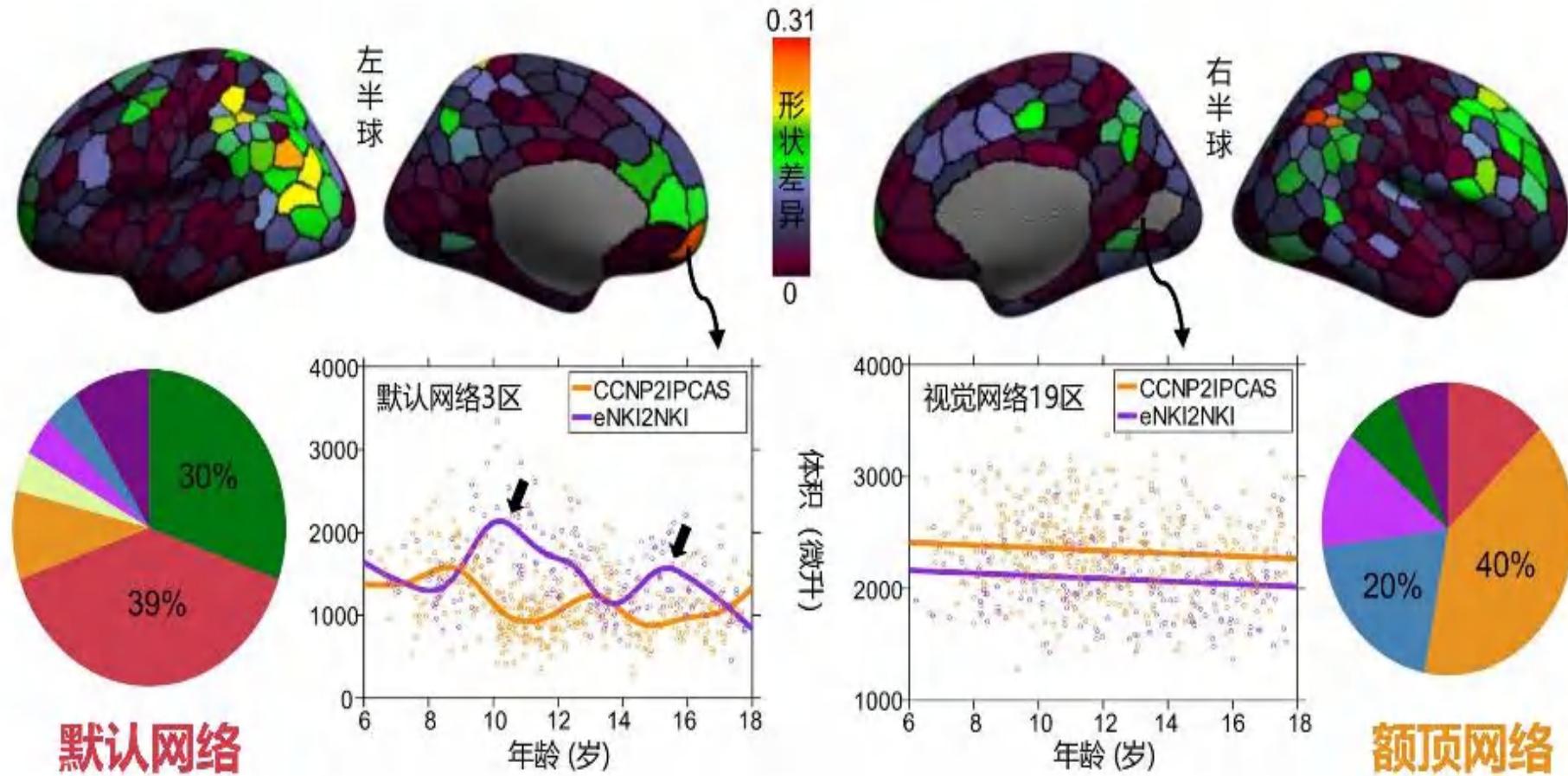
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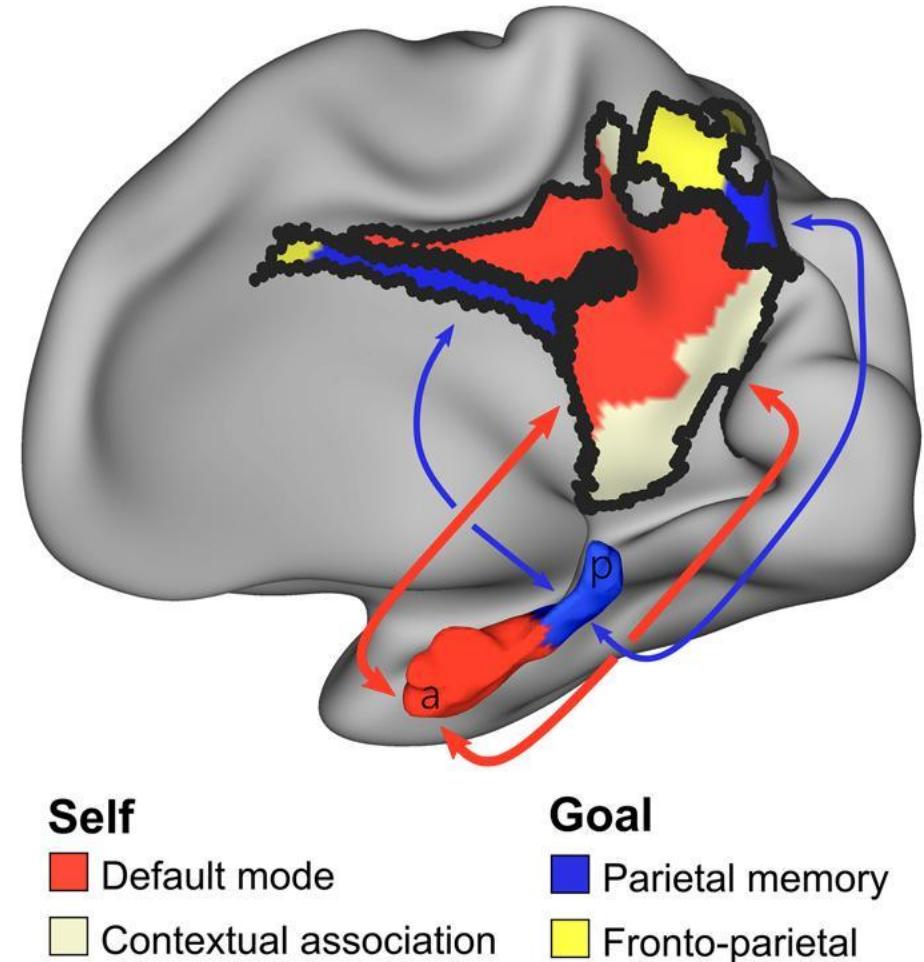
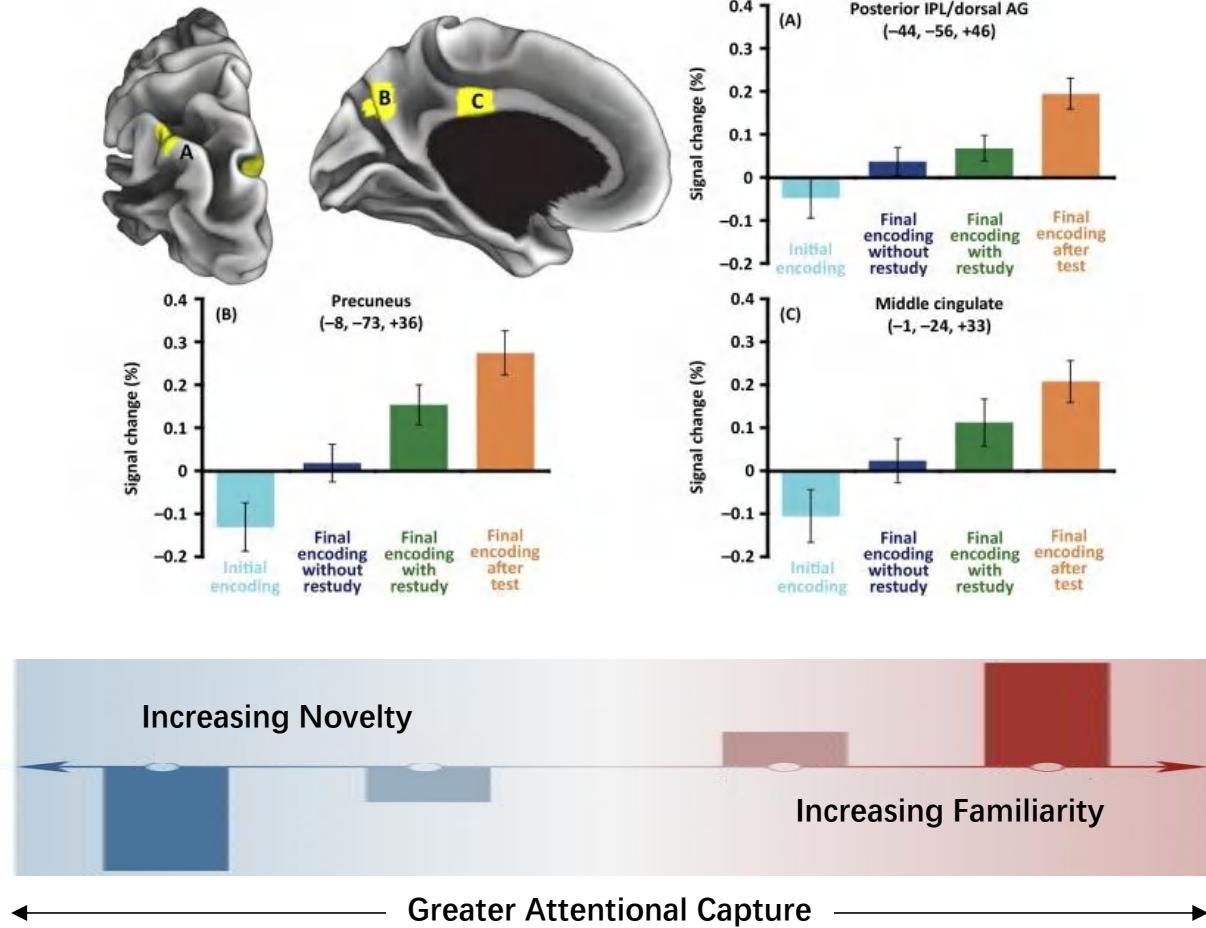
*Cerebral Cortex* (2016)



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# Brain-Mind Development across The Human Lifespan

Trends in Cognitive Sciences

Opinion

## Network Neuroscience Theory of Human Intelligence

Aron K. Barbey<sup>1,2,3,4,5,6,\*,@</sup>

An enduring aim of research in the psychological and brain sciences is to understand the nature of individual differences in human intelligence, examining the stunning breadth and diversity of intellectual abilities and the remarkable neurobiological mechanisms from which they arise. This Opinion article surveys recent neuroscience evidence to elucidate how general intelligence,  $g$ , emerges from individual differences in the network architecture of the human brain. The reviewed findings motivate new insights about how network topology and dynamics account for individual differences in  $g$ , represented by the Network Neuroscience Theory. According to this framework,  $g$  emerges from the small-world topology of brain networks and the dynamic reorganization of its community structure in the service of system-wide flexibility and adaptation.

### Spearman's Enigmatic $g$

Research in the psychological and brain sciences has long sought to understand the nature of individual differences in human intelligence, examining the stunning breadth and diversity of intellectual abilities and the remarkable cognitive and neurobiological mechanisms from which they emerge. The foundations of modern research in this effort were established in the early 20th century by Charles Spearman, who developed the correlation method and applied this technique to examine academic achievement within four branches of school study (i.e., English, French, classics, and mathematics) [1,2].

Spearman discovered that correlations in performance reflected characteristics of each discipline, observing that 'English and French, for instance, agree with one another in having a higher correlation with Classics than with Mathematics' [1]. Evidence that all branches of school study were not equally correlated motivated Spearman to conclude that they were influenced, in part, by mental abilities that were specific to each discipline. Beyond identifying the contribution of specific mental abilities, Spearman observed that the correlations among the four branches of school study were always positive. This finding, which is now well-established and named the positive manifold, provided evidence that all cognitive tests measure something in common. Spearman referred to this commonality as the general factor,  $g$ , which represents the component of individual differences variance that is common across all tests of mental ability.

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REVIEWS

**Trends**  
Accumulating evidence from network neuroscience indicates that  $g$  depends on the dynamic reorganization of brain networks, modifying their topology and community structure in the service of system-wide flexibility and adaptation.

Whereas crystallized intelligence engages easy-to-reach network states that access prior knowledge and experience, fluid intelligence recruits difficult-to-reach network states that support cognitive flexibility and adaptive problem-solving.

The capacity to flexibly transition between network states therefore provides the basis for  $g$  – enabling rapid information exchange across networks and capturing individual differences in information processing at a global level.

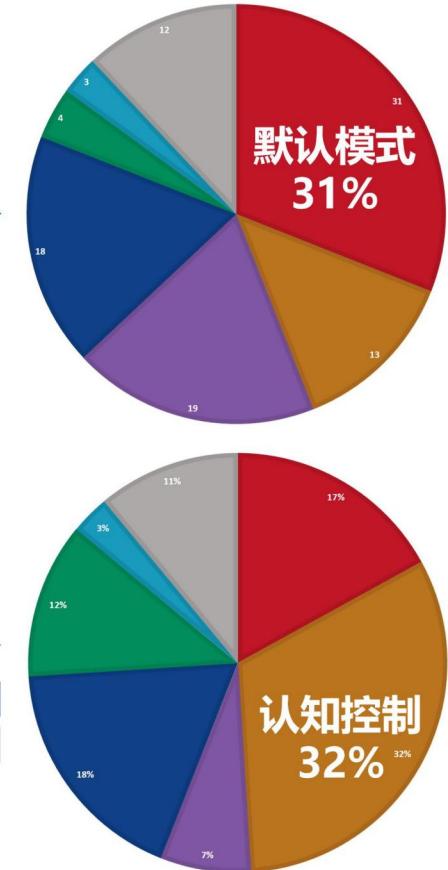
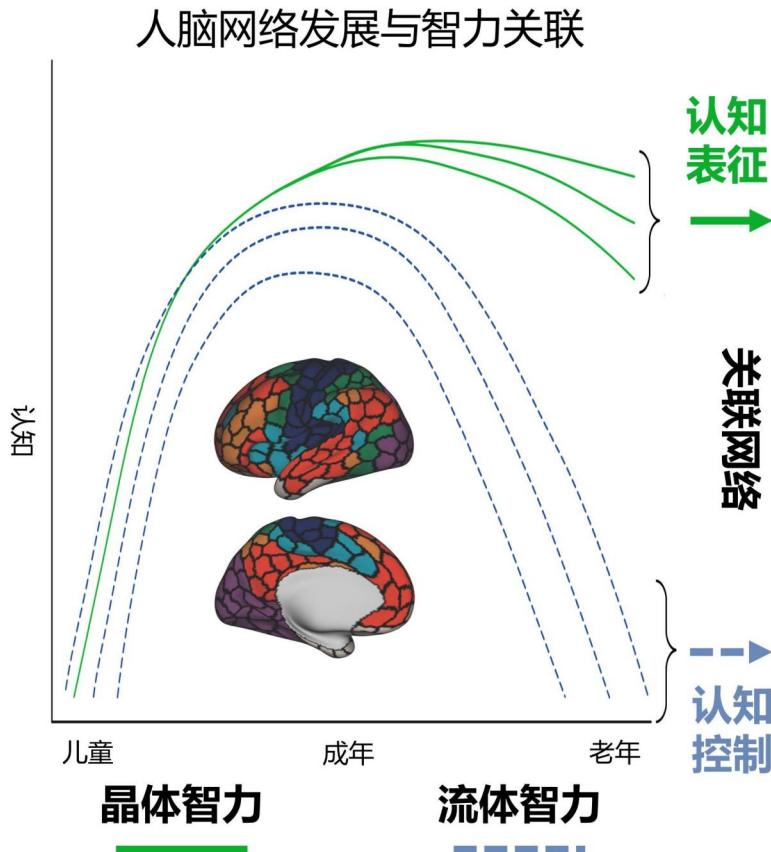
This framework sets the stage for new approaches to understanding the neural foundations of  $g$  – examining individual differences in brain network topology and dynamics.

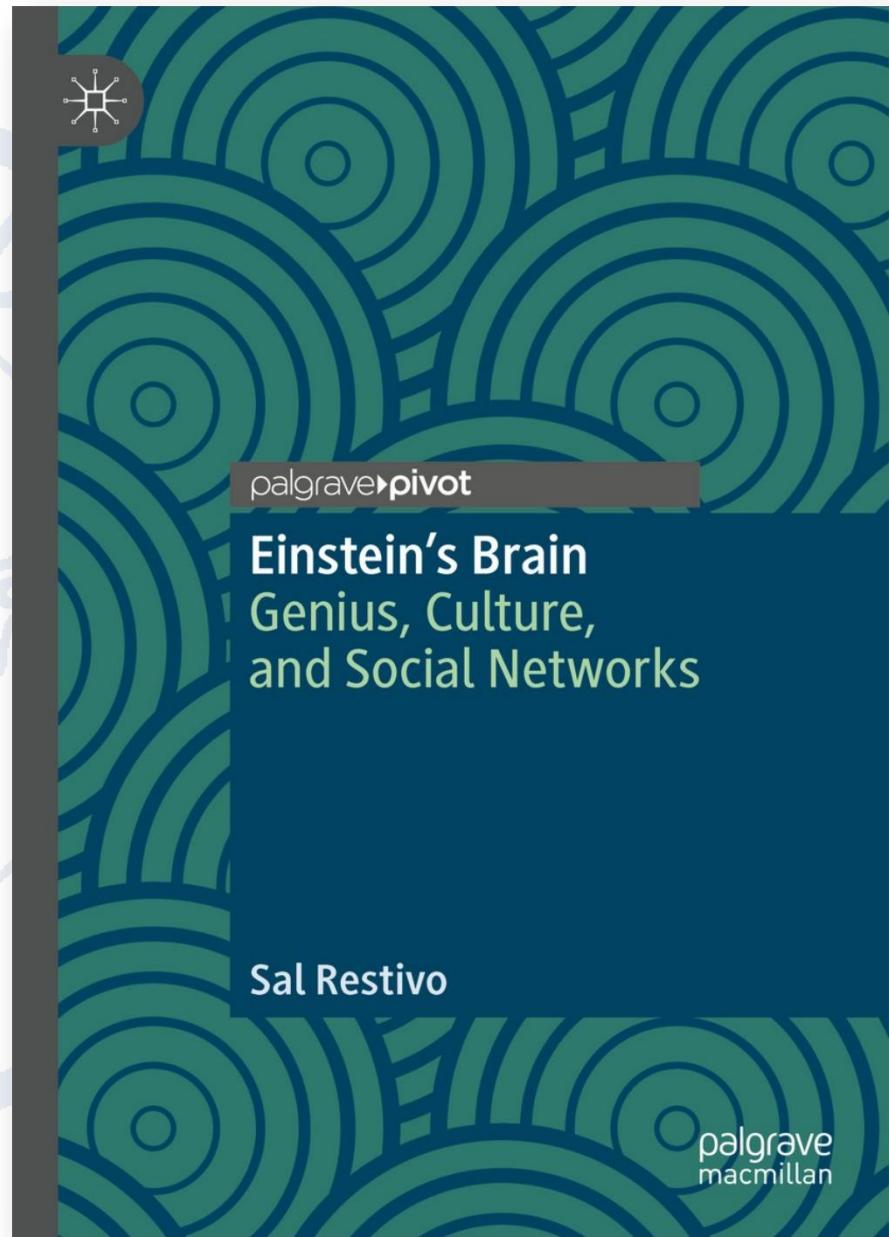
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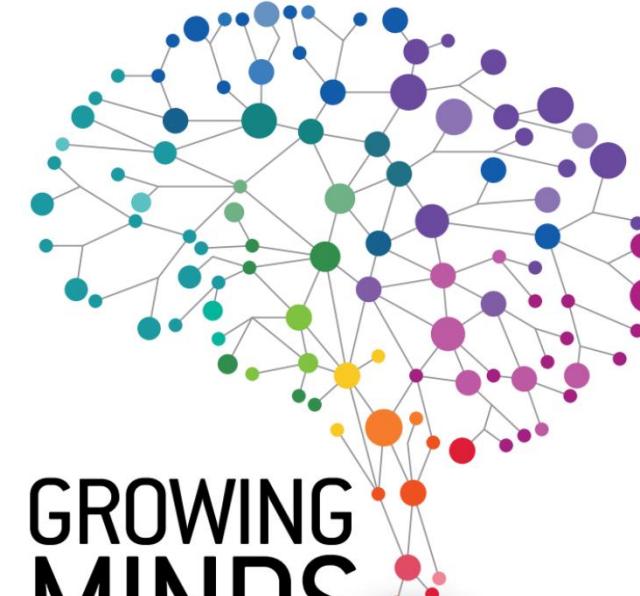
Increasing  
Intelligence



Norbert Jusšovec  
Anja Pabor

提智

ANDREAS DEMETRIOU  
& GEORGE SPANOUDIS



# GROWING MINDS



A Developmental Theory of  
Intelligence, Brain, and Education

