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**Sample-size estimation**

* You should state whether an appropriate sample size was computed when the study was being designed
* You should state the statistical method of sample size computation and any required assumptions
* If no explicit power analysis was used, you should describe how you decided what sample (replicate) size (number) to use

As this type of APEX2 study in mouse brain had not been conducted previously, we were unable to conduct power analysis for determination of sample sizes. We chose a number of biological replicates (mice) sufficient for differential expression analysis based on our experience in transcriptomics, under the assumption that proteomic data would behave similarly.

Please outline where this information can be found within the submission (e.g., sections or figure legends), or explain why this information doesn’t apply to your submission:

**Replicates**

* You should report how often each experiment was performed
* You should include a definition of biological versus technical replication
* The data obtained should be provided and sufficient information should be provided to indicate the number of independent biological and/or technical replicates
* If you encountered any outliers, you should describe how these were handled
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* High-throughput sequence data should be uploaded before submission, with a private link for reviewers provided (these are available from both GEO and ArrayExpress)

No technical replicates were included in this manuscript. The number of biological replicates (mice) used in each experiment is indicated in the relevant figure captions. The mass spectrometry proteomics data have been deposited to the ProteomeXchange Consortium via the PRIDE partner repository with the dataset identifier PXD026229.

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**Statistical reporting**

* Statistical analysis methods should be described and justified
* Raw data should be presented in figures whenever informative to do so (typically when N per group is less than 10)
* For each experiment, you should identify the statistical tests used, exact values of N, definitions of center, methods of multiple test correction, and dispersion and precision measures (e.g., mean, median, SD, SEM, confidence intervals; and, for the major substantive results, a measure of effect size (e.g., Pearson's r, Cohen's d)
* Report exact p-values wherever possible alongside the summary statistics and 95% confidence intervals. These should be reported for all key questions and not only when the p-value is less than 0.05.

A complete description of all statistical analysis methods used in this manuscript is found in the Materials and Methods section. Details regarding sample size, p values, and other test statistics are included in the relevant figure captions.

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(For large datasets, or papers with a very large number of statistical tests, you may upload a single table file with tests, Ns, etc., with reference to sections in the manuscript.)

**Group allocation**

* Indicate how samples were allocated into experimental groups (in the case of clinical studies, please specify allocation to treatment method); if randomization was used, please also state if restricted randomization was applied
* Indicate if masking was used during group allocation, data collection and/or data analysis

An equal number of DAT-Ires-Cre mice in each cage were randomly assigned to receive either injection of AAV-CAG-DIO-APEX2NES (APEX2+ group) or no virus (APEX2- group). Experimenters were not blinded to group assignment during subsequent experiments.

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**Additional data files (“source data”)**

* We encourage you to upload relevant additional data files, such as numerical data that are represented as a graph in a figure, or as a summary table
* Where provided, these should be in the most useful format, and they can be uploaded as “Source data” files linked to a main figure or table
* Include model definition files including the full list of parameters used
* Include code used for data analysis (e.g., R, MatLab)
* Avoid stating that data files are “available upon request”

In addition to deposition in the PRIDE proteomics repository, the raw proteomics data matrices are included as source data. Other relevant source data files are linked to each figure, such as complete output of Gene Ontology Analysis, Differential Expression Analysis, and complete list of all protein abbreviations used in the figures.

Please indicate the figures or tables for which source data files have been provided: