

Reporting Summary

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Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section).

n/a Confirmed

- ☐ ☒ The exact sample size (n) for each experimental group/condition, given as a discrete number and unit of measurement
- ☐ ☒ An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
- ☐ ☒ The statistical test(s) used AND whether they are one- or two-sided
Only common tests should be described solely by name; describe more complex techniques in the Methods section.
- ☒ ☐ A description of all covariates tested
- ☐ ☒ A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
- ☐ ☒ A full description of the statistics 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)
- ☐ ☒ For null hypothesis testing, the test statistic (e.g. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P value noted
Give P values as exact values whenever suitable.
- ☒ ☐ For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
- ☒ ☐ For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
- ☐ ☒ Estimates of effect sizes (e.g. Cohen's d , Pearson's r), indicating how they were calculated
- ☐ ☒ Clearly defined error bars
State explicitly what error bars represent (e.g. SD, SE, CI)

Our web collection on [statistics for biologists](#) may be useful.

Software and code

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

Data collection

Two forms of data were collected for this submitted manuscript: primarily electrophysiological trace records and numerical simulations. Raw data was obtained using pClamp 10, or using Ephus (<http://scanimage.vidriotechnologies.com/display/ephus/Ephus>), and saved as .ABF2 and MATLAB .MAT files, respectively. NEURON simulations produced .CSV files containing in-the-loop saved results. Simulations in MATLAB were saved as .MAT files. Meta analysis of ephys data was performed using Clampfit and MATLAB. All other analyses were performed in MATLAB.

Data analysis

All analysis of electrophysiological data was performed with Clampfit (Axon Instruments, CA, USA) and MATLAB (Mathworks, Natick MA, USA). Data were collated in Microsoft Excel, MATLAB and Graphpad Prism 7. All data was tested for normality and the appropriate statistic employed. All statistical tests, replicates tested, degrees of freedom, and statistical assumptions are presented in the legends and text pertaining to individual figures and the experimental methods section. All custom code used for this study is available on request, and code specific to running and analysing the numerical single-cell/network simulations is hosted on Github - please see below for accession links.

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/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research [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 list of figures that have associated raw data
- A description of any restrictions on data availability

All data will be made available on request, Simulation/analysis code is available on Github at: <https://github.com/apfdomanski/Thalamocortical-Synaptic-Integration-in-Fmr1-KO-cortex> and <https://github.com/apfdomanski/Fmr1-KO-cortical-layer-4-spiking-network>.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

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

Sample size	Sample size was determined with power-analysis, following preliminary examination of data. In brief, pilot experiments were performed with minimal biological replicates to determine variability and potential effect size of data. Following this initial assessment further data were collected to satisfy the calculated "n" required based on the observed effect size.
Data exclusions	No data was excluded
Replication	All experiments were performed in successive rounds (see sample size calculation), with a minimum of 2 rounds of experiments performed as routine, up to the number of replicates indicated by power analysis or by previous studies in the lab. The chosen replicate for all individual experiments was assumed as the animal, except where explicitly noted in the text/figure legends as pertaining to number of cells and brain slices use per animal.
Randomization	All animals were randomly chosen from each litter as they were used prior to genotyping. It is important to note that there are no outward phenotypes in Fmr1 knock-out mice that would potentially bias animal selection towards a particular genotype.
Blinding	All experiments and analysis were performed blind to genotype. As experiments were performed in young postnatal mice (day 10-11, see below) biopsies for genotyping were only collected on the day of experiment. Only once all data collection and analysis for a round of experiments was complete would genotyping be performed and the data unblinded. As such all data was collected in a blind and random fashion. All analysis was automated and run as batches on mixed genotype data using standardised parameter choices.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☒	☐ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☒	☐ Flow cytometry
☒	☐ MRI-based neuroimaging

Animals and other organisms

Policy information about [studies involving animals](#); [ARRIVE guidelines](#) recommended for reporting animal research

Laboratory animals	All mice used in the current study were of the C57/BL6J strain (Jackson Labs). Only male mice were used for the current study due to the X-linked nature of the Fmr1 gene. Mice were 10-11 days postnatal for all experiments in this study, as based on the
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first day pups were observed by handlers defined as postnatal day 0. All procedures were carried out according to UK Home Office and NIH IACUC guidelines for animal welfare.

Wild animals

N/A

Field-collected samples

N/A