One gene influences recovery from traumatic brain injury

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Researchers report that one change in the sequence of the BDNF gene causes some people to be more impaired by traumatic brain injury (TBI) than others with comparable wounds.

The study, described in the journal *PLOS ONE*, measured general intelligence in a group of 156 Vietnam War veterans who suffered penetrating head wounds during the war. All of the study subjects had damage to the prefrontal cortex, a brain region behind the forehead that is important to cognitive tasks such as planning, problem-solving, self-restraint and complex thought.

The researchers controlled for the size and location of subjects' brain injuries and other factors, such as intelligence prior to injury, which might have contributed to differences in cognitive function. (Prior to combat, the veterans had completed the Armed Forces Qualifications Test, which included measures of intelligence that provided a baseline for the new analysis.)

"We administered a large, cognitive battery of tests to investigate how they performed after their injury," said study leader Aron Barbey, a professor of speech and hearing science, of psychology and of neuroscience at the University of Illinois. "And we had a team of neurologists who helped characterize the nature and scope of the patients' brain injuries."

The researchers also collected blood for a genetic analysis, focusing on a gene known as BDNF (brain-derived neurotrophic factor).

The team found that a single polymorphism (a difference in one "letter" of the sequence) in the BDNF gene accounted for significant differences in intelligence among those with similar injuries and comparable intelligence before being injured.

"BDNF is a basic growth factor and it's related to neurogenesis, the production of new neurons," Barbey said. "What we found is that if people have a specific polymorphism in the BDNF gene, they recovered to a greater extent than those with a different variant of the gene."

The change in the gene alters the BDNF protein: The amino acid methionine (Met) is incorporated at a specific site in the protein instead of valine (Val). Since people inherit two versions of each gene, one from each parent, they have either Val/Val, Val/Met or Met/Met variants of the gene.

"The effects of this difference were large – very large," Barbey said. "If an individual had the Val/Val combination, then their performance on a battery of cognitive tests (conducted long after the injury occurred) was remarkably lower than that of individuals who had the Val/Met or Met/Met combination."

On average, those with the Val/Val polymorphism scored about eight IQ points lower on tests of general intelligence than those with the Val/Met or Met/Met variants, Barbey said. Those with the Val/Val variant also were significantly more impaired in "specific competencies for intelligence like verbal comprehension, perceptual organization, working memory and processing speed," he said.

To test these results, the researchers did the analysis over again "in a subset of individuals who had very similar (brain injuries) to the other group," Barbey said. "We found the same kind of effects, suggesting that lesion location isn't a factor influencing the difference between the groups."

The finding opens a new avenue of exploration for treatments to aid the process of recovery from TBI, Barbey said.

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