Neurodevelopmental and neurobehavioral characteristics in males and females with CDKL5 duplications.
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This is a report from the US on a group of children who were found to have mutations involving duplications of the CDKL5 gene. This has previously been reported in 1 individual and here, the authors present clinical and genetic details of a further 7 children (4 males and 3 females) and 4 of the mothers.

Clinical - All of the 7 children had an element of intellectual impairment and developmental delay.There were 3 males and 2 females who had an autism spectrum disorder while the same 3 males and 1 of the females also had an attention deficit hyperactivity disorder. These same 3 males also had an obsessive-compulsive disorder. Speech impairment or language delay was present in all the children while behavioural abnormalities were present in all females and all but 1 of the males. All the children seemed to be mobile although difficulties with various motor skills were present. Interestingly, none of the 7 had epileptic seizures and 3 of the 7 had macrocephaly as opposed to the microcephaly we can see in other CDKL5 mutations. Parental testing showed that the duplications were inherited from the mother in 4 cases and the father in 1 case. Testing was unavailable for the remaining 2 cases. Of the 4 mothers who were carriers, 2 reported having mild learning difficulties while 2 were said to be healthy.
Genetic - The CDKL5 duplications were associated with duplications of other genes in the region of the CDKL5 gene. Furthermore, 3 of the children were also found to have duplications affecting other chromosomes (chromosomes 9, 16 and 17). The authors did not feel that these other duplications contributed to the observed phenotypes. Blood testing revealed random X-inactivation in all the females.

Note – A very interesting report which is telling us that having too much CDKL5 protein does not seem to be as bad as having too little or none at all. The assumption here is that through the duplication of the CDKL5 gene, the brain is producing twice as much CDKL5 protein as would normally be present. This is something that is seen in other conditions including Rett syndrome. Whilst having too much is not as good as having normal levels, these individuals are clearly functioning relatively well compared to our children with mutations causing little of no CDKL5 protein activity. The fact that 2 of the mothers who were carriers were said to be healthy is also an interesting point in this report. The notion that we might be able cope better with too much than too little protein may have implications for therapeutic options in the future, particularly in relation to replacement therapies