AMERICAN BRAIN FOUNDATION
Research Advisory Committee Meeting
December 3, 2021
3:00 p.m. ET/ 2:00 p.m. CT/ 1:00 p.m. MT/ 12:00 p.m. PT
Conference Call

Zoom link: https://aan.zoom.us/j/3682078427

Committee Members	Robert Griggs, MD, Chair; Raymond Roos, MD, Vice Chair; Jose Biller, MD; Carsten Bonnemann, MD; Jose E. Cavazos, MD, PhD; Jacqueline French, MD; Na Tosha Gatson, MD, PhD; James Grotta, MD; Walter Koroshetz, MD; Mark Mehler, MD; Bruce Ovbiagele, MD, MSc, MAS; Ronald Petersen, MD, PhD; Ralph Sacco, MD; Eugene Scharf, MD; Ira Shoulson, MD; Gordon Smith, MD; Reisa Sperling, MD, MMSc; Phyllis C. Zee, MD; David Dodick, MD; Paul George, MD, PhD; Christy Phelps; Mary Post, MBA, CAE
Staff	Jane Ransom, ED; Julia Miglets-Nelson, PhD

AGENDA ITEM	PRESENTED BY
1. **Call to Order** *(:00)* **Approval of the October 1, 2021 minutes**	Robert Griggs, MD
2. **Thank You to Departing Members** *(:03)*	Robert Griggs, MD
3. **2021 Research Program Report** *(:10)*	Julia Miglets-Nelson, PhD
4. **Neuroinflammation Initiative** *(:20)*	Robert Griggs, MD Raymond Roos, MD
Adjourn	

Meeting Materials:

- Minutes of October 1, 2021 (p. 2)
- Draft LOI to prospective funders: Neuroinflammation (p. 4)

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American Brain Foundation
Research Advisory Committee Meeting
October 1, 2021
3:00 p.m. ET / 2:00 p.m. CT / 1:00 p.m. MT / 12:00 p.m. PT
Conference Call

Meeting Minutes

In Attendance: Robert Griggs, MD, Chair; Raymond Roos, MD, Vice Chair; Jose Biller, MD; Carsten Bonnemann, MD; Na Tosha N. Gatson, MD, PhD; Mark Mehler, MD; Bruce Ovbiagele, MD, MSc, MAS; Ralph Sacco, MD; Ira Shoulson, MD; Gordon Smith, MD; Reisa Sperling, MD; Phyllis C. Zee, MD, PhD; David Dodick, MD

Staff: Jane Ransom; Julia Miglets-Nelson, PhD; Lisa Dahlberg

Excused: Jose E. Cavazos, MD; Jacqueline French, MD; James Grotta, MD; Walter Koroshetz, MD; Ron Petersen, MD, PhD; Eugene Scharf, MD; Mary Post, MBA, CAE; Christy Phelps; Natalia Rost, MD

The meeting was called to order by Dr. Robert Griggs at 2:00 p.m. CT. The meeting minutes of August 6, 2021 were approved.

1. **Cure One, Cure Many Award in LBD Update:** John Morris, MD provided an update on the ABF's 2022 Cure One, Cure Many Award in LBD. Representatives from ABF, Alzheimer's Association, Michael J. Fox Foundation, and American Academy of Neurology worked together to develop the RFA, which went out in the summer 2021. The RFA was international in scope, and was open to researchers at both academic institutions and industry. The selection committee was comprised of representatives appointed by the ABF, AAN, Alzheimer's Association, and Michael J. Fox Foundation. Members of the committee are: John Morris, MD (Chair); Alice Chen-Plotkin, MD; Chadwick Hales, MD, PhD; Allan Levey, MD, PhD; Irene Litvan, MD; Oscar Lopez, MD; Karen Marder, MD, MPH; Ian McKeith, MD; Ronald Petersen, MD, PhD; Tanya Simuni, MD; Heather Snyder, PhD.

   The committee received 21 Letters of Inquiry by the July deadline, and met at end of August to determine which applicants would be invited to submit a full application for the $3M award. Ten of the 21 applicants were invited to submit full applications, which are due on October 29, 2021. The selection committee will meet at the end of the November to determine which application will receive the funding, and the selected individual will be notified by mid-December. The committee did consider making more than one award from the $3M pool of funds, but ultimately decided to make one major impact award through one $3M, 3-year investment, which was highlighted in the award announcement. The selection committee will discuss recipient reporting and monitoring at its December meeting.

   Dr. Morris advised that engaging a committed and knowledgeable panel of experts to design the award and review applications will be key for future Cure One, Cure Many initiatives.

Reisa Sperling, MD inquired about the rationale for the 3-year time frame of the award and whether this would be enough time for the recipient to complete the work. Dr. Morris noted that the award was constrained in part because of the ABF's desire to make a single, high impact award that would attract additional philanthropy that would lead to future awards. The RFA for this award was very clear about the three-year time frame for funding so that investigators could budget accordingly, but the ABF would like to raise more money to extend the length of the award, and to make additional awards.

Raymond Roos, MD suggested that the NINDS might be interested in partnering with the ABF to extend the duration of the award or to offer an additional award. Dr. Morris noted that the ABF has embarked on this initiative independently of NINDS in part to establish the ABF's major research initiatives and to ensure that the award is a flagship for the ABF to promote. However, it may be prudent to partner with the NINDS in the future.

2. **Health Disparities Discussion:** Bruce Ovbiagele, MD, MSc, MAS summarized the work of the Health Disparities Subcommittee to date, and asked for the committee's help in developing a prospect list to generate additional support for disparities initiatives. The key questions for developing a prospect list are: who could be funders? How can the ABF attract funders? Who are potential ABF point people, and who can help connect the ABF to prospective funders? What existing networks might the ABF be able to utilize? How much money is needed to advance these efforts? Is the ABF's focus on healthcare disparities, or workforce diversity?

   Jose Biller, MD recommended that the ABF consider approaching mega corporations that utilize resources from developing countries for funding for disparities and diversity initiatives.

   Gordon Smith, MD emphasized the need to align the work of the ABF with that of the AAN to create a program of support that can be built around the ABF's current Next Generation Research Grant scholarships. Joseph Sirven, MD, Nimish Mohile, MD, and Jeffrey McClean II, MD are leading the AAN's diversity, equity, and inclusion efforts.

   Jane Ransom noted that the ABF is working to collaborate with the AAN on DEI programs, and that there has been interest from Genentech in funding a program that provides support to researchers who are underrepresented in medicine.

   Ralph Sacco, MD added that the AAN's Academic Subcommittee is overseeing many of the AAN's diversity efforts, and that multiple pharmaceutical companies are interested in supporting diversity in the neurology pipeline.

   Na Tosha N. Gatson, MD, PhD encouraged the subcommittee to also look at the work being done by Yazmin Odia, MD.

3. **Next Generation Discussion:** Gordon Smith, MD outlined the challenges within the Next Generation Research Grants Program, specifically the need to engage additional funders and partners to support awards, while also bringing in awards that are broad enough to satisfy the AAN Science Committee's request for awards that are not restricted to specific disease areas. There is also concern that some prospective applicants for ABF-funded awards are unable to apply because their institutions will not support the 70% protected time currently required to accept a Next Generation grant. So far, the Next Generation Subcommittee has discussed strategies to address the misalignment between applicants and award opportunities, by better educating and marketing these opportunities, and redeveloping current awards to fill the gap, and generating new funding opportunities.

Reisa Sperling, MD suggested that there may be ways to define what is expected from 70% protected time, that the requirement is for research time that may include clinical duties, but that the award is not expected to cover 70% of a recipients' salary.

Robert Griggs, MD proposed that ABF start a discussion with the AAN about protected time in the Next Generation program for consideration before the RFAs for the 2023 awards are finalized.

4. **Special Initiatives Discussion:** Raymond Roos, MD updated the committee on the outlines of the ABF's proposed multi-million dollar research initiative in neuroinflammation, a topic which encompasses a number of related diseases. One approach may be to focus on diseases with inflammation that have not been researched as closely with regard to the immune system, such as stroke. Other contemporary issues, like COVID-19 and CAR-T therapy, are also promising targets, as is artificial intelligence. The Research Advisory Committee now needs to narrow down the target of the proposed initiative to the specific diseases and immunological parameters of focus.

   Na Tosha N. Gatson, MD, PhD asked for the committee's input on her draft of a Letter of Inquiry that outlines the proposed scope of a neuroinflammation for prospective funders. The LOI emphasizes the need to understand both the reparative and pathogenic effects of inflammation.

   Robert Griggs, MD requested that the committee think about the research targets and potential funders for a major research initiative in neuroinflammation before the committee's next meeting in December, which will be focused around fleshing out the parameters of the initiative.

Adjourned 2:57 p.m. CT.

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September ___, 2021

[NAME]

[ADDRESS]

Harnessing Neuroinflammation – A cross-cutting mechanism of brain disease and the aging brain

Dear [NAME],

Central Nervous System diseases such as multiple sclerosis, brain tumor, epilepsy, Parkinson's Disease, Huntington's Disease, Alzheimer's Disease, stroke, Amyotrophic Lateral Sclerosis, migraine, neuropathy, traumatic brain injury, meningitis, and COVID-19 associated brain disease, affect at least 3 billion people worldwide and 60% of the US population. These diseases attack the essence of humanness: thought, speech, emotion, and movement.

Neuroinflammation is a crucial underlying mechanism that contributes to each of these neurological diseases and many therapeutic breakthroughs in neurological disease have targeted mediators of inflammation and the immune system. Inflammation is also thought to play a role in mental health conditions such as depression as well as the deleterious effects on the brain from chronic stress.

Neuroinflammation is of such importance to the field of neuroscience, the future of brain diseases, and the aging of the brain, that the thematic emphasis of a recent European Academy of Neurology annual meeting focused on Neuroinflammation. In addition, the US National Institutes of Health convened a workshop on disease-promoting chronic inflammation to identify the challenges and needs in the development of clinically feasible strategies for monitoring a person's inflammation status before, during and after disease occurrence.

Understanding the shared mechanisms that underlie many neurological diseases has been the guiding principle of the research funded by the American Brain Foundation (ABF). We believe that a cure for one will lead to a cure for many. Therefore, we are excited to announce a new major funding initiative of the American Brain Foundation entitled *Harnessing Neuroinflammation*.

Pathological neuroinflammation (NI) may be intrinsic to the brain and related to activation of resident immune cells including glial cells. NI may also be related to factors extrinsic to the brain such as the recruitment and transport of peripheral inflammatory mediators or immune response molecules across the blood brain barrier and into the brain. Furthermore, the role of the brain's lymphatic system (glymphatic system) in eliminating damaging inflammatory molecules from the brain has also emerged as a potentially important factor in the development of neurodegenerative diseases such as Alzheimer's disease and for repair after brain injury. The clearance of inflammatory molecules and substances that generate inflammation may also play a vital role in age-related diseases such as Alzheimer's disease as well as in the aging of the brain itself – a phenomenon referred to as *inflammaging*. A better understanding of the precise

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mechanisms of inflammatory mediated mechanisms involved in brain disease and age-related brain pathology is essential to identifying potential therapeutic targets and developing targeted pharmacological approaches acting at different points along these inflammatory cascades.

ABF is backed by the 36,000 neurologists of the American Academy of Neurology (AAN), our founder and research partner. The largest organization of neurologists in the world, AAN will supply its top scientists to vet research proposals for the *Harnessing Neuroinflammation* initiative, assuring that only those proposals that have the potential to result in truly transformational and translational advances will be supported.

The American Brain Foundation and the American Academy of Neurology has been and continues to be dedicated to developing the future of brain disease research by investing in the most promising young researchers. Nearly 90% of our funded junior researchers go on to secure extramural funding from the National Institutes of Health as well as other government and foundational research support. This initiative will focus on both revolutionary (high risk/high reward) as well as evolutionary (high quality, incremental) research proposals.

To execute *Harnessing Neuroinflammation,* ABF seeks $ million to invest in innovative scientific neuroinflammation research that is focused on one or more of domains listed below. We ask that you consider meeting with leaders from ABF and AAN to further discuss this initiative. Our executive director Jane Ransom will be following up with you regarding this letter. Please feel free to contact her at jransom@americanbrainfoundation.org.

Sincerely,

David Dodick, MD
Board Chair

Harnessing Inflammation Research Funding Priorities

The American Brain Foundation's Harnessing Neuroinflammation initiative will prioritize revolutionary and evolutionary proposals that seeks to advance knowledge in one of the following critical domains:

- Determine the role of immune cells and their subsets in the development of chronic brain disease
- Develop detection platforms and instruments that can perform multiple measurements of genetic, epigenetic and protein inflammation biomarkers related to brain disease
- Design and analyze population studies based on molecular, cellular and 'trans-omics' data
- Analyze and discover inflammatory biomarkers from metabolome, microbiome, secretome, proteome and other large biological data resources
- Develop computational platforms and tools to integrate and analyze cross-platform measurements of inflammatory markers

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- Determine whether chronic brain disease and disability are diminished by therapeutic interventions that target high-value inflammation molecules or pathways

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