Asian family research answers questions on fatty acid in brain

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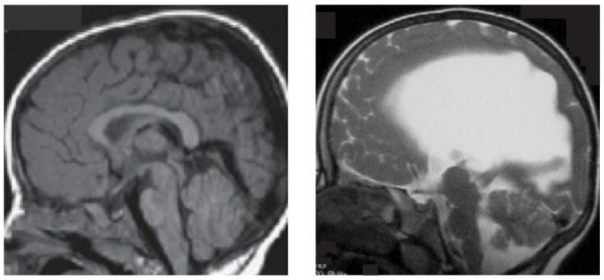

The difference between a brain with a normal Mfsd2a gene and a brain with a mutated Mfsd2a gene. Credit: Guemez-Gamboa et al./ Nature Genetics

New research conducted in a rural community in Pakistan highlights the crucial role that essential fatty acids play in human brain growth and function.

A team co-led by the University of Exeter, working with experts in Singapore, has published findings in *Nature Genetics* which show that mutations in the protein Mfsd2a cause impaired brain development in humans. Mfsd2a is the transporter in the brain for a special type of fat called lysophosphatidylcholines (LPCs)—which are composed of essential fatty acids like omega-3. This shows the crucial role of these fats in human brain growth and function.

The study was funded in the UK by the Medical Research Council and the Newlife Foundation for Disabled Children. Professor Andrew Crosby, from the University of Exeter medical School, who co-led the study, said: "This exciting finding teaches us about the crucial role that certain special fats in our blood play in brain growth development. It tells us which types of fats are important, and teaches us how the brain absorbs them. Although we discovered the gene in families from Pakistan, there will be people elsewhere in the world who also have this condition, and others like it. These findings provide us with a new focus for the potential treatment of these neurological disorders in the future."

The team worked with members from a large family from a village in North Pakistan, who all descend from the same lineage, and share common features in their DNA. Many of these family members inherited the same genetic mutation in the MFSD2A gene, which the research team showed impairs gene function, rather than destroying it. Individuals who inherited two copies of the gene mutation were found to have microcephaly (small head size), progressive intellectual disability, limb stiffness and absent speech.

One important finding of the study stemmed from the availability of patient blood plasma samples, which permitted biochemical studies in close collaboration with the study co-lead Dr David Silver from Duke-NUS Graduate Medical School Singapore. This pinpointed the crucial role of MFSD2A as the main transporter of omega fatty acids to the brain.

More information: A partially inactivating mutation in the sodium-dependent lysophosphatidylcholine transporter MFSD2A causes a non-lethal microcephaly syndrome, DOI: 10.1038/ng.3313

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