Size of brain areas does matter -- but bigger isn't necessarily better

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The ability to hit a baseball or play a piano well is part practice and part innate talent. One side of the equation required for skilled performances has its roots in the architecture of the brain genetically determined before birth, say scientists at the Salk Institute for Biological Studies. Practice takes no explaining, just persistence.

In this week's early online edition of the *Proceedings of the National Academy of Sciences*, the Salk researchers report that in mice, functional subdivisions of the cortex – the brain's powerful central processing unit responsible for higher functions – must be just the right size relative to other brain architecture, or mice will underperform in tests of their skill at the relevant behaviors.

These functionally-specialized subdivisions are known as areas, and are responsible for sensory perception, movements, and the coordination of these and other complex phenomena. The same area of the cortex can vary two-fold in size among normal humans, but the question of whether such variations in area size can influence behavioral performance has been left unanswered. Now, Salk investigators have answered this question by genetically manipulating area sizes in mice and testing the effect on behavioral performance.

They find that if areas of the cortex involved in body sensations and motor control are either smaller or larger than normal, mice will not be able to run an obstacle course, keep from falling off a rotating rod, or perform other tactile and motor behaviors that require balance and coordination as well as other mice can.

"It has been assumed that if a cortical area is larger, it would be more effective in processing information," says the senior author, Dennis O'Leary, Ph.D., professor in the Molecular Neurobiology Laboratory at the Salk Institute. "However", adds Axel Leingartner, Ph.D., co-first author together with Sandrine Thuret, Ph.D., "our findings suggest that the area size that gives optimal performance is the one that is best tuned to the context of the neural system within which that area functions."

In other words, the cortex needs to fit the functional profile of the "pipeline" of information, "read-outs" of body sensations and peripheral sensory structures such as the eye, that is taken in by brain neurons and sent to the cortex for processing and ultimately a behavioral response.

Thuret, formerly in the Laboratory of Genetics at the Salk and now at the Centre for the Cellular Basis of Behaviour at King's College in London, concludes that "If cortical areas are not properly sized, the information will not be processed effectively, resulting in diminished performance."

This study built upon a previous discovery by O'Leary and colleagues, that Emx2, a gene common to mice and men, controls how the cortex in mice is divided during embryonic development into its functionally specialized areas. The researchers wanted to know what would happen to behavioral performance if they altered area sizes by changing the levels of Emx2. Leingartner engineered one group of mice to express too much, which resulted in reductions in the sizes of "sensorimotor" areas of the cortex. These mice exhibited significant deficiencies in tactile and motor behaviors. But surprisingly, tactile and motor behaviors were also diminished in a second group of mice that had too little Emx2, resulting in an expansion of the sensorimotor areas.

In a final critical experiment, the first group of mice was bred to the second to perform a "genetic rescue." The scientists found that levels of Emx2, area sizes, and behavioral performance all returned to normal. "To us this rescue experiment was compelling, and even a bit shocking, because the offspring that performed normally were the progeny of the two lines of mice that performed poorly," O'Leary says. "Findings from the first two lines of mice tested show a correlation between area size and performance, but the genetic rescue proves the relationship between area size and performance."

The Salk scientists say that the two-fold variability in cortical area size likely explains at least in part variability in human performance and behavior and could also provide insight into developmental cognitive disorders. O'Leary says that establishing such a correlation between area size in human cortex size and behavior is possible by combining, in the same individuals, tests of behavioral performance with functional MRI that can be used to measure the size of a cortical area based on neural activity.

"There is no doubt that people vary considerably in performance in everything from hitting a baseball to playing a piano to even a simple measure such as visual acuity–indeed the full spectrum of sensory, motor, and cognitive function," he says. "Just as the size of a cortical area can vary considerably between people, so can human behavioral performance. Our studies in mice lead us to conclude that in humans, variations in cortical area size figures prominently in explaining variations in behavioral performance."

Alterations in the size and shape of cortical areas could also underlie some cognitive strengths and weaknesses, the researchers say, for example those associated with the genetically based disorder, Williams Syndrome, as recently reported by Salk professor Ursula Bellugi and her colleagues.

O'Leary stresses though that he is making no statements about variability in intelligence. "Neuroscientists have yet to develop an understanding of the biological underpinnings of intelligence. The behaviors we have studied are based on sensory and motor modalities. However, for most issues in biology, in the end, researchers conclude that both an environmental component and a genetic component contribute to the final outcome."

Source: Salk Institute