

Reporting Summary

Nature Research 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 Research 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 (n) 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. F , t , r) with confidence intervals, effect sizes, degrees of freedom and P 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 checked="" 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 checked="" type="checkbox"/> | Estimates of effect sizes (e.g. Cohen's d , Pearson's r), 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

Data analysis

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 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

Raw and processed data reported in this study using brain tissue from the lateral amygdala are publicly available via the Gene Expression Omnibus, with accession GSE151827, at: <https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE151827>. Source data are provided with this paper for all figures. RNA-Sequencing data generated using brain tissue from the anterior cingulate cortex is available upon request.

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	Sample size calculation was not performed. However, we justified experiment sample size based on several previously published reports using similar or even smaller sample sizes (Lutz et al, Am J Psychiatry 2017, 174(12):1185-1194; Labonté et al, Am J Psychiatry 2013, 170(5):511-20; Labonté et al, Arch Gen Psychiatry 2012 69(7):722-31; Sibille et al, Am J Psychiatry 2009 166(9):1011-24) and showing the power to detect significant statistical differences.
Data exclusions	No statistical outlier was removed.
Replication	Validity of our dataset was assessed by conducting systematic comparisons among multiple epigenetic layers, and against gene expression. Each library preparation and sequencing experiment was performed once.
Randomization	Given the nature of our experimental post-mortem design in humans, groups were not randomized. However, they were balanced for the following covariates: age, post-mortem interval and brain pH. In addition, groups were characterized by the same psychological autopsy methods, therefore avoiding the occurrence of systematic biases.
Blinding	Investigators were blinded to group allocation during data collection and analysis.

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 checked="" type="checkbox"/>	<input type="checkbox"/> Animals and other organisms
<input type="checkbox"/>	<input checked="" type="checkbox"/> Human research participants
<input checked="" type="checkbox"/>	<input type="checkbox"/> Clinical data
<input checked="" type="checkbox"/>	<input type="checkbox"/> Dual use research of concern

Methods

n/a	Involved in the study
<input type="checkbox"/>	<input checked="" 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	H3K4me1: Cell Signaling Technologies, cat #5326BF, lot #2 H3K4me3: Cell Signaling Technologies, cat #9751BF, lot#6 H3K9me3: Abcam, cat #Ab8898, lot #GR93671-1 H3K27me3: Cell Signaling Technologies, cat #9733S, lot #6 H3K27ac: Diagenode, cat #pAB-196-050, lot #A1723-0041D H3K36me3: Active motif, cat #MABI0333, lot #12003
Validation	H3K4me1: see https://www.cellsignal.com/products/primary-antibodies/mono-methyl-histone-h3-lys4-d1a9-xp-rabbit-mab/5326 H3K4me3: https://www.cellsignal.com/products/primary-antibodies/tri-methyl-histone-h3-lys4-c42d8-rabbit-mab/9751 H3K9me3: see https://www.abcam.com/histone-h3-tri-methyl-k9-antibody-chip-grade-ab8898.html H3K27me3: see https://www.cellsignal.com/products/primary-antibodies/tri-methyl-histone-h3-lys27-c36b11-rabbit-mab/9733 H3K27ac: see https://www.diagenode.com/en/p/h3k27ac-polyclonal-antibody-premium-50-mg-18-ml?utm_source=CiteAb&utm_medium=listing&utm_campaign=Ab H3K36me3: see https://www.activemotif.com/catalog/details/61021/histone-h3-trimethyl-lys36-antibody-clone-mab-clonemabi-0333

Human research participants

Policy information about [studies involving human research participants](#)

Population characteristics

Brain tissue was obtained from the Douglas Bell Canada Brain Bank (DBCBB; Douglas Mental Health Institute, Verdun, Québec; www.douglasbrainbank.ca). All subjects were Caucasians of French–Canadian descent, a population with a well identified founder effect. Sociodemographic and clinical information are listed in Supplementary Table 1. Inclusion criteria for both cases and controls were the following: the subject had to be Caucasian and of French Canadian origin and the subject had to die suddenly without prolonged agonal state. Tissue dissection was performed by histopathologists using reference neuroanatomical maps. Information concerning psychiatric history and socio-demographics was obtained by way of psychological autopsies performed by trained clinicians with the informants best acquainted with the deceased. Diagnoses were obtained using DSM-IV criteria by means of SCID-I interviews adapted for psychological autopsies. Control (C) and early-life adversity (ELA) groups were matched for age, gender, post mortem interval and RNA integrity values, all meaningful covariates.

Recruitment

The Douglas-Bell Canada Brain Bank (www.douglasbrainbank.ca) collects brain tissue in collaboration with the Montréal coroner office as described in the text. Psychological autopsies were performed by trained clinicians on both controls and cases, with the informants best-acquainted with the deceased, as validated by our group and others. Diagnoses were assigned based on DSM IV criteria. Characterization of early-life histories was based on adapted Childhood Experience of Care and Abuse (CECA) interviews assessing experiences of sexual and physical abuse, psychological abuse, as well as neglect, and for which scores from siblings are highly concordant. We considered as severe early-life adversity reports of non-random major physical and/or sexual abuse during childhood (up to 15 years). Only cases with the maximum severity ratings of 1 and 2 were included. This information was then complemented with medical charts and coroner records. Ethical approval was obtained from the Institutional Review Board of the Douglas Mental Health University Institute. Written informed consent was obtained from the families of each of the deceased subjects prior to inclusion in the study.

Ethics oversight

This study was approved by our IRB (Douglas Mental Health Institute Research Ethics Board), and signed informed consent was obtained from next of kin.

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

ChIP-seq

Data deposition

- Confirm that both raw and final processed data have been deposited in a public database such as [GEO](#).
- Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links

May remain private before publication.

<https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE151827>

Files in database submission

Raw files:
 S1_BS.bam
 S2_BS.bam
 S3_BS.bam
 S4_BS.bam
 S5_BS.bam
 S6_BS.bam
 S7_BS.bam
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Processed files:

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S2.profile
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S5.profile
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 S3_12_38_Pool6_H3K4me1.bw
 S3_12_38_Pool6_H3K4me3.bw
 S3_12_38_Pool6_H3K9me3.bw
 S3_12_38_Pool6_Input.bw
 S4_5_15_20_26_36_Pool1_H3K27ac.bw
 S4_5_15_20_26_36_Pool1_H3K27me3.bw
 S4_5_15_20_26_36_Pool1_H3K36me3.bw
 S4_5_15_20_26_36_Pool1_H3K4me1.bw
 S4_5_15_20_26_36_Pool1_H3K4me3.bw
 S4_5_15_20_26_36_Pool1_H3K9me3.bw
 S4_5_15_20_26_36_Pool1_Input.bw
 S6_7_Pool4_H3K27ac.bw
 S6_7_Pool4_H3K27me3.bw
 S6_7_Pool4_H3K36me3.bw
 S6_7_Pool4_H3K4me1.bw
 S6_7_Pool4_H3K4me3.bw
 S6_7_Pool4_H3K9me3.bw
 S6_7_Pool4_Input.bw
 S8_30_31_35_Pool7_H3K27ac.bw
 S8_30_31_35_Pool7_H3K27me3.bw
 S8_30_31_35_Pool7_H3K36me3.bw
 S8_30_31_35_Pool7_H3K4me1.bw
 S8_30_31_35_Pool7_H3K4me3.bw
 S8_30_31_35_Pool7_H3K9me3.bw
 S8_30_31_35_Pool7_Input.bw
 S9_27_39_Pool3_H3K27ac.bw
 S9_27_39_Pool3_H3K27me3.bw
 S9_27_39_Pool3_H3K36me3.bw

Genome browser session
(e.g. [UCSC](https://genome.ucsc.edu))

[http://genome.ucsc.edu/cgi-bin/hgTracks?](http://genome.ucsc.edu/cgi-bin/hgTracks?db=hg19&lastVirtModeType=default&lastVirtModeExtraState=&virtModeType=default&virtMode=0&nonVirtPosition=&position=chrX%3A15578261%2D15621068&hgsid=842700757_BMUbvvoSamAiEMdbGagOu9lp1XXvm)
 db=hg19&lastVirtModeType=default&lastVirtModeExtraState=&virtModeType=default&virtMode=0&nonVirtPosition=&posit
 ion=chrX%3A15578261%2D15621068&hgsid=842700757_BMUbvvoSamAiEMdbGagOu9lp1XXvm

Methodology

Replicates

No technical replicates were analyzed. Because of the small size of the amygdala lateral nucleus, and the large amounts of tissue required for multiple immune-precipitations and the ChIP-seq analysis of 6 histone marks, tissue from 17 C and 21 ELA subjects were distributed into 7 ELA and 4 C pools, and the 6 marks were analyzed in each of the 11 resulting pools.

Sequencing depth

Sequencing was performed using the Illumina HiSeq2000 to achieve at least 30 and 60 million reads for narrow (H3K27ac, H3K4me3) and broad (H3K27me3, H3K36me3, H3K4me1, H3K9me3) marks, respectively (see Supplementary Figure S1a), following standard

	recommendations from the International Human Epigenome Consortium.
Antibodies	H3K4me1: Cell Signaling Technologies, cat #5326BF, lot #2 H3K4me3: Cell Signaling Technologies, cat #9751BF, lot#6 H3K9me3: Abcam, cat #Ab8898, lot #GR93671-1 H3K27me3: Cell Signaling Technologies, cat #9733S, lot #6 H3K27ac: Diagenode, cat #pAB-196-050, lot #A1723-0041D H3K36me3: Active motif, cat #MABI0333, lot #12003
Peak calling parameters	No peak calling was conducted. Groups were compared by looking for differential enrichment of ChIP-Seq reads using diffReps, as well as by comparing ChromHMM maps of chromatin states across groups.
Data quality	Coverage profiles were visualized using IGV. Duplicate read removal and GC bias correction were performed with PICARD and deepTools, respectively. Relative and normalized strand cross correlations cutoffs were 0.8 and 1.05, respectively, for narrow marks. ChIP-Seq signal consistency throughout the cohort was assessed through hierarchical clustering of Pearson correlations using deepTools. Identification of differential enrichment sites for each histone mark was done using diffReps with window size 1000bp and sliding step 100bp. A FDR <10% and $p < 0.0001$ for negative binomial test were used as significance cutoffs.
Software	Trimmomatic, BWA, Picard and deepTools were used to pre-process and align the sequencing reads. Global visualization for the ChIP-seq data was done using IGV and ngs.plot. Inter-sample correlations and hierarchical clustering were achieved using deepTools. Identification of differential enrichment sites for each histone mark was done using diffReps. ChromHMM was used to annotate chromatin states.