

August 7, 2025

Dear Evelyn F. McKnight Brain Research Foundation Trustees ,

Thank you for your support of our McKnight Brain Aging Registry continuation. Please find attached the original signed Memo outlining the budget and terms. The current document is the year-end report outlining accomplishments in year 1, which completed 6/30/2025.

These deliverables per the MBAR memo are described here, along with the use of funds (numbering is consistent with the original Memo – numbers skipped are deliverables only applicable after year 2).

1. An organized, efficient, and PHI-friendly method for getting raw data for analysis to McKnight investigators.

- We developed and implemented a method for data transfer, facilitated by our data curator, Paul Stewart, that allows data to be transferred from our centralized data storage to various MBRF-affiliated labs. We use the Box file sharing platform, which is approved for potentially sensitive data, though no sensitive data is shared in this method (that is, we redact ages over 89, as well as all potentially identifiable information).
- Requests for access to blood are coordinated with investigators at University of Florida. They ship frozen blood or thaw and aliquot blood biomarkers as needed for further analyses done by other investigators. The current budget does not cover the processing of blood biomarkers, thus that processing (which is often costly) is done by interested investigators who have obtained independent funding to work with the blood provided by this project. Currently, Dr. Rundek's group is performing some processing of blood biomarkers to identify blood-based biomarkers including pTau217 in the sample.
- We send emails quarterly to all members of the four McKnight sites, reminding them of the availability of these datasets. These emails include links to our researcher-facing website (see item 3, go.uab.edu/mbar). This website, among other things, details the procedure for obtaining datasets. This involves filling out a Data Access Form (including details about the data requested and information about a power analysis about the question being addressed in the proposed analysis). This form will be collated by the data curator and assessed by the McKnight Brain Aging Registry Scientific Advisory Committee which meets monthly.

2. Generation of minimally preprocessed data from our datasets, as well as generation of selected early analyses

- While sophisticated users of data frequently want to start their analyses with raw datasets to apply the tools most appropriate for their exact research question, a dataset like the MBAR involves a wide range of different types of datasets which many investigators may not have sufficient expertise to process. For this reason, we

make several levels of processed data available. This approach decreases the effort and time required by researchers to analyze these datasets accurately.

- We have added several forms of tabular data to our dataset, including outputs of a brain-age measurement, GABA concentrations in Anterior Cingulate Cortex for each participant, and summarized alcohol-use variables. We have also included processed files to the dataset (not available as tabularized data), including GANNET pre-processed GABA files, which will be useful for investigators who are sophisticated in the use of MR Spectroscopy datasets and wish to do their own processing of those data, in order to be consistent with processing done on a different dataset. This strategy allows for use of this oldest-old dataset as a comparator to other datasets.

3. A researcher-facing website that shows exactly what data exists from our datasets and documents indicating how to go about accessing this data

- Any researcher interested in using the MBAR data has a full, detailed description of the data available to them at our website <https://go.uab.edu/mbar>. This includes a detailed list of demographic and behavioral data. The website contains detailed descriptions of how each scan and behavioral measure was collected, and relevant technical parameters that could help them determine whether this dataset will be appropriate for their research (see <https://uab-it.github.io/mbar/resources>, especially the link to the Manual of Procedures here: <https://uab.app.box.com/v/MBAR-Manual-of-procedures>). This represents Phase 1 of the website. Phase 2 (see item 7 in original memo; Phase 2 is a deliverable in year 2) will incorporate components for the lay public. Development of Phase 1 of the website involved careful documentation of the full dataset, and was a project in year 1 for Paul Stewart along with Hannah Cowart, who worked on the MBAR project while an undergraduate, and who has a strong understanding of the details of data acquisition.
- New Data Access forms for new projects within the past year are in the table below. These are in addition to the 16 proposals reviewed and described in the previous memo, several of which have been published (see item 6).

Investigator	Project title	investigator's home institution
Mishra	Understanding correlations between neuropsychological variables and harmonized structural MRI-derived features during healthy aging.	UAB
Britton/Gullett	Predictors and Cognitive Correlates of Brain-Predicted Age Discrepancy in Oldest-Old Adults	UF
Ling	Is executive function linked to dynamic functional connectivity in an older population?	UAB
Lubin	Identification and Characterization of Circular RNA and Competing Endogenous RNA Networks in Healthy Aging	UAB
Waters	Relationship between effective connectivity, heart-rate variability, and brain aging, in older adults	UF
Santos	Lifestyle, Psychosocial, and Health-related Facilitators of Cognitive Health in the Oldest-Old	UF
McGregor	Relationship of GABA to Functional Network Segregation and GABA in the Oldest Old	UAB
Rundek	Examining blood based biomarkers in the MBAR cohort: aBeta 40/42, pTau 217, NFL	UM

6. Quantification of the research products (papers/grants/etc.) that come from this effort.

- (note that this item is labeled “6” to match the original memo, where deliverables 4 and 5 are for year 2 and so are skipped here). We organize detailed information about the papers, grants, and any other work created with this dataset using an internal database. Additionally, any papers using this data are listed on our public-facing website here <https://uab-it.github.io/mbar/publications>. Our data curator, Paul Stewart has been following up with users of the data, asking for information about status of future or ongoing research involving the data. This is where much of the new tabular data described in item 2 arises from. We will continue to follow up with these users, especially those who have identified new projects within the past year.
- The published papers that have come from this effort include:
 - Britton, M.K., Jensen, G., Edden, R.A. *et al.* “Surviving and Thriving”: evidence for cortical GABA stabilization in cognitively-intact oldest-old adults. *Translational Psychiatry*, 15,79 (2025). <https://doi.org/10.1038/s41398-025-03302-w>
 - Ho, B.D., Gullett, J.M., Anton, S., Franchetti, M.K., Bharadwaj, P.K., Raichlen, D.A., Alexander, G.E., Rundek, T., Levin, B., Visscher, K., Woods, A.J., & Cohen, R.A. (2024). Associations between physical exercise type, fluid intelligence, executive function, and processing speed in the oldest-old (85+). *GeroScience*, 46(1), 491–503
 - Nolin, S.A., Faulkner, M.E., Stewart, P., Fleming, L., Merritt, S., Rezaei, R.F., Bharadwaj, P.K., Franchetti, M.K., Raichlen, D.A., Jessup, C.J., Edwards, L., Hishaw, G.A., Van Etten, E.J., Trouard, T.P., Geldmacher, D., Wadley, V.G.,

- Alperin, N., Porges, E.C., Woods, A.J., Cohen, R.A., Levin, B.E., Rundek, T., Alexander, G.E., Visscher, K.M. (2025) Network segregation is associated with processing speed in the cognitively healthy oldest-old. *eLife*, 14:e78076
- Nolin, S.A., Cowart, H., Merritt, S., McInerney, K., Bharadwaj, P.K., Franchetti, M.K., Raichlen, D.A., Jessup, C.J., Hishaw, G.A., Van Etten, E.J., Trouard, T.P., Geldmacher, D.S., Wadley, V.G., Porges, E.S., Woods, A.J., Cohen, R.A., Levin, B.E., Rundek, T., Alexander, G.E., & Visscher, K.M. (2023). Validity of the NIH toolbox cognitive battery in a healthy oldest-old 85+ sample. *Journal of the International Neuropsychological Society JINS*, 29(6), 605–614. <https://doi.org/10.1017/S1355617722000443>
 - Under review:
 - Britton, M. K., Hoogerwoerd, H., Juhasz, J., Johnson, K. J., Stewart, P. D., Merritt, S. S., Jessup, C. J., Wright, C. B., Raichlen, D. A., Hishaw, G. A., Del Bene, V. A., Wadley, V. G., Trouard, T. P., Alperin, N., Levin, B. E., Rundek, T., Visscher, K. M., Alexander, G. E., Cohen, R. A., Porges, E. C., ... Gullett, J. M. (2025). Your Brain Doesn't Look a Day Past 70! Cross-Sectional Associations with Brain-Predicted Age in the Cognitively-Intact Oldest-Old. *bioRxiv: the preprint server for biology*, 2025.05.26.655855. <https://doi.org/10.1101/2025.05.26.655855>
 - Parpura, V., Caceres, H.S., Sims, S.A., Ver Hoef, L., Ramaniharan, A.K., Merritt, S., Rezaei, R.F., Bharadwaj, P.K., Franchetti, M.K., Raichlen, D.A., Jessup, C.J., Hishaw, A.G., Van Etten, E.J., Trouard, T.P., Geldmacher, D.S., Wadley, V.G., Alperin, N., Porges, E.S., Woods, A.J., Cohen, R.A., Levin, B.E., Rundek, T., Alexander, G.E., Visscher, K.M. (2022). Larger and more dentated hippocampal structure is associated with better memory in the oldest-old. *bioRxiv: the preprint server for biology*, 2022.04.10.487750. <https://doi.org/10.1101/2022.04.10.487750>

Access to Biospecimens: In addition, you requested information about the criteria used to approve requests for access to biospecimens. Any investigator wishing to have access to the biospecimens should fill out the same data access form available for all other data access. It is linked to and described in the overview website described in Item 3, above. The form itself can be found here: <https://uab.app.box.com/v/MBAR-proposal-data-access>

These forms, when submitted, are discussed by the scientific advisory council, which meets on the second Friday of the month, via zoom. As with the other studies, the criteria used are that the work described fits within the scope of McKnight goals (brain health and cognitive aging, very broadly construed), and the rough power analyses, as described in the data access form will have enough power to be publishable, if publication is the goal described in the data access form. Alternatively, if publication is not the goal described, we assess whether the proposed goal is scientifically consistent with the analysis proposed. In practice, we have only had 2 proposed projects request biospecimens (Dr. Farah Lubin and team, and Dr. Tanja Rundek and team). Despite a concerted effort to request applications, and we have not received other data access forms requesting the biospecimens yet. Dr. Lubin's request is to perform a costly test of circular RNA, for which they only wish to sample up to 4 of the participants' data. Dr. Rundek's analysis of the biospecimens is to identify aBeta 40/42, pTau2017, and NFL in

each sample. Dr. Lubin's team aims to identify circular RNA measures. One goal for the coming year is to improve the number of data request forms which will use biospecimens. The frozen blood samples are held at the University of Florida, and we ship them as needed to other sites.

Use of funds: Funds were used, consistent with the Budget per the original memo, for contributions toward Paul Stewart's Salary, and publication costs for the journal eLife for \$3000 for the Nolin et al. paper published this year.

Thank you for your past and continued support of this important endeavor. Please let me know if you have any questions.

Sincerely,



Kristina Visscher, Ph.D.

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Associate Director, UAB Evelyn F. McKnight Brain Institute