**Supplementary Material for the Article:**

**Adolescent cannabis use and adult psychoticism:**

**A longitudinal co-twin control analysis using data from two cohorts**

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**Supplemental Table 1.** Results fromindividual-level models predicting adult psychoticism as a function of the cannabis use index as well as mean scores on its constituent items (i.e., frequency of cannabis use, number of uses).

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  |  | **Individual-level models** | | |
| **Exposure** | **Psychoticism Scale** | **N** | **Estimate (95% CI)** | ***p* value** | |
| Cumulative Adolescent Cannabis Use Index | PID-5 Psychoticism | 1544 | 0.14 (0.09, 0.19) | <0.001 | |
| *Unusual Beliefs & Experiences* | 0.12 (0.07, 0.17) | <0.001 | |
| *Eccentricity* | 0.10 (0.05, 0.15) | <0.001 | |
| *Perceptual Dysregulation* | 0.16 (0.11, 0.21) | <0.001 | |
| Frequency of Cannabis Use | PID-5 Psychoticism | 1544 | 0.13 (0.08, 0.18) | <0.001 | |
| *Unusual Beliefs & Experiences* | 0.11 (0.06, 0.16) | <0.001 | |
| *Eccentricity* | 0.10 (0.05, 0.15) | <0.001 | |
| *Perceptual Dysregulation* | 0.14 (0.09, 0.19) | <0.001 | |
| Number of Uses | PID-5 Psychoticism | 1544 | 0.13 (0.08, 0.19) | <0.001 | |
| *Unusual Beliefs & Experiences* | 0.12 (0.07, 0.17) | <0.001 | |
| *Eccentricity* | 0.10 (0.05, 0.15) | <0.001 | |
| *Perceptual Dysregulation* | 0.15 (0.10, 0.20) | <0.001 | |

*Notes.* Individual-level analyses examined associations between cumulative adolescent cannabis use index or mean scores on constituent items and young adult scores on the PID-5 Psychoticism factor or its facets. Estimates are reported as standardized betas, reflecting the standard deviation increase in Psychoticism associated with each standard deviation increase in each measure of cumulative cannabis use. The number of complete pairs contributing data to each set of analyses is 679 for the cannabis use index and 644 for cannabis use disorder. The number of families contributing data to each set of analyses is 865 for the cannabis use index and 814 for cannabis use disorder. All models included participant age, sex, zygosity, and cohort as covariates. CI = confidence interval.

**Supplemental Table 2.** Results fromco-twin control models predicting adult psychoticism as a function of the cannabis use index as well as mean scores on its constituent items (i.e., frequency of cannabis use, number of uses).

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  | **Co-twin control models** | | | | | | |
|  |  |  | **Between-pair effect** | | |  | | **Within-pair effect** | | |
| **Exposure** | **Psychoticism Scale** | **N** |  | **Estimate (95% CI)** | ***p* value** | |  | | **Estimate (95% CI)** | ***p* value** |
| Cumulative Adolescent Cannabis Use Index | PID-5 Psychoticism | 1544 |  | 0.18 (0.12, 0.24) | <0.001 | |  | | 0.00 (-0.10, 0.10) | 0.965 |
| *Unusual Beliefs & Experiences* |  | 0.16 (0.11, 0.22) | <0.001 | |  | | -0.01 (-0.12, 0.09) | 0.840 |
| *Eccentricity* |  | 0.14 (0.08, 0.20) | <0.001 | |  | | 0.00 (-0.09, 0.10) | 0.930 |
| *Perceptual Dysregulation* |  | 0.20 (0.14, 0.26) | <0.001 | |  | | 0.01 (-0.09, 0.12) | 0.805 |
| Frequency of Cannabis Use | PID-5 Psychoticism | 1544 |  | 0.19 (0.13, 0.25) | <0.001 | |  | | -0.02 (-0.11, 0.07) | 0.598 |
| *Unusual Beliefs & Experiences* |  | 0.17 (0.11, 0.23) | <0.001 | |  | | -0.04 (-0.14, 0.05) | 0.380 |
| *Eccentricity* |  | 0.15 (0.09, 0.21) | <0.001 | |  | | -0.01 (-0.10, 0.08) | 0.813 |
| *Perceptual Dysregulation* |  | 0.21 (0.15, 0.26) | <0.001 | |  | | -0.01 (-0.11, 0.08) | 0.779 |
| Number of Uses | PID-5 Psychoticism | 1544 |  | 0.17 (0.11, 0.23) | <0.001 | |  | | 0.02 (-0.08, 0.12) | 0.696 |
| *Unusual Beliefs & Experiences* |  | 0.15 (0.10, 0.21) | <0.001 | |  | | 0.02 (-0.09, 0.12) | 0.750 |
| *Eccentricity* |  | 0.13 (0.07, 0.19) | <0.001 | |  | | 0.02 (-0.08, 0.12) | 0.691 |
| *Perceptual Dysregulation* |  | 0.19 (0.13, 0.25) | <0.001 | |  | | 0.01 (-0.09, 0.12) | 0.810 |

*Notes.*Co-twin control analyses decompose effects from individual-level models into between-pair (reflecting pre-existing, shared familial liability) and within-pair (cannabis exposure) effects.Estimates are reported as standardized betas, reflecting the standard deviation increase in Psychoticism associated either with each standard deviation increase in each measure of cumulative cannabis use. Because standardization was conducted at the phenotypic level, betas for the within-pair effects of the adolescent cannabis use index should be interpreted in terms of the SD for the entire sample rather than the SD of twin differences. The number of complete pairs contributing data to each set of analyses is 679 for the cannabis use index and 644 for cannabis use disorder. The number of families contributing data to each set of analyses is 865 for the cannabis use index and 814 for cannabis use disorder. All models included participant age, sex, zygosity, and cohort as covariates. CI = confidence interval.

**Supplemental Table 3.** Full results from individual-level models testing for associations between adolescent cannabis exposure and adult psychoticism.

1. **Cumulative Adolescent Cannabis Use Index**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | |  | **Outcome** | | | |
| **Predictors** | **N** |  | **Psychoticism** | | | **Unusual Beliefs & Experiences** | **Eccentricity** | **Perceptual Dysregulation** |
| Cannabis Use Index |  |  | 0.14\*\*\* | | | 0.12\*\*\* | 0.10\*\*\* | 0.16\*\*\* |
|  |  | ( 0.09, 0.19) | | | ( 0.07, 0.17) | ( 0.05, 0.15) | ( 0.11, 0.21) |
| Sex (ref: female) |  |  | 0.39\*\*\* | | | 0.34\*\*\* | 0.40\*\*\* | 0.23\*\*\* |
|  |  | ( 0.26, 0.51) | | | ( 0.22, 0.46) | ( 0.28, 0.53) | ( 0.11, 0.36) |
| Zygosity (ref: DZ) | 1544 |  | -0.04 | | | -0.01 | -0.04 | -0.04 |
|  |  | (-0.15, 0.08) | | | (-0.12, 0.10) | (-0.15, 0.07) | (-0.15, 0.07) |
| Age |  |  | -0.35\* | | | -0.18 | -0.37\* | -0.36\* |
|  |  | (-0.63, -0.07) | | | (-0.46, 0.10) | (-0.65, -0.09) | (-0.64, -0.08) |
| Cohort (ref: Cohort 2) |  |  | -0.28 | | | -0.11 | -0.31 | -0.31 |
|  |  | (-0.85, 0.28) | | | (-0.67, 0.45) | (-0.88, 0.25) | (-0.87, 0.25) |

1. **Adolescent Cannabis Use Disorder**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | |  | **Outcome** | | | |
| **Predictors** | **N** |  | **Psychoticism** | | | **Unusual Beliefs & Experiences** | **Eccentricity** | **Perceptual Dysregulation** |
| Cannabis Use Disorder (ref: absent) |  |  | 0.35\*\*\* | | | 0.31\*\*\* | 0.29\*\*\* | 0.36\*\*\* |
|  |  | ( 0.20, 0.50) | | | ( 0.16, 0.47) | ( 0.14, 0.44) | ( 0.21, 0.52) |
| Sex (ref: female) |  |  | 0.40\*\*\* | | | 0.35\*\*\* | 0.41\*\*\* | 0.26\*\*\* |
|  |  | ( 0.27, 0.53) | | | ( 0.22, 0.48) | ( 0.28, 0.54) | ( 0.13, 0.38) |
| Zygosity (ref: DZ) | 1458 |  | -0.03 | | | 0.01 | -0.03 | -0.05 |
|  |  | (-0.14, 0.09) | | | (-0.11, 0.12) | (-0.15, 0.08) | (-0.16, 0.07) |
| Age |  |  | -0.37\* | | | -0.21 | -0.38\* | -0.39\*\* |
|  |  | (-0.67, -0.08) | | | (-0.50, 0.08) | (-0.68, -0.09) | (-0.68, -0.09) |
| Cohort (ref: Cohort 2) |  |  | -0.31 | | | -0.15 | -0.32 | -0.35 |
|  |  | (-0.90, 0.27) | | | (-0.73, 0.43) | (-0.91, 0.26) | (-0.93, 0.23) |

*Notes.* Individual-level analyses examined associations between (A) cumulative adolescent cannabis use index or (B) adolescent cannabis use disorder diagnosis and young adult scores on the PID-5 Psychoticism factor and its facets. Estimates for continuous predictors are reported as standardized betas with 95% confidence intervals, reflecting the standard deviation increase in each outcome associated with a standard deviation increase in each predictor. Estimates for binary predictors are standardized betas with 95% confidence intervals reflecting the difference in each outcome associated with scoring a “1” on this variable (vs. “0” for the reference category). The number of complete pairs contributing data to each set of analyses is 679 for the cannabis use index and 644 for cannabis use disorder. The number of families contributing data to each set of analyses is 865 for the cannabis use index and 814 for cannabis use disorder. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001

**Supplemental Table 4.** Results from cohort-specificindividual-level models of adolescent cannabis exposure and adult psychoticism.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | **Combined sample** | | |  | | **Cohort 1** | | | | |  | **Cohort 2** | | | |
| **Exposure** | **Psychoticism Scale** | **N** | **Estimate (95% CI)** | ***p* value** | |  | | **N** | **Estimate (95% CI)** | ***p* value** |  | | | **N** | **Estimate (95% CI)** | ***p* value** |
| Cumulative Adolescent Cannabis Use Index | PID-5 Psychoticism | 1544 | 0.14 (0.09, 0.19) | <0.001 | |  | | 724 | 0.16 (0.08, 0.24) | <0.001 |  | | | 820 | 0.12 (0.06, 0.18) | <0.001 |
| *Unusual Beliefs & Experiences* | 0.12 (0.07, 0.17) | <0.001 | |  | | 0.14 (0.06, 0.22) | <0.001 |  | | | 0.11 (0.04, 0.17) | 0.001 |
| *Eccentricity* | 0.10 (0.05, 0.15) | <0.001 | |  | | 0.12 (0.04, 0.21) | 0.004 |  | | | 0.09 (0.03, 0.15) | 0.006 |
| *Perceptual Dysregulation* | 0.16 (0.11, 0.21) | <0.001 | |  | | 0.19 (0.10, 0.27) | <0.001 |  | | | 0.13 (0.07, 0.19) | <0.001 |
| Adolescent Cannabis Use Disorder | PID-5 Psychoticism | 1458 | 0.35 (0.20, 0.50) | <0.001 | |  | | 688 | 0.60 (0.35, 0.84) | <0.001 |  | | | 770 | 0.13 (-0.05, 0.31) | 0.160 |
| *Unusual Beliefs & Experiences* | 0.31 (0.16, 0.47) | <0.001 | |  | | 0.57 (0.33, 0.81) | <0.001 |  | | | 0.09 (-0.11, 0.28) | 0.379 |
| *Eccentricity* | 0.29 (0.14, 0.44) | <0.001 | |  | | 0.48 (0.24, 0.73) | <0.001 |  | | | 0.13 (-0.06, 0.31) | 0.178 |
| *Perceptual Dysregulation* | 0.36 (0.21, 0.52) | <0.001 | |  | | 0.60 (0.34, 0.85) | <0.001 |  | | | 0.17 (-0.01, 0.35) | 0.067 |

*Note:* Individual-level analyses examined associations between cumulative adolescent cannabis use index or adolescent cannabis use disorder diagnosis and young adult scores on the PID-5 Psychoticism factor and its facets. Estimates are reported as standardized betas, reflecting the standard deviation increase in Psychoticism associated either (a) with each standard deviation increase in cumulative adolescent cannabis use or (b) with an adolescent cannabis use disorder diagnosis (vs. not receiving this diagnosis). The number of complete pairs contributing data to each set of analyses is 679 for the cannabis use index and 644 for cannabis use disorder. The number of families contributing data to each set of analyses is 865 for the cannabis use index and 814 for cannabis use disorder. All models included participant age, sex, zygosity, and cohort as covariates. CI = confidence interval.

**Supplemental Table 5.** Cohort-specificco-twin control models of adolescent cannabis exposure and adult psychoticism.

**A. Full Analytic Sample**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Between-pair effect** | | |  | | **Within-pair effect** | | |
| **Exposure** | **Psychoticism Scale** | **N** | **Estimate (95% CI)** | ***p* value** |  | | **Estimate (95% CI)** | | ***p* value** |
| Cumulative Adolescent Cannabis Use Index | PID-5 Psychoticism | 1544 | 0.18 (0.12, 0.24) | <0.001 |  | | 0.00 (-0.10, 0.10) | | 0.965 |
| *Unusual Beliefs & Experiences* | 0.16 (0.11, 0.22) | <0.001 |  | | -0.01 (-0.12, 0.09) | | 0.840 |
| *Eccentricity* | 0.14 (0.08, 0.20) | <0.001 |  | | 0.00 (-0.09, 0.10) | | 0.930 |
| *Perceptual Dysregulation* | 0.20 (0.14, 0.26) | <0.001 |  | | 0.01 (-0.09, 0.12) | | 0.805 |
| Adolescent Cannabis Use Disorder | PID-5 Psychoticism | 1458 | 0.55 (0.36, 0.74) | <0.001 |  | | 0.02 (-0.22, 0.26) | | 0.865 |
| *Unusual Beliefs & Experiences* | 0.48 (0.29, 0.67) | <0.001 |  | | 0.00 (-0.27, 0.26) | | 0.980 |
| *Eccentricity* | 0.43 (0.24, 0.62) | <0.001 |  | | 0.06 (-0.18, 0.31) | | 0.607 |
| *Perceptual Dysregulation* | 0.59 (0.40, 0.78) | <0.001 |  | | -0.04 (-0.29, 0.22) | | 0.784 |

**B. Cohort 1**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Between-pair effect** | | |  | | **Within-pair effect** | | |
| **Exposure** | **Psychoticism Scale** | **N** |  | **Estimate (95% CI)** | ***p* value** | |  | | **Estimate (95% CI)** | ***p* value** |
| Cumulative Adolescent Cannabis Use Index | PID-5 Psychoticism | 724 |  | 0.20 (0.11, 0.30) | <0.001 | |  | | 0.00 (-0.19, 0.18) | 0.960 |
| *Unusual Beliefs & Experiences* |  | 0.17 (0.08, 0.26) | <0.001 | |  | | 0.01 (-0.19, 0.20) | 0.936 |
| *Eccentricity* |  | 0.16 (0.06, 0.25) | 0.001 | |  | | -0.01 (-0.20, 0.17) | 0.890 |
| *Perceptual Dysregulation* |  | 0.23 (0.14, 0.33) | <0.001 | |  | | 0.00 (-0.19, 0.19) | 0.988 |
| Adolescent Cannabis Use Disorder | PID-5 Psychoticism | 688 |  | 0.78 (0.49, 1.08) | <0.001 | |  | | 0.22 (-0.21, 0.64) | 0.318 |
| *Unusual Beliefs & Experiences* |  | 0.66 (0.38, 0.95) | <0.001 | |  | | 0.32 (-0.14, 0.78) | 0.170 |
| *Eccentricity* |  | 0.61 (0.32, 0.91) | <0.001 | |  | | 0.21 (-0.22, 0.64) | 0.335 |
| *Perceptual Dysregulation* |  | 0.86 (0.56, 1.16) | <0.001 | |  | | 0.00 (-0.45, 0.45) | 0.995 |

**C. Cohort 2**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Between-pair effect** | | |  | | **Within-pair effect** | | |
| **Exposure** | **Psychoticism Scale** | **N** |  | **Estimate (95% CI)** | ***p* value** | |  | | **Estimate (95% CI)** | ***p* value** |
| Cumulative Adolescent Cannabis Use Index | PID-5 Psychoticism | 820 |  | 0.16 (0.09, 0.24) | <0.001 | |  | | 0.00 (-0.11, 0.12) | 0.939 |
| *Unusual Beliefs & Experiences* |  | 0.16 (0.08, 0.23) | <0.001 | |  | | -0.02 (-0.14, 0.10) | 0.719 |
| *Eccentricity* |  | 0.12 (0.05, 0.19) | 0.002 | |  | | 0.01 (-0.10, 0.13) | 0.823 |
| *Perceptual Dysregulation* |  | 0.18 (0.11, 0.24) | <0.001 | |  | | 0.02 (-0.09, 0.13) | 0.730 |
| Adolescent Cannabis Use Disorder | PID-5 Psychoticism | 770 |  | 0.32 (0.08, 0.56) | 0.010 | |  | | -0.11 (-0.39, 0.16) | 0.432 |
| *Unusual Beliefs & Experiences* |  | 0.30 (0.05, 0.55) | 0.020 | |  | | -0.22 (-0.52, 0.08) | 0.150 |
| *Eccentricity* |  | 0.24 (0.00, 0.49) | 0.050 | |  | | -0.03 (-0.32, 0.25) | 0.827 |
| *Perceptual Dysregulation* |  | 0.33 (0.10, 0.56) | 0.006 | |  | | -0.06 (-0.34, 0.22) | 0.662 |

*Note:* Co-twin control analyses decompose effects from individual-level models into between-pair (reflecting pre-existing, shared familial liability) and within-pair (cannabis exposure) effects. Because standardization was conducted at the phenotypic level, betas for the within-pair effects of the adolescent cannabis use index should be interpreted in terms of the SD for the entire sample rather than the SD of twin differences. All models included participant age, sex, zygosity, and cohort as covariates. CI = confidence interval.

**Supplemental Table 6.** Full results from co-twin control models testing for associations between adolescent cannabis exposure and adult psychoticism.

1. **Cumulative Adolescent Cannabis Use Index**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | |  | **Outcome** | | | |
| **Predictors** | **N** |  | **Psychoticism** | | | **Unusual Beliefs & Experiences** | **Eccentricity** | **Perceptual Dysregulation** |
| Between-Pair Effect | 1544 |  | 0.18\*\*\* | | | 0.16\*\*\* | 0.14\*\*\* | 0.20\*\*\* |
|  | ( 0.12, 0.24) | | | ( 0.11, 0.22) | ( 0.08, 0.20) | ( 0.14, 0.26) |
| Within-Pair Effect |  | 0.00 | | | -0.01 | 0.00 | 0.01 |
|  | (-0.10, 0.10) | | | (-0.12, 0.09) | (-0.09, 0.10) | (-0.09, 0.12) |
| Sex (ref: female) |  | 0.38\*\*\* | | | 0.33\*\*\* | 0.40\*\*\* | 0.23\*\*\* |
|  | ( 0.25, 0.50) | | | ( 0.21, 0.46) | ( 0.27, 0.52) | ( 0.10, 0.35) |
| Zygosity (ref: DZ) |  | -0.03 | | | -0.01 | -0.03 | -0.03 |
|  | (-0.14, 0.08) | | | (-0.12, 0.10) | (-0.15, 0.08) | (-0.14, 0.08) |
| Age |  | -0.35\* | | | -0.18 | -0.37\*\* | -0.36\* |
|  | (-0.64, -0.07) | | | (-0.46, 0.10) | (-0.66, -0.09) | (-0.64, -0.08) |
| Cohort (ref: Cohort 2) |  | -0.29 | | | -0.11 | -0.32 | -0.31 |
|  | (-0.85, 0.27) | | | (-0.67, 0.45) | (-0.88, 0.25) | (-0.87, 0.25) |

1. **Adolescent Cannabis Use Disorder**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  |  | | |  | **Outcome** | | | |
| **Predictors** | **N** |  | **Psychoticism** | | | **Unusual Beliefs & Experiences** | **Eccentricity** | **Perceptual Dysregulation** |
| Between-Pair Effect | 1458 |  | 0.55\*\*\* | | | 0.48\*\*\* | 0.43\*\*\* | 0.59\*\*\* |
|  | ( 0.36, 0.74) | | | ( 0.29, 0.67) | ( 0.24, 0.62) | ( 0.40, 0.78) |
| Within-Pair Effect |  | 0.02 | | | -0.00 | 0.06 | -0.04 |
|  | (-0.22, 0.26) | | | (-0.27, 0.26) | (-0.18, 0.31) | (-0.29, 0.22) |
| Sex (ref: female) |  | 0.39\*\*\* | | | 0.34\*\*\* | 0.40\*\*\* | 0.24\*\*\* |
|  | ( 0.26, 0.51) | | | ( 0.21, 0.47) | ( 0.27, 0.53) | ( 0.11, 0.37) |
| Zygosity (ref: DZ) |  | -0.02 | | | 0.01 | -0.03 | -0.04 |
|  | (-0.13, 0.09) | | | (-0.10, 0.13) | (-0.14, 0.09) | (-0.15, 0.08) |
| Age |  | -0.39\*\* | | | -0.22 | -0.40\*\* | -0.41\*\* |
|  | (-0.68, -0.10) | | | (-0.51, 0.07) | (-0.69, -0.10) | (-0.70, -0.11) |
| Cohort (ref: Cohort 2) |  | -0.34 | | | -0.17 | -0.34 | -0.39 |
|  | (-0.93, 0.24) | | | (-0.75, 0.41) | (-0.93, 0.24) | (-0.97, 0.20) |

*Notes.* Co-twin control analyses decompose effects from individual-level models into between-pair (reflecting pre-existing, shared familial liability) and within-pair (cannabis exposure) effects. Estimates for continuous predictors are reported as standardized betas with 95% confidence intervals, reflecting the standard deviation increase in each outcome associated with a standard deviation increase in each predictor. Estimates for binary predictors are standardized betas with 95% confidence intervals reflecting the difference in each outcome associated with scoring a “1” on this variable (vs. “0” for the reference category). Because standardization was conducted at the phenotypic level, betas for the within-pair effects of the adolescent cannabis use index should be interpreted in terms of the SD for the entire sample rather than the SD of twin differences. The number of complete pairs contributing data to each set of analyses is 679 for the cannabis use index and 644 for cannabis use disorder. The number of families contributing data to each set of analyses is 865 for the cannabis use index and 814 for cannabis use disorder. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001

**Supplemental Table 7.** Results from discordant twin analyses involving only pairs in which one twin scored ≥2 on our cannabis use index for at least one wave and the other twin reported complete cannabis abstinence.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Psychoticism Scale** | **N** |  | **Estimate (95% CI)** | ***p* value** |
| PID-5 Psychoticism | 82 |  | 0.06 (-0.29, 0.40) | 0.750 |
| *Unusual Beliefs & Experiences* |  | -0.09 (-0.42, 0.24) | 0.593 |
| *Eccentricity* |  | 0.13 (-0.23, 0.49) | 0.470 |
| *Perceptual Dysregulation* |  | 0.07 (-0.26, 0.41) | 0.660 |

*Note:* Estimates from discordant twin analyses reflect the standardized mean difference in Psychoticism scores between twins with at least one period of at least moderate adolescent cannabis use (score of ≥ 2 on our cannabis use index at any wave) and co-twins who reported no adolescent cannabis use. All models included participant age, sex, zygosity, and cohort as covariates. CI = confidence interval.

**Supplemental Table 8.** Full model results from tests for incremental and interaction effects between adolescent cannabis exposure and polygenic risk of schizophrenia in predicting adult psychoticism.

**A. Psychoticism**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Predictors** | **Psychoticism** | | | |
| **1** | **2** | **3** |
| SCHZ-PGS | 0.08\*\* | 0.07\* | 0.17 |
| (0.03, 0.14) | (0.02, 0.13) | (-0.09, 0.43) |
| Cannabis Use Index | - | 0.12\*\*\* | 0.10 |
| (0.07, 0.18) | (-0.17, 0.36) |
| SCHZ-PGS \* Cannabis Use Index | - | - | 0.01 |
| (-0.05, 0.07) |
| PC1 | 0.00 | -0.01 | 0.02 |
| (-0.06, 0.05) | (-0.06, 0.05) | (-0.05, 0.09) |
| PC2 | 0.01 | 0.01 | 0.01 |
| (-0.04, 0.07) | (-0.05, 0.07) | (-0.05, 0.07) |
| PC3 | 0.03 | 0.04 | 0.02 |
| (-0.03, 0.09) | (-0.02, 0.10) | (-0.04, 0.08) |
| PC4 | -0.03 | -0.04 | -0.06\* |
| (-0.09, 0.02) | (-0.02, 0.10) | (-0.12, -0.00) |
| PC5 | 0.05 | 0.04 | 0.04 |
| (-0.01, 0.10) | (-0.02, 0.10) | (-0.02, 0.11) |
| PC6 | -0.02 | -0.02 | 0.00 |
| (-0.08, 0.04) | (-0.07, 0.04) | (-0.06, 0.06) |
| PC7 | -0.04 | -0.04 | -0.03 |
| (-0.10, 0.01) | (-0.10, 0.02) | (-0.09, 0.03) |
| PC8 | -0.03 | -0.03 | -0.03 |
| (-0.09, 0.03) | (-0.08, 0.03) | (-0.09, 0.03) |
| PC9 | 0.02 | 0.02 | 0.01 |
| (-0.04, 0.08) | (-0.08, 0.04) | (-0.06, 0.07) |
| PC10 | -0.02 | -0.02 | -0.03 |
| (-0.08, 0.04) | (-0.08, 0.04) | (-0.09, 0.04) |
| Sex (ref: female) | 0.37\*\*\* | 0.36\*\*\* | 0.33\*\*\* |
| (0.24, 0.51) | (0.23, 0.49) | ( 0.20, 0.47) |
| Cohort (ref: Cohort 2) | -0.27 | -0.33 | -0.28 |
| (-0.88, 0.34) | (-0.93, 0.28) | (-0.88, 0.32) |
| Age | -0.34\* | -0.38\* | -0.35\* |
| (-0.64, -0.04) | (-0.68, -0.08) | (-0.65, -0.05) |
| Zygosity (ref: DZ) | -0.06 | -0.05 | -0.04 |
| (-0.18, 0.06) | (-0.17, 0.06) | (-0.16, 0.08) |
| SCHZ-PGS \* PC1 | - | - | -0.05 |
| (-0.10, 0.00) |
| SCHZ-PGS \* PC2 | - | - | 0.01 |
| (-0.04, 0.07) |
| SCHZ-PGS \* PC3 | - | - | -0.03 |
| (-0.09, 0.02) |
| SCHZ-PGS \* PC4 | - | - | 0.01 |
| (-0.05, 0.07) |
| SCHZ-PGS \* PC5 | - | - | -0.02 |
| (-0.08, 0.04) |
| SCHZ-PGS \* PC6 | - | - | 0.03 |
| (-0.03, 0.09) |
| SCHZ-PGS \* PC7 | - | - | -0.02 |
| (-0.08, 0.04) |
| SCHZ-PGS \* PC8 | - | - | 0.04 |
| (-0.02, 0.10) |
| SCHZ-PGS \* PC9 | - | - | 0.03 |
| (-0.04, 0.10) |
| SCHZ-PGS \* PC10 | - | - | 0.03 |
| (-0.03, 0.09) |
| SCHZ-PGS \* Sex | - | - | 0.01 |
| (-0.12, 0.14) |
| SCHZ-PGS \* Cohort | - | - | -0.27 |
| (-0.87, 0.33) |
| SCHZ-PGS \* Age | - | - | -0.08 |
| (-0.38, 0.23) |
| SCHZ-PGS \* Zygosity | - | - | 0.04 |
| (-0.07, 0.16) |
| Cannabis Use Index \* PC1 | - | - | 0.10\*\*\* |
| ( 0.04, 0.15) |
| Cannabis Use Index \* PC2 | - | - | -0.06\* |
| (-0.12, -0.01) |
| Cannabis Use Index \* PC3 | - | - | -0.04 |
| (-0.10, 0.02) |
| Cannabis Use Index \* PC4 | - | - | 0.01 |
| (-0.06, 0.07) |
| Cannabis Use Index \* PC5 | - | - | 0.01 |
| (-0.05, 0.07) |
| Cannabis Use Index \* PC6 | - | - | 0.08\*\* |
| ( 0.02, 0.14) |
| Cannabis Use Index \* PC7 | - | - | 0.02 |
| (-0.04, 0.09) |
| Cannabis Use Index \* PC8 | - | - | -0.04 |
| (-0.11, 0.03) |
| Cannabis Use Index \* PC9 | - | - | -0.05 |
| (-0.12, 0.03) |
| Cannabis Use Index \* PC10 | - | - | 0.01 |
| (-0.07, 0.08) |
| Cannabis Use Index \* Sex | - | - | -0.06 |
| (-0.18, 0.07) |
| Cannabis Use Index \* Cohort | - | - | 0.05 |
| (-0.51, 0.60) |
| Cannabis Use Index \* Age | - | - | 0.01 |
| (-0.26, 0.29) |
| Cannabis Use Index \* Zygosity | - | - | 0.04 |
| (-0.07, 0.15) |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Predictors** | **PID-5 Psychoticism** | | | |
| **1** | **2** | **3** |
| SCHZ-PGS | 0.08\*\* | 0.08\* | 0.17 |
| (0.03, 0.14) | (0.02, 0.13) | (-0.10, 0.44) |
| Cannabis Use Disorder | - | 0.28\*\*\* | 0.01 |
| (0.12, 0.43) | (-0.78, 0.79) |
| SCHZ-PGS \* Cannabis Use Disorder | - | - | 0.10 |
| (-0.06, 0.26) |
| PC1 | 0.00 | -0.01 | -0.02 |
| (-0.06, 0.05) | (-0.07, 0.04) | (-0.09, 0.06) |
| PC2 | 0.01 | 0.01 | 0.02 |
| (-0.04, 0.07) | (-0.05, 0.07) | (-0.04, 0.08) |
| PC3 | 0.03 | 0.04 | 0.04 |
| (-0.03, 0.09) | (-0.02, 0.10) | (-0.02, 0.11) |
| PC4 | -0.03 | -0.05 | -0.08\* |
| (-0.09, 0.02) | (-0.10, 0.01) | (-0.14, -0.01) |
| PC5 | 0.05 | 0.04 | 0.04 |
| (-0.01, 0.10) | (-0.02, 0.10) | (-0.03, 0.11) |
| PC6 | -0.02 | -0.02 | -0.03 |
| (-0.08, 0.04) | (-0.07, 0.04) | (-0.09, 0.03) |
| PC7 | -0.04 | -0.04 | -0.04 |
| (-0.10, 0.01) | (-0.10, 0.02) | (-0.10, 0.02) |
| PC8 | -0.03 | -0.03 | -0.02 |
| (-0.09, 0.03) | (-0.08, 0.03) | (-0.08, 0.05) |
| PC9 | 0.02 | 0.02 | 0.02 |
| (-0.04, 0.08) | (-0.04, 0.08) | (-0.04, 0.09) |
| PC10 | -0.02 | -0.02 | -0.03 |
| (-0.08, 0.04) | (-0.08, 0.04) | (-0.09, 0.03) |
| Sex (ref: female) | 0.37\*\*\* | 0.36\*\*\* | 0.33\*\*\* |
| (0.24, 0.51) | ( 0.22, 0.49) | ( 0.19, 0.47) |
| Cohort (ref: Cohort 2) | -0.27 | -0.22 | -0.19 |
| (-0.88, 0.34) | (-0.83, 0.39) | (-0.84, 0.46) |
| Age | -0.34\* | -0.33\* | -0.29 |
| (-0.64, -0.04) | (-0.63, -0.02) | (-0.62, 0.04) |
| Zygosity (ref: DZ) | -0.06 | -0.04 | -0.05 |
| (-0.18, 0.06) | (-0.16, 0.08) | (-0.18, 0.08) |
| SCHZ-PGS \* PC1 | - | - | -0.05 |
| (-0.10, 0.01) |
| SCHZ-PGS \* PC2 | - | - | -0.00 |
| (-0.06, 0.06) |
| SCHZ-PGS \* PC3 | - | - | -0.03 |
| (-0.08, 0.03) |
| SCHZ-PGS \* PC4 | - | - | 0.02 |
| (-0.05, 0.08) |
| SCHZ-PGS \* PC5 | - | - | -0.00 |
| (-0.06, 0.06) |
| SCHZ-PGS \* PC6 | - | - | 0.03 |
| (-0.03, 0.09) |
| SCHZ-PGS \* PC7 | - | - | -0.02 |
| (-0.07, 0.04) |
| SCHZ-PGS \* PC8 | - | - | 0.04 |
| (-0.03, 0.10) |
| SCHZ-PGS \* PC9 | - | - | 0.03 |
| (-0.04, 0.10) |
| SCHZ-PGS \* PC10 | - | - | 0.03 |
| (-0.03, 0.09) |
| SCHZ-PGS \* Sex | - | - | 0.02 |
| (-0.11, 0.16) |
| SCHZ-PGS \* Cohort | - | - | -0.30 |
| (-0.92, 0.31) |
| SCHZ-PGS \* Age | - | - | -0.10 |
| (-0.40, 0.21) |
| SCHZ-PGS \* Zygosity | - | - | 0.05 |
| (-0.07, 0.17) |
| Cannabis Use Disorder \* PC1 | - | - | 0.18\* |
| ( 0.03, 0.34) |
| Cannabis Use Disorder \* PC2 | - | - | -0.06 |
| (-0.21, 0.09) |
| Cannabis Use Disorder \* PC3 | - | - | -0.08 |
| (-0.26, 0.11) |
| Cannabis Use Disorder \* PC4 | - | - | 0.11 |
| (-0.07, 0.28) |
| Cannabis Use Disorder \* PC5 | - | - | -0.03 |
| (-0.19, 0.14) |
| Cannabis Use Disorder \* PC6 | - | - | 0.19\* |
| ( 0.02, 0.37) |
| Cannabis Use Disorder \* PC7 | - | - | 0.03 |
| (-0.16, 0.21) |
| Cannabis Use Disorder \* PC8 | - | - | 0.03 |
| (-0.18, 0.23) |
| Cannabis Use Disorder \* PC9 | - | - | -0.06 |
| (-0.27, 0.15) |
| Cannabis Use Disorder \* PC10 | - | - | 0.05 |
| (-0.14, 0.25) |
| Cannabis Use Disorder \* Sex | - | - | 0.06 |
| (-0.31, 0.44) |
| Cannabis Use Disorder \* Cohort | - | - | 0.33 |
| (-1.38, 2.04) |
| Cannabis Use Disorder \* Age | - | - | 0.00 |
| (-0.84, 0.85) |
| Cannabis Use Disorder \* Zygosity | - | - | 0.12 |
| (-0.20, 0.45) |

**B. Unusual Beliefs & Experiences**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Predictors** | **Unusual Beliefs & Experiences** | | | |
| **1** | **2** | **3** |
| SCHZ-PGS | 0.08\*\* | 0.07\* | 0.17 |
| (0.03, 0.14) | (0.02, 0.13) | (-0.09, 0.43) |
| Cannabis Use Index | - | 0.12\*\*\* | 0.10 |
| (0.07, 0.18) | (-0.17, 0.36) |
| SCHZ-PGS \* Cannabis Use Index | - | - | 0.01 |
| (-0.05, 0.07) |
| PC1 | -0.02 | -0.02 | -0.01 |
| (-0.08, 0.04) | (-0.08, 0.03) | (-0.08, 0.06) |
| PC2 | 0.02 | 0.02 | 0.02 |
| (-0.04, 0.08) | (-0.04, 0.07) | (-0.04, 0.07) |
| PC3 | 0.06 | 0.06\* | 0.05 |
| (-0.00, 0.11) | ( 0.00, 0.12) | (-0.01, 0.11) |
| PC4 | -0.03 | -0.04 | -0.06 |
| (-0.09, 0.02) | (-0.10, 0.01) | (-0.12, 0.00) |
| PC5 | 0.03 | 0.03 | 0.02 |
| (-0.02, 0.09) | (-0.03, 0.08) | (-0.05, 0.08) |
| PC6 | -0.02 | -0.02 | 0.00 |
| (-0.08, 0.03) | (-0.07, 0.04) | (-0.05, 0.06) |
| PC7 | -0.03 | -0.03 | -0.02 |
| (-0.09, 0.02) | (-0.09, 0.02) | (-0.08, 0.04) |
| PC8 | -0.04 | -0.04 | -0.04 |
| (-0.10, 0.02) | (-0.09, 0.02) | (-0.10, 0.02) |
| PC9 | 0.01 | 0.01 | -0.00 |
| (-0.05, 0.06) | (-0.05, 0.06) | (-0.06, 0.06) |
| PC10 | -0.01 | -0.01 | -0.01 |
| (-0.07, 0.04) | (-0.07, 0.05) | (-0.07, 0.05) |
| Sex (ref: female) | 0.31\*\*\* | 0.30\*\*\* | 0.28\*\*\* |
| ( 0.18, 0.44) | ( 0.17, 0.43) | ( 0.15, 0.42) |
| Cohort (ref: Cohort 2) | -0.04 | -0.10 | -0.08 |
| (-0.63, 0.55) | (-0.68, 0.49) | (-0.67, 0.51) |
| Age | -0.14 | -0.18 | -0.17 |
| (-0.44, 0.15) | (-0.47, 0.12) | (-0.46, 0.13) |
| Zygosity (ref: DZ) | -0.05 | -0.04 | -0.03 |
| (-0.16, 0.07) | (-0.15, 0.08) | (-0.14, 0.09) |
| SCHZ-PGS \* PC1 | - | - | -0.02 |
| (-0.08, 0.03) |
| SCHZ-PGS \* PC2 | - | - | -0.01 |
| (-0.06, 0.05) |
| SCHZ-PGS \* PC3 | - | - | -0.01 |
| (-0.07, 0.04) |
| SCHZ-PGS \* PC4 | - | - | -0.01 |
| (-0.07, 0.05) |
| SCHZ-PGS \* PC5 | - | - | -0.01 |
| (-0.07, 0.05) |
| SCHZ-PGS \* PC6 | - | - | 0.02 |
| (-0.04, 0.08) |
| SCHZ-PGS \* PC7 | - | - | -0.03 |
| (-0.09, 0.02) |
| SCHZ-PGS \* PC8 | - | - | 0.03 |
| (-0.03, 0.10) |
| SCHZ-PGS \* PC9 | - | - | 0.02 |
| (-0.05, 0.09) |
| SCHZ-PGS \* PC10 | - | - | 0.02 |
| (-0.04, 0.08) |
| SCHZ-PGS \* Sex | - | - | -0.05 |
| (-0.18, 0.08) |
| SCHZ-PGS \* Cohort | - | - | -0.15 |
| (-0.75, 0.45) |
| SCHZ-PGS \* Age | - | - | -0.02 |
| (-0.32, 0.28) |
| SCHZ-PGS \* Zygosity | - | - | 0.05 |
| (-0.06, 0.17) |
| Cannabis Use Index \* PC1 | - | - | 0.09\*\* |
| ( 0.03, 0.14) |
| Cannabis Use Index \* PC2 | - | - | -0.04 |
| (-0.09, 0.01) |
| Cannabis Use Index \* PC3 | - | - | -0.05 |
| (-0.12, 0.01) |
| Cannabis Use Index \* PC4 | - | - | 0.01 |
| (-0.05, 0.07) |
| Cannabis Use Index \* PC5 | - | - | 0.02 |
| (-0.04, 0.08) |
| Cannabis Use Index \* PC6 | - | - | 0.05 |
| (-0.01, 0.10) |
| Cannabis Use Index \* PC7 | - | - | 0.02 |
| (-0.05, 0.09) |
| Cannabis Use Index \* PC8 | - | - | -0.07 |
| (-0.14, 0.00) |
| Cannabis Use Index \* PC9 | - | - | -0.03 |
| (-0.10, 0.05) |
| Cannabis Use Index \* PC10 | - | - | 0.02 |
| (-0.06, 0.10) |
| Cannabis Use Index \* Sex | - | - | -0.06 |
| (-0.19, 0.07) |
| Cannabis Use Index \* Cohort | - | - | 0.13 |
| (-0.43, 0.69) |
| Cannabis Use Index \* Age | - | - | 0.06 |
| (-0.22, 0.34) |
| Cannabis Use Index \* Zygosity | - | - | 0.05 |
| (-0.06, 0.17) |

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| --- | --- | --- | --- | --- |
| **Predictors** | **Unusual Beliefs & Experiences** | | | |
| **1** | **2** | **3** |
| SCHZ-PGS | 0.08\*\* | 0.06\* | 0.15 |
| (0.02, 0.14) | (0.01, 0.12) | (-0.12, 0.41) |
| Cannabis Use Disorder | - | 0.26\*\* | -0.23 |
| (0.10, 0.41) | (-1.02, 0.57) |
| SCHZ-PGS \* Cannabis Use Disorder | - | - | -0.04 |
| (-0.20, 0.12) |
| PC1 | -0.02 | -0.03 | -0.04 |
| (-0.08, 0.04) | (-0.08, 0.03) | (-0.11, 0.03) |
| PC2 | 0.02 | 0.02 | 0.02 |
| (-0.04, 0.08) | (-0.04, 0.07) | (-0.04, 0.08) |
| PC3 | 0.06 | 0.06\* | 0.07\* |
| (-0.00, 0.11) | ( 0.01, 0.12) | ( 0.00, 0.13) |
| PC4 | -0.03 | -0.04 | -0.06\* |
| (-0.09, 0.02) | (-0.10, 0.01) | (-0.12, -0.00) |
| PC5 | 0.03 | 0.02 | 0.02 |
| (-0.02, 0.09) | (-0.03, 0.08) | (-0.05, 0.09) |
| PC6 | -0.02 | -0.02 | -0.02 |
| (-0.08, 0.03) | (-0.07, 0.04) | (-0.08, 0.04) |
| PC7 | -0.03 | -0.03 | -0.03 |
| (-0.09, 0.02) | (-0.09, 0.02) | (-0.09, 0.03) |
| PC8 | -0.04 | -0.03 | -0.03 |
| (-0.10, 0.02) | (-0.09, 0.02) | (-0.09, 0.03) |
| PC9 | 0.01 | 0.01 | 0.01 |
| (-0.05, 0.06) | (-0.05, 0.06) | (-0.05, 0.07) |
| PC10 | -0.01 | -0.01 | -0.02 |
| (-0.07, 0.04) | (-0.07, 0.04) | (-0.08, 0.04) |
| Sex (ref: female) | 0.31\*\*\* | 0.30\*\*\* | 0.29\*\*\* |
| ( 0.18, 0.44) | ( 0.17, 0.43) | ( 0.15, 0.43) |
| Cohort (ref: Cohort 2) | -0.04 | -0.03 | -0.09 |
| (-0.63, 0.55) | (-0.62, 0.57) | (-0.73, 0.55) |
| Age | -0.14 | -0.15 | -0.16 |
| (-0.44, 0.15) | (-0.45, 0.15) | (-0.48, 0.16) |
| Zygosity (ref: DZ) | -0.05 | -0.02 | -0.04 |
| (-0.16, 0.07) | (-0.13, 0.10) | (-0.16, 0.09) |
| SCHZ-PGS \* PC1 | - | - | -0.03 |
| (-0.08, 0.03) |
| SCHZ-PGS \* PC2 | - | - | -0.02 |
| (-0.08, 0.04) |
| SCHZ-PGS \* PC3 | - | - | -0.01 |
| (-0.06, 0.05) |
| SCHZ-PGS \* PC4 | - | - | 0.01 |
| (-0.05, 0.07) |
| SCHZ-PGS \* PC5 | - | - | 0.00 |
| (-0.06, 0.06) |
| SCHZ-PGS \* PC6 | - | - | 0.02 |
| (-0.04, 0.07) |
| SCHZ-PGS \* PC7 | - | - | -0.03 |
| (-0.09, 0.03) |
| SCHZ-PGS \* PC8 | - | - | 0.02 |
| (-0.04, 0.09) |
| SCHZ-PGS \* PC9 | - | - | 0.01 |
| (-0.06, 0.08) |
| SCHZ-PGS \* PC10 | - | - | 0.02 |
| (-0.04, 0.08) |
| SCHZ-PGS \* Sex | - | - | -0.03 |
| (-0.17, 0.10) |
| SCHZ-PGS \* Cohort | - | - | -0.21 |
| (-0.82, 0.39) |
| SCHZ-PGS \* Age | - | - | -0.06 |
| (-0.36, 0.25) |
| SCHZ-PGS \* Zygosity | - | - | 0.07 |
| (-0.05, 0.19) |
| Cannabis Use Disorder \* PC1 | - | - | 0.17\* |
| ( 0.01, 0.33) |
| Cannabis Use Disorder \* PC2 | - | - | 0.04 |
| (-0.11, 0.19) |
| Cannabis Use Disorder \* PC3 | - | - | -0.04 |
| (-0.23, 0.15) |
| Cannabis Use Disorder \* PC4 | - | - | 0.07 |
| (-0.11, 0.25) |
| Cannabis Use Disorder \* PC5 | - | - | -0.01 |
| (-0.17, 0.16) |
| Cannabis Use Disorder \* PC6 | - | - | 0.13 |
| (-0.05, 0.30) |
| Cannabis Use Disorder \* PC7 | - | - | 0.03 |
| (-0.16, 0.23) |
| Cannabis Use Disorder \* PC8 | - | - | 0.03 |
| (-0.18, 0.23) |
| Cannabis Use Disorder \* PC9 | - | - | -0.00 |
| (-0.21, 0.21) |
| Cannabis Use Disorder \* PC10 | - | - | 0.06 |
| (-0.14, 0.25) |
| Cannabis Use Disorder \* Sex | - | - | 0.06 |
| (-0.31, 0.44) |
| Cannabis Use Disorder \* Cohort | - | - | 0.79 |
| (-0.94, 2.52) |
| Cannabis Use Disorder \* Age | - | - | 0.24 |
| (-0.61, 1.09) |
| Cannabis Use Disorder \* Zygosity | - | - | 0.15 |
| (-0.18, 0.48) |

**C. Eccentricity**

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| --- | --- | --- | --- | --- |
| **Predictors** | **Eccentricity** | | | |
| **1** | **2** | **3** |
| SCHZ-PGS | 0.06\* | 0.06 | 0.10 |
| (0.01, 0.12) | (0.00, 0.11) | (-0.17, 0.37) |
| Cannabis Use Index | - | 0.09\*\*\* | 0.13 |
| (0.04, 0.14) | (-0.14, 0.39) |
| SCHZ-PGS \* Cannabis Use Index | - | - | 0.04 |
| (-0.02, 0.10) |
| PC1 | 0.00 | 0.00 | 0.04 |
| (-0.06, 0.06) | (-0.06, 0.06) | (-0.04, 0.11) |
| PC2 | -0.01 | -0.01 | -0.01 |
| (-0.06, 0.05) | (-0.07, 0.05) | (-0.07, 0.05) |
| PC3 | 0.01 | 0.02 | -0.00 |
| (-0.05, 0.07) | (-0.04, 0.08) | (-0.07, 0.06) |
| PC4 | -0.04 | -0.04 | -0.06 |
| (-0.09, 0.02) | (-0.10, 0.02) | (-0.12, 0.00) |
| PC5 | 0.05 | 0.04 | 0.05 |
| (-0.01, 0.10) | (-0.02, 0.10) | (-0.01, 0.12) |
| PC6 | -0.02 | -0.01 | 0.00 |
| (-0.08, 0.04) | (-0.07, 0.04) | (-0.06, 0.06) |
| PC7 | -0.04 | -0.04 | -0.03 |
| (-0.10, 0.02) | (-0.10, 0.02) | (-0.09, 0.03) |
| PC8 | -0.02 | -0.02 | -0.02 |
| (-0.08, 0.04) | (-0.08, 0.04) | (-0.08, 0.05) |
| PC9 | 0.02 | 0.02 | -0.00 |
| (-0.04, 0.07) | (-0.04, 0.08) | (-0.06, 0.06) |
| PC10 | -0.01 | -0.01 | -0.02 |
| (-0.07, 0.05) | (-0.07, 0.05) | (-0.08, 0.05) |
| Sex (ref: female) | 0.39\*\*\* | 0.37\*\*\* | 0.35\*\*\* |
| ( 0.25, 0.52) | ( 0.24, 0.51) | ( 0.21, 0.48) |
| Cohort (ref: Cohort 2) | -0.28 | -0.33 | -0.27 |
| (-0.90, 0.33) | (-0.94, 0.28) | (-0.88, 0.34) |
| Age | -0.35\* | -0.38\* | -0.35\* |
| (-0.66, -0.05) | (-0.68, -0.07) | (-0.65, -0.04) |
| Zygosity (ref: DZ) | -0.06 | -0.05 | -0.04 |
| (-0.18, 0.06) | (-0.17, 0.07) | (-0.16, 0.08) |
| SCHZ-PGS \* PC1 | - | - | -0.06\* |
| (-0.11, -0.01) |
| SCHZ-PGS \* PC2 | - | - | 0.02 |
| (-0.04, 0.08) |
| SCHZ-PGS \* PC3 | - | - | -0.03 |
| (-0.09, 0.03) |
| SCHZ-PGS \* PC4 | - | - | 0.01 |
| (-0.06, 0.07) |
| SCHZ-PGS \* PC5 | - | - | -0.01 |
| (-0.07, 0.05) |
| SCHZ-PGS \* PC6 | - | - | 0.03 |
| (-0.03, 0.09) |
| SCHZ-PGS \* PC7 | - | - | -0.01 |
| (-0.07, 0.05) |
| SCHZ-PGS \* PC8 | - | - | 0.04 |
| (-0.02, 0.10) |
| SCHZ-PGS \* PC9 | - | - | 0.04 |
| (-0.03, 0.11) |
| SCHZ-PGS \* PC10 | - | - | 0.05 |
| (-0.02, 0.11) |
| SCHZ-PGS \* Sex | - | - | 0.02 |
| (-0.11, 0.15) |
| SCHZ-PGS \* Cohort | - | - | -0.13 |
| (-0.74, 0.49) |
| SCHZ-PGS \* Age | - | - | -0.01 |
| (-0.32, 0.30) |
| SCHZ-PGS \* Zygosity | - | - | 0.01 |
| (-0.11, 0.13) |
| Cannabis Use Index \* PC1 | - | - | 0.08\*\* |
| ( 0.03, 0.14) |
| Cannabis Use Index \* PC2 | - | - | -0.07\* |
| (-0.12, -0.01) |
| Cannabis Use Index \* PC3 | - | - | -0.03 |
| (-0.09, 0.04) |
| Cannabis Use Index \* PC4 | - | - | 0.01 |
| (-0.05, 0.07) |
| Cannabis Use Index \* PC5 | - | - | -0.00 |
| (-0.06, 0.06) |
| Cannabis Use Index \* PC6 | - | - | 0.09\*\* |
| ( 0.03, 0.15) |
| Cannabis Use Index \* PC7 | - | - | 0.02 |
| (-0.04, 0.09) |
| Cannabis Use Index \* PC8 | - | - | -0.05 |
| (-0.12, 0.03) |
| Cannabis Use Index \* PC9 | - | - | -0.06 |
| (-0.14, 0.01) |
| Cannabis Use Index \* PC10 | - | - | -0.00 |
| (-0.08, 0.08) |
| Cannabis Use Index \* Sex | - | - | -0.02 |
| (-0.15, 0.11) |
| Cannabis Use Index \* Cohort | - | - | -0.12 |
| (-0.68, 0.44) |
| Cannabis Use Index \* Age | - | - | -0.06 |
| (-0.34, 0.21) |
| Cannabis Use Index \* Zygosity | - | - | 0.03 |
| (-0.08, 0.14) |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Predictors** | **Eccentricity** | | | |
| **1** | **2** | **3** |
| SCHZ-PGS | 0.06\* | 0.06\* | 0.07 |
| (0.01, 0.12) | (0.00, 0.12) | (-0.20, 0.35) |
| Cannabis Use Disorder | - | 0.23\*\* | 0.39 |
| (0.08, 0.39) | (-0.41, 1.18) |
| SCHZ-PGS \* Cannabis Use Disorder | - | - | 0.12 |
| (-0.04, 0.28) |
| PC1 | 0.00 | -0.01 | 0.00 |
| (-0.06, 0.06) | (-0.06, 0.05) | (-0.07, 0.08) |
| PC2 | -0.01 | -0.01 | 0.01 |
| (-0.06, 0.05) | (-0.07, 0.05) | (-0.06, 0.07) |
| PC3 | 0.01 | 0.02 | 0.02 |
| (-0.05, 0.07) | (-0.04, 0.08) | (-0.05, 0.08) |
| PC4 | -0.04 | -0.05 | -0.08\* |
| (-0.09, 0.02) | (-0.10, 0.01) | (-0.14, -0.01) |
| PC5 | 0.05 | 0.04 | 0.05 |
| (-0.01, 0.10) | (-0.02, 0.10) | (-0.02, 0.12) |
| PC6 | -0.02 | -0.01 | -0.03 |
| (-0.08, 0.04) | (-0.07, 0.05) | (-0.09, 0.03) |
| PC7 | -0.04 | -0.04 | -0.04 |
| (-0.10, 0.02) | (-0.10, 0.02) | (-0.10, 0.02) |
| PC8 | -0.02 | -0.02 | -0.00 |
| (-0.08, 0.04) | (-0.08, 0.04) | (-0.06, 0.06) |
| PC9 | 0.02 | 0.02 | 0.02 |
| (-0.04, 0.07) | (-0.04, 0.08) | (-0.04, 0.09) |
| PC10 | -0.01 | -0.01 | -0.02 |
| (-0.07, 0.05) | (-0.07, 0.05) | (-0.08, 0.05) |
| Sex (ref: female) | 0.39\*\*\* | 0.37\*\*\* | 0.34\*\*\* |
| ( 0.25, 0.52) | ( 0.23, 0.50) | ( 0.19, 0.48) |
| Cohort (ref: Cohort 2) | -0.28 | -0.23 | -0.10 |
| (-0.90, 0.33) | (-0.85, 0.39) | (-0.76, 0.56) |
| Age | -0.35\* | -0.33\* | -0.25 |
| (-0.66, -0.05) | (-0.65, -0.02) | (-0.58, 0.09) |
| Zygosity (ref: DZ) | -0.06 | -0.04 | -0.05 |
| (-0.18, 0.06) | (-0.16, 0.08) | (-0.18, 0.08) |
| SCHZ-PGS \* PC1 | - | - | -0.06\* |
| (-0.11, -0.00) |
| SCHZ-PGS \* PC2 | - | - | 0.01 |
| (-0.05, 0.07) |
| SCHZ-PGS \* PC3 | - | - | -0.03 |
| (-0.08, 0.03) |
| SCHZ-PGS \* PC4 | - | - | 0.01 |
| (-0.06, 0.07) |
| SCHZ-PGS \* PC5 | - | - | -0.00 |
| (-0.06, 0.06) |
| SCHZ-PGS \* PC6 | - | - | 0.03 |
| (-0.02, 0.09) |
| SCHZ-PGS \* PC7 | - | - | -0.01 |
| (-0.07, 0.05) |
| SCHZ-PGS \* PC8 | - | - | 0.04 |
| (-0.02, 0.11) |
| SCHZ-PGS \* PC9 | - | - | 0.05 |
| (-0.02, 0.12) |
| SCHZ-PGS \* PC10 | - | - | 0.05 |
| (-0.01, 0.11) |
| SCHZ-PGS \* Sex | - | - | 0.03 |
| (-0.11, 0.16) |
| SCHZ-PGS \* Cohort | - | - | -0.10 |
| (-0.72, 0.52) |
| SCHZ-PGS \* Age | - | - | 0.01 |
| (-0.30, 0.32) |
| SCHZ-PGS \* Zygosity | - | - | 0.01 |
| (-0.11, 0.13) |
| Cannabis Use Disorder \* PC1 | - | - | 0.15 |
| (-0.01, 0.31) |
| Cannabis Use Disorder \* PC2 | - | - | -0.13 |
| (-0.28, 0.02) |
| Cannabis Use Disorder \* PC3 | - | - | -0.06 |
| (-0.25, 0.13) |
| Cannabis Use Disorder \* PC4 | - | - | 0.08 |
| (-0.10, 0.26) |
| Cannabis Use Disorder \* PC5 | - | - | -0.01 |
| (-0.17, 0.16) |
| Cannabis Use Disorder \* PC6 | - | - | 0.22\* |
| ( 0.04, 0.40) |
| Cannabis Use Disorder \* PC7 | - | - | 0.03 |
| (-0.16, 0.22) |
| Cannabis Use Disorder \* PC8 | - | - | -0.04 |
| (-0.25, 0.16) |
| Cannabis Use Disorder \* PC9 | - | - | -0.14 |
| (-0.35, 0.07) |
| Cannabis Use Disorder \* PC10 | - | - | 0.03 |
| (-0.17, 0.22) |
| Cannabis Use Disorder \* Sex | - | - | 0.05 |
| (-0.33, 0.43) |
| Cannabis Use Disorder \* Cohort | - | - | -0.57 |
| (-2.30, 1.16) |
| Cannabis Use Disorder \* Age | - | - | -0.39 |
| (-1.25, 0.46) |
| Cannabis Use Disorder \* Zygosity | - | - | 0.14 |
| (-0.19, 0.47) |

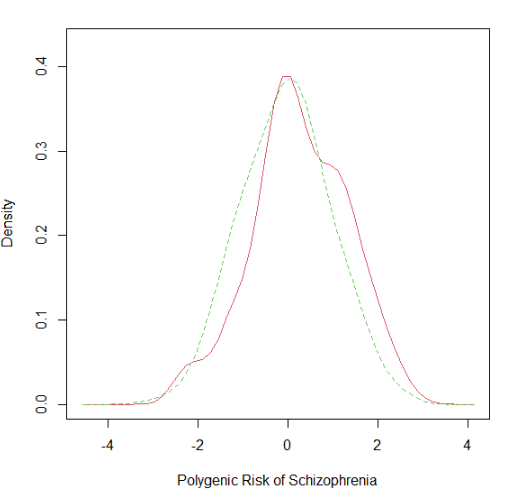
**D. Perceptual Dysregulation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Predictors** | **Eccentricity** | | | |
| **1** | **2** | **3** |
| SCHZ-PGS | 0.09\*\* | 0.08\*\* | 0.27 |
| (0.03, 0.15) | (0.02, 0.14) | (0.00, 0.54) |
| Cannabis Use Index | - | 0.14\*\*\* | 0.08 |
| (0.09, 0.20) | (-0.18, 0.35) |
| SCHZ-PGS \* Cannabis Use Index | - | - | 0.02 |
| (-0.04, 0.08) |
| PC1 | 0.01 | 0.00 | 0.02 |
| (-0.05, 0.07) | (-0.05, 0.06) | (-0.06, 0.09) |
| PC2 | 0.03 | 0.03 | 0.03 |
| (-0.03, 0.09) | (-0.03, 0.08) | (-0.03, 0.09) |
| PC3 | 0.03 | 0.03 | 0.01 |
| (-0.03, 0.09) | (-0.02, 0.09) | (-0.05, 0.08) |
| PC4 | -0.02 | -0.03 | -0.05 |
| (-0.07, 0.04) | (-0.08, 0.03) | (-0.11, 0.01) |
| PC5 | 0.04 | 0.03 | 0.03 |
| (-0.02, 0.10) | (-0.02, 0.09) | (-0.04, 0.10) |
| PC6 | -0.01 | -0.01 | 0.00 |
| (-0.07, 0.04) | (-0.07, 0.05) | (-0.06, 0.06) |
| PC7 | -0.04 | -0.04 | -0.03 |
| (-0.10, 0.02) | (-0.10, 0.02) | (-0.09, 0.03) |
| PC8 | -0.02 | -0.01 | -0.01 |
| (-0.08, 0.04) | (-0.07, 0.04) | (-0.07, 0.05) |
| PC9 | 0.03 | 0.03 | 0.03 |
| (-0.03, 0.09) | (-0.03, 0.09) | (-0.03, 0.09) |
| PC10 | -0.04 | -0.03 | -0.04 |
| (-0.10, 0.02) | (-0.09, 0.02) | (-0.10, 0.02) |
| Sex (ref: female) | 0.26\*\*\* | 0.24\*\*\* | 0.21\*\* |
| ( 0.12, 0.39) | ( 0.11, 0.37) | ( 0.08, 0.35) |
| Cohort (ref: Cohort 2) | -0.41 | -0.49 | -0.40 |
| (-1.03, 0.20) | (-1.09, 0.12) | (-1.01, 0.20) |
| Age | -0.41\*\* | -0.45\*\* | -0.41\*\* |
| (-0.72, -0.10) | (-0.76, -0.15) | (-0.72, -0.10) |
| Zygosity (ref: DZ) | -0.06 | -0.05 | -0.03 |
| (-0.18, 0.06) | (-0.17, 0.07) | (-0.15, 0.09) |
| SCHZ-PGS \* PC1 | - | - | -0.03 |
| (-0.09, 0.02) |
| SCHZ-PGS \* PC2 | - | - | 0.02 |
| (-0.04, 0.08) |
| SCHZ-PGS \* PC3 | - | - | -0.04 |
| (-0.10, 0.01) |
| SCHZ-PGS \* PC4 | - | - | 0.03 |
| (-0.03, 0.09) |
| SCHZ-PGS \* PC5 | - | - | -0.03 |
| (-0.09, 0.03) |
| SCHZ-PGS \* PC6 | - | - | 0.02 |
| (-0.03, 0.08) |
| SCHZ-PGS \* PC7 | - | - | 0.00 |
| (-0.06, 0.06) |
| SCHZ-PGS \* PC8 | - | - | 0.02 |
| (-0.04, 0.08) |
| SCHZ-PGS \* PC9 | - | - | 0.00 |
| (-0.07, 0.07) |
| SCHZ-PGS \* PC10 | - | - | -0.01 |
| (-0.08, 0.05) |
| SCHZ-PGS \* Sex | - | - | 0.06 |
| (-0.07, 0.20) |
| SCHZ-PGS \* Cohort | - | - | -0.54 |
| (-1.16, 0.07) |
| SCHZ-PGS \* Age | - | - | -0.23 |
| (-0.54, 0.08) |
| SCHZ-PGS \* Zygosity | - | - | 0.06 |
| (-0.06, 0.18) |
| Cannabis Use Index \* PC1 | - | - | 0.08\*\* |
| ( 0.03, 0.13) |
| Cannabis Use Index \* PC2 | - | - | -0.06\* |
| (-0.11, -0.01) |
| Cannabis Use Index \* PC3 | - | - | -0.03 |
| (-0.09, 0.04) |
| Cannabis Use Index \* PC4 | - | - | -0.01 |
| (-0.08, 0.05) |
| Cannabis Use Index \* PC5 | - | - | 0.03 |
| (-0.03, 0.09) |
| Cannabis Use Index \* PC6 | - | - | 0.06\* |
| ( 0.01, 0.12) |
| Cannabis Use Index \* PC7 | - | - | 0.02 |
| (-0.05, 0.09) |
| Cannabis Use Index \* PC8 | - | - | 0.02 |
| (-0.06, 0.09) |
| Cannabis Use Index \* PC9 | - | - | -0.02 |
| (-0.10, 0.05) |
| Cannabis Use Index \* PC10 | - | - | 0.00 |
| (-0.07, 0.08) |
| Cannabis Use Index \* Sex | - | - | -0.09 |
| (-0.22, 0.04) |
| Cannabis Use Index \* Cohort | - | - | 0.18 |
| (-0.39, 0.75) |
| Cannabis Use Index \* Age | - | - | 0.06 |
| (-0.22, 0.34) |
| Cannabis Use Index \* Zygosity | - | - | 0.03 |
| (-0.08, 0.14) |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Predictors** | **Perceptual Dysregulation** | | | |
| **1** | **2** | **3** |
| SCHZ-PGS | 0.09\*\* | 0.08\*\* | 0.28\* |
| (0.03, 0.15) | (0.02, 0.14) | (0.00, 0.55) |
| Cannabis Use Disorder | - | 0.29\*\*\* | -0.30 |
| (0.13, 0.45) | (-1.11, 0.51) |
| SCHZ-PGS \* Cannabis Use Disorder | - | - | 0.17\* |
| (0.01, 0.34) |
| PC1 | 0.01 | -0.00 | -0.02 |
| (-0.05, 0.07) | (-0.06, 0.05) | (-0.09, 0.06) |
| PC2 | 0.03 | 0.03 | 0.04 |
| (-0.03, 0.09) | (-0.03, 0.09) | (-0.02, 0.10) |
| PC3 | 0.03 | 0.03 | 0.03 |
| (-0.03, 0.09) | (-0.03, 0.09) | (-0.03, 0.10) |
| PC4 | -0.02 | -0.03 | -0.07\* |
| (-0.07, 0.04) | (-0.09, 0.03) | (-0.13, -0.00) |
| PC5 | 0.04 | 0.04 | 0.03 |
| (-0.02, 0.10) | (-0.02, 0.10) | (-0.04, 0.10) |
| PC6 | -0.01 | -0.01 | -0.03 |
| (-0.07, 0.04) | (-0.07, 0.05) | (-0.09, 0.04) |
| PC7 | -0.04 | -0.04 | -0.03 |
| (-0.10, 0.02) | (-0.09, 0.02) | (-0.10, 0.03) |
| PC8 | -0.02 | -0.02 | -0.02 |
| (-0.08, 0.04) | (-0.08, 0.04) | (-0.09, 0.04) |
| PC9 | 0.03 | 0.03 | 0.04 |
| (-0.03, 0.09) | (-0.03, 0.09) | (-0.03, 0.10) |
| PC10 | -0.04 | -0.04 | -0.05 |
| (-0.10, 0.02) | (-0.10, 0.02) | (-0.12, 0.01) |
| Sex (ref: female) | 0.26\*\*\* | 0.24\*\*\* | 0.22\*\* |
| ( 0.12, 0.39) | ( 0.10, 0.38) | ( 0.07, 0.37) |
| Cohort (ref: Cohort 2) | -0.41 | -0.35 | -0.38 |
| (-1.03, 0.20) | (-0.97, 0.27) | (-1.04, 0.29) |
| Age | -0.41\*\* | -0.39\* | -0.38\* |
| (-0.72, -0.10) | (-0.70, -0.08) | (-0.71, -0.04) |
| Zygosity (ref: DZ) | -0.06 | -0.04 | -0.04 |
| (-0.18, 0.06) | (-0.17, 0.08) | (-0.17, 0.09) |
| SCHZ-PGS \* PC1 | - | - | -0.03 |
| (-0.09, 0.02) |
| SCHZ-PGS \* PC2 | - | - | 0.01 |
| (-0.05, 0.07) |
| SCHZ-PGS \* PC3 | - | - | -0.03 |
| (-0.09, 0.02) |
| SCHZ-PGS \* PC4 | - | - | 0.03 |
| (-0.04, 0.09) |
| SCHZ-PGS \* PC5 | - | - | -0.01 |
| (-0.07, 0.05) |
| SCHZ-PGS \* PC6 | - | - | 0.02 |
| (-0.03, 0.08) |
| SCHZ-PGS \* PC7 | - | - | 0.01 |
| (-0.05, 0.06) |
| SCHZ-PGS \* PC8 | - | - | 0.02 |
| (-0.04, 0.08) |
| SCHZ-PGS \* PC9 | - | - | 0.01 |
| (-0.06, 0.08) |
| SCHZ-PGS \* PC10 | - | - | -0.01 |
| (-0.08, 0.05) |
| SCHZ-PGS \* Sex | - | - | 0.07 |
| (-0.06, 0.21) |
| SCHZ-PGS \* Cohort | - | - | -0.61 |
| (-1.24, 0.01) |
| SCHZ-PGS \* Age | - | - | -0.26 |
| (-0.58, 0.05) |
| SCHZ-PGS \* Zygosity | - | - | 0.07 |
| (-0.05, 0.19) |
| Cannabis Use Disorder \* PC1 | - | - | 0.19\* |
| ( 0.03, 0.35) |
| Cannabis Use Disorder \* PC2 | - | - | -0.04 |
| (-0.19, 0.11) |
| Cannabis Use Disorder \* PC3 | - | - | -0.11 |
| (-0.30, 0.08) |
| Cannabis Use Disorder \* PC4 | - | - | 0.15 |
| (-0.03, 0.33) |
| Cannabis Use Disorder \* PC5 | - | - | -0.06 |
| (-0.23, 0.11) |
| Cannabis Use Disorder \* PC6 | - | - | 0.14 |
| (-0.04, 0.32) |
| Cannabis Use Disorder \* PC7 | - | - | -0.00 |
| (-0.20, 0.19) |
| Cannabis Use Disorder \* PC8 | - | - | 0.15 |
| (-0.06, 0.36) |
| Cannabis Use Disorder \* PC9 | - | - | 0.02 |
| (-0.20, 0.23) |
| Cannabis Use Disorder \* PC10 | - | - | 0.08 |
| (-0.12, 0.28) |
| Cannabis Use Disorder \* Sex | - | - | 0.03 |
| (-0.36, 0.41) |
| Cannabis Use Disorder \* Cohort | - | - | 1.09 |
| (-0.67, 2.85) |
| Cannabis Use Disorder \* Age | - | - | 0.36 |
| (-0.51, 1.23) |
| Cannabis Use Disorder \* Zygosity | - | - | 0.04 |
| (-0.29, 0.38) |

*Notes.* Tables show results from individual-level models testing for (1) associations between polygenic risk of schizophrenia (SCHZ-PGS) and adult Psychoticism, (2) incremental contributions to Psychoticism from adolescent cannabis exposure and polygenic risk of schizophrenia, and (3) interactions between adolescent cannabis exposure and polygenic risk of schizophrenia. Estimates for continuous predictors are reported as standardized betas with 95% confidence intervals, reflecting the standard deviation increase in each outcome associated with a standard deviation increase in each predictor. Estimates for binary predictors are standardized betas with 95% confidence intervals reflecting the difference in each outcome associated with scoring a “1” on this variable (vs. “0” for the reference category). All models included participant age, sex, zygosity, cohort, and the first 10 genetic principal components (PCs) as covariates. Models testing for interaction between polygenic risk of schizophrenia and cannabis exposure additionally included terms adjusting for possible interactions between the schizophrenia PGS or cannabis exposure measures with covariates. \*p<0.05, \*\*p<0.01, \*\*\*p<0.001

**Supplemental Figure 1.** Kernel density plot showing the distribution of schizophrenia polygenic risk scores for twin participants both with and without adolescent cannabis use disorder diagnoses.



*Notes.* Solid red line depicts density plot of schizophrenia polygenic risk scores for twins who met criteria for an adolescent cannabis use disorder diagnosis (*n* = 169). Dotted green line depicts the corresponding density plot for twins who did not meet criteria (*n*  = 1122). The shape and extent of overlap of the two distributions suggests similar levels of polygenic risk in both groups.