

Life stressors trigger neurological disorders, researchers find

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When mothers are exposed to trauma, illness, alcohol or other drug abuse, these stressors may activate a single molecular trigger in brain cells that can go awry and activate conditions such as schizophrenia, post-traumatic stress disorder and some forms of autism.

Until now, it has been unclear how much these stressors have impacted the <u>cells</u> of a developing brain. Past studies have shown that when an expectant mother exposes herself to alcohol or drug abuse or she experiences some trauma or illness, her baby may later develop a psychiatric disorder, including some forms of autism or <u>post-traumatic stress disorder</u>, later in life. But the new findings, published online in *Neuron*, identifies a molecular mechanism in the prenatal brain that may help explain how cells go awry when exposed to certain environmental conditions.

Kazue Hasimoto-Torii, PhD, Principal Investigator of the Center for Neuroscience, Children's National Health System, and a Scott-Gentle Foundation investigator, is lead author of the paper. Torii was previously at Yale, whose researchers were co-authors in the report. The research was funded primarily through National Institutes of Health grants.

Researchers found that mouse embryos exposed to alcohol, methylmercury, or maternal seizures activate a single gene, HSF1, also known as heat shock factor, in cerebral cortex. The HSF1 "plays a crucial role in the response of <u>brain cells</u> to prenatal environmental insults," the researchers reported. "The gene protects and enables brain cells to



survive prenatal assaults. Mice lacking the HSF1 gene showed structural brain abnormalities and were prone to seizures after birth following exposures to very low levels of toxins."

Even in mice where the HSF1 gene was properly activated to combat environmental insults, the <u>molecular mechanism</u> alone may permanently change how brain cells respond, and may be a reason why someone may be more susceptible to neuropsychiatric disorders later in life.

Innovative work with stem cells also provided findings that supported the theory that stress induces vulnerable cells to malfunction, the researchers reported. For the study, researchers created stem cells from biopsies of people diagnosed with schizophrenia. Stem cells are capable of becoming many different tissue types, including neurons. In the study, genes from the stem cells of those with schizophrenia responded more dramatically when exposed to environmental insults than <u>stem cells</u> from non-schizophrenic individuals.

While it has been generally accepted that exposure to harmful environmental factors increase the susceptibility of the brain to neurological and psychiatric disorders, new types of environmental agents are continuingly added to the mix, requiring evolving studies, Hasimoto-Torii says.

Hashimoto-Torii notes that autism rates have increased substantially and "more people are having these exposures to environmental stressors," she says. While there have been many studies that have identified singular stressors, such as alcohol, there have not been enough studies to focus on many different environmental factors and their impacts, such as heavy metals as well as alcohol and other toxic exposure, she adds.

Identifying many risk factors helped Hashimoto-Torii and other researchers identify the gene that may be linked to neurological



problems. "Different stressors may have different stress responses," she says. She examined risk factors specifically involving epilepsy, ADHD, autism and <u>schizophrenia</u>. Eventually, it may open the door "to provide therapy in the future to reduce the risk" and protect vulnerable cells.

Provided by Children's National Medical Center

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