

# United in Hope: PWS 2025 – Clinical and Scientific Conference

## Keynote Speaker

### **Laura Holsen, PhD**

Associate Professor of Psychiatry, Harvard Medical School

Director of Research Training, Connors Center for Women's Health, Brigham and Women's Hospital

Psychologist, Division of Women's Health, Department of Medicine, Brigham and Women's Hospital

Research Psychologist, Department of Psychiatry, Brigham and Women's Hospital

**Background:** Laura Holsen is an Associate Professor of Psychiatry at Harvard Medical School (HMS), and faculty member in the Division of Women's Health, Department of Medicine and in the Department of Psychiatry at the Brigham and Women's Hospital (BWH). She also serves as Director of Research Training for the Connors Center for Women's Health and Gender Biology at BWH. Dr. Holsen received an M.S. in Developmental Psychology from Vanderbilt University. As a graduate student in Child and Developmental Psychology from the University of Kansas, where she received her Ph.D. under the mentorship of Dr. Cary Savage, she completed one of the first functional MRI studies on hyperphagia in Prader-Willi Syndrome. She then completed postdoctoral training in affective neuroscience with Dr. Richard Davidson at the University of Wisconsin – Madison. Research in Dr. Holsen's lab at BWH/HMS examines the interaction between eating behavior, stress, and reward using functional MRI and neuroendocrine assessment in eating and mood disorders and obesity, with a goal of ameliorating the negative health outcomes of these conditions through identification of modifiable neurobiological targets that drive appetite, eating behaviors, and weight change.

### **Title of Presentation: Mapping Brain Circuitry Involved in Hyperphagia in Prader-Willi Syndrome to Identify Novel Treatment Targets**

**Abstract:** Among the phenotypic characteristics of PWS, hyperphagia remains one of the most challenging factors to cope with for individuals with PWS and their families. Severity of hyperphagia in PWS is associated with greater caregiver burden, poorer overall quality of life, and greater morbidity and mortality. Behavior, emergent from brain function, likely governs several primary sources of hyperphagia in PWS. In this talk, I will review findings from neuroimaging data which reveal insights into circuits involved in the pathophysiology of hyperphagia in PWS. Additionally, I will describe our recent reverse-translational work which identified the novel involvement of the cerebellum in regulating food-related responsivity in PWS, with preclinical data suggesting cerebellar-mediated attenuation of food reward related activity in the striatum. These results informed an ongoing pilot clinical trial using transcranial magnetic stimulation (TMS) targeted to the cerebellar-striatal network to modulate hyperphagic behavior in PWS, with data indicating evidence of feasibility for the study protocol and initial efficacy in reducing scores on the Hyperphagia

Questionnaire and brain activation in relevant circuits. Findings will be discussed with reference to confounds such as uncontrolled environments and effects on other behavioral characteristics of PWS. Taken together, extant neuroimaging data provide mechanistic understanding of hyperphagia in PWS, with more recent findings informing strategies to leverage the neuromodulatory effects of cerebellar TMS in PWS at neural and behavioral levels, offering critical insight into development of cerebellar TMS as a standalone or add-on treatment for PWS.