Growth hormone improves social impairments in those with autism-linked disorder

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Quinn, an autistic boy, and the line of toys he made before falling asleep. Repeatedly stacking or lining up objects is a behavior commonly associated with autism. Credit: Wikipedia.

A growth hormone can significantly improve the social impairment associated with autism spectrum disorder (ASD) in patients with a related genetic syndrome, according to a pilot study conducted at the

Icahn School of Medicine at Mount Sinai and published yesterday on Pub Med, a public database of biomedical topics maintained by the National Institutes of Health (study originally published in the December 12 issue of the journal *Molecular Autism*).

The study results focus specifically on the use of insulin-like growth factor-1 (IGF-1) to treat Phelan-McDermid syndrome (PMS), a disorder caused by a deletion or mutation of the SHANK3 gene on chromosome 22. Along with facing developmental and language delays and motor skill deficits, most people with PMS also have autism spectrum disorder.

SHANK3 is a focus of research in the field because of its essential role in the function of synapses, the gaps between nerve cells that "decide" whether messages continue along nerve pathways as they regulate bodily processes. While Phelan-McDermid syndrome is a rare disorder, advanced genetic technology has revealed it to be a relatively common cause of ASD.

"Ours is the first controlled trial of any treatment for Phelan-McDermid syndrome," says Alexander Kolevzon, MD, Clinical Director of the Seaver Autism Center at the Icahn School of Medicine at Mount Sinai. "Because different genetic causes of ASD converge on common underlying chemical signaling pathways, the findings of this study may have implications for many forms of ASD."

IGF-1 is a commercially available compound that promotes nerve cell survival, synaptic maturation and synaptic plasticity, the ability of synapses to strengthen or weaken over time, in response to increases or decreases in their activity. It is currently approved by the Food and Drug Administration for the treatment of short stature.

The Mount Sinai study is the first to suggest that IGF-1 is safe, tolerable and associated with significant improvement in both social impairment

and restrictive behaviors (fascination with one subject or activity; strong attachment to one specific object; preoccupation with part[s] of an object rather than the whole object; preoccupation with movement or things that move) in people with Phelan-McDermid syndrome, said the study authors.

Researchers enrolled nine children aged 5-15 years who were diagnosed with Phelan-McDermid syndrome in a placebo-controlled, double-blind, cross-over design study. All participants were exposed to three months of treatment with IGF-1 and three months of placebo, in random order. Compared to placebo, the IGF-1 phase was associated with significant improvement in social withdrawal and restrictive behaviors as measured by the Aberrant Behavior Checklist and the Repetitive Behavior Scale respectively, both standard behavior scales used to assess treatment effects in ASD.

Preclinical studies of SHANK3 deficient mouse models developed at Mount Sinai and human neuronal models derived from pluripotent stem cells (stem cells that have the capacity to produce several distinct biological responses) of humans with SHANK3 deficiency previously suggested that IGF-1 can reverse synaptic plasticity and motor learning deficits. These studies formed the basis of this clinical trial and the results provide support for the ongoing effort to develop related drug treatments.

"This clinical trial is part of a paradigm shift to develop targeted, disease modifying medicines specifically to treat the core symptoms of ASD," says Joseph Buxbaum, PhD, Director of the Seaver Autism Center and Professor of Psychiatry, Genetics and Genomic Sciences and Neuroscience at Mount Sinai. "Results from this pilot trial will facilitate larger studies that more definitively inform efficacy and better targeted therapeutic treatments."

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