SUPPLEMENTAL INFORMATION

Neuroimaging Meta-Analysis of Cannabis-Use Studies Reveals Convergent Functional Alterations in Brain Regions Supporting Cognitive Control and Reward Processing

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SUPPLEMENTAL CONTENT

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Table S1. Meta-Analytic Connectivity Modeling (MACM) Coordinates for Cannabis-Affected Regions

Cluster No.	MACM Extrema Label (within +/-5mm)	BA	Hemisphere	x	y	z
1 (ACC)						
	Cingulate Gyrus	32	L	-4	18	38
	Insula	13	L	-32	18	4
	Insula	NA	R	32	20	2
	Thalamus	NA	L	-10	-18	8
	Anterior Cingulate Gyrus	32	L	-4	30	22
	Thalamus	NA	R	8	-18	8
	Inferior Frontal Gyrus	9	L	-44	4	32
	Lentiform Nucleus	NA	R	14	4	6
	Inferior Frontal Gyrus	9	L	-44	12	24
	Inferior Frontal Gyrus	9	R	44	8	30
	Lentiform Nucleus	NA	L	-20	6	4
	Superior Parietal Lobule	7	L	-28	-62	44
	Middle Frontal Gyrus	9	R	40	30	26
	Superior Parietal Lobule	7	R	28	-62	40
	Inferior Parietal Lobule	40	R	40	-48	40
	Precentral Gyrus	6	L	-28	-8	48
	Precentral Gyrus	6	L	-40	-4	46
	Middle Frontal Gyrus	10	L	-36	42	22
	Precentral Gyrus	6	R	46	-4	44
	Inferior Parietal Lobule	40	L	-46	-40	40
	Insula	40	R	54	-20	16
	Postcentral Gyrus	40	R	56	-22	20
	Postcentral Gyrus	40	L	-58	-24	20
	Cingulate Gyrus	23	L	0	-30	28
	Middle Frontal Gyrus	10	L	-36	48	10
	Lentiform Nucleus	NA	R	18	-2	-8
	Inferior Parietal Lobule	40	L	-54	-42	22
	Supramarginal Gyrus	40	R	54	-38	28
	Middle Frontal Gyrus	6	R	26	-4	50
	Supramarginal Gyrus	40	R	52	-42	34
	Middle Temporal Gyrus	22	L	-50	-40	4
	Middle Frontal Gyrus	10	R	32	48	20
	Precuneus	7	L	-10	-68	46
	Precentral Gyrus	6	L	-50	-12	34
	Sub-Gyral Gray Matter	6	R	26	4	52
	Precuneus	7	R	6	-70	44
	Superior Temporal Gyrus	22	R	46	-30	0
	Thalamus	NA	L	-24	-24	0
	Precuneus	31	L	-24	-80	28

Note. Table continued on next page.

Table S1 (continued).

Cluster No.	MACM Extrema Label (within +/-5mm)	BA	Hemisphere	x	y	z
2 (DL-PFC)						
	Precentral Gyrus	6	R	44	4	34
	Insula	13	R	32	18	6
	Lentiform Nucleus	NA	R	20	2	6
	Middle Frontal Gyrus	9	R	44	22	28
	Insula	13	R	44	12	12
	Lentiform Nucleus	NA	L	-20	2	6
	Caudate	NA	R	14	-2	16
	Caudate	NA	L	-14	0	12
	Middle Frontal Gyrus	9	R	42	32	26
	Thalamus	NA	R	10	-8	8
	Middle Frontal Gyrus	10	R	34	44	24
	Parahippocampal Gyrus	NA	L	-18	-6	-10
	Precentral Gryrus	6	L	-44	-2	36
	Precentral Gyrus	6	L	-28	-10	50
	Inferior Parietal Lobule	40	L	-42	-38	40
	Fusiform Gyrus	37	L	-46	-58	-12
	Insula	13	L	-46	-40	16
	Postcentral Gyrus	40	L	-38	-26	44
	Transverse Temporal Gyrus	41	L	-40	-32	12
	Precentral Gyrus	6	R	48	2	36
	Superior Temporal Gyrus	22	R	48	-32	4
	Superior Temporal Gyrus	22	R	50	-28	4
	Superior Temporal Gyrus	22	R	50	6	2
	Superior Temporal Gyrus	22	R	50	-10	2
	Postcentral Gyrus	40	R	56	-24	24
	Inferior Parietal Lobule	40	R	56	-32	34
	Insula	13	L	-32	18	8
	Inferior Frontal Gyrus	9	L	-46	8	30
	Middle Frontal Gyrus	46	L	-44	22	26
	Middle Frontal Gyrus	10	L	-38	42	22
	Superior Parietal Lobule	7	R	30	-58	44
	Inferior Occipital Gyrus	19	R	36	-76	-4
	Supramarginal Gyrus	40	R	54	-36	36
	Lingual Gyrus	18	R	26	-80	-8

Note. Table continued on next page.

Table S1 (continued).

Cluster No.	MACM Extrema Label (within +/-5mm)	BA	Hemisphere	x	y	z
3 (Striatum)						
	Claustrum	NA	R	32	16	2
	Caudate	NA	R	12	6	6
	Insula	13	L	-32	18	4
	Lentiform Nucleus	NA	L	-12	4	4
	Thalamus	NA	L	-12	-16	8
	Thalamus	NA	R	6	-16	8
	Inferior Frontal Gyrus	9	R	44	6	28
	Inferior Parietal Lobule	40	L	-32	-54	42
	Inferior Frontal Gyrus	9	L	-46	4	28
	Middle Frontal Gyrus	46	R	40	34	24
	Precentral Gyrus	6	L	-42	-4	44
	Middle Frontal Gyrus	46	L	-42	26	24
	Middle Frontal Gyrus	6	R	42	-2	46
	Middle Frontal Gyrus	10	R	34	46	20
	Precentral Gyrus	6	L	-28	-8	50
	Precentral Gyrus	6	R	30	-6	50
	Middle Frontal Gyrus	10	L	-36	42	22
	Sub-Gyral Gray Matter	6	R	28	2	54
	Middle Frontal Gyrus	10	R	30	52	6
	Supramarginal Gyrus	40	L	-54	-48	30
	Insula	40	L	-48	-24	16
	Superior Temporal Gyrus	13	L	-54	-40	20
	Inferior Frontal Gyrus	46	R	44	36	8
	Precentral Gyrus	4	R	46	-14	38
	Medial Frontal Gyrus	32	L	-2	8	46
	Cingulate Gyrus	32	L	0	18	40
	Anterior Cingulate Gyrus	24	L	-2	32	14
	Superior Parietal Lobule	7	R	28	-62	40
	Inferior Parietal Lobule	40	R	38	-48	40
	Inferior Parietal Lobule	40	R	46	-40	42
	Inferior Parietal Lobule	40	R	54	-44	30
	Postcentral Gyrus	40	R	58	-24	20
	Middle Temporal Gyrus	21	R	52	-42	8
	Precuneus	31	R	28	-74	22
	Precuneus	7	R	8	-72	44

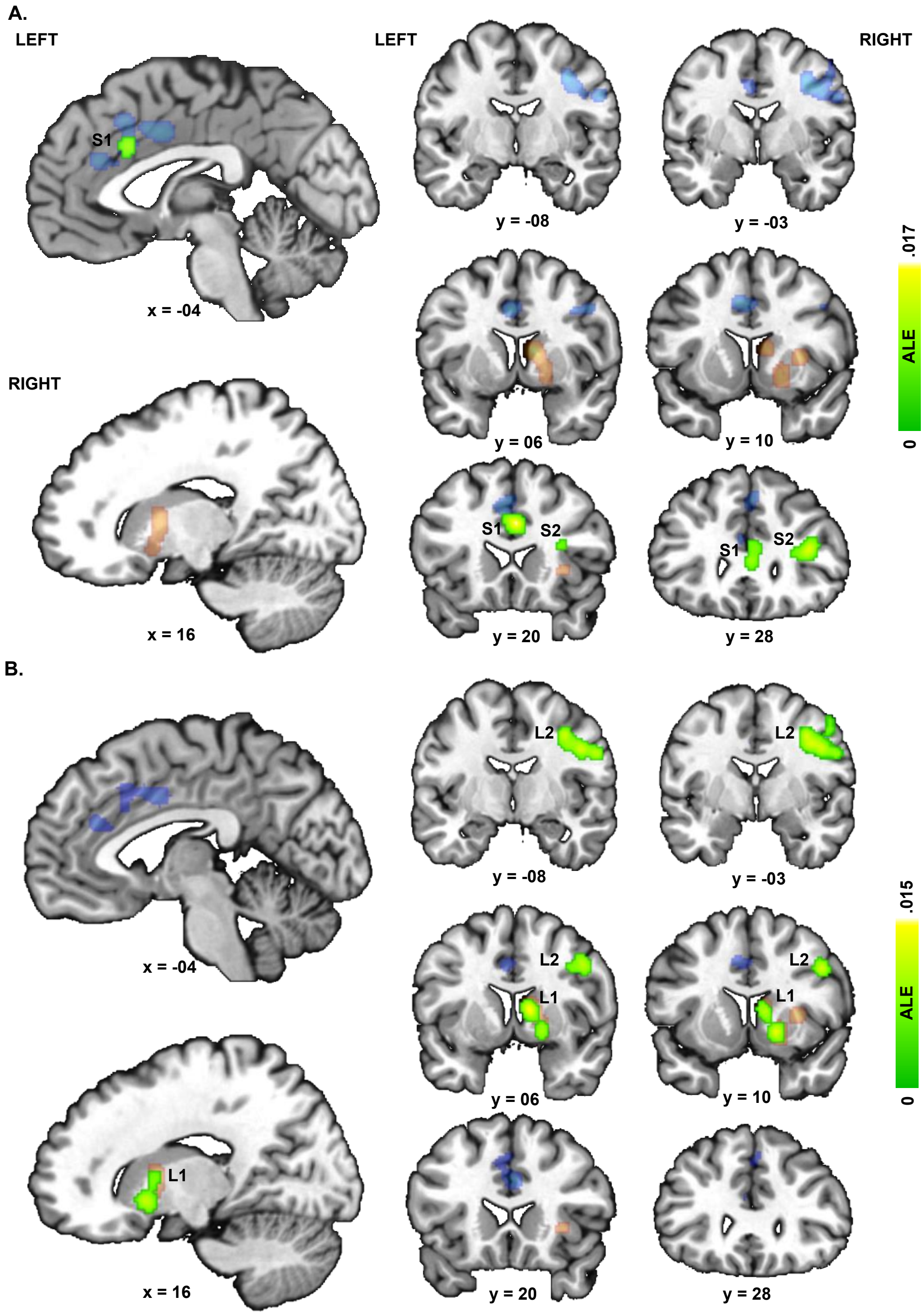
Note: Local extrema coordinates and associated labels of MACM maps shown in main text Figure 3. Coordinates (x, y, z) are reported in Talairach Space and extrema labels were determined via the Talairach Daemon. BA, Brodmann Area; NA, not applicable; R, right; L, left.

Table S2. Forward-Inference Analysis for Cannabis-Affected Regions

Cluster No.	Task Classification	Liklihood Ratio
Decreases (Users < Non-Users)		
1 (ACC)	Flanker Task	2.99*
	Stroop Task	1.97*
	Pain Monitor/Discrimination	1.75*
	Go/No-Go	1.12
	Passive Listening	0.46
2 (DL-PFC)		
	Saccades	2.83*
	Visual Pursuit/Tracking	2.05
	Recitation/Repetition	1.90
	Flexion/Extension	1.68
	Delayed Match to Sample	1.43
	Reading	1.43
	Film Viewing	1.41
	Go/No-Go	1.26
	Reward	0.52
Increases (Users > Non-Users)		
3 (Striatum)	Reward	2.46*
	Pain Monitor/Discrimination	1.66*
	Go/No-Go	1.27
	Passive Listening	0.52

Note: Forward-inference estimates [P(Activation|Process] used to compute reverse-inference estimates [P(Process|Activation)] using Bayes' rule. * statistically significant ($p_{FDR\text{-}corrected}<0.05$).

Figure S1: Cannabis Abstinence Stratified ALE Meta-Analysis Results



Note. (**A**) An exploratory assessment examined convergence across included studies involving *short-term* abstinence among users (i.e., ≤ 48 hours since last cannabis-use episode; n = 19, mean = 22.71 hours) identified regional alterations among short-term abstinent users versus non-users. Specifically, convergent alterations were observed in two clusters, one encompassing the anterior cingulate cortex (A, S1, green), and a second encompassing the right middle frontal gyrus, right inferior frontal gyrus, and right insula (A, S2, green). These clusters showed considerable spatial overlap with Cluster 1 (ACC) described in Table 2 and Figure 2 of the main text. (**B**) Among studies that assessed users involving *long-term* abstinence (i.e., > 48 hours since last cannabis-use episode; n = 14, mean = 98.89 days), convergent alterations were observed in two clusters, one encompassing the caudate and putamen (B, L1, green), and a second encompassing the right precentral gyrus and right middle frontal gyrus (B, L2, green). These clusters showed considerable spatial overlap with Cluster 3 (Striatum) and Cluster 2 (DL-PFC), respectfully, described in Table 2 and Figure 2 of the main text. Areas of decreased activation (transparent blue) and increased activation (transparent red) among cannabis users as observed in the primary meta-analysis reported in the main text are included for visual comparison. Current methodological recommendations regarding ALE meta-analyses indicate that ~20 studies are needed to achieve sufficient statistical power allowing for the detection of moderately sized effects (Eickhoff et al., 2016). For this reason, stratified meta-analysis results were obtained using an exploratory approach ($p_{\text{cluster-corrected}}<0.1$; $p_{\text{voxel-level}}< 0.01$) that involved combining coordinates across the included studies – irrespective of statistical contrast direction – to enable enhanced understanding about cannabis abstinence. ALE maps were computed in Talairach space. Given these exploratory outcomes, it is plausible that the primary meta-analysis results reported in Table 2 and Figure 2 represent distinct neurobiological effects of cannabis: effects associated with *short-term* abstinence (i.e., recent intoxication) and effects associated with *long-term* abstinence (i.e., chronic differences between previous cannabis users versus non-users). It is worth noting that in combining coordinates across studies, neurobiological interpretations regarding directionality become unclear. Nevertheless, exploratory results reported here may augment our primary meta-analysis outcomes, pointing towards potential targets for subsequent studies on the differential effects of cannabis with respect to abstinence.