## Supplementary Methods

## Materials and Methods

## Human subjects

Brain specimens were obtained during autopsies conducted at the Allegheny County Office of the Medical Examiner (Pittsburgh, PA) following consent from next-of-kin. An independent committee of experienced research clinicians made consensus DSM-IV diagnoses (American Psychiatric Association, 2000) for each subject using structured interviews with family members and review of medical records(1, 2). The same approach was used to confirm the absence of psychiatric diagnoses in comparison subjects. In order to control for experimental variance, subjects with schizophrenia or schizoaffective disorder ( $\mathrm{N}=62$ ) were matched individually to one unaffected comparison subject for sex and as closely as possible for other measures (see Table S1 for individual subject details).

## Laser Microdissection Procedure

The right hemisphere of each brain was blocked coronally, frozen and stored at $-80^{\circ} \mathrm{C}$. Frozen tissue blocks containing the middle portion of the right superior frontal sulcus were confirmed to contain DLPFC area 9 using Nissl-stained sections for each subject. For all procedures, samples from each subject in a given pair were processed together in order to control for experimental variance. Tissue sections $(12 \mu \mathrm{~m})$ containing DLPFC area 9 were cut on a cryostat, mounted on glass polyethylene naphthalate membrane slides (Leica Microsystems, Bannockburn, IL, USA) that were previously treated with ultraviolet light at 254 nm for 30 minutes, which were blinded to diagnosis, and stained with thionin for Nissl substance. We used the Leica laser microdissection system (LMD6500) to dissect DLPFC layer

3 and 5 pyramidal cells, and used the same technique to dissect layer 3 parvalbumin interneurons as described(3-5).

## Microarray Analyses

For each sample, the RNA from the resulting pools of individually dissected pyramidal and parvalbumin cells was extracted using the QIAGEN RNeasy Plus Micro Kit, transcribed into cDNA, subjected to a single round of amplification using the Ovation Pico WTA System (NuGEN Technologies, Inc, San Carlos, California) and labeled using the Encore Biotin module. These samples were then loaded on an Affymetrix GeneChip ${ }^{\circledR}$ HT HG-U133 ${ }^{+}$PM Array plate (Affymetrix, Santa Clara, CA) designed to assess transcript levels from the human genome.

## Quantitative Polymerase Chain Reaction

For each subject in the full cohort ( $\mathrm{N}=62$ pairs), the gray white matter boundary in each tissue block containing DLPFC area 9 was carefully scored with a scalpel blade where the gray matter had uniform thickness and was cut perpendicular to the pial surface. Standardized dilutions of total RNA (10 ng/ $\mu \mathrm{l}$ ) were used to synthesize complementary DNA (cDNA) for each subject using a High Capacity cDNA Reverse Transcription Kit (Life Technologies, Carlsbad, CA). All primer sets (Table S2) demonstrated high amplification efficiency across a wide range of cDNA dilutions and specific single products in dissociation curve analyses. Individual standard curve analysis was performed for each primer set using a range of four different cDNA dilutions and was used to determine the slope. The primer efficiency for each transcript is computed using the formula: Efficiency=(10^(-1/slope)-1) *100. Quantitative PCR was performed using the comparative cycle threshold (CT) method with Power SYBR Green dye and the Vii-7 ${ }^{\text {TM }}$ Real-Time PCR System (Applied Biosystems) as previously described(6).

## Antipsychotic-exposed monkeys

Experimentally naïve, male, young adult, long-tailed macaque monkeys (Macaca fascicularis) received oral doses of placebo, olanzapine or haloperidol ( $\mathrm{N}=6$ monkeys per group) twice daily for 17-27 months(7). The doses administered to the monkeys produced trough serum levels in the therapeutic range in the treatment of schizophrenia. Animals were euthanized in triads and the tissue was processed as previously described(1). For each monkey ( $\mathrm{N}=18$ ), 150 pyramidal cells from each of DLPFC layers deep 3 and 5 were dissected as described above. The cDNA from all subjects was loaded on GeneChip® Rhesus Macaque Genome Array (Affymetrix, Santa Clara, CA) with all samples from a given triad processed together. All studies were carried out in compliance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals and were approved by the University of Pittsburgh Institutional Animal Care and Use Committee.

## Data Analysis and Statistics

## Analysis of potential confounding factors

We also assessed the potential influence of factors frequently comorbid with a diagnosis of schizophrenia using ANCOVA models. For these analyses, we compared expression levels of the transcripts of interest between schizophrenia subjects with or without each of the following: diagnosis of schizoaffective disorder; history of substance dependence or abuse; use of nicotine, antipsychotics, antidepressants, or benzodiazepines and/or sodium valproate at the time of death; and death by suicide. In each analysis, sex, age, tissue storage time, brain pH , PMI and RIN were used as covariates.

## Analysis of antipsychotic-exposed monkeys

For the antipsychotic-exposed monkey study, ANCOVAs with ARP2/3 complex transcript levels as dependent variables, treatment group as the main effect, and triad as a blocking factor were employed. All statistical tests were conducted with $\alpha=0.05$.

Table S1. Demographic, postmortem, and clinical characteristics of human subjects used in this study

| Subject Group ${ }^{\text {a }}$ | Case No. | S/R/A ${ }^{\text {b }}$ | PMI ${ }^{\text {c }}$ | pH | RIN | Storage time ${ }^{\text {a }}$ | Cause of death ${ }^{\text {e }}$ | $\begin{array}{r} D \\ \text { Diag } \\ \text { Pri } \\ \text { Sub } \end{array}$ | DSM IV gnoses ${ }^{\text {f }}$ rimary stance ${ }^{g}$ | Antipsychotics ATOD | Antidepressants ATOD | $\begin{aligned} & \text { BZ/VPA } \\ & \text { ATOD }^{\text {n }} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| $1 \bullet$ | 592 | M/B/41 | 22.1 | 6.7 | 9.0 | 203 | ASCVD | N |  |  |  |  |
|  | 533 | M/W/40 | 29.1 | 6.8 | 8.4 | 213 | Accidental Asphyxiation | US |  | Y | N | N |
| $2 \cdot$ | 567 | FW/46 | 15.0 | 6.7 | 8.9 | 208 | Mitral valve prolapse | N |  |  |  |  |
|  | 537 | F/W/37 | 14.5 | 6.7 | 8.6 | 213 | Suicide by hanging | SA |  | N | N | N |
| $3 \cdot$ | 1322 | M/W/62 | 16.5 | 6.8 | 8.6 | 73 | ASCVD | N |  |  |  |  |
|  | 630\# | M/W/65 | 21.2 | 7.0 | 9.0 | 198 | ASCVD | N |  |  |  |  |
|  | 566 | M/W/63 | 18.3 | 6.8 | 8.0 | 193 | ASCVD | US | AAR | Y | Y | Y |
| $4 \bullet$ | 604 | M/W/39 | 19.3 | 7.1 | 8.6 | 201 | Hypoplastic coronary artery | N |  |  |  |  |
|  | 581 | M/W/46 | 28.1 | 7.2 | 7.9 | 206 | Accidental combined drug overdose | PS | $\begin{aligned} & \text { ADC; } \\ & \text { OAC } \end{aligned}$ | Y | N | Y |
| $5 \cdot$ | 546 | F/W/37 | 23.5 | 6.7 | 8.6 | 211 | ASCVD | N |  |  |  |  |
|  | 587 | F/B/38 | 17.8 | 7.0 | 9.0 | 204 | Myocardial hypertrophy | US | AAR | Y | N | Y |
| $6 \bullet$ | 551 | M/W/61 | 16.4 | 6.6 | 8.3 | 210 | Cardiac tamponade | N |  |  |  |  |
|  | 625 | M/B/49 | 23.5 | 7.3 | 7.6 | 198 | ASCVD | DS | AAC | Y | Y | N |
| $7 \bullet$ | 681 | M/W/51 | 11.6 | 7.2 | 8.9 | 191 | Hypertrophic cardiomyopathy | N |  |  |  |  |
|  | 640 | M/W/49 | 5.2 | 6.9 | 8.4 | 196 | Pulmonary embolism | PS |  | Y | Y | N |
| $8 \cdot$ | 806 | M/W/57 | 24.0 | 6.9 | 7.8 | 170 | Pulmonary embolism | N |  |  |  |  |
|  | 665 | M/B/59 | 28.1 | 6.9 | 9.2 | 194 | Intestinal hemorrhage | PS | ADC | Y | Y | N |
| $9 \bullet$ | 822 | M/B/28 | 25.3 | 7.0 | 8.5 | 167 | ASCVD | N |  |  |  |  |
|  | 787 | M/B/27 | 19.2 | 6.7 | 8.4 | 173 | Suicide by gun shot | SA | ODC | Y | N | N |
| 10 | 727 | M/B/19 | 7.0 | 7.2 | 9.2 | 184 | Trauma | N |  |  |  |  |
|  | 829 | M/W/25 | 5.0 | 6.8 | 9.3 | 165 | Suicide by drug overdose | SA | ADC; OAR | N | N | Y |
| $11 \bullet$ | 871 | M/W/28 | 16.5 | 7.1 | 8.5 | 156 | Trauma | N |  |  |  |  |
|  | 878 | M/W/33 | 10.8 | 6.7 | 8.9 | 156 | Myocardial fibrosis | DS | ADC | Y | Y | Y |
| 12 | 700 | M/W/42 | 26.1 | 7.0 | 8.7 | 188 | ASCVD | N |  |  |  |  |
|  | 539 | M/W/50 | 40.5 | 7.1 | 8.1 | 212 | Suicide by combined drug overdose | SA | ADR | Y | Y | Y |
| $13 \cdot$ | 988 | M/W/82 | 22.5 | 6.2 | 8.4 | 135 | Trauma | N |  |  |  |  |
|  | 621 | M/W/83 | 16.0 | 7.3 | 8.7 | 199 | Accidental asphyxiation | US |  | N | N | N |
| 14. | 686 | FW/52 | 22.6 | 7.0 | 8.5 | 190 | ASCVD | N |  |  |  |  |
|  | 656 | F/B/47 | 20.1 | 7.3 | 9.2 | 195 | Suicide by gun shot | SA | ADC | Y | N | N |
| $15 \cdot$ | 634 | M/W/52 | 16.2 | 7.0 | 8.5 | 197 | ASCVD | N |  |  |  |  |
|  | 722 | M/B/45 | 9.1 | 6.7 | 9.2 | 185 | Upper GI bleeding | US | ODR; | Y | N | N |


| Subject Group ${ }^{\text {a }}$ |  | Case No. | S/R/A ${ }^{\text {b }}$ | PMI ${ }^{\text {c }}$ | pH | RIN | Storage time | Cause of death ${ }^{\text {e }}$ | DSM IVDiagnosesPrimarySubstance $^{\text {g }}$ |  | Antipsychotics ATOD | Antidepressants ATOD | $\begin{aligned} & \text { BZ/VPA } \\ & \text { ATOD }^{\text {a }} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 16• | C | 852 | M/W/54 | 8.0 | 6.8 | 9.1 | 159 | Cardiac tamponade | N |  |  |  |  |
|  | S | 781 | M/B/52 | 8.0 | 6.7 | 7.7 | 174 | Peritonitis | SA | ADR | Y | Y | N |
| $17 \bullet$ | C | 987 | F/W/65 | 21.5 | 6.8 | 9.1 | 135 | ASCVD | N |  |  |  |  |
|  | S | 802 | F/W/63 | 29.0 | 6.4 | 9.2 | 170 | Right ventricular dysplasia | SA | ADC; ODR | Y | N | Y |
| 18• | C | 857 | M/W/48 | 16.6 | 6.7 | 8.9 | 158 | ASCVD | N |  |  |  |  |
|  | S | 930 | M/W/47 | 15.3 | 6.2 | 8.2 | 145 | ASCVD | DS | ADR; OAR | Y | N | Y |
| $19 \bullet$ | C | 739 | M/W/40 | 15.8 | 6.9 | 8.4 | 183 | ASCVD | N |  |  |  |  |
|  | S | 933 | M/W/44 | 8.3 | 5.9 | 8.1 | 144 | Myocarditis | DS |  | Y | Y | Y |
| $20 \cdot \dagger$ | C | 1047 | M/W/43 | 13.8 | 6.6 | 9.0 | 126 | ASCVD | N |  |  |  |  |
|  | S | 1209 | M W/35 | 9.1 | 6.5 | 8.7 | 107 | Diphenhydramine overdose | SA |  | Y | N | N |
| $21 . \dagger$ | C | 1086 | MW/51 | 24.2 | 6.8 | 8.1 | 120 | ASCVD | N |  |  |  |  |
|  | S | 10025 | MB/52 | 27.1 | 6.7 | 7.8 | 99 | ASCVD | DS | OAR | N | N | N |
| $22 . \dagger$ | C | 1092 | F/B/40 | 16.6 | 6.8 | 8.0 | 120 | Mitral valve prolapse | N |  |  |  |  |
|  | S | 1178 | F/B/37 | 18.9 | 6.1 | 8.4 | 111 | Pulmonary embolism | SA |  | Y | N | Y |
| 23.1 | C | 1336 | M/W/65 | 18.4 | 6.8 | 8.0 | 85 | Cardiac tamponade | N |  |  |  |  |
|  | S | 1173 | M/W/62 | 22.9 | 6.4 | 7.7 | 111 | ASCVD | DS | ADR | Y | N | N |
| $24 . \dagger$ | C | 1122 | M/W/55 | 15.4 | 6.7 | 7.9 | 116 | Cardiac tamponade | N |  |  |  |  |
|  | S | 1105 | M/W/53 | 7.9 | 6.2 | 8.9 | 118 | ASCVD | SA |  | Y | N | N |
| 25 | C | 1284 | M/W/55 | 6.4 | 6.8 | 8.7 | 95 | ASCVD | N |  |  |  |  |
|  | S | 1188 | M/W/58 | 7.7 | 6.2 | 8.4 | 109 | ASCVD | US | AAR; OAR | Y | N | Y |
| $26 \cdot$ | C | 1191 | M/B/59 | 19.4 | 6.2 | 8.4 | 109 | ASCVD | N |  |  |  |  |
|  | S | 1263 | M/W/62 | 22.7 | 7.1 | 8.5 | 98 | Asphyxiation | US | ADR | Y | Y | N |
| 27• $\dagger$ | C | 970 1222 | M/W/42 M/W/32 | 25.9 30.8 | 6.4 | 7.2 7.5 | 137 105 | ASCVD ${ }_{\text {Combined drug overdose }}$ | N US | AAC | Y | Y | N |
| 28• | C | 1247 | FW/58 | 22.7 | 6.4 | 8.4 | 101 | ASCVD | N |  |  |  |  |
|  | S | 1240 | F/B/50 | 22.9 | 6.3 | 7.7 | 101 | ASCVD | US | ADR | Y | N | N |
| 29•† | C | 1324 | M/W/43 | 22.3 | 7.0 | 7.3 | 87 | Aortic dissection | N |  |  |  |  |
|  | S | 10020 | M/W/38 | 28.8 | 6.6 | 7.4 | 101 | Salicylate overdose | PS | $\begin{aligned} & \text { AAC; } \\ & \text { OAC } \end{aligned}$ | Y | Y | Y |
| 30• $\dagger$ | C | 1099 10023 | F/W/24 | $\begin{gathered} 9.1 \\ 20.1 \end{gathered}$ | 6.5 6.7 | 8.6 7.4 | 119 100 | Cardiomyopathy Suicide by drowning | N DS |  | Y | Y | Y |
| $31 . \dagger$ | C | 1307 | M/B/32 | 4.8 | 6.7 | 7.6 | 90 | ASCVD | N |  |  |  |  |


| Subject Group ${ }^{\text {a }}$ |  | $\begin{gathered} \text { Case } \\ \text { No. } \end{gathered}$ | $\begin{gathered} \mathrm{S} / \mathrm{R} / \mathrm{A}^{\mathrm{b}} \\ \hline \mathrm{M} / \mathrm{B} / 37 \end{gathered}$ | $\begin{gathered} \text { PMI }^{\mathbf{C}} \\ \hline 6.0 \end{gathered}$ | pH | RIN$7.5$ | Storage time$99$ | Cause of death ${ }^{\text {e }}$ASCVD | DSM IVDiagnoses $^{\boldsymbol{f}}$PrimarySubstance ${ }^{\text {g }}$PS |  | Antipsychotics ATOD <br> N | Antidepressants ATOD <br> N | BZ/VPA ATOD ${ }^{\text {h }}$ <br> N |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | S |  |  |  |  |  |  |  |  |  |  |  |  |
| 32•† | C | 1391 | F/W/51 | 7.8 | 6.6 | 7.1 | 76 | ASCVD | N |  |  |  |  |
|  | S | 1189 | F/W/47 | 14.4 | 6.4 | 8.3 | 109 | Combined drug overdose | SA | AAR | Y | Y | Y |
| $33 \bullet \dagger$ | C | 1282 | F/W/39 | 24.5 | 6.8 | 7.5 | 95 | ASCVD | N |  |  |  |  |
|  | S | 1211 | F/W/41 | 20.1 | 6.3 | 7.8 | 107 | Sudden unexpected death | SA |  | Y | Y | N |
| 34•† | C | 1159 | M/W/51 | 16.7 | 6.5 | 7.6 | 113 | ASCVD | N |  |  |  |  |
|  | S | 1296 | M/W/48 | 7.8 | 6.5 | 7.3 | 93 | Pneumonia | US |  | Y | Y | N |
| $35 \bullet \dagger$ | C | 1326 | M/W/58 | 16.4 | 6.7 | 8.0 | 87 | ASCVD | N |  |  |  |  |
|  | S | 1314 | M/W/50 | 11.0 | 6.2 | 7.2 | 89 | ASCVD | US |  | Y | Y | Y |
| 36•† | C | 902 | M/W/60 | 23.6 | 6.7 | 7.7 | 152 | ASCVD | N |  |  |  |  |
|  | S | 1361 | M/W/63 | 23.2 | 6.4 | 7.7 | 82 | Cardiomyopathy | SA | ODC | Y | N | Y |
| 37 | C | 1374 | M/W/43 | 21.7 | 6.6 | 7.2 | 79 | ASCVD | N |  |  |  |  |
|  | S | 904 | M/W/33 | 28.0 | 6.2 | 7.1 | 150 | Pneumonia | SA |  | Y | N | Y |
| 38 | C | 1555 | M/W/17 | 15.1 | 6.9 | 7.9 | 44 | Trauma | N |  |  |  |  |
|  | S | 1649 | M/B/17 | 21.4 | 6.9 | 8.1 | 29 | Hanging | US |  | Y | Y | N |
| 39 | C | 1268 | M/B/49 | 19.9 | 7.1 | 7.9 | 96 | ASCVD | N |  |  |  |  |
|  | S | 1230 | M/W/50 | 16.9 | 6.6 | 8.2 | 102 | Doxepin overdose | US |  | Y | Y | N |
| 40 | C | 1466 | F/B/64 | 20.0 | 6.7 | 8.8 | 61 |  |  |  |  |  |  |
|  | S | 1341 | F/W/44 | 24.5 | 6.6 | 8.8 | 83 | Trauma | SA | ODC | Y | N | Y |
| 41 | C | 1518 | M/W/50 | 20.7 | 6.4 | 7.7 | 50 | ASCVD | N |  |  |  |  |
|  | S | 1367 | M/W/47 | 28.9 | 6.6 | 7.2 | 80 | Combined drug overdose | SA | $\begin{aligned} & \text { ADC; } \\ & \text { ODR } \end{aligned}$ | N | N | N |
| 42 | C | 1386 | M/W/46 | 21.2 | 6.7 | 8.3 | 75 | ASCVD | N |  |  |  |  |
|  | S | 1420 | M/W/47 | 23.4 | 6.8 | 8.2 | 69 | Jump | SA | AAR; ODC; OAR | Y | Y | N |
| 43 | C | 1472 | M/W/61 | 23.8 | 6.5 | 8.0 | $60$ | Pulmonary embolism |  |  |  |  |  |
|  | S | 1453 | M/W/62 | 11.1 | 6.4 | 8.2 | 63 | Trauma | PS | ADR | Y | N | Y |
| 44 | C | 1026 | M/W/59 | 19.8 | 6.3 | 7.4 | 128 | ASCVD | N |  |  |  |  |
|  | S | 1454 | M/W/59 | 24.1 | 6.1 | 7.6 | 62 | Trauma | PS | AAR; ODC | Y | Y | N |
| 45 | C | 694 | M/W/38 | 20.7 | 7.0 | 7.7 | 189 | Subarachnoid hemorrhage | N |  |  |  |  |
|  | S | 1455 | M/W/42 | 8.2 | 6.4 | 7.7 | 62 | Peritonitis | PS | AAR; <br> OAC | Y | N | Y |
| 46 | C | 1350 | M/W/21 | 24.2 | 6.4 | 7.3 | 82 | Trauma | N |  |  |  |  |


| Subject Group ${ }^{\text {a }}$ |  | Case No. | S/R/A ${ }^{\text {b }}$ | PMI ${ }^{\text {c }}$ | pH | RIN | Storage time | Cause of death ${ }^{\text {e }}$ | DSM IVDiagnosesPrimarySubstance ${ }^{\text {g }}$ |  | Antipsychotics ATOD | Antidepressants ATOD | $\begin{aligned} & \text { BZ/VPA } \\ & \text { ATOD }^{\text {a }} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 47 | S | 1474 | M/W/37 | 39.9 | 6.7 | 7.0 | 60 | Hanging | SA | ADR | N | N | N |
|  | C | 1792 | F/W/36 | 28.1 | 6.5 | 7.5 | 5 | Pulmonary embolism | N |  |  |  |  |
|  | S | 1506 | F/W/47 | 14.1 | 6.6 | 7.5 | 55 | Combined drug overdose | SA | ADC | Y | Y | N |
| 48 | C | 1524 | MW/66 | 9.4 | 6.4 | 8.1 | 48 | Intestinal infarction | N |  |  |  |  |
|  | S | 1542 | M/W/65 | 17.4 | 6.7 | 7.8 | 45 | Combined drug overdose | PS |  | Y | Y | Y |
| 49 | C | 1270 | F/W/73 | 19.7 | 6.7 | 7.7 | 96 | Trauma | N |  |  |  |  |
|  | S | 1579 | F/W/69 | 16.1 | 6.7 | 7.7 | 39 | ASCVD | SA | ADR; ODC | Y | N | Y |
| 50 | C | 1372 | M/W/37 | 20.5 | 6.6 | 9.0 | 79 | Asphyxiation | N |  |  |  |  |
|  | S | 1581 | M/W/32 | 18.4 | 6.8 | 9.0 | 39 | ASCVD | PS | $\begin{aligned} & \text { ODC; } \\ & \text { OAC } \end{aligned}$ | Y | Y | N |
| 51 | C | 1543 | F/W/45 | 17.9 | 6.8 | 7.4 | 45 | Subarachnoid hemorrhage | N |  |  |  |  |
|  | S | 10026 | F/W/46 | 23.8 | 6.6 | 7.6 | 98 | Thermal injuries | US |  | Y | Y | N |
| 52 | C | 1583 | M/W/58 | 19.1 | 6.8 | 8.2 | 39 | Trauma | N |  |  |  |  |
|  | S | 1686 | M/B/56 | 14.1 | 6.2 | 8.3 | 22 | ASCVD | PS | AAR | Y | Y | Y |
| 53 | C | 1554 | M/W/50 | 23.2 | 6.5 | 7.6 | 44 | ASCVD | N |  |  |  |  |
|  | S | 1691 | M/W/51 | 31.9 | 6.6 | 7.7 | 20 | Combined drug overdose | PS | ADR; ODC | Y | N | Y |
| 54 | C | 1635 | M/W/66 | 25.3 | 6.8 | 8.2 | 31 | Cardiac tamponade | N |  |  |  |  |
|  | S | 1706 | M/B/60 | 28.1 | 6.8 | 8.4 | 17 | Sepsis | SA | AAR; <br> ODC; <br> OAR | Y | N | N |
| 55 | C | 1384 | M/W/67 | 21.9 | 6.6 | 7.0 | 77 | ASCVD | N |  |  |  |  |
|  | S | 1712 | M/W/63 | 15.1 | 6.2 | 7.1 | 15 | ASCVD | SA | ADR; ODC | Y | Y | Y |
| 56 | C | 1558 | M/W/54 | 24.4 | 6.9 | 7.7 | 43 | ASCVD | N |  |  |  |  |
|  | S | 1734 | M/W/54 | 28.6 | 6.1 | 7.7 | 12 | Pneumonia | US | AAR; <br> ODC; <br> OAR | Y | N | N |
| 57 | C | 516 | M/B/20 | 14.0 | 6.9 | 8.4 | 215 | Homicide by gun shot | N |  |  |  |  |
|  | S | 547 | M/B/27 | 16.5 | 7.0 | 7.4 | 211 | Heat stroke | SA |  | Y | Y | Y |
| 58 | C | 685 | M/W/56 | 14.5 | 6.6 | 8.1 | 191 | Hypoplastic coronary artery | N |  |  |  |  |
|  | S | 622 | M/W/58 | 18.9 | 6.8 | 7.4 | 198 | Right MCA infarction | US |  | N | N | N |
| 59 | C | 575 | F/B/55 | 11.3 | 6.8 | 9.6 | 206 | ASCVD | N |  |  |  |  |
|  | S | 517 | F/W/48 | 3.7 | 6.7 | 9.3 | 215 | Intracerebral hemorrhage | DS | ADC | Y | N | N |


| Subject Group ${ }^{\text {a }}$ |  | Case No. | S/R/A ${ }^{\text {b }}$ | PMI ${ }^{\text {c }}$ | pH | RIN | Storage time | Cause of death ${ }^{\text {e }}$ | DSM IV Diagnoses Primary Substance ${ }^{\text {g }}$ | Antipsychotics ATOD | Antidepressants ATOD | $\begin{aligned} & \text { BZ/VPA } \\ & \text { ATOD }^{\text {n }} \end{aligned}$ |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
| 60 | C | 818 | F/W/67 | 24.0 | 7.1 | 8.4 | 168 | Anaphylactic reaction | N |  |  |  |
|  | S | 917 | F/W/71 | 23.8 | 6.8 | 7.0 | 148 | ASCVD | US | Y | N | N |
| 61 | C | 10005 | M/W/42 | 23.5 | 6.7 | 7.4 | 107 | Trauma | N |  |  |  |
|  | S | 1256 | M/W/34 | 27.4 | 6.4 | 7.9 | 99 | Hanging | US | Y | N | N |
| 62 | C | 10003 | M/W/49 | 21.2 | 6.5 | 8.4 | 109 | Trauma | N |  |  |  |
|  | S | 1088 | M/W/49 | 21.5 | 6.5 | 8.1 | 120 | Combined drug overdose | US ADC; | Y | Y | N |






 benzodiazepines; VPA, Sodium valproate; ATOD, at time of death; Y, yes; N, no.

TABLE S2. Sequences and priming efficiency for all human qPCR primer sets used in this study

| Gene | $\begin{array}{c}\text { Forward Primer (F) } \\ \text { Reverse Primer (R) }\end{array}$ |
| :---: | :--- |
| Beta actin | $\begin{array}{c}\text { (F) GATGTGGATCAGCAAGCA } \\ \text { (R) AGAAAGGGTGTAACGCAACTA }\end{array}$ |
| Cyclophilin | (F) GCAGACAAGGTCCCAAAG |
| (R) GAAGTCACCACCCTGACAAC |  |$)$

TABLE S3. Summary of differences* by transcript in pyramidal cells in DLPFC layer 3 and layer 5 and gray matter

| Transcript | Pyramidal Cell |  |  |  | Gray Matter |  |  |  |
| :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: | :---: |
|  | Layer 3 ( $\mathrm{N}=36$ pairs) |  | Layer 5 (N=34 pairs) |  | qPCR (N=36 pairs) |  | qPCR ( $\mathrm{N}=62$ pairs) |  |
|  | \% Change | P-value | \% Change | P-value | \% Change | $P$-value | \% Change | P-value |
| ACTR2 | -10.9\% | 0.021 | -12.2\% | 0.048 | 0.2\% | 0.934 | -0.7\% | 0.558 |
| ACTR3 | -15.2\% | 0.002 | -23.7\% | <0.001 | -3.2\% | 0.081 | -3.5\% | 0.012 |
| ARPC1A | 3.6\% | 0.481 | 2.6\% | 0.732 | 0.1\% | 0.940 | 0.3\% | 0.559 |
| ARPC1B | -4.5\% | 0.302 | -2.3\% | 0.562 | 5.0\% | 0.392 | 15.5\% | 0.010 |
| ARPC2 | -14.9\% | <0.001 | -16.9\% | 0.013 | -1.5\% | 0.190 | -1.6\% | 0.097 |
| ARPC3 | -15.9\% | 0.001 | -16.8\% | 0.005 | 3.8\% | 0.034 | 4.3\% | 0.018 |
| ARPC4 | -11.2\% | <0.001 | -10.4\% | 0.014 | -2.0\% | 0.040 | -3.5\% | <0.001 |
| ARPC5 | -10.2\% | 0.015 | -14.8\% | 0.007 | -6.0\% | 0.017 | -7.4\% | <0.001 |
| CTTN | -16.4\% | 0.052 | -27.3\% | 0.002 | 5.9\% | 0.014 | 7.5\% | 0.004 |
| WASL | -10.1\% | 0.010 | -17.9\% | 0.014 | 3.4\% | 0.009 | 3.5\% | 0.023 |
| CYFIP1 | -14.3\% | 0.088 | -17.7\% | 0.006 | 5.9\% | 0.645 | 7.5\% | 0.118 |
| WASF1 | 4.6\% | 0.076 | 2.5\% | 0.303 | 3.4\% | 0.065 | 3.5\% | 0.009 |

*All reported p-values are from paired ANCOVAs.

FIGURE S1.


FIGURE $\mathbf{S 2}$.


## References

1. Hashimoto T, Arion D, Unger T, Maldonado-Aviles JG, Morris HM, Volk DW, Mirnics K, Lewis DA. Alterations in GABA-related transcriptome in the dorsolateral prefrontal cortex of subjects with schizophrenia. Mol Psychiatry. 2008;13:147-161.
2. Volk DW, Matsubara T, Li S, Sengupta EJ, Georgiev D, Minabe Y, Sampson A, Hashimoto T, Lewis DA. Deficits in transcriptional regulators of cortical parvalbumin neurons in schizophrenia. Am J Psychiatry. 2012;169:1082-1091.
3. Arion D, Corradi JP, Tang S, Datta D, Boothe F, He A, Cacace AM, Zaczek R, Albright CF, Tseng G, Lewis DA. Distinctive transcriptome alterations of prefrontal pyramidal neurons in schizophrenia and schizoaffective disorder. Mol Psychiatry. 2015.
4. Datta D, Arion D, Corradi JP, Lewis DA. Altered Expression of CDC42 Signaling Pathway Components in Cortical Layer 3 Pyramidal Cells in Schizophrenia. Biol Psychiatry. 2015.
5. Georgiev D, Arion D, Enwright JF, Kikuchi M, Minabe Y, Corradi JP, Lewis DA, Hashimoto T. Lower gene expression for KCNS3 potassium channel subunit in parvalbumin-containing neurons in the prefrontal cortex in schizophrenia. Am J Psychiatry. 2014;171:62-71.
6. Volk DW, Chitrapu A, Edelson JR, Roman KM, Moroco AE, Lewis DA. Molecular Mechanisms and Timing of Cortical Immune Activation in Schizophrenia. Am J Psychiatry. 2015;172:1112-1121.
7. Dorph-Petersen KA, Pierri JN, Perel JM, Sun Z, Sampson AR, Lewis DA. The influence of chronic exposure to antipsychotic medications on brain size before and after tissue fixation: a comparison of haloperidol and olanzapine in macaque monkeys. Neuropsychopharmacology. 2005;30:1649-1661.
