REQUEST FOR PROPOSALS

The National Organization for Rare Disorders (NORD) Rare Disease Research Grants Program

Announces a research grant opportunity for one grant
up to $50,000 US for

Neuropsychological Effects of Oxytocin Deficiency in Children with Acquired Pituitary and/or Hypothalamic Dysfunction

DEADLINE FOR LETTER OF INTENT (*OPTIONAL*): December 10, 2024 (11:59 PT)
DEADLINE FOR APPLICATIONs: February 10, 2025 (11:59 pm PT)

NORD, with funding from the Michael Finkelstein and Sue-Ann Friedman Foundation and The Lesley and Roslyn Goldstein Foundation, is accepting applications for one grant of up to $50,000 (USD), for scientific and/or clinical research studies related to the neuropsychological effects of and/or therapeutic strategies to mitigate acquired deficiencies of oxytocin in children.

Oxytocin is a neuropeptide hormone with diverse functions that include roles in lactation, social bonding, emotional regulation, and some aspects of cognitive function. Oxytocin is produced in the hypothalamus, distributed centrally within the brain, and also stored in the posterior pituitary gland, from which it is released into the blood stream, in response to certain stimuli. A growing body of research has focused on the neurocognitive effects of oxytocin deficiency in children, particularly given its potential involvement in neurodevelopmental disorders, including autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), and other conditions characterized by social and cognitive deficits. This current NORD call for research proposals is focused specifically on neuropsychological effects of oxytocin deficiency acquired in childhood due to damage or dysfunction of the hypothalamus and/or the posterior pituitary gland. Unlike congenital conditions, acquired hypothalamic/pituitary dysfunction presents with unique features, opportunities, and challenges, as previously typical neurocognitive and social functioning may be disrupted due to the sudden neurohormonal changes.

Children with acquired oxytocin deficiency can experience significant challenges in social cognition and emotional regulation. Previously well-adjusted children may suddenly exhibit difficulties with social interactions, reduced empathy, and/or impaired abilities to recognize and respond to social cues, such as facial expressions and emotional tone. Several case reports and studies have documented marked changes in social behaviors following pituitary dysfunction, particularly in children with pituitary tumors or traumatic brain injuries. These children may struggle to maintain friendships, engage in reciprocal social interactions, and may withdraw from social activities they previously enjoyed.[1,2,3,4]

Research Objectives

Research projects proposed in response to this call for applications may involve a clinical trial of oxytocin therapy in applicable patients or should add to the knowledge needed to design and conduct such trials. At least two careful, recent reviews discuss: the evidence for significant neuropsychological effects of oxytocin deficiency due to acquired hypothalamic and/or pituitary dysfunction; the potential benefits of oxytocin replacement therapy in such cases; early clinical findings leaning in that direction; and remaining uncertainties.[5,6] Challenges include an incomplete understanding of the regulation and mechanisms of action of oxytocin, difficulties in accurately measuring oxytocin levels and in establishing a diagnosis of oxytocin deficiency, the choice of methods for measuring the resulting neuropsychiatric signs and symptoms, and a need to determine the optimal dosing and mode of administration for oxytocin replacement therapy. Although animal studies have been performed in different model systems, these may not be predictive of human responses, and there have been to date only a few published studies of oxytocin replacement therapy in human patients with acquired hypothalamic/pituitary oxytocin deficiency.[7,8]

Regardless of whether applicants propose a clinical trial or propose specific research needed to better plan a clinical trial, all proposals must carefully consider and cite evidence supporting their approach. Some of the factors that must be stipulated and justified in a proposed clinical trial plan, or that may need to be explored in preliminary research include:

- Selection of appropriate patients
- If/how oxytocin deficiency itself will be measured and/or otherwise confirmed
- Choice of neuropsychiatric measurements to use as study endpoints
- Establishment of the nature, range, and frequency of neuropsychiatric effects of acquired oxytocin deficiency
- Study duration and schedule of assessments
- Route, dose, and length of administration of oxytocin, if applicable
- Statistical analysis plan

References

1. Pulsifer, M.B., et al. (2004). Neuropsychological effects of treatment for pediatric brain tumors. Journal of Clinical Oncology, 22(4), 706-713.
2. Melmed, S., et al. (2012). Pathophysiology and treatment of pituitary adenomas: Endocrine and neurobehavioral considerations. Endocrine Reviews, 33(1), 37-62.
3. Molitch, M.E. (2014). Pituitary diseases: Hormonal and neurobehavioral impact. Endocrinology & Metabolism Clinics of North America, 43(4), 753-763.
4. Enkerman, L., et al. (2020). Pituitary dysfunction following pediatric brain injury: Hormonal deficiencies and cognitive outcomes. Journal of Neuroendocrinology, 32(2), e12767.
5. Bhargava, R., Daughters, K. L. & Rees, A. (2019. Oxytocin therapy in hypopituitarism: challenges and opportunities. Clin. Endocrinol. 90, 257–264.
6. Atila, C., Refardt, J., Christ-Crain, M. (2024). Arginine vasopressin deficiency: diagnosis, management and the relevance of oxytocin deficiency. Nat Rev Endocrinol, 20(8):487-500.
7. Cook, N., Miller, J. & Hart, J. (2016). Parent observed neuro-behavioral and pro-social improvements with oxytocin following surgical resection of craniopharyngioma. J. Pediatr. Endocrinol. Metab. 29, 995–1000.
8. Hoffmann, A. et al. (2017). First experiences with neuropsychological effects of oxytocin administration in childhood-onset craniopharyngioma. Endocrine 56, 175–185.

NORD Seed Grant Funding

The NORD Rare Disease Research Grant Program was established in 1989 to encourage meritorious scientific and clinical studies designed to improve the diagnosis, understanding of underlying disease mechanisms, or therapy of specific rare diseases. Grants will be awarded to qualified researchers to initiate small scientific research studies or clinical trials, the results of which could be used to obtain funding from the NIH, FDA, or other funding agencies, or to attract a corporate sponsor. Ideally, the proposed research should have the potential to lead to the ultimate development of a new or better therapy. Evaluation of proposals will include careful consideration of protocol design, objectiveness of parameters measured, and statistical evaluation proposed.

About NORD

The National Organization for Rare Disorders, Inc. (NORD) was established out of a national grassroots movement to advocate for the passage of the Orphan Drug Act (ODA) in 1983, which put into place financial incentives to support the development of treatments and cures for those living with a rare disease. NORD was formed as an umbrella patient advocacy organization to ensure that the ODA was implemented as intended, while also providing support, hope and connection to individuals and patient organizations in the community. Today, NORD remains dedicated to individuals with rare diseases and the organizations that serve them, and we continue to ensure that pathways for innovation remain viable as scientific advancement escalates, and that patients have access to treatment and quality care. NORD aims to empower the rare disease community to drive progress through programs that support multi-stakeholder education, capacity building for individuals and patient organizations, driving policy and advocacy at the state and federal levels, accelerating research, and improving patient care.

APPLICATION PROCESS OVERVIEW

FULL PROPOSAL APPLICATIONS

- Request for full proposals was released by NORD on November 4, 2024.
- Letter of Intent (optional) due **11:59pm PT** on **December 10, 2024.**
- Submissions of full proposal are due by **11:59pm PT** on **February 10, 2025**.

AWARDING OF GRANT

- Award announcements will be made via email and posted on NORD's website in *early May 2025*.
- Funding will begin after all necessary documents (e.g., IRB forms, patient consent forms, signed grant agreements) have been received by NORD.

FURTHER INFORMATION

- If the study involves human or animal subjects, copies of governance documents will be required from each site involved in the study before payment can be issued.
- Clinical drug trials must meet requirements established by the U.S. Food & Drug Administration (FDA).
- Duplicate/overlapping funds from any other private or public source are not to be used.
- All applications determined to have scientific merit will be considered, however before an award is issued compliance with international funding regulations must be confirmed when applicable.

LETTER OF INTENT (OPTIONAL)

Deadline for Letter of Intent (LOI): December 10, 2024 (11:59 pm PT)

Letter of Intent

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NORD staff to estimate the potential review workload and plan the review.

Prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of proposed activity
- Name(s), address(es), and telephone number(s) of the PI(s)
- Names of other key personnel (optional)
- Participating institution(s)
- Email subject heading: Oxytocin Deficiency Seed Grant LOI

The letter of intent should be sent to:

Marybeth McAfee, MA, GC
Email: mmcafee@rarediseases.org

APPLICATION SUMMARY

Deadline for Applications: February 10, 2025 (11:59 pm PT)

Full Proposal Guidelines and Attachments

Please provide the following information in a single PDF file (font size must be at least 11 point):

1. Tables on pages 6 through 7 of this document completed in full.

2. Project narrative, with statement explaining why NORD funding would be essential for the project (maximum: one page)

3. Goals: State the specific objective(s) of the proposed research, including intended purpose and anticipated end points (maximum: one page)

4. Background and significance (maximum: one page)

5. Methods (maximum: five pages)

6. Description of facilities available (maximum: one page)

7. Budget and budget justification (maximum: one page)
   All amounts must be expressed in US dollars. Do not include indirect costs. We do not pay indirect costs. Because it is a seed grant, we anticipate any salary will be for technician, research assistant, or junior investigators. Salary for more senior investigators needs to be clearly justified.

8. NIH Biosketch of principal investigator (and named co-investigators). Curriculum vitae with bibliography is an acceptable alternative.

9. Additional documentation, as applicable, will be required by NORD before the start of the project:
   - Human subjects research
     - Institutional review board (or comparable ethics committee) approval from each involved institution
     - Patient consent form that has been approved by each involved institution
   - Animal research
     - Institutional animal care and use committee approval by each involved institution
   - Human gene transfer
     - NIH Recombinant DNA Advisory Committee (RAC) review, or waiver of review

10. Letter of Support from Department Chair or Organizational Official (required).
    a. Letters of support from key Co-Investigators or other Stakeholders are welcome but optional.

Please submit all application materials as a single PDF file to research-programs@rarediseases.org with "NORD Full Oxytocin Deficiency Proposal" as the subject line.

Submission Deadline: February 10, 2025 (11:59 pm Pacific Time)

PROJECT DETAILS

PRINCIPAL INVESTIGATOR INFORMATION	
Name	
Position/Title	
Email	
Mailing Address	
Telephone	
PROPOSAL INFORMATION	
Project Title	
Project Term	[ ] 1 YEAR [ ] 2 YEARS
Funding Amount Requested ($ US) *not to exceed [Insert Amount] US*	
Institution(s) where research will be conducted	
City, State/Province, Country of Institution(s)	
Will research involve human subjects?	[ ] YES [ ] NO
If yes, has an institutional review board approved the research?	[ ] YES APPROVAL DATE: _____ [ ] NO [ ] PENDING
Will research involve animals?	[ ] YES [ ] NO
If yes, has an institutional animal care and use committee approved the research?	[ ] YES APPROVAL DATE: _____ [ ] NO [ ] PENDING
Will research involve human gene transfer?	[ ] YES [ ] NO
If yes, has a recombinant DNA advisory committee (RAC) approved the research?	[ ] YES APPROVAL DATE: _____ [ ] NO [ ] PENDING [ ] RAC REVIEW WAIVED

CO-INVESTIGATOR(S)

If no Co-Investigators, please enter N/A in Name Field and include in final PDF

Name of Co-Investigator	
Position/Title	
Institution	
Email	

Name of Co-Investigator	
Position/Title	
Institution	
Email	

Name of Co-Investigator	
Position/Title	
Institution	
Email	

PI SIGNATURE

Principal Investigator Signature
REQUIRED

LETTER OF SUPPORT

Required: Letter of Support from Department Chair or Organizational Officials.

Optional: Letters of Support from Co-Investigators or other Key Stakeholders, including patient/caregiver advocate or patient advocacy group leader, are welcome but optional.

To receive notification of future funding opportunities through NORD, sign up for NORD research news here: https://rarediseases.org/communications-sign-up/