> This is the first study to formally document that SNL affects the salvaged penumbra in humans

that microglia drive the neuronal loss and could, therefore, represent a primary therapeutic target in the effort to improve penumbral rescue. However, the new findings in humans indicate that prevention of SNL by more direct means — for example, by increasing oxygenation or perfusion of the penumbral tissue before or during recanalization of the occluded vessel — would be a more constructive approach.

"This is the first study to formally document that SNL affects the salvaged penumbra in humans," comments Baron. "Contrary to our hypothesis based on rat studies, we found that microglial activation does not substantially influence the salvaged penumbra in humans and, hence, targeting microglial activation with drugs is unlikely to prevent SNL in the penumbra."

Heather Wood

ORIGINAL ARTICLE Morris, R. S. et al. Relationships between selective neuronal loss and microglial activation after ischaemic stroke in man. *Brain* https://doi.org/10.1093/brain/awy121 (2018)
FURTHER READING Baron, J.-C. et al. Protecting the ischaemic penumbra as an adjunct to thrombectomy for acute stroke. *Nat. Rev. Neurol.* https://doi.org/10.1038/s41582-018-0002-2 (2018)

> We hope this study helps lead to the FDA approval of this plant-based cannabidiol liquid formulation

"We hope this study helps lead to the FDA approval of this plant-based cannabidiol liquid formulation as an option for patients with seizures in Lennox–Gastaut syndrome," says co-first author Anup Patel.

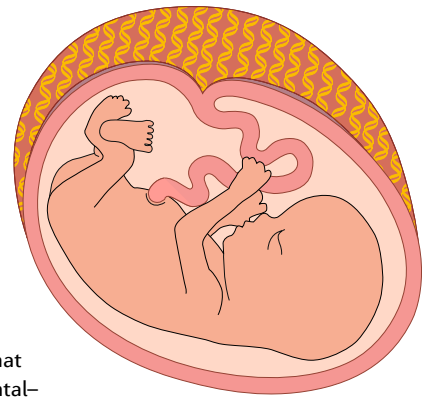
The team are now turning to unanswered questions, such as whether cannabidiol might be effective as a monotherapy, and whether doses lower than 10 mg/kg daily might elicit a similar reduction in seizures with even fewer adverse events. Broader controversies regarding the use of cannabis-based therapies for epilepsy also remain to be addressed. "Many lay individuals with epilepsy and parents of children with epilepsy believe that cannabidiol with tetrahydrocannabinol is more effective to control seizures than cannabidiol alone. There is no animal or human scientific data to support this, but it would be worth studying," Devinsky concludes.

Charlotte Ridler

ORIGINAL ARTICLE Devinsky, O. et al. Effect of cannabidiol on drop seizures in the Lennox–Gastaut syndrome. *N. Engl. J. Med.* https://doi.org/10.1056/NEJMoa1714631 (2018)

NEUROPSYCHIATRIC DISORDERS

Placental gene expression linked to schizophrenia risk



Credit: Philip Patenall/Macmillan Publishers Limited

Serious complications during pregnancy are associated with upregulation of schizophrenia-related genes in the placenta, according to new research reported in *Nature Medicine*. The findings suggest a role for placental health in modifying the risk of schizophrenia and other developmental–behavioural disorders in the offspring.

"There is abundant evidence that the risk of virtually all developmental–behavioural disorders involves both genes and the environment," explains study leader Daniel Weinberger, who is the director of the Lieber Institute for Brain Development (LIBD) in Baltimore, USA. "Complications in the early-life environment, as reflected in complicated pregnancies, have been implicated as risk factors in these disorders."

Weinberger and colleagues calculated polygenic risk scores (PRSs) — a predictive measure of disease susceptibility based on genetic factors — in a discovery cohort and four separate replication cohorts, comprising 2,038 patients with schizophrenia and 847 healthy controls in total. The PRS for schizophrenia was weighed up against the occurrence of early-life complications (ELCs), including pre-eclampsia and intrauterine growth restriction (IUGR).

The researchers found that serious ELCs were associated with an increase in the PRS for schizophrenia in the patients but not in the controls. These findings suggest that genomic risk and ELCs act synergistically to modify the risk of schizophrenia.

To further investigate the link between ELCs and schizophrenia risk, the team analysed the expression of schizophrenia-related genes in the placenta. In pregnancies that were complicated by pre-eclampsia and/or IUGR, sets of genes that had previously been linked to schizophrenia were shown to be upregulated in the fetal portion of the placenta.

Schizophrenia-related genes were found to be more highly expressed in placentas from male than from female offspring. This finding mirrors the elevated risk of schizophrenia in men that has been reported in a number of epidemiological studies.

"These results are consistent with animal work showing that complicated pregnancies elicit an immune–inflammatory response in the placenta, and also with epidemiological and observational data regarding pregnancy complications and risk of schizophrenia," comments Weinberger. "This work represents a new frontier in developmental neuroscience, with placental health providing a novel opportunity for model building and potential preventive interventions."

The researchers are now planning to extend their investigations to other developmental disorders. In addition, another group at the LIBD is using pluripotent stem cells to develop placental models to further study the gene–environment interactions that are implicated in schizophrenia.

Heather Wood

ORIGINAL ARTICLE Ursini, G. et al. Convergence of placenta biology and genetic risk for schizophrenia. *Nat. Med.* https://doi.org/10.1038/s41591-018-0021-y (2018)

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