Medical Xpress

A promising tool for translational research into Phelan-McDermid syndrome and autism spectrum disorders

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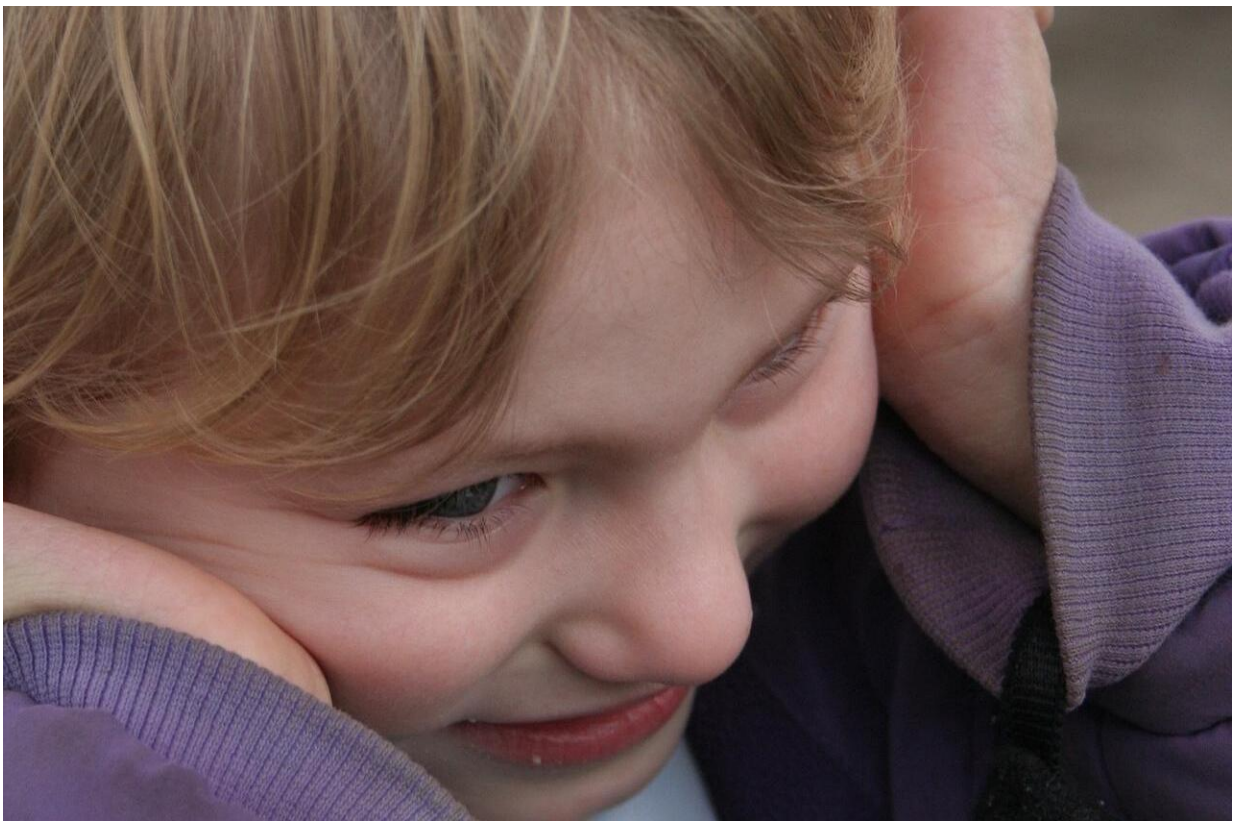

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Researchers at the Seaver Autism Center for Research and Treatment at Mount Sinai have identified specific transient visual evoked potential

waveform abnormalities in individuals with Phelan-McDermid syndrome (PMS), proving the method to be an effective, noninvasive technique to gather objective data from a range of individuals, including those who are profoundly affected. The study results were published online July 23 in the *Journal of the American Academy of Child and Adolescent Psychiatry* (*JAACAP*).

A visual evoked potential measures electrical activity in the brain by evoking a brain response to a visual stimulus, such as an alternating checkerboard on a computer screen. Responses are recorded from electrodes that are placed on the scalp and are observed as a reading on an electroencephalogram. Phelan-McDermid syndrome is a rare disorder caused by mutations in the *SHANK3* gene and is a leading single-gene cause of autism.

The study results suggest that there is a link between the magnitude of loss of function in the *SHANK3* gene and subsequent dysregulation of glutamate, a powerful excitatory neurotransmitter that plays an important role in learning and memory.

"Visual evoked potentials (VEPs) can be collected rapidly, repeated frequently, and are a cost-effective method with strong translational potential across human and animal studies," said Paige Siper, Ph.D., Chief Psychologist at the Seaver Autism Center and first author of the publication. "With this approach, the availability of treatments targeting core mechanistic disturbances in Pheland-McDermid syndrome and autism may progress more rapidly, thereby making a significant clinical contribution."

The data collected from the study also provide information about the underlying neurophysiology of Phelan-McDermid syndrome, offering a noninvasive method to examine excitatory and inhibitory neurotransmission that holds promise for stratification and surrogate

endpoints in ongoing clinical trials for Pheland-McDermid syndrome and autism.

The results are based on data from 175 children, including 31 with Phelan-McDermid syndrome, 79 with idiopathic autism, 45 typically developing controls, and 20 unaffected siblings of children with the syndrome. Stimuli included standard and short-duration contrast-reversing checkerboard conditions.

The results show that gene deletion size is significantly correlated with the amplitude of an initial negative peak, thought to reflect excitatory activity—while no significant differences between the typically developing and sibling control groups were identified. Both control groups showed significantly stronger VEPs responses compared to the syndrome group, while a subset of children with idiopathic autism displayed a similar response pattern to the Phelan-McDermid syndrome group.

VEPs will now be examined as a biomarker of Phelan-McDermid syndrome and will measure treatment efficacy in ongoing clinical trials in the syndrome.

More information: Paige M. Siper et al, Visual Evoked Potential Abnormalities in Phelan-McDermid Syndrome, *Journal of the American Academy of Child & Adolescent Psychiatry* (2021). DOI: 10.1016/j.jaac.2021.07.006

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