

Proceedings of the International SSADH Deficiency 2020 Conference

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Given the exigencies of the COVID-19 pandemic that persisted throughout 2020 and well into 2021, the planned conference for physicians, investigators, and families on SSADH deficiency was moved from a promising venue in Boston to a virtual space but retained a sense of enthusiasm and progress that has held promise since these meetings began nearly two decades ago. Starting with a conference sponsored by the Pediatric Neurotransmitter Disease Association, NIH Office of Rare Disorders, and NINDS (published as a special supplement to the *Annals of Neurology* 2003), with two intervening conferences in the Washington, DC metropolitan area (published in the *J Inher Metab Dis*) and a 2016 meeting held in Boston, the SSADH Association together with NIH/NINDS (1R13NS116963-01) sponsored our virtual meeting July 9 to 10, 2020 to a highly engaged audience of internationally represented researchers and families. Over 125 participants attended each day from 20 different countries around the world. Scientific sessions were held along with patient/family education workshops, and herein are the manuscripts of invited scientific papers.

Succinic semialdehyde dehydrogenase (SSADH) deficiency is an ultra-rare disorder of the metabolism of the major inhibitor neurotransmitter, GABA (gamma-amino butyric acid), with myriad biochemical and clinical manifestations. The cardinal biochemical defect, endogenous elevation of gamma-hydroxybutyric acid, and enzymatic identification of SSADH deficiency were discovered forty years ago in the laboratory of Gibson, Jakobs, and Nyhan^{1,2}, followed by phenotyping and a series of translational investigations³⁻⁵ that have continued to the present time. This sequential series of studies and an overview of the current NICHD funded natural history study comprise the overview paper of the 2020 conference and these proceedings.

Other studies presented in this volume are important results from our accumulating biorepository including post-mortem analyses, imaging findings using edited MR spectroscopy and sequences for metabolic imaging, and our current animal model of enzyme replacement therapy accounting for developmental changes in GABAergic transmission. The results of the randomized controlled trial of SGS-742, a GABA(B) receptor antagonist, held in the intramural NINDS program were presented, as well as papers on epidemiology, analysis of the pervasive expressive language impairment vis a vis the supplementary motor cortex, and quality of life survey data.

The conference in particular afforded an opportunity to bring together an international cadre of investigators focused on this

challenging disorder, now collaborating as the SDIC (SSADH Investigators Consortium), and working together to further our understanding and offer promising strategies for patients and families. Perhaps the most powerful part of the conference was having families from a global network come together and sense the strength of mutual support and progress across borders and countries. We gratefully acknowledge their support and wish to share their special note to our organizing committee following the meeting:

“We would like to express our gratitude to the conference organizers and speakers who made the 2020 SSADHD International On-Line Conference a huge success. When faced with logistical challenges resulting from the COVID-19 pandemic, the organizing committee and speakers were able to seamlessly shift from an in-person meeting to an online zoom event and wrap it up with this informative publication.

It is hard to find the words to express the appreciation that we hold for those participating in the conference as well as the unwavering support through research and ongoing studies that continue to emerge. For being an ultra-rare disorder, your initiative, creativity and guidance have made monumental strides in research over the last twenty five years.

Facing the daily struggles of SSADHD would be exhausting without the *hope* you provide by so diligently navigating through government regulations, international relations and grant requirements, while entertaining new ideas and collaborating with others on the latest scientific advancements.

On behalf of the SSADH Association along with the patients and families we represent, please accept our sincere thank-you for your time, effort and talent!

Gratefully,
Brad and Carolyn Hoffman
SSADH Association

It is our fervent hope that these Proceedings help to further advance the field and ameliorate the plight of affected patients and families.

References

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