Experts outline research methods to study puberty suppression impacts on brains of transgender youth

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A new set of expert consensus-based recommendations lays out how best to study possible neurodevelopmental impacts of pubertal suppression treatment in transgender youth. Developed by a consensus panel of 24 international scientists, the recommendations were published in the journal *Transgender Health*.

While early evidence suggests suppressing puberty has positive effects on the mental health of transgender adolescents, little is known about how this standard of care treatment affects an adolescent's brain development.

"We don't know how stopping puberty for a year or more affects a transgender adolescent's neurocognitive development. Clearly, pubertal suppression is important for many transgender youth, but at this time, we can't speak to a family's questions about how this medical treatment might affect brain development," said Diane Chen, Ph.D., co-lead author of the study and Behavioral Health Director for the Potocsnak Family Division of Adolescent and Young Adult Medicine at the Ann & Robert H. Lurie Children's Hospital of Chicago.

John Strang, Psy.D., co-lead author and director of Research for the Children's National Hospital Gender Development Program, continued, "We need high quality research to understand the impacts of this treatment—impacts which may be positive in some ways and potentially

negative in others. This information about benefits and risks will help young people make informed decisions and assist providers in knowing how best to provide this treatment for optimal outcomes."

Transgender youth, who are on the verge of developing sex-based characteristics that don't align with their gender identity, often work with their care providers to suppress pubertal development via gonadotropin releasing hormone agonists (GnRHa). This medication approach suspends the production of gonadal (sex) hormones for as long as GnRHa is administered, which is often 1-2 years.

Employing a Delphi consensus method that included 24 international experts from the fields of adolescent neurodevelopment, gender development, neuroendocrinology and measurement science, the authors identified three primary domains of neurodevelopment that should be measured in these studies: mental health, executive function/cognitive control and social awareness/functioning.

In addition, the authors identified 44 study design elements, that all experts agreed were crucial components, out of the original 160 identified at study start. The consensus elements include:

- Measuring neurodevelopment domains repeatedly over time, before and during treatment
- Identifying an individual's stage of puberty prior to treatment
- Applying analytical approaches that account for the heterogeneity, or broad range of differences that exist between transgender individuals
- Incorporating comparisons between multiple groups, including untreated transgender youth at the same pubertal stage, cisgender youth at the same pubertal stage and an independent sample from available largescale youth databases.

"This is a critical topic for transgender youth and their families. It is also a difficult topic to study because we would never randomly assign transgender youth to treatment and no treatment groups—that would be harmful and unethical," says Dr. Strang.

Dr. Chen concludes, "Instead, we gathered the world's experts in relevant fields to work together and design the best possible research approaches to study the effects of this treatment without relying on a randomized treatment design."

More information: Diane Chen et al, Consensus Parameter: Research Methodologies to Evaluate Neurodevelopmental Effects of Pubertal Suppression in Transgender Youth, *Transgender Health* (2020). DOI: 10.1089/trgh.2020.0006

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