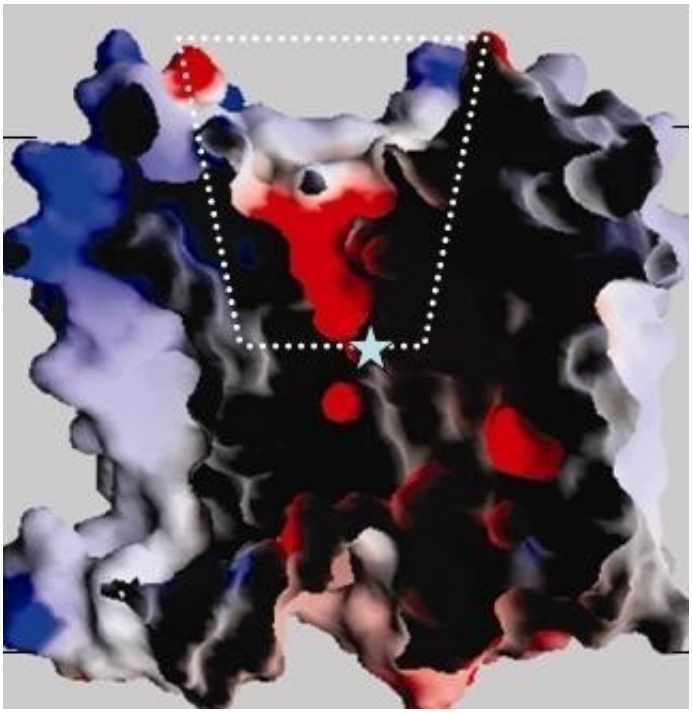
A new molecular mechanism related to epilepsy and intellectual disability

May 15 2017



Epilepsy and intellectual disability, which usually have their onset during childhood, are in some cases linked to mutations in the gene KIAA1202, which contains the information to produce the protein Shrm4. An international study published in *Nature Communications*, coordinated by Maria Passafaro, at the Institute of Neuroscience of the National Research Council (IN-CNR), demonstrated one possible mechanism by

which these mutations could cause those pathologies.

"The research community has been always interested in understanding the link between different mutations and the onset of these pathologies, and recent studies have shown a direct relation between mutations on the KIA1202 gene and the insurgence of these diseases in some families," Passafaro states. "Our work provides a step further for the knowledge of these disorders, unravelling the role of Shrm4 protein. This protein is crucial since it is responsible for the correct positioning of $GABA_B$ receptors. We observed that this activity occurs through the molecular motor Dynein, and that Shrm4 acts as an adaptor between the motor and $GABA_B$ receptors, thus allowing its correct localization in synapses (the contact points that allow the communication between neurons and with other cells). What we found is that when Shrm4 is absent, $GABA_B$ receptors cannot reach synapses and thus cannot exert their function."

The researchers registered electric currents in the hippocampus of animals deprived of Shrm4, and found a reduction of the inhibitory component. "The consequence of this is an increase in epileptic seizures in these animals, together with other defects such as increased anxious behaviours, and impairments in learning and sociability. From these results, we can start to hypothesize new treatments for patients that harbour these mutations," Passafaro concludes.

More information: Jonathan Zapata et al. Epilepsy and intellectual disability linked protein Shrm4 interaction with GABABRs shapes inhibitory neurotransmission, *Nature Communications* (2017). DOI: 10.1038/ncomms14536

Provided by National Research Council of Italy