Mouse studies reveal possible benefits of CBD and metformin for treating behavioral difficulties

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Studies of mouse models of Fragile X syndrome and Phelan-McDermid syndrome show that treatment with cannabidiol (CBD) and the diabetes drug metformin can alleviate behavioral difficulties, according to research presented today (Wednesday) at the Federation of European Neuroscience Societies (FENS) Forum 2024.

Fragile X syndrome and Phelan-McDermid syndrome are two genetic conditions that cause a variety of neurodevelopmental difficulties throughout life. Both conditions have a high incidence of autism spectrum disorder, including speech delay, social difficulties and repetitive behavior.

The research was presented by Dr. Ilse Gantois from McGill University, Montreal, Canada. She said, "There are several drugs used to treat depression, anxiety, epilepsy and aggression in people with Fragile X. Most of these drugs have many side effects. Similarly, for Phelan McDermid syndrome, current treatments mostly target epilepsy and anxiety. There has been limited research on this condition."

"During my career, I often meet parents of children with Fragile X and hear how they try to help their children to live a more comfortable life. So, with my experience in behavioral neuroscience, I want to look for safe treatments that might improve behavioral difficulties in children with these conditions."

In previous research, Dr. Gantois and her colleagues have successfully used metformin to treat adult mice that were bred to model Fragile X syndrome. Metformin is the most widely used treatment for type 2 diabetes.

Now the researchers have tested metformin on newborn mice, also bred to model Fragile X syndrome. This research shows that metformin can correct a biochemical difference in the mouse's brain that underlies the
condition. The researchers also found that metformin stopped the young mice from developing impaired speech, which in mice manifests as very high-pitched squeaking, and repetitive behavior, which manifests as excessive grooming.

The research team has also used metformin with mice bred to model Phelan-McDermid syndrome and similarly found that they can reduce impaired speech and repetitive behavior, as well as improving the mice's impaired learning and memory behavior.

Cannabidiol or CBD is the non-psychoactive component of cannabis. Dr. Gantois and her colleagues gave CBD to mice bred to model Fragile X syndrome from three weeks after birth. These mice are equivalent to young children. By the time the mice reached adulthood, their repetitive and social behaviors were the same as a control mouse. The researchers found similar improvements when treating mice bred to model Phelan-McDermid syndrome with CBD. The team is now studying how CBD interacts in the mouse brain to better understand why the drug affects behavior in this way.

Several other research groups in Canada and the U.S. are now running patient trials of metformin and CBD for Fragile X syndrome.

Dr. Gantois said, "This research and the outcome of the clinical trials could have a major impact on behavioral difficulties that people with Fragile X syndrome and Phelan-McDermid syndrome experience. The major strengths of these studies are that we are using approved drugs that can be taken throughout lifetime and have minimal side effects. Taken at an early age, these drugs could ultimately improve speech delay, social interaction and repetitive behavior in these developmental conditions.

"Using mouse models makes it possible to look in detail at what is
happening in the brain, define the underlying cause of these conditions, and study behavior and the effect of targeted drugs. Of course, mouse brains are not the same as human brains. However, we can often translate the mouse behavior we study to human behaviors."

The researchers are also studying the effects of these drugs on mouse models of other autism spectrum disorder-related conditions to see if they could have broader use.

Professor Richard Roche is chair of the FENS Forum communication committee and Deputy Head of the Department of Psychology at Maynooth University, Maynooth, County Kildare, Ireland, and was not involved in the research. He said, "We need a lot more research to help us understand conditions like Fragile X and Phelan-McDermid and to find out how these developmental conditions can be treated to give children the best possible chance in life. Mouse models of these conditions give us a vital window into what is happening mechanistically inside the brain and allow us to study the possible benefits of new treatments."

**More information:** "Repurposing of drugs for the treatment of Fragile X and Phelan McDermid syndromes", by Ilse Gantois, Part of Scientific Symposia: S08 Dissecting mechanisms of disease in ASD models for developing and testing personalized treatments, 10:53 – 11:11 hrs CEST, Wednesday 26 June – Hall H, fens2024.abstractserver.com/pr ... ils/presentations/71

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