Online Supplementary Material

Methods for RNA-sequencing of the postmortem brain sample

Sample extraction: RNA was extracted from the gray matter of the dorsolateral prefrontal cortex using Qiagen's miRNeasy mini kit (cat. no. 217004) and the RNase free DNase Set (cat. no. 79254). The samples were quantified by Nanodrop and quality was evaluated by Agilent Bioanalyzer.

Library Preparation: cDNA libraries were compiled on the Broad Institutes's Genomics Platform using the strand specific dUTP method with poly-A selection [Adiconis X et al., Nature Methods 2013]. This method begins with poly-A selection followed by first strand specific cDNA synthesis, and then uses dUTP for second strand specific cDNA synthesis followed by fragmentation and Illumina adapter ligation for library construction. RNA-Seq data of all samples met quality (Bioanalyzer RNA integrity (RIN) score >5) and quantity thresholds (5ug).

Sequencing: Sequencing was performed on the Illumina HiSeq with 101bp paired-end reads and achieved coverage of 150M reads. The libraries were constructed and pooled according to the RNA Integrity Number (RIN) scores such that similar RIN scores would be pooled together. Varying RIN scores results in a larger spread of insert sizes during library construction and leads to uneven coverage distribution throughout the pool.

Data processing and quality control: RNA-Seq data were processed by our parallelized and automatic pipeline. These pipeline include trimming the beginning and ending bases from each read, identifying and trimming adapter sequences from reads, detecting and removing rRNA reads, aligning reads to reference genome. We used the non-gapped aligner Bowtie to align reads to transcriptome reference and then applied RSEM to estimate expression levels for all transcripts. The FPKM values were the outcome of our data RNA-Seq pipeline. We applied quantile normalization method to FPKM first and then used combat package to remove potential batch effect.