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☐ Initial submission ☐ Revised version ☒ Final submission

# Life Sciences Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form is intended for publication with all accepted life science papers and provides structure for consistency and transparency in reporting. Every life science submission will use this form; some list items might not apply to an individual manuscript, but all fields must be completed for clarity.

For further information on the points included in this form, see Reporting Life Sciences Research. For further information on Nature Research policies, including our data availability policy, see Authors & Referees and the Editorial Policy Checklist.

## Experimental design

1. Sample size

Describe how sample size was determined.

No statistical methods were used to pre-determine sample sizes but our sample sizes are similar to those reported in Sharma et al's study of the mouse brain (Nature Neuroscience 2015).

2. Data exclusions

Describe any data exclusions.

No data were excluded from the analysis.

3. Replication

Describe whether the experimental findings were reliably reproduced.

Of the proteins we tested by immunoblotting in the DFC vs V1C, 3 out of 4 proteins validated.

4. Randomization

Describe how samples/organisms/participants were allocated into experimental groups.

Samples were run on the LC-MS/MS in regional blocks, with control samples interspersed throughout to allow for correction of batch effects.

5. Blinding

Describe whether the investigators were blinded to group allocation during data collection and/or analysis.

Data collection and analysis were not performed blind to the conditions of the experiments

Note: all studies involving animals and/or human research participants must disclose whether blinding and randomization were used.

6. Statistical parameters

For all figures and tables that use statistical methods, confirm that the following items are present in relevant figure legends (or in the Methods section if additional space is needed).

| n/a | Confirmed | |
|---|---|---|
| ☐ | ☒ | The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement (animals, litters, cultures, etc.) |
| ☐ | ☒ | A description of how samples were collected, noting whether measurements were taken from distinct samples or whether the same sample was measured repeatedly |
| ☒ | ☐ | A statement indicating how many times each experiment was replicated |
| ☐ | ☒ | The statistical test(s) used and whether they are one- or two-sided (note: only common tests should be described solely by name; more complex techniques should be described in the Methods section) |
| ☐ | ☒ | A description of any assumptions or corrections, such as an adjustment for multiple comparisons |
| ☐ | ☒ | The test results (e.g. *P* values) given as exact values whenever possible and with confidence intervals noted |
| ☐ | ☒ | A clear description of statistics including central tendency (e.g. median, mean) and variation (e.g. standard deviation, interquartile range) |
| ☒ | ☐ | Clearly defined error bars |

*See the web collection on statistics for biologists for further resources and guidance.*

## Software

Policy information about availability of computer code

7. Software

| | |
|---|---|
| Describe the software used to analyze the data in this study. | Maxquant v1.5.2.1 to map/quantify peptides & proteins<br>ComBat to correct for batch effects in the proteomic data<br>STAR aligner v2.4.2a to map RNAseq reads<br>RSEQ tools to compute RNA abundance<br>Custom R/Bioconductor code provided in accompanying zip file to analyse differential expression/enrichment/ generate figures |

For manuscripts utilizing custom algorithms or software that are central to the paper but not yet described in the published literature, software must be made available to editors and reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). *Nature Methods* guidance for providing algorithms and software for publication provides further information on this topic.

## Materials and reagents

Policy information about availability of materials

8. Materials availability

| | |
|---|---|
| Indicate whether there are restrictions on availability of unique materials or if these materials are only available for distribution by a for-profit company. | All materials used (not including the samples themselves) are available through standard commercial vendors. |

9. Antibodies

| | |
|---|---|
| Describe the antibodies used and how they were validated for use in the system under study (i.e. assay and species). | Primary antibodies used were anti mGluR2/3 (GRM2/3, EMD Millipore, 06-676, 1:1000), anti CB1 (CNR1, Cell Signalling, D5N5C, 1:1000), anti PDE4D (Millipore ABS22, 1:1000), anti TrkC (NTRK3, Cell Signalling, C44H5, 1:1000) and anti GAPDH (Calbiochem CB1001, 1:5000). They have been validated for this assay in other species, but not in human brain. The bands we observe are of equivalent size to those shown in validation data. Comprehensive validation of antibodies for use in human brain tissue is extremely difficult, as discussed by the Antibody Validation Working group (Uhlen et al, Nature Methods, Oct 2016), but given that for all antibodies except TrKC the antibodies show a comparable pattern of expression to the LC-MS/MS data, and bands of the appropriate size, we can presume these antibodies are working appropriately. In TrkC's case, the disagreement may depend on the epitope used by the antibody, drop out of peptides due to post translational modification, or a lack of sensitivity by the antibodies for a relatively modest change. |

10. Eukaryotic cell lines

| | |
|---|---|
| a. State the source of each eukaryotic cell line used. | N/A |
| b. Describe the method of cell line authentication used. | N/A |
| c. Report whether the cell lines were tested for mycoplasma contamination. | N/A |
| d. If any of the cell lines used are listed in the database of commonly misidentified cell lines maintained by ICLAC, provide a scientific rationale for their use. | N/A |

## Animals and human research participants

Policy information about studies involving animals; when reporting animal research, follow the ARRIVE guidelines

11. Description of research animals

| | |
|---|---|
| Provide details on animals and/or animal-derived materials used in the study. | N/A |

Policy information about studies involving human research participants

12. Description of human research participants

| | |
|---|---|
| Describe the covariate-relevant population characteristics of the human research participants. | All demographic infomation regarding the human samples used can be found in Table S1. |