Sensory stimuli improves brain damage in mouse models of preterm birth

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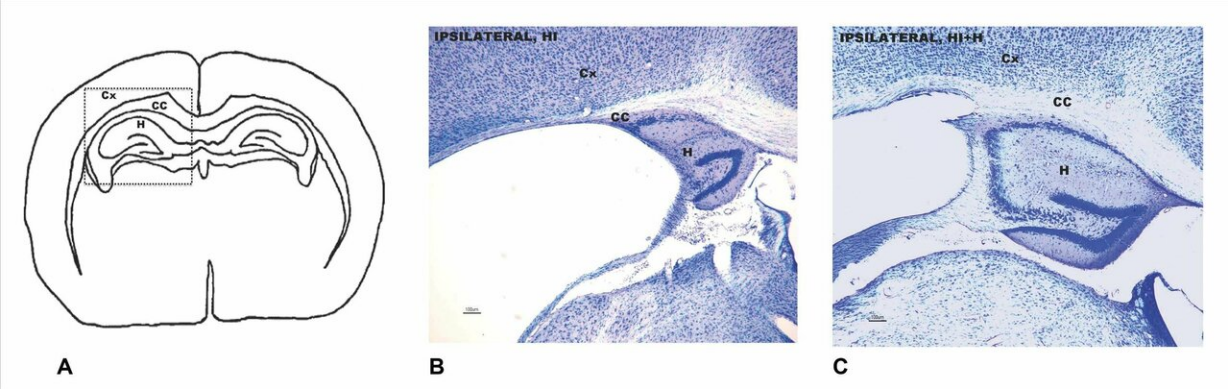

A: Brain area affected by hypoxic and ischemic injury. B: Neuropathological analysis demonstrating brain damage in adult mice that as newborns suffered hypoxic and ischemic injuries and did not received sensory stimulation. C: Neuropathological analysis on the same area in adult mice that were stimulated.

Perinatal brain injuries hinder neurological capabilities throughout life, causing fine motor problems and severe cognitive limitations, and therapies currently available are very limited. Researchers are seeking other types of interventions to counter these effects.

A new study by researchers from the Institute of Neuroscience of the Universitat Autònoma de Barcelona (INc-UAB), led by Dr. Lydia Giménez-Llort, demonstrates that tactile and proprioceptive stimulation related to tactile perception and the body's position, muscle, bone,

balance and the coordination of movements improves the effects of perinatal hypoxic and ischemic brain injuries in mice. This improvement mainly benefits male mice, in which the neurological damage is reduced by half.

The study, published in *Frontiers of Behavioral Neuroscience*, was conducted with mouse models of preterm birth. "We currently know that the immature brain of preterm infants, equivalent to that of mice when born, is at a larger risk for hypoxic-ischemic damage, and male newborns are more susceptible and respond worse to protective and therapeutic interventions," says co-author of the study Mireia Recasens. "Our work provides important information on this serious health problem with a damage of 1-3.5 and 6 of every thousand births in developed and developing countries, respectively."

Sensory stimulation was applied from before the injury occurred until the final stages of infancy, a period in preterm infants equivalent to being born at seven months until two years. The manipulation consisted in tactile and propioceptive stroking and massaging of the mice three times within an eight-minute period, twice a day.

The results revealed that this intervention had a notable neurological protection on both genders throughout their lives, but researchers highlight that the effects were especially positive among males. The histopathological analysis in males demonstrated 50 percent less brain damage compared to the non-stimulated mice. There was a 30 percent decrease among female mice. The neurological protection in both genders was correlated to the improvement of functional capacities, reflexes, and an improvement in memory results.

In relation to brain areas, the region involved with motor control and learning and memory (caudate/putamen) was the one to register the largest difference in males, with 80 percent less damage. In females, the

main improvement was a 66 percent reduction in atrophy to the corpus callosum, a nerve tract connecting the left and right brain hemispheres.

"The study illustrates the preventive and therapeutic potential of these types of stimulations in newborns with brain injuries, in a short yet very intense period at levels of brain development and plasticity. It also gives support to the different scientific approaches advocating for the transcendence of perinatal conditions from sensory stimulation to maternal contact and a warm and protective environment, and its role as an adjuvant to current therapies," says Dr. Giménez-Llort, who is also a member of the International Gender Medicine (IGM) and the ISNA, an international association of sensory stimulation and snoezelen, which studies its effects.

One same injury with different effects according to gender

The research also analysed the impact of perinatal hypoxic and ischemic brain injuries, demonstrating that although the same degree of neuropathological severity exists, the damage affects each gender's functional, neurological, cognitive and emotional capacities differently depending on the stage of life and task undertaken.

"During the infant stage, the damage affects balance, particularly among females, and prehension in males, but both aspects improve as they grow, and only reflexes remain damaged. Male mice exhibited infantile hyperactivity, which normalised as they became adults. In contrast, the anxiety and emotional traits of these injuries lasted throughout their lives. Both genders showed poorer learning processes at short and long terms, but there was more damage to memory among the males," explains Aida Muntsant, Ph.D. student at the INc-UAB and first author of the paper. The functional evaluations were correlated with the degree

of severity of the affected brain areas: hippocampus, caudate/putamen, thalamus, neocortex and corpus callosum.

Rehabilitation targets

"As a whole, the study shows the different neuronal substrates needed to satisfy functional demands and points to the most resilient neuroanatomical targets to repair these functions through postnatal stimulation," says Dr. Kalpana Shrisvastava, specialist in neuroimmunology and co-first author of the paper.

"Despite the obvious differences between rodents and humans, the study shows the complex relationship between different regions of the brain, risk factors, vulnerability and resilience, and all dependant on gender and age. It also provides new data on behavioural neuroscience within the field of neonatology and the area of paediatric functional rehabilitation, defining a translational scenario in which to study the underlying mechanisms of the functional and neuropathological correlates found," concludes Dr. Lydia Giménez-Llort.

More information: Severe Perinatal Hypoxic-Ischemic Brain Injury Induces Long-term Sensorimotor Deficits, Anxiety-like Behaviors and Cognitive Impairment in a Sex-, Age- and Task-Selective Manner in C57BL76 Mice but Can Be Modulated by Neonatal Handling. *Frontiers in Behavioral Neuroscience* (2019). 10.3389/fnbeh.2019.00007 , www.frontiersin.org/articles/1 … nbeh.2019.00007/full

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