Protective brain protein reveals gender implications for autism, Alzheimer's research

February 3 2015

For parents of children struggling with autism, the dearth of information is heartbreaking. Medical professionals are hard put to answer the primary questions: Who is autistic? What causes autism? What treatments are available? The situation is similar for Alzheimer's patients and relatives, who are helpless before the aggressive disease devouring a sufferer's identity.

A new study by Tel Aviv University's Prof. Illana Gozes, published in *Translational Psychiatry*, may offer insight into the pathology of both autism and Alzheimer's by revealing that different activities of certain proteins in males and females cause gender-specific tendencies toward

these diseases. While the three-to-one ratio of autism in boys to girls is well known, as is the greater number of female Alzheimer's patients, the reasons for these phenomena are less clear.

According to Prof. Gozes, "If we understand how ADNP, an activity-related neuroprotective protein which is a major regulatory gene, acts differently in males and females, we can try to optimize drugs for potential future therapeutics to treat both autism and Alzheimer's disease."

Prof. Gozes is the incumbent of the Lily and Avraham Gildor Chair for the Investigation of Growth Factors, Head of the Elton Laboratory for Molecular Neuroendocrinology at TAU's Sackler Faculty of Medicine, a member of TAU's Adams Super Center for Brain Studies and the Sagol School of Neuroscience. Research for the study was conducted by graduate students Anna Malishkevich, Noy Amram and Gal Hacohen-Kleiman, in collaboration with post-doctoral fellow Dr. Iddo Magen, and staff scientist Dr. Eliezer Giladi, all of TAU.

The gender factor

For the purpose of the new study, Prof. Gozes and her team examined the behavioral response of male and female mice, both ADNP-altered and normal, to different cognitive challenges and social situations. To do so, they removed one copy of the ADNP gene—which regulates over 400 proteins involved in development—from some mice, and then examined their respective responses to unfamiliar objects, odors, and other mice.

Their results revealed sex-specific learning and memory differences in the mice, reflecting hippocampal expression changes in ADNP, resulting in ADNP-controlled autism and in genes which indicate a risk for Alzheimer's disease. For example, ADNP-deficient male mice exhibited

deficiencies in object recognition and social memory, whereas ADNP-altered female mice were more socially deficient compared to the non-altered females.

Providing new hope?

"ADNP may be new to the world of autism, but I have been studying it for 15 years," said Prof. Gozes. "Its gender-dependent expression changes male and female chemical tendencies toward different neurological disorders. Male and female mice may look the same and their brains may look the same, but they are not. When the expression of ADNP is different, it may cause different behaviors and different cognitive abilities.

"This study emphasizes the need to analyze men and women separately in clinical trials to find cures for diseases because they may respond differently," she concludes.

Prof. Gozes hopes the new study will prompt further research into the drug Davunetide (NAP) as a means of treating social and cognitive deficits with special attention to gender differences. Prof. Gozes discovered Davunetide (NAP), a snippet of ADNP, by looking at the nerve cell protective activity of ADNP fragments. Proof-of-concept clinical studies performed in adults have shown that Davunetide protects memory in patients suffering from the mild cognitive impairment that precedes Alzheimer's disease as well as functional activity in schizophrenia patients.

Provided by Tel Aviv University

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