**Supplementary Material**

**Role of orbitofrontal sulcogyral pattern on lifetime cannabis use and depressive symptoms**

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**Supplementary Table 1** Scanner Information by Imaging Site

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | *Amsterdam* | *Barcelona* | *Wollongong* | *Melbourne* |
| Manufacturer and Model | Phillips Intera | GE Signa Excite | Phillips Intera | Siemens Trio |
| Field Strength (Tesla, T) | 3 | 1.5 | 3 | 3 |
| Number of Channels | 8 | 8 | 8 | 32 |
| Repetition Time, TR (ms) | 9600 | 11.8 | 6.4 | 1900 |
| Echo Time, TE (ms) | 4.6 | 3.2 | 2.9 | 2.15 |
| Sequence | Turbo field echo | 3D inversion recovery prepared fast spoiled gradient | 3D spoiled gradient-recalled echo | 3D MP-RAGE |

**Supplementary Table 2** Overview of Demographic, IQ, Substance Use Levels, and Orbitofrontal Cortex (OFC) Pattern Distribution of Healthy Controls (HC) and Cannabis (CB) Users by Imaging Site (Mean (SD))

|  |  |  |
| --- | --- | --- |
|  | *HC c* | *CB c* |
|  | *Amsterdam**N = 43* | *Barcelona**N = 30* | *Wollongong**N = 18* | *Melbourne**N = 37* | *Amsterdam**N = 33* | *Barcelona**N = 30* | *Wollongong**N = 16* | *Melbourne**N = 67* |
| Age  | 21.98 (2.46) | 22.57 (3.36) | 35.00 (10.08) | 29.95 (11.29) | 21.32 (2.39) | 21.03 (2.34) | 38.99 (9.24) | 32.67 (11.07) |
| Gender (% M / F) | 62.79 / 37.21 | 100.00 / 0.00 | 88.89 / 11.11 | 48.65 / 51.35 | 66.67 / 33.33 | 100.00 / 0.00 | 93.75 / 6.25 | 46.27 / 53.73 |
| IQ*a* | 104.86 (7.25) | 109.26 (10.47)1 | 113.45 (8.07) | 112.32 (12.72) | 104.18 (5.44) | 103.58 (10.71) | 109.37 (6.16) | 101.83 (12.96)2 |
| Depressive Symptoms *b* | -0.26 (0.71)3 | -0.75 (0.26)4 | -0.25 (0.58) | -0.41 (0.73) | 0.23 (0.80)5 | -0.50 (0.91) | 0.78 (0.98) | 0.49 (1.35) |
| Alcohol (StDr/mth) *c* | 21.44 (26.76) | 12.43 (10.52)6 | 28.12 (21.79)7 | 19.79 (26.72) | 23.64 (23.85) | 21.14 (15.38)1 | 40.29 (26.37)7 | 22.89 (28.06)2 |
| Tobacco (Cig/mth) *c* | 41.73 (106.41) | 24.22 (103.97)8 | 25.35 (100.20) | 22.46 (77.77) | 211.99 (218.91) | 168.41 (152.35)1 | 482.86 (274.73) | 266.12 (233.14)2 |
| Cannabis Use |  |  |  |  |  |  |  |  |
|  Onset Regular Use (years) | - | - | - | - | 18.85 (2.26) | 18.12 (2.05)9 | 20.14 (5.25) | 16.72 (3.27) |
|  Current Use (cones/month) | - | - | - | - | 158.51 (115.95) | 224.13 (138.20)4 | 634.13 (545.45) | 404.97 (308.94) |
|  Lifetime Use (cones) | - | - | - | - | 4,738.64 (4,275.06) | 15,611.28 (12,577.01)1 | 177,772.50 (205,672.08) | 74,579.21 (75,833.71)10 |
| Right OFC *c* sulcogyral pattern, n (%) |
|  Type I | 17 (40) | 20 (67) | 7 (39) | 19 (51) | 17 (52) | 14 (47) | 7 (44) | 31 (46) |
|  Type II | 11 (26) | 4 (13) | 4 (22) | 2 (5) | 7 (21) | 8 (27) | 4 (25) | 12 (18) |
|  Type III | 15 (35) | 6 (20) | 7 (39) | 16 (43) | 9 (27) | 8 (27) | 5 (31) | 24 (36) |
| Left OFCsulcogyral pattern, n (%) |
|  Type I | 23 (54) | 14 (47) | 9 (50) | 18 (49) | 13 (39) | 18 (60) | 8 (50) | 31 (46) |
|  Type II | 8 (19) | 7 (23) | 3 (19) | 7 (19) | 8 (24) | 4 (13) | 3 (19) | 12 (18) |
|  Type III | 12 (28) | 9 (30) | 6 (33) | 12 (32) | 12 (36) | 8 (27) | 5 (31) | 24 (36) |

*a* Estimated IQ measured with the Dutch version of the National Adult Reading Test (DART) (Schmand et al., 1991) (Amsterdam), the vocabulary subscale of the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III) (Barcelona) (Wechsler, 1997); the National Adult Reading Test (NART) (Wollongong) (Nelson, 1982); and the Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) (Melbourne).

*b* Depressive symptoms measured with the Beck Depression Inventory (BDI) (Beck et al., 1961) (Amsterdam, Barcelona, Melbourne) and Hamilton Depression Rating Scale (HAMD) (Hamilton, 1960) (Wollongong); and subsequently standardized to a z-score based on reported population means (Crawford et al., 2011; Zimmerman et al., 2004).

*c* StDr/mth = standard drinks per month; Cig/mth = cigarettes smoked per month; OFC = orbitofrontal cortex; HC = healthy control; CB = cannabis

1n = 29, 2n = 64, 3n = 41, 4n = 27, 5n = 31, 6n = 28, 7n = 15, 8n = 27, 9n = 25, 10n = 66

**Supplementary Table 3** Comparison of Differences in Orbitofrontal Cortex (OFC) Pattern Distribution in Healthy Controls (HC) or Cannabis (CB) Users by Imaging Site

|  |  |  |  |
| --- | --- | --- | --- |
| Variable of Interest | Comparison | *HC a**N = 128* | *CB a**N = 146* |
|  |  | *χ2* | *p* | *χ2* | *P* |
| Right OFC *a* sulcogyral pattern | Within continent – Amst vs. Barc *a* | 5.22 | .07 | 0.27 | .87 |
| Within continent – Woll vs. Melb  | 3.59 | .17 | 0.43 | .81 |
| Across continents – Europe vs. Australia | 3.41 | .18 | 1.16 | .56 |
| Across sites – Amst vs. Barc vs. Woll vs. Melb | 11.34 | .08 | 1.86 | .93 |
| Left OFC sulcogyral pattern | Within continent – Amst vs. Barc | 0.38 | .83 | 2.80 | .25 |
| Within continent – Woll vs. Melb  | 0.04 | .98 | 0.12 | .94 |
| Across continents – Europe vs. Australia | 0.27 | .88 | 0.16 | .92 |
| Across sites – Amst vs. Barc vs. Woll vs. Melb | 0.70 | .99 | 3.13  | .79 |

*a* OFC = orbitofrontal cortex; Amst = Amsterdam, Barc = Barcelona, Woll = Wollongong, Melb = Melbourne; HC = healthy control; CB = cannabis



**Supplementary Fig. 1** Cumulative lifetime cannabis (CB) use, IQ, and tobacco use as mediator between right orbitofrontal cortex (OFC) pattern type (categorical, Type III vs. non-Type III) and depressive symptoms in CB users; relative indirect effect of lifetime CB use, *b* = 0.13, 95% CI = [0.02, 0.31].

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