

Table S1. Demographic, postmortem, and clinical characteristics of schizophrenia and unaffected comparison subjects

| Unaffected Comparison Subjects | | | | | | | | | Subjects with Schizophrenia | | | | | | | | | | | | | | | |
|--------------------------------|--------|--------------|-----|------------------|------------------------------|-----|-----|-----------------------------|-----------------------------|--------------------------------------------------|--------------|-----|------------------|------------------------------|-----|-----|-----------------------------------|---------------|-----------------|----------------------------|-----------------------------|-------------------------------------------|-----------------|--------------------------|
| Pair | Case | Sex/ Race | Age | PMI ^a | Storage Time ^b | RIN | pH | Cause of Death | Case | DSM IV diagnosis | Sex/ Race | Age | PMI ^a | Storage Time ^b | RIN | pH | Cause of Death | LGM Member | Tobacco ATOD | Anti- psychotic ATOD | Anti- depressant ATOD | Benzodiazepine/ Anticonvulsant ATOD | Lithium ATOD | Cannabis Use Disorder |
| 1 | 592 | M/B | 41 | 22.1 | 212 | 9.0 | 6.7 | ASCVD | 533 | Chronic undifferentiated schizophrenia | M/W | 40 | 29.1 | 222 | 8.4 | 6.8 | Accidental Asphyxiation | No | Unknown | Yes | No | No | No | No |
| 2 | 630 | M/W | 65 | 21.2 | 206 | 9.0 | 7.0 | ASCVD | 566 | Chronic undifferentiated schizophrenia; AAR | M/W | 63 | 18.3 | 217 | 8.0 | 6.8 | ASCVD | No | Yes | Yes | Yes | Yes | No | No |
| 3 | 604 | M/W | 39 | 19.3 | 210 | 8.6 | 7.1 | Hypoplastic coronary artery | 581 | Chronic paranoid schizophrenia; ADC; OAC | M/W | 46 | 28.1 | 214 | 7.9 | 7.2 | Accidental combined drug overdose | Yes | Unknown | Yes | No | Yes | No | No |
| 4 | 546 | F/W | 37 | 23.5 | 220 | 8.6 | 6.7 | ASCVD | 587 | Chronic undifferentiated schizophrenia; AAR | F/B | 38 | 17.8 | 213 | 9.0 | 7.0 | Myocardial hypertrophy | No | Yes | Yes | No | Yes | Yes | No |
| 5 | 551 | M/W | 61 | 16.4 | 219 | 8.3 | 6.6 | Cardiac tamponade | 625 | Chronic disorganized schizophrenia; AAC | M/B | 49 | 23.5 | 207 | 7.6 | 7.3 | ASCVD | No | Yes | Yes | Yes | No | No | No |
| 6 | 685 | M/W | 56 | 14.5 | 199 | 8.1 | 6.6 | Hypoplastic coronary artery | 622 | Chronic undifferentiated schizophrenia | M/W | 58 | 18.9 | 207 | 7.4 | 6.8 | Right MCA infarction | No | Unknown | No | No | No | No | No |
| 7 | 681 | M/W | 51 | 11.6 | 200 | 8.9 | 7.2 | Hypertrophic cardiomyopathy | 640 | Chronic paranoid schizophrenia | M/W | 49 | 5.2 | 205 | 8.4 | 6.9 | Pulmonary embolism | No | Unknown | Yes | Yes | No | No | No |
| 8 | 806 | M/W | 57 | 24.0 | 178 | 7.8 | 6.9 | Pulmonary embolism | 665 | Chronic paranoid schizophrenia; ADC | M/B | 59 | 28.1 | 202 | 9.2 | 6.9 | Intestinal hemorrhage | Yes | Yes | Yes | Yes | No | No | No |
| 9 | 871 | M/W | 28 | 16.5 | 165 | 8.5 | 7.1 | Trauma | 878 | Disorganized schizophrenia; ADC | M/W | 33 | 10.8 | 164 | 8.9 | 6.7 | Myocardial fibrosis | No | Yes | Yes | Yes | Yes | No | No |
| 10 | 575 | F/B | 55 | 11.3 | 215 | 9.6 | 6.8 | ASCVD | 517 | Disorganized schizophrenia; ADC | F/W | 48 | 3.7 | 223 | 9.3 | 6.7 | Intracerebral hemorrhage | Yes | Yes | Yes | No | No | No | No |
| 11 | 988 | M/W | 82 | 22.5 | 144 | 8.4 | 6.2 | Trauma | 621 | Chronic undifferentiated schizophrenia | M/W | 83 | 16.0 | 207 | 8.7 | 7.3 | Accidental asphyxiation | Yes | Unknown | No | No | No | No | No |
| 12 | 634 | M/W | 52 | 16.2 | 205 | 8.5 | 7.0 | ASCVD | 722 | Chronic undifferentiated schizophrenia; ODR; OAR | M/B | 45 | 9.1 | 193 | 9.2 | 6.7 | Upper GI bleeding | No | Yes | Yes | No | No | No | No |
| 13 | 818 | F/W | 67 | 24.0 | 177 | 8.4 | 7.1 | Anaphylactic reaction | 917 | Chronic undifferentiated schizophrenia | F/W | 71 | 23.8 | 157 | 7.0 | 6.8 | ASCVD | Yes | Yes | Yes | No | No | No | No |
| 14 | 857 | M/W | 48 | 16.6 | 167 | 8.9 | 6.7 | ASCVD | 930 | Disorganized schizophrenia; ADR; OAR | M/W | 47 | 15.3 | 153 | 8.2 | 6.2 | ASCVD | Yes | Yes | Yes | No | Yes | No | No |
| 15 | 739 | M/W | 40 | 15.8 | 192 | 8.4 | 6.9 | ASCVD | 933 | Disorganized schizophrenia | M/W | 44 | 8.3 | 153 | 8.1 | 5.9 | Myocarditis | Yes | No | Yes | Yes | Yes | No | No |
| 16 | 1086* | M/W | 51 | 24.2 | 128 | 8.1 | 6.8 | ASCVD | 10025 | Disorganized schizophrenia; OAR | M/B | 52 | 27.1 | 107 | 7.8 | 6.7 | ASCVD | Yes | Yes | No | No | No | No | Abuse, Current |
| 17 | 10005 | M/W | 42 | 23.5 | 115 | 7.4 | 6.7 | Trauma | 1256 | Undifferentiated schizophrenia | M/W | 34 | 27.4 | 107 | 7.9 | 6.4 | Suicide by hanging | No | No | Yes | No | No | No | No |
| 18 | 1336 | M/W | 65 | 18.4 | 93 | 8.0 | 6.8 | Cardiac tamponade | 1173 | Disorganized schizophrenia; ADR | M/W | 62 | 22.9 | 120 | 7.7 | 6.4 | ASCVD | Yes | Yes | Yes | No | No | No | No |
| 19 | 1284 | M/W | 55 | 6.4 | 103 | 8.7 | 6.8 | ASCVD | 1188 | Undifferentiated schizophrenia; AAR; OAR | M/W | 58 | 7.7 | 118 | 8.4 | 6.2 | ASCVD | No | Yes | Yes | No | No | No | No |
| 20 | 1191 | M/B | 59 | 19.4 | 117 | 8.4 | 6.2 | ASCVD | 1263 | Undifferentiated schizophrenia; ADR | M/W | 62 | 22.7 | 106 | 8.5 | 7.1 | Accidental asphyxiation | Yes | Yes | Yes | Yes | No | No | No |
| 21 | 970 | M/W | 42 | 25.9 | 146 | 7.2 | 6.4 | ASCVD | 1222 | Undifferentiated schizophrenia; AAC | M/W | 32 | 30.8 | 113 | 7.5 | 6.4 | Suicide by combined drug overdose | Yes | No | Yes | Yes | No | No | Dependence, Current |
| 22 | 10003* | M/W | 49 | 21.2 | 117 | 8.4 | 6.5 | Trauma | 1088 | Undifferentiated schizophrenia; ADC; OAC | M/W | 49 | 21.5 | 128 | 8.1 | 6.5 | Accidental combined drug overdose | No | Yes | Yes | Yes | No | No | No |
| 23 | 1247* | F/W | 58 | 22.7 | 109 | 8.4 | 6.4 | ASCVD | 1240 | Undifferentiated schizophrenia; ADR | F/B | 50 | 22.9 | 110 | 7.7 | 6.3 | ASCVD | Yes | Yes | Yes | No | No | No | Abuse, Past |
| 24 | 1324* | M/W | 43 | 22.3 | 96 | 7.3 | 7 | Aortic dissection | 10020 | Schizophrenia, paranoid type; AAC; OAC | M/W | 38 | 28.8 | 109 | 7.4 | 6.6 | Suicide by salicylate overdose | Yes | Yes | Yes | Yes | Yes | No | No |
| 25 | 1099 | F/W | 24 | 9.1 | 127 | 8.6 | 6.5 | Cardiomyopathy | 10023 | Disorganized schizophrenia | F/B | 25 | 20.1 | 108 | 7.4 | 6.7 | Suicide by drowning | No | No | Yes | No | Yes | No | No |
| 26 | 1307 | M/B | 32 | 4.8 | 99 | 7.6 | 6.7 | ASCVD | 10024 | Paranoid schizophrenia | M/B | 37 | 6.0 | 108 | 7.5 | 6.1 | ASCVD | No | No | No | No | No | No | Abuse, Current |
| 27 | 1159 | M/W | 51 | 16.7 | 121 | 7.6 | 6.5 | ASCVD | 1296 | Undifferentiated schizophrenia | M/W | 48 | 7.8 | 101 | 7.3 | 6.5 | Pneumonia | Yes | Yes | Yes | Yes | No | No | No |
| 28 | 1326 | M/W | 58 | 16.4 | 95 | 8.0 | 6.7 | ASCVD | 1314 | Undifferentiated schizophrenia | M/W | 50 | 11.0 | 97 | 7.2 | 6.2 | ASCVD | No | No | Yes | Yes | No | No | No |
| 29 | 1555 | M/W | 17 | 15.1 | 53 | 7.9 | 6.9 | Trauma | 1649 | Undifferentiated schizophrenia | M/B | 17 | 21.4 | 38 | 8.1 | 6.9 | Suicide by hanging | No | No | Yes | Yes | No | No | No |
| 30 | 1268 | M/B | 49 | 19.9 | 105 | 7.9 | 7.1 | ASCVD | 1230 | Undifferentiated schizophrenia | M/W | 50 | 16.9 | 111 | 8.2 | 6.6 | Suicide by doxepin overdose | Yes | Yes | Yes | Yes | No | No | No |
| 31 | 1472 | M/W | 61 | 23.8 | 69 | 8.0 | 6.5 | Pulmonary embolism | 1453 | Paranoid schizophrenia; ADR | M/W | 62 | 11.1 | 72 | 8.2 | 6.4 | Trauma | No | Yes | Yes | No | Yes | No | No |

| Unaffected Comparison Subjects | | | | | | | | | Subjects with Schizophrenia | | | | | | | | | | | | | | | |
|--------------------------------|------|--------------|------|------------------|------------------------------|-----|-----|-------------------------|-----------------------------|-----------------------------------------------------|--------------|------|------------------|------------------------------|-----|-----|-----------------------------|---------------|-----------------|----------------------------|-----------------------------|-------------------------------------------|-----------------|--------------------------|
| Pair | Case | Sex/ Race | Age | PMI ^a | Storage Time ^b | RIN | pH | Cause of Death | Case | DSM IV diagnosis | Sex/ Race | Age | PMI ^a | Storage Time ^b | RIN | pH | Cause of Death | LGM Member | Tobacco ATOD | Anti- psychotic ATOD | Anti- depressant ATOD | Benzodiazepine/ Anticonvulsant ATOD | Lithium ATOD | Cannabis Use Disorder |
| 32 | 1026 | M/W | 59 | 19.8 | 136 | 7.4 | 6.3 | ASCVD | 1454 | Paranoid schizophrenia; AAR; ODC | M/W | 59 | 24.1 | 71 | 7.6 | 6.1 | Trauma | Yes | Yes | Yes | Yes | No | No | No |
| 33 | 694 | M/W | 38 | 20.7 | 197 | 7.7 | 7.0 | Subarachnoid hemorrhage | 1455 | Paranoid schizophrenia; AAR; OAC | M/W | 42 | 8.2 | 71 | 7.7 | 6.4 | Peritonitis | No | Yes | Yes | No | Yes | No | No |
| 34 | 1524 | M/W | 66 | 9.4 | 57 | 8.1 | 6.4 | Intestinal infarction | 1542 | Paranoid schizophrenia | M/W | 65 | 17.4 | 54 | 7.8 | 6.7 | Combined drug overdose | Yes | Yes | Yes | Yes | Yes | No | No |
| 35 | 1372 | M/W | 37 | 20.5 | 88 | 9.0 | 6.6 | Asphyxiation | 1581 | Paranoid schizophrenia; ODC; OAC | M/W | 32 | 18.4 | 48 | 9.0 | 6.8 | ASCVD | No | Yes | Yes | Yes | No | No | No |
| 36 | 1543 | F/W | 45 | 17.9 | 54 | 7.4 | 6.8 | Subarachnoid hemorrhage | 10026 | Undifferentiated schizophrenia | F/W | 46 | 23.8 | 107 | 7.6 | 6.6 | Suicide by thermal injuries | No | Yes | Yes | Yes | No | No | No |
| 37 | 1583 | M/W | 58 | 19.1 | 48 | 8.2 | 6.8 | Trauma | 1686 | Schizophrenia, paranoid type; AAR | M/B | 56 | 14.1 | 31 | 8.3 | 6.2 | ASCVD | No | Yes | Yes | Yes | Yes | No | No |
| 38 | 1554 | M/W | 50 | 23.2 | 53 | 7.6 | 6.5 | ASCVD | 1691 | Schizophrenia, paranoid type; ADR; ODC | M/W | 51 | 31.9 | 29 | 7.7 | 6.6 | Combined drug overdose | Yes | Yes | Yes | No | Yes | Yes | Yes |
| 39 | 1558 | M/W | 54 | 24.4 | 52 | 7.7 | 6.9 | ASCVD | 1734 | Schizophrenia, undifferentiated type; AAR; ODC; OAR | M/W | 54 | 28.6 | 21 | 7.7 | 6.1 | Pneumonia | Yes | Yes | Yes | No | No | No | No |
| | Mean | 49.8 | 18.5 | 135.5 | 8.2 | 6.7 | | | | | | 48.8 | 18.7 | 128.7 | 8.0 | 6.6 | | 19Y/20N | 27Y/7N/ 5Unk | 35Y/4N | 19Y/20N | 13Y/26N | 2Y/37N | 4Y/35N |
| | SD | 12.9 | 5.2 | 56.3 | 0.6 | 0.3 | | | | | | 12.9 | 8.1 | 61.6 | 0.6 | 0.3 | | | | | | | | |

^a subject also included as unaffected comparison subject in bipolar disorder cohort (Supplemental Table S2); ^a PMI, postmortem interval (hours); ^b Storage time (months) at -80C; Other abbreviations: ASCVD, arteriosclerotic cardiovascular disease; MCA, middle cerebral artery; ATOD, at time of death; ADC, alcohol dependence, current at time of death; ADR, alcohol dependence, in remission at time of death; AAC, alcohol abuse, current at time of death; AAR, alcohol abuse, in remission at time of death; ODC, other substance dependence, current at time of death; ODR, other substance dependence, in remission at time of death; OAC, other substance abuse, current at time of death; OAR, other substance abuse, in remission at time of death; U, unknown; M, male; F, female; W, white; B, black.

Table S2. Demographic, postmortem, and clinical characteristics of schizoaffective disorder and unaffected comparison subjects

| Unaffected Comparison Subjects | | | | | | | | | | Subjects with Schizoaffective Disorder | | | | | | | | | | | | | | |
|--------------------------------|-------|--------------|------|------------------|------------------------------|-----|-----|-----------------------|------|--------------------------------------------|--------------|------|------------------|------------------------------|-----|-----|-------------------------------------|---------------|-----------------|----------------------------|-----------------------------|-------------------------------------------|-----------------|-----------------------------|
| Pair | Case | Sex/ Race | Age | PMI ^a | Storage Time ^b | RIN | pH | Cause of Death | Case | DSM IV diagnosis | Sex/ Race | Age | PMI ^a | Storage Time ^b | RIN | pH | Cause of Death | LGM Member | Tobacco ATOD | Anti- psychotic ATOD | Anti- depressant ATOD | Benzodiazepine/ Anticonvulsant ATOD | Lithium ATOD | Cannabis Use Disorder |
| 1 | 567 | F/W | 46 | 15.0 | 216 | 8.9 | 6.7 | Mitral valve prolapse | 537 | Schizoaffective disorder | F/W | 37 | 14.5 | 221 | 8.6 | 6.7 | Suicide by hanging | No | Unknown | No | No | No | No | No |
| 2 | 516 | M/B | 20 | 14.0 | 224 | 8.4 | 6.9 | Homicide by gun shot | 547 | Schizoaffective disorder | M/B | 27 | 16.5 | 220 | 7.4 | 7.0 | Heat Stroke | Yes | Unknown | Yes | Yes | Yes | Yes | No |
| 3 | 822 | M/B | 28 | 25.3 | 176 | 8.5 | 7.0 | ASCVD | 787 | Schizoaffective disorder; ODC | M/B | 27 | 19.2 | 182 | 8.4 | 6.7 | Suicide by gun shot | No | No | Yes | No | No | No | Abuse, Past |
| 4 | 727 | M/B | 19 | 7.0 | 193 | 9.2 | 7.2 | Trauma | 829 | Schizoaffective disorder; ADC; OAR | M/W | 25 | 5.0 | 174 | 9.3 | 6.8 | Suicide by salicylate overdose | Yes | Yes | No | No | Yes | No | No |
| 5 | 700 | M/W | 42 | 26.1 | 197 | 8.7 | 7.0 | ASCVD | 539 | Schizoaffective disorder; ADR | M/W | 50 | 40.5 | 221 | 8.1 | 7.1 | Suicide by combined drug overdose | Yes | Unknown | Yes | Yes | Yes | No | No |
| 6 | 686* | F/W | 52 | 22.6 | 199 | 8.5 | 7.0 | ASCVD | 656 | Schizoaffective disorder; ADC | F/B | 47 | 20.1 | 203 | 9.2 | 7.3 | Suicide by gun shot | No | Yes | Yes | No | No | No | No |
| 7 | 852 | M/W | 54 | 8.0 | 168 | 9.1 | 6.8 | Cardiac tamponade | 781 | Schizoaffective disorder; ADR | M/B | 52 | 8.0 | 183 | 7.7 | 6.7 | Peritonitis | Yes | Yes | Yes | Yes | No | No | No |
| 8 | 987 | F/W | 65 | 21.5 | 144 | 9.1 | 6.8 | ASCVD | 802 | Schizoaffective disorder; ADC; ODR | F/W | 63 | 29.0 | 179 | 9.2 | 6.4 | Right ventricular dysplasia | No | Yes | Yes | No | Yes | No | Abuse, Past |
| 9 | 1047* | M/W | 43 | 13.8 | 135 | 9.0 | 6.6 | ASCVD | 1209 | Schizoaffective disorder | M/W | 35 | 9.1 | 115 | 8.7 | 6.5 | Suicide by diphenhydramine overdose | No | No | Yes | No | No | Yes | No |
| 10 | 1092* | F/B | 40 | 16.6 | 128 | 8.0 | 6.8 | Mitral valve prolapse | 1178 | Schizoaffective disorder | F/B | 37 | 18.9 | 119 | 8.4 | 6.1 | Pulmonary embolism | No | Yes | Yes | No | Yes | No | No |
| 11 | 1122 | M/W | 55 | 15.4 | 124 | 7.9 | 6.7 | Cardiac tamponade | 1105 | Schizoaffective disorder | M/W | 53 | 7.9 | 126 | 8.9 | 6.2 | ASCVD | No | Yes | Yes | No | No | No | No |
| 12 | 1391* | F/W | 51 | 7.8 | 84 | 7.1 | 6.6 | ASCVD | 1189 | Schizoaffective disorder; AAR | F/W | 47 | 14.4 | 117 | 8.3 | 6.4 | Suicide by combined drug overdose | No | Yes | Yes | Yes | Yes | No | No |
| 13 | 1282* | F/W | 39 | 24.5 | 103 | 7.5 | 6.8 | ASCVD | 1211 | Schizoaffective disorder | F/W | 41 | 20.1 | 115 | 7.8 | 6.3 | Sudden unexplained death | No | Yes | Yes | Yes | No | No | No |
| 14 | 902 | M/W | 60 | 23.6 | 160 | 7.7 | 6.7 | ASCVD | 1361 | Schizoaffective disorder; ODC | M/W | 63 | 23.2 | 90 | 7.7 | 6.4 | Cardiomyopathy | Yes | Yes | Yes | No | Yes | No | No |
| 15 | 1374* | M/W | 43 | 21.7 | 88 | 7.2 | 6.6 | ASCVD | 904 | Schizoaffective disorder | M/W | 33 | 28.0 | 159 | 7.1 | 6.2 | Pneumonia | Yes | Yes | Yes | No | Yes | No | No |
| 16 | 1466 | F/B | 64 | 20.0 | 69 | 8.8 | 6.7 | Trauma | 1341 | Schizoaffective disorder; ODC | F/W | 44 | 24.5 | 91 | 8.8 | 6.6 | Trauma | Yes | No | Yes | No | Yes | No | No |
| 17 | 1518 | M/W | 50 | 20.7 | 58 | 7.7 | 6.4 | ASCVD | 1367 | Schizoaffective disorder; ADC; ODR | M/W | 47 | 28.9 | 89 | 7.2 | 6.6 | Combined drug overdose | Yes | No | No | No | No | No | No |
| 18 | 1386 | M/W | 46 | 21.2 | 84 | 8.3 | 6.7 | ASCVD | 1420 | Schizoaffective disorder; AAR; ODC; OAR | M/W | 47 | 23.4 | 77 | 8.2 | 6.8 | Suicide by jump | No | Yes | Yes | Yes | No | No | No |
| 19 | 1350 | M/W | 21 | 24.2 | 90 | 7.3 | 6.4 | Trauma | 1474 | Schizoaffective disorder; ADR | M/W | 37 | 39.9 | 69 | 7.0 | 6.7 | Suicide by hanging | No | No | No | No | No | No | No |
| 20 | 1792 | F/W | 36 | 28.1 | 14 | 7.5 | 6.5 | Pulmonary embolism | 1506 | Schizoaffective disorder; ADC | F/W | 47 | 14.1 | 65 | 7.5 | 6.6 | Combined drug overdose | Yes | Yes | Yes | Yes | No | No | No |
| 21 | 1270 | F/W | 73 | 19.7 | 104 | 7.7 | 6.7 | Trauma | 1579 | Schizoaffective disorder; ADR; ODC | F/W | 69 | 16.1 | 48 | 7.7 | 6.7 | ASCVD | Yes | Yes | Yes | No | Yes | No | No |
| 22 | 1635 | M/W | 66 | 25.3 | 40 | 8.2 | 6.8 | Cardiac tamponade | 1706 | Schizoaffective disorder; AAR; ODC; OAR | M/B | 60 | 28.1 | 26 | 8.4 | 6.8 | Sepsis | No | Yes | Yes | No | No | No | No |
| 23 | 1384 | M/W | 67 | 21.9 | 86 | 7 | 6.6 | ASCVD | 1712 | Schizoaffective disorder; ADR; ODC | M/W | 63 | 15.1 | 24 | 7.1 | 6.2 | ASCVD | Yes | No | Yes | Yes | Yes | No | No |
| | Mean | 47.0 | 19.3 | 125.3 | 8.1 | 6.7 | | | | | 45.7 | 20.2 | 126.6 | 8.1 | 6.6 | | | 11Y/12N | 14Y/6N/ 3Unk | 19Y/4N | 8Y/15N | 11Y/12N | 2Y/21N | 2Y/21N |
| | SD | 15.4 | 6.1 | 58.3 | 0.7 | 0.2 | | | | | 12.5 | 9.4 | 62.3 | 0.7 | 0.3 | | | | | | | | | |

^a subject also included as healthy comparison subject in bipolar disorder cohort (Supplemental Table S2); ^aPMI, postmortem interval (hours); ^b Storage time (months) at -80C; Other abbreviations: ASCVD, arteriosclerotic cardiovascular disease; MCA, middle cerebral artery; ATOD, at time of death; ADC, alcohol dependence, current at time of death; ADR, alcohol dependence, in remission at time of death; AAC, alcohol abuse, current at time of death; AAR, alcohol abuse, in remission at time of death; ODC, other substance dependence, current at time of death; ODR, other substance dependence, in remission at time of death; OAC, other substance abuse, current at time of death; OAR, other substance abuse, in remission at time of death; U, unknown; M, male; F, female; W, white; B, black.

Table S3. Demographic, postmortem, and clinical characteristics of bipolar disorder and unaffected comparison subjects

| Unaffected Comparison Subjects | | | | | | | | | Bipolar Disorder Subjects | | | | | | | | | | | | | | | |
|--------------------------------|--------|--------------|-----|------------------|------------------------------|-----|-----|--------------------------------------------|---------------------------|---------------------------------|--------------|-----|------------------|------------------------------|-----|-----|------------------------------------|---------------|-----------------|----------------------------|-----------------------------|-------------------------------------------|-----------------|--------------------------|
| Pair | Case | Sex/ Race | Age | PMI ^a | Storage Time ^b | RIN | pH | Cause of Death | Case | DSM IV diagnosis | Sex/ Race | Age | PMI ^a | Storage Time ^b | RIN | pH | Cause of Death | LGM Member | Tobacco ATOD | Anti- psychotic ATOD | Anti- depressant ATOD | Benzodiazepine/ Anticonvulsant ATOD | Lithium ATOD | Cannabis Use Disorder |
| 1 | 10003* | M/W | 49 | 21.2 | 119 | 8.4 | 6.5 | Trauma | 1102 | Bipolar NOS; ADR; ODC; OAC; OAR | M/W | 50 | 12.1 | 129 | 8.3 | 6.7 | ASCVD | No | Yes | No | Yes | Yes | No | No |
| 2 | 1374* | M/W | 43 | 21.7 | 90 | 7.2 | 6.6 | ASCVD | 1121 | Bipolar I +P; ADR | M/W | 40 | 18.5 | 127 | 8.3 | 6.4 | Pulmonary embolism | No | No | Yes | No | Yes | No | No |
| 3 | 1282* | F/W | 39 | 24.5 | 106 | 7.5 | 6.8 | ASCVD | 957 | Bipolar I | F/W | 39 | 22.2 | 150 | 8.4 | 6.7 | Suicide by drowning | No | Unknown | No | Yes | No | No | No |
| 4 | 1298 | M/W | 48 | 24.5 | 103 | 7.9 | 6.5 | ASCVD | 886 | Bipolar I; ADC | M/W | 45 | 27.2 | 165 | 8.3 | 7.1 | Suicide by gun shot | No | Yes | No | No | No | No | No |
| 5 | 1047* | M/W | 43 | 13.8 | 137 | 9.0 | 6.6 | ASCVD | 1020 | Bipolar I +P; ADC; ODC | M/W | 42 | 12.5 | 141 | 8.5 | 6.7 | Accidental combined drug overdose | No | Yes | No | Yes | Yes | No | No |
| 6 | 795 | M/W | 68 | 11.8 | 182 | 8.2 | 6.8 | Ruptured aortic aneurysm | 1130 | Bipolar I +P; AAR | M/W | 65 | 8.9 | 126 | 8.0 | 6.7 | Esophageal cancer | No | Unknown | Yes | Yes | Yes | No | No |
| 7 | 1789 | F/W | 53 | 13.7 | 15 | 8.5 | 6.8 | ASCVD | 1048 | Bipolar I +P | F/W | 51 | 21.5 | 136 | 7.7 | 6.7 | Suicide by asphyxiation | No | Yes | No | Yes | No | No | No |
| 8 | 1324* | M/W | 43 | 22.3 | 97 | 7.3 | 6.7 | Aortic dissection | 697 | Bipolar I +P | M/W | 39 | 24.2 | 200 | 7.8 | 6.6 | Suicide by incised wounds | No | Unknown | No | No | Yes | No | Abuse, Past |
| 9 | 1444 | M/W | 46 | 22.0 | 77 | 8.4 | 6.3 | Pulmonary embolism | 1069 | Bipolar I; AAR | M/W | 48 | 18.1 | 133 | 8.1 | 6.9 | ASCVD | No | No | No | No | No | No | No |
| 10 | 1086* | M/W | 51 | 24.2 | 131 | 8.1 | 6.6 | ASCVD | 1244 | Bipolar I +P; AAR; ODC; OAC | M/W | 52 | 23.5 | 111 | 8.0 | 6.7 | Accidental asphyxiation | No | Yes | Yes | Yes | Yes | No | No |
| 11 | 1391* | F/W | 51 | 7.8 | 86 | 7.1 | 6.6 | ASCVD | 10004 | Bipolar I; ODC | F/W | 50 | 11.7 | 118 | 8.5 | 6.4 | Accidental combined drug overdose | Yes | Unknown | Yes | No | No | No | No |
| 12 | 1196 | F/W | 36 | 14.5 | 119 | 8.2 | 6.4 | Asphyxiation | 1180 | Bipolar I +P | F/W | 28 | 22.3 | 121 | 7.5 | 6.3 | Suicide by jump | No | No | No | Yes | No | No | Abuse, Current |
| 13 | 1293 | F/W | 65 | 18.5 | 104 | 7.0 | 6.5 | Trauma | 10006 | Bipolar I +P; ADR | F/W | 55 | 17.5 | 117 | 8.1 | 6.4 | Suicide by gun shot | No | Yes | No | No | No | No | Abuse, Past |
| 14 | 1153 | M/W | 55 | 28.0 | 123 | 8.0 | 6.1 | ASCVD | 716 | Bipolar I; ADC; OAC | M/W | 58 | 27.7 | 196 | 8.3 | 6.8 | Suicide by gun shot | No | Unknown | No | No | No | No | No |
| 15 | 789 | M/W | 22 | 20.1 | 184 | 7.8 | 6.8 | Asphyxiation | 1181 | Bipolar I +P; ODC; OAR | M/W | 28 | 27.4 | 121 | 8.0 | 6.2 | Accidental morphine overdose | Yes | Yes | No | Yes | Yes | No | Dependence, Remission |
| 16 | 686* | F/W | 52 | 22.6 | 201 | 8.5 | 7.1 | ASCVD | 1328 | Bipolar NOS | F/W | 49 | 21.5 | 97 | 7.5 | 6.7 | ASCVD | No | No | No | Yes | Yes | Yes | No |
| 17 | 1247* | F/W | 58 | 22.7 | 111 | 8.4 | 6.4 | ASCVD | 1044 | Bipolar I +P | F/W | 56 | 24.5 | 137 | 7.1 | 6.1 | ASCVD | No | No | Yes | Yes | Yes | No | No |
| 18 | 1092* | F/B | 40 | 16.6 | 130 | 8.0 | 6.8 | Mitral valve prolapse | 984 | Bipolar I +P | F/W | 42 | 31.2 | 146 | 8.0 | 6.5 | Accidental combined drug overdose | Yes | Yes | Yes | Yes | No | Yes | No |
| 19 | 840 | F/W | 41 | 15.4 | 172 | 9.1 | 6.6 | ASCVD | 945 | Bipolar I; AAC | F/W | 43 | 31.9 | 152 | 7.2 | 6.7 | Suicide by asphyxiation | Yes | Yes | Yes | Yes | Yes | No | Abuse, Current |
| 20 | 1031 | M/W | 53 | 23.2 | 139 | 8.9 | 6.8 | ASCVD | 849 | Bipolar II | M/W | 52 | 22.1 | 171 | 7.0 | 7.3 | Suicide by alprazolam overdose | Yes | No | No | No | Yes | No | No |
| 21 | 841 | M/W | 70 | 21.2 | 172 | 7.2 | 7.2 | Hypertrophic cardiomyopathy | 982 | Bipolar II; ADR | M/W | 79 | 31.1 | 146 | 8.4 | 6.7 | Accidental smoke inhalation | Yes | Yes | No | Yes | Yes | No | No |
| 22 | 1394 | M/W | 45 | 17.3 | 85 | 7.3 | 6.6 | ASCVD | 1207 | Bipolar NOS; ADC; ODC | M/W | 48 | 18.0 | 117 | 8.1 | 6.4 | ASCVD | No | Unknown | Yes | Yes | Yes | No | Abuse, Current |
| 23 | 1081 | F/W | 57 | 14.9 | 131 | 9.0 | 6.8 | Chronic obstructive pulmonary disease | 1449 | Bipolar II | F/W | 57 | 19.1 | 75 | 8.0 | 6.4 | ASCVD | No | Yes | No | Yes | No | No | No |
| 24 | 1598 | M/W | 50 | 23.8 | 48 | 7.8 | 6.9 | Acute myocardial infarction | 1473 | Bipolar II; AAC | M/W | 51 | 22.3 | 72 | 8.1 | 6.6 | Accidental electrocution | No | Unknown | No | Yes | No | No | No |
| 25 | 1694 | F/W | 67 | 8.5 | 31 | 8.9 | 6.7 | Acute myocarditis | 1483 | Bipolar II; ADC; OAC | F/W | 56 | 5.8 | 70 | 8.3 | 6 | Chronic alcoholism | Yes | No | No | No | No | No | Abuse, Past |
| 26 | 1403 | F/W | 45 | 12.3 | 84 | 8.2 | 6.4 | ASCVD | 1537 | Bipolar II; ADR | F/W | 52 | 21.1 | 58 | 8.9 | 6.8 | Bilateral pulmonary emboli | No | Yes | No | Yes | Yes | No | Abuse, Past |
| 27 | 1770 | M/W | 52 | 28.2 | 19 | 8.2 | 6.8 | Asphyxiation | 1565 | Bipolar NOS; ADC | M/W | 45 | 27.6 | 53 | 8.3 | 6.8 | Acute & chronic myocardial infarct | Yes | Yes | Yes | Yes | No | No | No |
| 28 | 1605 | F/W | 21 | 23.9 | 47 | 8.2 | 6.9 | Arrhythmogenic right ventricular dysplasia | 1589 | Bipolar NOS; ADC; ODC; OAC | F/W | 25 | 27.6 | 50 | 7.1 | 6.1 | Accidental combined drug overdose | Yes | Yes | Yes | Yes | No | No | No |
| 29 | 1489 | M/W | 25 | 16.9 | 70 | 8.3 | 5.9 | Hypoglycemia | 1603 | Bipolar I; ADC; ODC | M/W | 31 | 12.0 | 47 | 7.6 | 6.8 | Suicide by hanging | No | Yes | No | Yes | No | No | Dependence, Current |

| Unaffected Comparison Subjects | | | | | | | | | Bipolar Disorder Subjects | | | | | | | | | | | | | | | | |
|--------------------------------|-------|--------------|------|------------------|------------------------------|-----|-----|--------------------------------------------|---------------------------|--------------------------|--------------|------|------------------|------------------------------|-----|-----|-----------------------------------|---------------|------------------|----------------------------|-----------------------------|-------------------------------------------|-----------------|--------------------------|----|
| Pair | Case | Sex/ Race | Age | PMI ^a | Storage Time ^b | RIN | pH | Cause of Death | Case | DSM IV diagnosis | Sex/ Race | Age | PMI ^a | Storage Time ^b | RIN | pH | Cause of Death | LGM Member | Tobacco ATOD | Anti- psychotic ATOD | Anti- depressant ATOD | Benzodiazepine/ Anticonvulsant ATOD | Lithium ATOD | Cannabis Use Disorder | |
| 30 | 10019 | F/B | 41 | 19.3 | 112 | 7.6 | 6.6 | Complications of postpartum cardiomyopathy | 1632 | Bipolar II; ODC | F/B | 31 | 19.1 | 43 | 8.5 | 6.6 | Undetermined | Yes | No | No | No | No | No | No | |
| 31 | 1482 | M/W | 25 | 20.2 | 70 | 9.1 | 6.6 | ASCVD | 10014 | Bipolar NOS; ADC; ODC | M/W | 24 | 23.1 | 115 | 7.8 | 6.1 | Suicide by gun shot | No | Yes | No | No | No | No | No | |
| 32 | 838 | M/W | 58 | 16.5 | 173 | 8.5 | 7 | ASCVD | 1461 | Bipolar I; AAR | M/W | 57 | 7.6 | 73 | 8.7 | 6.8 | ASCVD | No | No | Yes | Yes | No | No | No | |
| 33 | 1637 | M/W | 46 | 16.6 | 42 | 8.2 | 6.9 | ASCVD | 1584 | Bipolar I; ODC; ODR | M/W | 46 | 16.6 | 50 | 7.6 | 6.8 | Suicide by oxymorphone overdose | No | Yes | No | Yes | Yes | Yes | Yes | No |
| 34 | 1783 | F/W | 23 | 15.9 | 16 | 8.5 | 6.8 | Trauma | 1573 | Bipolar II | F/W | 27 | 11.2 | 52 | 9.0 | 6.7 | Status asthmaticus | No | No | No | No | No | No | Dependence, Current | |
| 35 | 1429 | M/B | 44 | 23.9 | 79 | 7.5 | 6.8 | Dilated cardiomyopathy & cardiomegaly | 1695 | Bipolar I; ADR; ODC; OAR | M/W | 33 | 29.1 | 31 | 7.7 | 6.8 | Accidental combined drug overdose | No | Yes | Yes | No | Yes | No | No | |
| | Mean | 46.4 | 19.1 | 103.0 | 8.1 | 6.7 | | | | | | 45.5 | 20.5 | 109.9 | 8.0 | 6.6 | | 10Y/25N | 18Y/10N/ 7Unk | 12Y/23N | 22Y/13N | 16Y/19N | 3Y/32N | 10Y/25N | |
| | SD | 12.7 | 5.1 | 49.8 | 0.6 | 0.3 | | | | | | 12.2 | 7.0 | 45.1 | 0.5 | 0.3 | | | | | | | | | |

^a subject also included as unaffected comparison subject in schizophrenia cohort (Supplemental Table S1); ^aPMI, postmortem interval (hours); ^b Storage time (months) at -80C; Other abbreviations: ASCVD, arteriosclerotic cardiovascular disease; MCA, middle cerebral artery; ATOD, at time of death; ADC, alcohol dependence, current at time of death; ADR, alcohol dependence, in remission at time of death; AAC, alcohol abuse, current at time of death; AAR, alcohol abuse, in remission at time of death; Bipolar I +P, bipolar I disorder with psychotic features; Bipolar NOS, bipolar disorder not otherwise specified; ODC, other substance dependence, current at time of death; ODR, other substance dependence, in remission at time of death; OAC, other substance abuse, current at time of death; OAR, other substance abuse, in remission at time of death; U, unknown; M, male; F, female; W, white; B, black

Supplemental Table S4: qPCR primer design

| Gene | Accession # | Amplicon Size (bp) | Position | Melting Temperature | Efficiency | Forward Primer (F) Reverse Primer (R) |
|--------------------------------------------------|--------------------|---------------------------|-----------------|----------------------------|-------------------|-------------------------------------------------------|
| Glutamate decarboxylase 67 kDa (GAD67) | NM_000817 | 86 | 2495-2580 | 79°C | 97% | (F) GTTTCCCGCTCCAAGAGAAT (R) TGGAGTTGTTGGACAAGCTG |
| Parvalbumin | NM_002854 | 99 | 112-210 | 78°C | 102% | (F) CTACCGACTCCTTCGACCA (R) CCTTGTCAGCATGTGAAA |
| Somatostatin | NM_001048 | 93 | 319-411 | 81°C | 99% | (F) ATGCCCTGGAACCTGAAGAT (R) CCATAGCCGGGTTTGAGTTA |
| Lhx6 | NM_014368 | 96 | 642-737 | 83°C | 100% | (F) CGACACCATGATTGAGAACC (R) TTGGGTTGACTGTCCTGTTC |
| Beta actin | NM_001101 | 101 | 1146-1246 | 81°C | 100% | (F) GATGTGGATCAGCAAGCA (R) AGAAAGGGTGTAACGCAACTA |
| Cyclophilin | NM_021130 | 126 | 159-284 | 78°C | 98% | (F) GCAGACAAGGTCCCAAAG (R) GAAGTCACCACCCTGACAC |
| Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) | NM_002046 | 87 | 556-642 | 81°C | 97% | (F) TGCACCACCAACTGCTTAGC (R) GGCATGGACTGTGGTCATGAG |

Supplemental Table S5. Mean Non-Adjusted GABA Neuron-Related Transcript Levels in Schizophrenia, Schizoaffective Disorder, and Bipolar Disorder Subjects with and without the Low GABA Marker Molecular Phenotype

| | <i>Low GABA Marker (LGM) Molecular Phenotype</i> | | | | | <i>Non-LGM Molecular Phenotype</i> | | | | | LGM vs NonLGM % Diff | Statistics² |
|---------------------------------|--------------------------------------------------|----------------------|-------------------------------------|---------------|--------------------------------------|------------------------------------|--------------------------|-------------------------------------|---------------|--------------------------------------|-----------------------------|---------------------------------------|
| | N | LGM Mean (SD) | Matched Unaffected Mean (SD) | % Diff | Statistics¹ | N | Non-LGM Mean (SD) | Matched Unaffected Mean (SD) | % Diff | Statistics¹ | | |
| Schizophrenia | | | | | | | | | | | | |
| <i>GAD67</i> | 19 | 0.043 (0.010) | 0.057 (0.008) | -24% | t ₁₈ = -5.05 p < .0001 | 20 | 0.062 (0.008) | 0.062 (0.008) | -0.5% | t ₁₉ = -0.10 p = 0.92 | -30% | t ₃₇ = -6.48 p < .0001 |
| <i>Parvalbumin</i> | 19 | 0.029 (0.007) | 0.041 (0.007) | -29% | t ₁₈ = -5.66 p < .0001 | 20 | 0.039 (0.010) | 0.041 (0.007) | -4% | t ₁₉ = -0.67 p = 0.51 | -25% | t ₃₇ = -3.59 p = .0009 |
| <i>Somatostatin</i> | 19 | 0.039 (0.024) | 0.090 (0.022) | -57% | t ₁₈ = -6.21 p < .0001 | 20 | 0.091 (0.035) | 0.106 (0.021) | -14% | t ₁₉ = -2.06 p = 0.05 | -57% | t ₃₇ = -5.38 p < .0001 |
| <i>Lhx6</i> | 19 | 0.0067 (0.0010) | 0.0083 (0.0010) | -19% | t ₁₈ = -4.05 p = .0007 | 20 | 0.0090 (0.0015) | 0.0086 (0.0007) | 5% | t ₁₉ = -1.17 p = 0.25 | -25% | t ₃₇ = -5.62 p < .0001 |
| Schizoaffective Disorder | | | | | | | | | | | | |
| <i>GAD67</i> | 11 | 0.039 (0.012) | 0.060 (0.006) | -35% | t ₁₀ = -4.99 p = .0005 | 12 | 0.062 (0.005) | 0.059 (0.009) | 6% | t ₁₁ = 1.66 p = 0.13 | -37% | t ₂₁ = -6.34 p < .0001 |
| <i>Parvalbumin</i> | 11 | 0.026 (0.008) | 0.049 (0.012) | -46% | t ₁₀ = -6.97 p < .0001 | 12 | 0.035 (0.008) | 0.042 (0.007) | -15% | t ₁₁ = -1.30 p = 0.22 | -25% | t ₂₁ = -2.59 p = 0.02 |
| <i>Somatostatin</i> | 11 | 0.045 (0.025) | 0.093 (0.032) | -52% | t ₁₀ = -4.53 p = .001 | 12 | 0.095 (0.026) | 0.105 (0.023) | -10% | t ₁₁ = -1.12 p = 0.29 | -53% | t ₂₁ = -4.71 p = .0001 |
| <i>Lhx6</i> | 11 | 0.0067 (0.0008) | 0.0087 (0.0009) | -23% | t ₁₀ = -5.73 p = .0002 | 12 | 0.0089 (0.0010) | 0.0088 (0.0009) | 1% | t ₁₁ = 1.00 p = 0.34 | -25% | t ₂₁ = -5.76 p < .0001 |
| Bipolar Disorder | | | | | | | | | | | | |
| <i>GAD67</i> | 10 | 0.043 (0.008) | 0.061 (0.006) | -29% | t ₉ = -5.47 p = .0004 | 25 | 0.063 (0.007) | 0.062 (0.007) | 2% | t ₂₄ = -0.02 p = 0.99 | -32% | t ₃₃ = -7.32 p < .0001 |
| <i>Parvalbumin</i> | 10 | 0.029 (0.007) | 0.042 (0.007) | -32% | t ₉ = -6.37 p = .0001 | 25 | 0.037 (0.008) | 0.044 (0.007) | -15% | t ₂₄ = -3.65 p = 0.001 | -23% | t ₃₃ = -2.92 p = .006 |
| <i>Somatostatin</i> | 10 | 0.052 (0.018) | 0.105 (0.028) | -50% | t ₉ = -4.87 p = .0009 | 25 | 0.098 (0.027) | 0.103 (0.021) | -4% | t ₂₄ = -1.03 p = 0.31 | -47% | t ₃₃ = -4.99 p < .0001 |
| <i>Lhx6</i> | 10 | 0.0073 (0.0013) | 0.0087 (0.0009) | -16% | t ₉ = -2.22 p = 0.05 | 25 | 0.0099 (0.0013) | 0.0091 (0.0011) | 8% | t ₂₄ = 1.53 p = 0.14 | -26% | t ₃₃ = -5.40 p < .0001 |
| All Disorders | | | | | | | | | | | | |
| <i>GAD67</i> | 40 | 0.042 (0.010) | 0.059 (0.007) | -29% | t ₃₉ = -8.70 p < .0001 | 57 | 0.063 (0.007) | 0.062 (0.008) | 2% | t ₅₆ = 0.77 p = 0.45 | -33% | t ₉₅ = -11.99 p < .0001 |
| <i>Parvalbumin</i> | 40 | 0.028 (0.007) | 0.043 (0.009) | -35% | t ₃₉ = -9.68 p < .0001 | 57 | 0.037 (0.009) | 0.042 (0.007) | -11% | t ₅₆ = -3.30 p = 0.002 | -24% | t ₉₅ = -5.43 p < .0001 |
| <i>Somatostatin</i> | 40 | 0.044 (0.023) | 0.095 (0.026) | -54% | t ₃₉ = -9.30 p < .0001 | 57 | 0.095 (0.030) | 0.104 (0.021) | -9% | t ₅₆ = -2.53 p = 0.01 | -54% | t ₉₅ = -9.18 p < .0001 |
| <i>Lhx6</i> | 40 | 0.0068 (0.0011) | 0.0085 (0.0010) | -20% | t ₃₉ = -6.22 p < .0001 | 57 | 0.0094 (0.0014) | 0.0089 (0.0010) | 6% | t ₅₆ = -2.20 p = 0.03 | -27% | t ₉₅ = -9.84 p < .0001 |

¹ Paired t test

² Unpaired two sample t test