Brain-on-a-chip axonal strain injury model highlights mitochondrial membrane potential threshold

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Researchers from the Biomedical Engineering Department of Rutgers, The State University of New Jersey recently demonstrated the use of their "Brain-on-a-Chip" microsystem to assess specific effects of traumatic axonal injury. While their model uses the three dimensional cell structure and networks found in intact animals, it is capable of visualizing individual axons and their responses to mechanical injury. This is done by utilizing organotypic slices taken from specific areas in the brain that are susceptible to injury during a traumatic brain injury event.

"What's really nice about the system is that it is very versatile, in that specific physiologically relevant pathways or networks can be monitored depending on the orientation of the slices placed in the device, or by which brain slices are used," says Jean-Pierre Doll, Ph.D, lead author. Through the use of very small microchannels, the authors direct the natural response of brain slices to extend axons to connect one brain slice to another. Once the extending axons have traversed the distance and made functional connections between the brain slices, these axons are ready to be selectively injured.

This innovative approach was used to characterize the biochemical changes that are induced following traumatic axonal injury and highlights an apparent injury threshold that exists in axonal mitochondria. Their research shows that below the injury threshold

mitochondria undergo a delayed hyperpolarization, whereas above the threshold they immediately depolarize. Using their system, the authors tested a novel therapeutic candidate, in which they showed that the sodium/hydrogen exchange inhibitor EIPA could significantly reduce the mitochondrial responses to injury resulting in an overall improvement in axonal health.

"Since therapeutic options are currently limited, these results are exciting and highlight the value of our brain-on-a-chip technology that can be used for high-throughput screens of potential agents to ameliorate the consequences of diffuse axonal injury, which often accompanies traumatic brain injury" says senior author Martin Yarmush MD, Ph.D.

More information: Additional co-authors of the *TECHNOLOGY* paper are Rene R. Schloss Ph.D from Biomedical Engineering, Rutgers University and Barclay Morrison III Ph.D from Biomedical Engineering, Columbia University.

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