

Data supplement

	Psychotic experiences		OR (95% CI) ^a	<i>P</i> ^a
	Absent	Present		
Table DS1 Number of individuals (%) endorsing definite psychotic experiences in relation to <i>COMT</i> genotypes				
<i>COMT</i> rs737865				
TT	1197	127 (9.6)		
TC	929	76 (7.6)		
CC	191	18 (9.1)	0.87 (0.70–1.09)	0.239
<i>COMT</i> rs2097603				
AA	680	68 (9.1)		
AG	1097	98 (8.2)		
GG	420	45 (9.7)	1.02 (0.83–1.25)	0.853
<i>COMT</i> rs6269				
AA	812	77 (8.7)		
AG	1007	101 (9.1)		
GG	364	33 (8.3)	0.99 (0.81–1.21)	0.948
<i>COMT</i> rs4818				
CC	838	77 (8.4)		
CG	1005	100 (9.1)		
GG	367	33 (8.3)	1.01 (0.82–1.23)	0.944
<i>COMT</i> rs165599				
AA	1084	92 (7.8)		
AG	914	100 (9.9)		
GG	207	21 (9.2)	1.16 (0.94–1.43)	0.170
Haplotype (G–G–G) ^b				
0 copies	811	76 (8.6)		
1 copy	990	98 (9.0)		
2 copies	353	32 (8.3)	1.00 (0.81–1.22)	0.985
Haplotype (A–C–G) ^b				
0 copies	1834	174 (8.7)		
1 copy	298	30 (9.2)		
2 copies	22	2 (8.3)	1.04 (0.73–1.49)	0.827
a. Per minor allele/copy. b. rs6269–rs4818–rs4680.				

Table DS2 Association between cumulative cannabis use and self-reported psychotic experience stratified by *COMT* genotypes and cannabis × *COMT* interactions

	<i>n</i>	Odds ratio (95% CI)		
		Association between cannabis and psychotic experience	Cannabis × <i>COMT</i> interaction	<i>P</i>
rs4068				
AA (met/met)	715	1.56 (1.05–2.31)		
AG (met/val)	1274	1.68 (1.23–2.28)		
GG (val/val)	578	1.47 (0.85–2.26)		
Total	2567		1.00 (0.73–1.36)	0.981
rs737865				
TT	1355	1.73 (1.31–2.29)		
TC	1025	1.34 (0.89–1.99)		
CC	203	2.33 (0.78–6.95)		
Total	2583		0.87 (0.58–1.29)	0.488
rs2097603				
AA	817	1.69 (1.10–2.58)		
AG	1293	1.39 (0.97–1.99)		
GG	504	2.01 (1.29–3.13)		
Total	2614		1.10 (0.79–1.51)	0.574
rs6269				
AA	957	1.82 (1.25–2.67)		
AG	1208	1.58 (1.14–2.19)		
GG	426	1.46 (0.82–2.61)		
Total	2591		0.89 (0.64–1.24)	0.499
rs4818				
CC	984	1.95 (1.34–2.82)		
CG	1212	1.40 (1.01–1.98)		
GG	431	1.48 (0.83–2.64)		
Total	2627		0.83 (0.60–1.18)	0.304
rs165599				
AA	1270	1.80 (1.33–2.44)		
AG	1111	1.48 (1.03–2.13)		
GG	243	1.33 (0.52–3.41)		
Total	2624		0.85 (0.60–1.21)	0.362
Haplotype (G–G–G) ^a				
0 copies	951	1.79 (1.25–2.57)		
1 copy	1184	1.47 (1.07–2.01)		
2 copies	413	1.35 (0.80–2.26)		
Total	2548		0.86 (0.59–1.23)	0.373
Haplotype (A–C–G) ^a				
0 copies	2196	1.54 (1.24–1.91)		
1 copy	328	1.52 (0.55–4.16)		
2 copies	24	21 (0.69–642)		
Total	2548		1.33 (0.58–3.05)	0.499

a. rs6269–rs4818–rs4680.

Table DS3 Sensitivity analyses for the associations between cannabis, *COMT* (rs4680) and the interaction between these exposures on risk of self-reported psychotic experiences

(a) Cannabis main effect									
Odds ratio (95% CI)									
	Primary Outcome			Frequent distressing symptoms			Definite hallucinations		
	Main sample	Restricted sample	Cross-sectional sample	Main sample	Restricted sample	Cross-sectional sample	Main sample	Restricted sample	Cross-sectional sample
Cumulative use	1.60 (1.28–1.99)	1.60 (1.18–2.17)	1.39 (1.29–1.51)	1.52 (1.11–2.09)	1.23 (0.70–2.17)	1.36 (1.22–1.51)	1.68 (1.27–2.23)	1.73 (1.15–2.60)	1.46 (1.32–1.62)
Frequency	2.74 (1.61–4.67)	2.63 (1.32–5.26)	1.93 (1.61–2.31)	1.91 (0.81–4.49)	1.14 (0.22–5.96)	1.72 (1.34–2.19)	4.00 (2.18–7.34)	3.88 (1.77–8.48)	2.01 (1.61–2.52)
Ever use	2.48 (1.62–3.77)	2.15 (1.16–3.96)	1.92 (1.56–2.36)	2.94 (1.62–5.34)	1.91 (0.74–4.93)	1.85 (1.39–2.47)	2.37 (1.29–4.35)	1.64 (0.58–4.68)	2.22 (1.67–2.93)
(b) <i>COMT</i> rs4680 main effect									
Odds ratio (95% CI)									
	Primary Outcome			Frequent distressing symptoms			Definite hallucinations		
	Main sample	Restricted sample	Cross-sectional sample	Main sample	Restricted sample	Cross-sectional sample	Main sample	Restricted sample	Cross-sectional sample
<i>COMT</i> rs4680	1.01 (0.83–1.22)	1.10 (0.85–1.43)	0.99 (0.86–1.14)	0.94 (0.70–1.28)	0.89 (0.59–1.33)	1.01 (0.83–1.23)	1.07 (0.80–1.42)	1.32 (0.86–2.01)	1.05 (0.87–1.28)
(c) Cannabis × <i>COMT</i> rs4680 interaction									
Odds ratio (95% CI)									
	Primary Outcome			Frequent distressing symptoms			Definite hallucinations		
	Main sample	Restricted sample	Cross-sectional sample	Main sample	Restricted sample	Cross-sectional sample	Main sample	Restricted sample	Cross-sectional sample
Cumulative × <i>COMT</i>	1.00 (0.73–1.36)	0.67 (0.41–1.08)	1.10 (0.99–1.23)	1.27 (0.81–2.00)	1.01 (0.47–2.18)	1.06 (0.91–1.23)	0.87 (0.57–1.31)	0.50 (0.23–1.08)	1.16 (1.01–1.34)
Frequency × <i>COMT</i>	0.59 (0.27–1.27)	0.38 (0.12–1.21)	1.21 (0.94–1.56)	1.07 (0.35–3.33)	1.18 (0.15–9.35)	1.21 (0.86–1.71)	0.58 (0.24–1.41)	0.32 (0.08–1.25)	1.11 (0.81–1.53)
Ever use × <i>COMT</i>	1.45 (0.79–2.65)	0.85 (0.35–2.08)	1.21 (0.91–1.62)	1.65 (0.70–3.86)	0.97 (0.24–3.90)	1.17 (0.78–1.76)	0.96 (0.40–2.31)	0.28 (0.05–1.54)	1.51 (1.01–2.24)