

Reporting Summary

Nature Portfolio wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Portfolio policies, see our [Editorial Policies](#) and the [Editorial Policy Checklist](#).

Statistics

For all statistical analyses, confirm that the following items are present in the figure legend, table legend, main text, or Methods section.

n/a	Confirmed
<input type="checkbox"/>	<input checked="" type="checkbox"/> The exact sample size (<i>n</i>) for each experimental group/condition, given as a discrete number and unit of measurement
<input type="checkbox"/>	<input checked="" type="checkbox"/> A statement on whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
<input type="checkbox"/>	<input checked="" type="checkbox"/> The statistical test(s) used AND whether they are one- or two-sided <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
<input type="checkbox"/>	<input checked="" type="checkbox"/> A description of all covariates tested
<input type="checkbox"/>	<input checked="" type="checkbox"/> A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
<input type="checkbox"/>	<input checked="" type="checkbox"/> A full description of the statistical parameters including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
<input type="checkbox"/>	<input checked="" type="checkbox"/> For null hypothesis testing, the test statistic (e.g. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
<input checked="" type="checkbox"/>	<input type="checkbox"/> For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
<input type="checkbox"/>	<input type="checkbox"/> For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
<input type="checkbox"/>	<input type="checkbox"/> Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection	Behavior data were collected using Anymaze (7.16). Echocardiographic measurements were collected using Visual Sonic Vevo (3100 system). Data on brain plaques were collected in Image J (1.53k). Western blots data were collected with Image J (1.53k) and BioRad ImageLab (6.1). Immunofluorescence 3D renders were created in Imaris Viewer (9.9.1).
Data analysis	All data were analyzed according to the specialized softwares. Data for analysis were anonymized. 1. Statistical test used and whether they are one- or two-sided. • Linear regression models (LMs) were fit for models that did not include repeated measurements. The significance of each individual predictor in a LM was derived from two-sided t-tests with a significance level of 0.05. Linear mixed regression models (LMMs) were fit for models that did include repeated measurements. The significance of each individual coefficient in a LMM was derived from approximate ad hoc two-sided Wald tests with a significance level of 0.05. Sensitivity analyses was performed, but since the removal of these observations did not change the results presented in the manuscript we maintained all data points. 2. Identification of the appropriate level for tests and full reporting of outcomes for hierarchical and complex designs. • We used hierarchical models to control for the repeated measures of outcomes in the linear mixed regression models (LMMs) that were fit. Each model specification incorporated random effects to account for the variability within each subject. Results from these models included estimates for both fixed and random effects, their standard errors, confidence intervals, and the derived significance of each coefficient using two-sided Wald tests. Additionally, model fit statistics such as the AIC were obtained, alongside diagnostic plots to validate model assumptions. 3. Estimates of effect sizes (e.g. Cohen's <i>d</i> , Pearson's <i>r</i>) calculation • For the LMs, the estimates of effect sizes were obtained using the method of least squares, which minimizes the sum of squared differences between the observed and predicted outcome values. For the LMMs, the estimates of effect sizes were obtained using restricted maximum likelihood (REML) estimation.

4. Software and Code.

• The application of our models was implemented with the R version 4.1.3 using the base (for LMs) and lme4 (for LMMs) packages. All models fit were assessed for fit using diagnostics to validate model assumptions.

5. Code availability statement.

• The analysis scripts will be deposited at https://github.com/everparkeller/PM_Cardiac_Brain_Alzheimers_Mice. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio [guidelines for submitting code & software](#) for further information.

Data

Policy information about [availability of data](#)

All manuscripts must include a [data availability statement](#). This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our [policy](#)

All experimental data supporting the finding of the study are presented within the paper and in its Supplementary Material. Mice strain is indicated in the text and specific details are available from Jaxson Laboratory. Raw experimental data are presented in the Supplementary Material and stored in the MUSC storage service (Box). Data will be available upon request. • The analysis scripts are available at https://github.com/everparkeller/PM_Cardiac_Brain_Alzheimers_Mice. The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender

Reporting on race, ethnicity, or other socially relevant groupings

Population characteristics

Recruitment

Ethics oversight

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one below that is the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see [nature.com/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size

Data exclusions

Replication

Randomization

Blinding

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experimental systems

n/a	Involved in the study
<input type="checkbox"/>	<input checked="" type="checkbox"/> Antibodies
<input checked="" type="checkbox"/>	<input type="checkbox"/> Eukaryotic cell lines
<input checked="" type="checkbox"/>	<input type="checkbox"/> Palaeontology and archaeology
<input type="checkbox"/>	<input checked="" type="checkbox"/> Animals and other organisms
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern
<input checked="" type="checkbox"/>	<input type="checkbox"/> Plants

Methods

n/a	Involved in the study
<input checked="" type="checkbox"/>	<input type="checkbox"/> ChIP-seq
<input checked="" type="checkbox"/>	<input type="checkbox"/> Flow cytometry
<input checked="" type="checkbox"/>	<input type="checkbox"/> MRI-based neuroimaging

Antibodies

Antibodies used	<p>Amyloid beta-40 (D8Q7I) (Cell Signaling; catalog#12990S, lot#3)</p> <p>Amyloid beta-42 (D3E10) (Cell Signaling; catalog#12843S, lot#1)</p> <p>SOD1 (Invitrogen; catalog#PA18497, lot#XG3649353)</p> <p>OC (Millipore Sigma; catalog#2286, lot#NG1865063)</p> <p>VIA (gift from the lab of Rakez Kayed at UTMB)</p> <p>A11-19 (gift from the lab of Rakez Kayed at UTMB)</p> <p>Tropomyosin (Millipore Sigma; catalog#AB5441, lot#3760045)</p> <p>Anti-rabbit IgG HRP Linked (Cell Signaling; catalog #7074, lot#32)</p> <p>Donkey Anti-Rabbit AF568 (Invitrogen; catalog#A10042, lot#2433862)</p> <p>Donkey anti-Sheep AF488 (Jackson ImmunoResearch; catalog#713-545-003, lot#168058)</p>
Validation	<p>Amyloid beta-40 (D8Q7I); This Cell Signaling antibody was validated to ensure optimal performance for western blot per the manufacturer's website.</p> <p>Amyloid beta-42 (D3E10); This Cell Signaling antibody was validated to ensure optimal performance for western blot per the manufacturer's website.</p> <p>SOD1; This Invitrogen antibody was validated for western blot by H2O2 cell treatment and CRISPR-Cas9 SOD1 knockout per the manufacturer's website.</p> <p>OC; This Millipore Sigma antibody underwent quality control testing and was validated for the target for dot blot per the manufacturer's website.</p> <p>VIA; This antibody from the Kayed Lab has been validated and published: (DOI: 10.1021/acschemneuro.5b00231)</p> <p>A11-19; This antibody from the Kayed Lab has been validated and published: (DOI: 10.1186/1750-1326-2-18 ; DOI: 10.1074/jbc.R800016200)</p> <p>Tropomyosin; This antibody from Millipore Sigma has been validated for IHC per the manufacturer's website.</p> <p>Anti-rabbit IgG HRP Linked; This Cell Signaling antibody was validated to ensure optimal performance for western blot per the manufacturer's website.</p> <p>Donkey Anti-Rabbit AF568; This Invitrogen antibody was validated for immunofluorescence per the manufacturer's website.</p> <p>Donkey anti-Sheep AF488; This Jackson ImmunoResearch antibody was validated for immunofluorescence per the manufacturer's website.</p>

Animals and other research organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research, and [Sex and Gender in Research](#)

Laboratory animals	APPswe/PSEN1dE9 double transgenic and C57Bl/6J WT control mice were obtained from Jackson Laboratories (Bar Harbor, ME) (Jax 000664 and MMRC 034832, respectively). Mice were obtained at three month of age and were euthanized at six months of age following a three month exposure period.
Wild animals	This study did not involve wild animals.
Reporting on sex	Male and female mice were used in this study. Sex was a covariate in all analyzes where applicable.
Field-collected samples	This study did not involve field collected samples.
Ethics oversight	The study complies with the National Institute of Health Guide for the Care and Use of Laboratory Animals (Protocol #2020-01084). Male and female mice were included in the study.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Plants

Seed stocks	This study did not involve plants.
Novel plant genotypes	This study did not involve plants.
Authentication	This study did not involve plants.