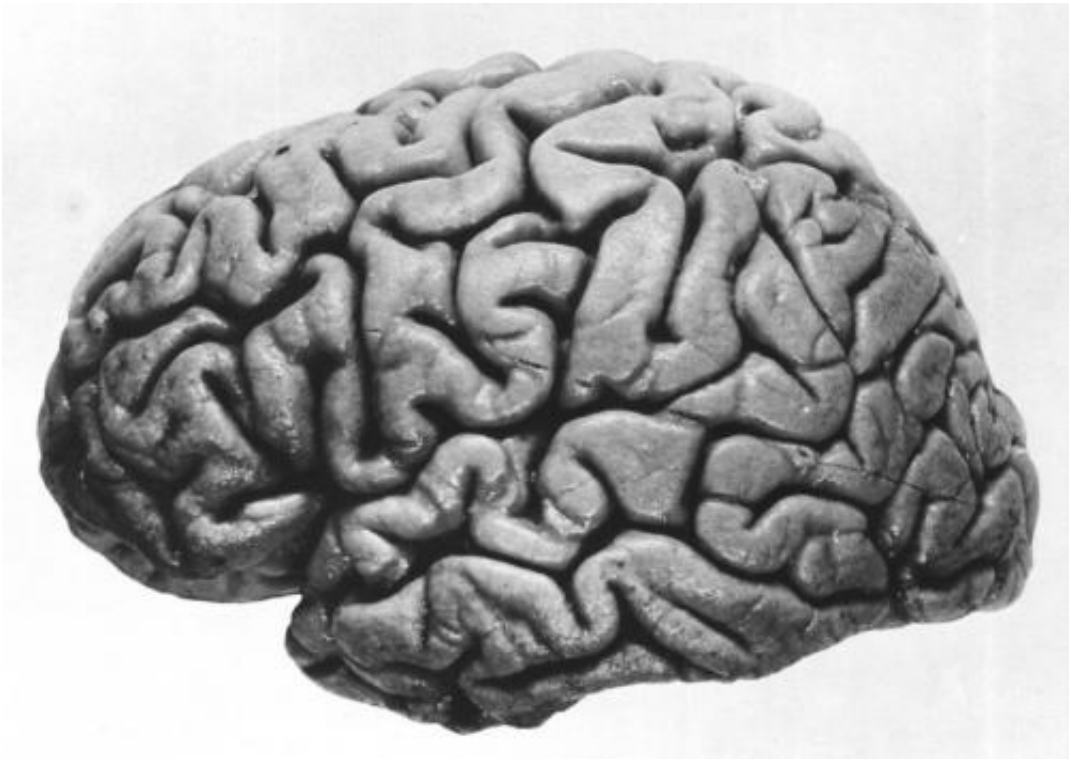
A paradox revealed: Cues associated with infant abuse may help reduce stress in adult brain

January 14 2015, by David March



Left hemisphere of J. Piłsudski's brain, lateral view. Credit: public domain

Neurobiologists at NYU Langone Medical Center and elsewhere have found a surprising and paradoxical effect of abuse-related cues in rat pups: those cues also can lower depressive-like behavior when the rat pups are fully grown.

These paradoxical properties may help shed light on why certain cues such as pictures or odors associated with early life abuse can sometimes reduce stress in those same individuals as adults.

In experiments conducted in infant and adult rats, the NYU Langone team found that trauma and pain experienced in infancy clearly led to higher rates of adult rat depression-like behavior. But - in an ironic twist - presenting odor cues associated with the early life trauma during depressive episodes in the same rats - now fully grown—lowered depression-like behavior. Results also showed that the adult rats' brain biology had been altered by the trauma linked cues, much like what happens in the human brain on antidepressant drugs involving serotonin.

Senior study investigator Regina Sullivan, PhD and graduate student Millie Rincón-Cortés, PhD, in a report published in the *Proceedings of the National Academy of Sciences* (*PNAS*) online Jan. 5, say these results are surprising because cues associated with trauma experienced as adults provoke fear and do not rescue depressive behavior. Previous work by the Sullivan team showed that the infant brain has limited ability to link trauma to fear areas in the brain, such as the amygdala, and instead, activate areas of the brain important in approach and attachment. Once these cues are linked to the attachment circuitry in the brain, they remain capable of activating the attachment circuit throughout the lifespan.

Sullivan says her team's results show important details about the biological effect of infant trauma in mammals, and reveals how the brain may react to such trauma among humans, as well.

A key finding of the study is the trauma-related paradoxical—and opposite—effect of serotonin in infancy and adulthood. The trauma experienced by the infant rats increased serotonin, and the study showed that giving rat pups antidepressant drugs, such as selective serotonin reuptake inhibitors (SSRI) was sufficient to mimic the effects of trauma

and produced depression in these rats during later life.

"It is possible that giving SSRI medications to children could be detrimental to mental health in adulthood," Dr. Sullivan says. "We believe that our research offers the first evidence for the impact of serotonin pathways. The infant trauma increases serotonin to produce brain programming of later life depression and the infant trauma cue increases serotonin to alleviate the adult depressive like symptoms."

Later tests on the same rats when they matured showed that the infant trauma linked cues continued to trigger a similar serotonin response. But instead, in adults,, the investigators say, the production of more serotonin helped to alleviate the depression, similar to SSRIs. The odor cues' effects, researchers showed, altered overall gene activity in the amygdala region of the brain, which is responsible for processing emotions, such as fear and pleasure. The adult rats experienced the same mood-uplifting effects from increased serotonin as other rats did when researchers blocked stress pathways in the brain and just added serotonin.

"Starting with our results in this study, we can use the same rat model system to better understand other aberrant behaviors and investigate whether changes in serotonin, or other neurotransmitters, can similarly influence adult behavior," says Dr. Sullivan, a professor at the NYU School of Medicine and its affiliated Nathan S. Kline Institute for Psychiatric Research.

More information: *PNAS*, www.pnas.org/content/early/201 … /1416065112.abstract

Provided by New York University School of Medicine