

SUPPLEMENTARY MATERIAL

Figures and Tables

Table S1. Plasma concentrations of acylethanolamides (NAEs) in the control, SUD without antipsychotics and SUD + antipsychotics groups.

| NAEs | CONTROL (<i>n</i> = 175) | SUD (<i>n</i> =293) | SUD +Antipsychotic (<i>n</i> = 40) | <i>p</i> Value |
|---------------------------------|------------------------------|-------------------------|--|----------------|
| AEA median (IQR) | 0.33 (0.21-.048) | 0.43 (0.30-.061) | 0.58 (0.42-0.80) | 0.000 |
| DEA median (IQR) | 0.08 (0.05-0.14) | 0.12 (0.09-0.17) | 0.16 (0.13-0.22) | 0.000 |
| DGLEA median (IQR) | 0.07 (0.04-0.09) | 0.08 (0.06-0.12) | 0.07 (0.11-0.14) | 0.000 |
| DHEA median (IQR) | 0.42 (0.27-0.61) | 0.52 (0.36-0.70) | 0.55 (0.42-0.78) | 0.000 |
| LEA median (IQR) | 0.70 (0.51-0.93) | 1.07 (0.85-1.37) | 1.31 (0.99-1.61) | 0.000 |
| OEA median (IQR) | 1.88 (1.33-3.15) | 3.32 (2.47-4.47) | 3.85 (2.91-5.49) | 0.000 |
| PEA median (IQR) | 1.59 (1.27-2.45) | 3.37 (2.26-5.65) | 3.38 (2.21-6.35) | 0.000 |
| POEA median (IQR) | 0.29 (0.16-0.39) | 0.30 (0.19-0.42) | 0.39 (0.22-0.53) | 0.143 |
| SEA median (IQR) | 4.30 (0.90-5.90) | 1.90 (1.24-4.18) | 3.01 (1.6-4.36) | 0.599 |

P-value from the Kruskal-Wallis test. *P*-value in bold indicates a statistically significant difference.

Table S2. Logistic regression model for distinguishing patients with SUD from controls.

| Logistic regression model | | | | | | | | |
|----------------------------------|------------|-------------|-------------|-----------|---------------------------|---------------|--------------------------|--------------|
| Variable | B | S.E. | Wald | df | <i>p</i> Value | Exp(B) | 95% CI for EXP(B) | |
| | | | | | | | Lower | Upper |
| Sex | 1.209 | 0.603 | 4.019 | 1 | 0.045 | 3.349 | 1.027 | 10.914 |
| Age | - 0.017 | 0.023 | 0.553 | 1 | 0.457 | 0.983 | 0.940 | 1.028 |
| BMI | - 0.021 | 0.062 | 0.121 | 1 | 0.728 | 0.979 | 0.867 | 1.104 |
| AEA^(a) | 7.708 | 2.768 | 7.753 | 1 | 0.005 | 2225.302 | 9.798 | 505429.601 |
| DEA^(a) | - 3.638 | 1.735 | 4.399 | 1 | 0.036 | 0.026 | 0.001 | 0.788 |
| DGLEA^(a) | 1.456 | 2.458 | 0.351 | 1 | 0.554 | 4.289 | 0.035 | 530.219 |
| DHEA^(a) | - 4.217 | 1.722 | 5.996 | 1 | 0.014 | 0.015 | 0.001 | 0.431 |
| LEA^(a) | - 0.257 | 2.622 | 0.010 | 1 | 0.922 | 0.773 | 0.005 | 131.766 |
| OEA^(a) | 1.346 | 3.261 | 0.170 | 1 | 0.680 | 3.842 | 0.006 | 2293.625 |
| PEA^(a) | 5.256 | 2.365 | 4.937 | 1 | 0.026 | 191.634 | 1.859 | 19758.811 |
| POEA^(a) | - 1.049 | 1.084 | 0.937 | 1 | 0.333 | 0.350 | 0.042 | 2.931 |
| SEA^(a) | - 8.782 | 2.029 | 18.737 | 1 | 0.000 | 0.000 | 0.000 | 0.008 |
| Constant | - 0.299 | 4.286 | 0.005 | 1 | 0.944 | 0.742 | | |

^(a)Log10 values

Abbreviations: B = coefficient; BMI = body mass index; CI = confidence interval; df = degrees of freedom; S.E. = standard error; W = Wald test.

Table S3. Logistic regression model for distinguishing patients with SUD and antipsychotic treatment from patients with SUD.

| Logistic regression model | | | | | | | | |
|----------------------------|--------|-------|-------|----|-------------------|---------|-------------------|-------------|
| Variable | B | S.E. | Wald | df | <i>p</i> Value | Exp(B) | 95% CI for EXP(B) | |
| | | | | | | | Lower | Upper |
| Sex | 0.991 | 1.220 | 0.660 | 1 | 0.417 | 2.693 | 0.247 | 29.404 |
| Age | -0.022 | 0.030 | 0.523 | 1 | 0.470 | 0.978 | 0.922 | 1.038 |
| BMI | 0.004 | 0.062 | 0.003 | 1 | 0.953 | 1.004 | 0.890 | 1.132 |
| AEA^(a) | 5.711 | 4.594 | 1.546 | 1 | 0.214 | 302.305 | 0.037 | 2459340.555 |
| DEA^(a) | -1.161 | 2.886 | 0.162 | 1 | 0.688 | 0.313 | 0.001 | 89.642 |
| DGLEA^(a) | 3.384 | 2.930 | 1.334 | 1 | 0.248 | 29.474 | 0.095 | 9186.582 |
| DHEA^(a) | 0.737 | 2.113 | 0.122 | 1 | 0.727 | 2.090 | 0.033 | 131.370 |
| LEA^(a) | 4.114 | 2.850 | 2.083 | 1 | 0.149 | 61.165 | 0.229 | 16312.512 |
| OEA^(a) | -6.249 | 5.344 | 1.367 | 1 | 0.242 | 0.002 | 0.000 | 68.405 |
| PEA^(a) | 0.741 | 3.063 | 0.059 | 1 | 0.809 | 2.098 | 0.005 | 848.644 |
| POEA^(a) | 0.017 | 1.742 | 0.000 | 1 | 0.992 | 1.017 | 0.033 | 30.888 |
| SEA^(a) | -0.504 | 2.531 | 0.040 | 1 | 0.842 | 0.604 | 0.004 | 86.167 |
| Constant | 5.689 | 6.884 | 0.683 | 1 | 0.409 | 295.575 | | |

^(a)Log10 values

Abbreviations: B = coefficient; BMI = body mass index; CI = confidence interval; df = degrees of freedom; S.E. = standard error; W = Wald test.

Figure S1

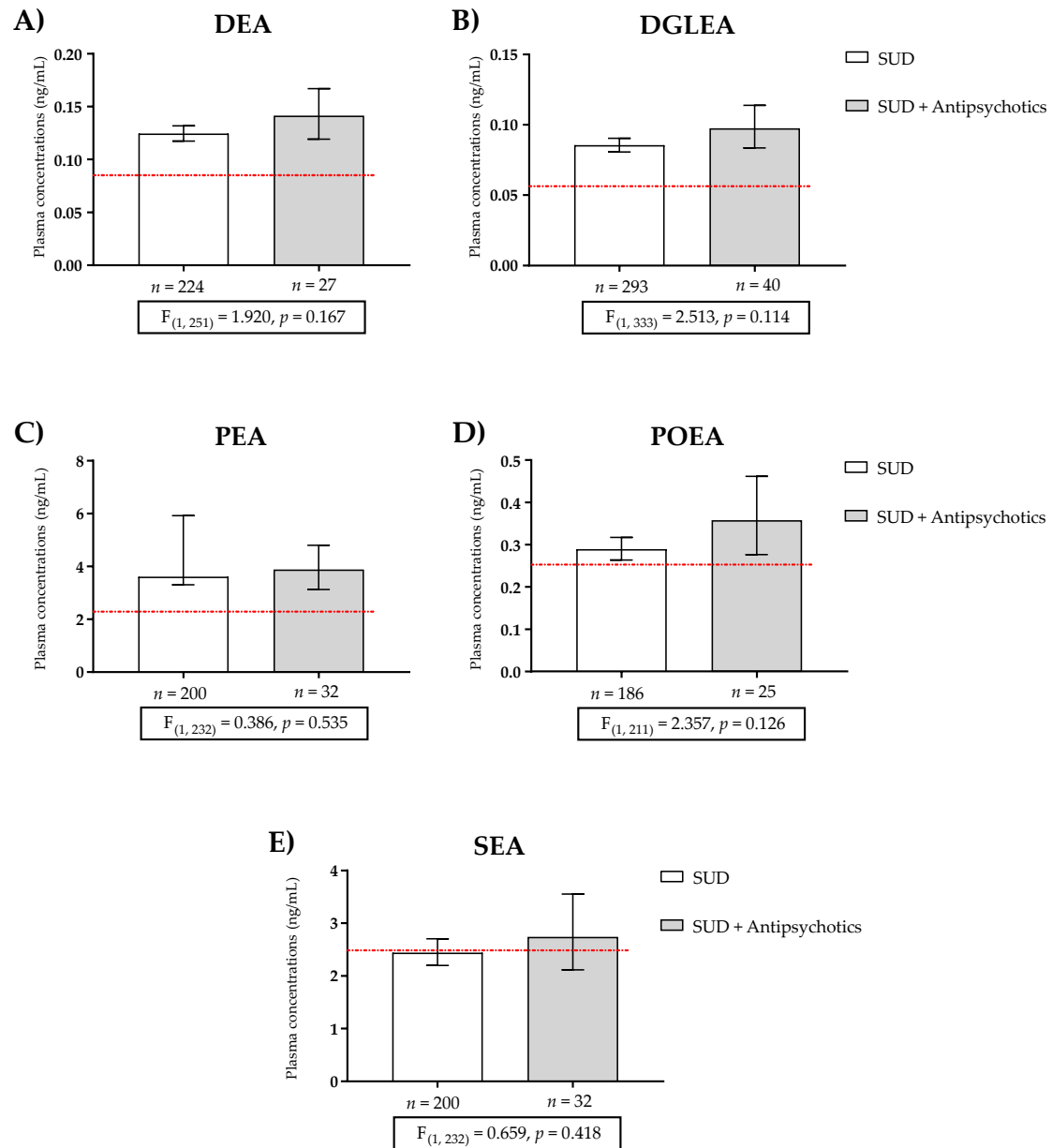


Figure S1. Plasma concentrations of (A) docosatetraenylethanolamide (DEA); (B) dihomog- γ -linolenylethanolamide (DGLEA); (C) palmitoylethanolamide (PEA); (D) palmitoleoylethanolamide (POEA); and (E) stearoylethanolamide (SEA) in patients with substance use disorder (SUD) not using antipsychotics, and patients with SUD using antipsychotics. Red line represents the mean plasma concentration of the control group. Data were analyzed by one-way analysis of covariance (ANCOVA). Bars are the estimated marginal means and 95% confidence intervals (CI).

Figure S2

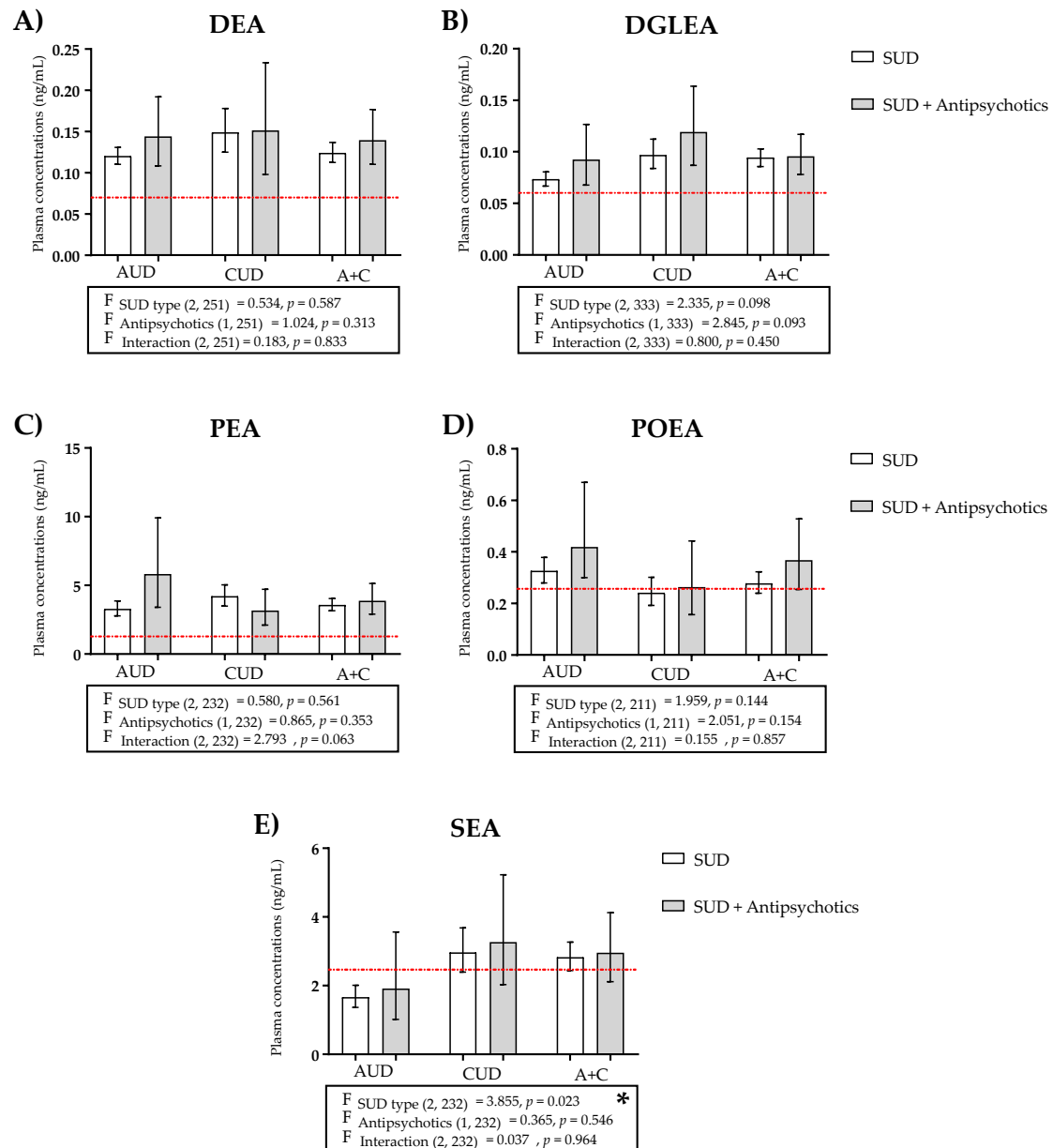


Figure S2. Plasma concentrations of (A) DEA; (B) DGLEA; (C) PEA; (D) POEA; and (E) SEA in patients with SUD not using antipsychotics and patients of SUD using antipsychotics classified on the basis of AUD, CUD or AUD + CUD diagnosis. Red line represents the mean plasma concentration of the control group. Data were analyzed by two-way ANCOVA. Bars are estimated marginal means and 95% CI. (*) $p < 0.05$ for factors (F).