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Standardization of structural and functional brain integration in cannabis users

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Abstract

Cannabis is one of the most widely used and commercialized illegal drugs worldwide, notably amid young adults. The neuro-biological mechanisms of cannabis, particularly in adolescents, have yet to be identified. The purpose of this study was to evaluate a cohort of 73 cannabis users (ages 22-36, 19 females) and his 73 healthy controls (ages 22-36, females). We observed some momentous differences in local structural/functional network measures (such as grade along with clustering coefficient), extended in the insular and anterior cranial cortices, and in the lateral/medial temporal cortex . An abundant structural network of clubs showed a normal tendency to distribute in the bilateral frontal, temporal, and occipital regions. However, slight differences between the two groups were found in the superior and inferior temporal gyri. Functionally rich clavate nodes were located primarily in the parietal and posterior regions, with minor differences between the groups that were found primarily in the centrotemporal and parietal regions. Regional network measures of structural/functional networks have been associated with time of cannabis use (TUC) in several regions. Structural/functional networks showed small-world ownership in both groups, but no differences were found between cannabis users and healthy control of global network measures, no association with cannabis use. After FDR alteration, all significant associations among network measurements and TUC were found to be insignificant, except for the association between termination within the subicule region and TUC . In summary, our results revealed changes in the local topological properties of structural and functional networks in cannabis users, but global brain network organization remained intact.

Introduction

Cannabis is one of the foremost commonly utilized illegal drugs around the world, and its utilization has been on the rise in later a long time, coinciding with its legalization in numerous countries1. Investigate has appeared that reliance on cannabis is related with a extend of neurocognitive shortages, counting disabled long winded memory2, engagement in unsafe behaviors, and destitute execution on cognitive errands that require executive function1,3. Within the past decades, morphometry and arrange examinations have been commonly utilized in most thinks about to explore the affiliation between cannabis utilize and brain structure and work. The morphometry based approach is utilized to think about changes within the nearby concentration (volume/thickness) of brain tissues4. Early considers found no critical morphological changes within the brain related with incessant cannabis use5. In any case, later ponders have appeared that the utilize of cannabis may lead to hippocampal, parahippocampal and horizontal atrophy6,7,8,9. Changes in brain work and structure may not be simply due to nearby changes in brain morphology, it can be moreover a result of changes in morphology between brain locales.

By modeling the brain as a network, several studies have used resting-state functional and diffusion-weighted imaging data to examine changes in

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functional and structural brain connectivity resulting from chronic cannabis use. I'm here. Previous studies on large-scale brain networks have reported heterogeneous results regarding the association between structural and functional brain connectivity patterns and cannabis in cannabis users. Preliminary results, using graph-theoretical means, show that structural brain network efficiency is low, in addition to changes in regional structural connectivity in zonal regions in a group of cannabis users. 12. One of the first studies to examine the effects of long-term cannabis use on axonal connectivity found impaired structural connectivity in the spleen of the corpus callosum, fornix, and commissural fibers 15 . Increased structural fractional anisotropy was found in regular cannabis users, but decreased with frequent use3. Other studies 16,17,18 found no significant differences in global characteristics of brain structural networks between cannabis users and controls. Although most studies focus on specific brain regions that use cognitive tasks, long-term cannabis use has been shown to be associated with various changes in functional connectivity. Several studies have examined resting-state functional connectivity across large brain networks16,21. Manza et al.11 found increased regional functional connectivity in the ventral striatum, midbrain, brainstem, and lateral thalamus. While using seed-based connectivity analysis, they reported no significant differences in brain-wide functional connectivity between cannabis users and healthy controls who used the above regions as seeds. Ramaekers et al.22 found widespread hyper-connectivity within key brain networks such as dorsal attention, limbic, subcortical, and cerebellar networks in chronic cannabis users compared to acute cannabis users. Did. Using graph theory analysis, no differences were found in the global and regional characteristics of resting-state functional networks between cannabis users and non-users 21. Interested in identifying densely connected nodes within brain networks (so-called 'rich clubs') that have recently been shown to play a key role in information integration across structural and functional brain networks is rising. Few studies have examined the abundance of associated tissues in the structural brain networks of cannabis users compared to non-users16,17. Despite a large body of research, changes in functional and structural connectivity of brain networks in cannabis users have not been fully investigated.

Table 1 : *Summary of Socio-demographic and substance use characteristics of the subjects included in the study.*

		Cannabis users	Healthy controls	p-value	t-statistic	df
N of total		73	73			
Mean Agea (SD)		28.58 (3.69)	27.72 (3.56)	0.1352	1.51	72
Gender (N of Male (%))		54 (73.97%)	59 (80.82%)			
Mean BMI (SD)		26.99 (4.91)	27.06 (4.54)	0.9309	− 0.087	72
Education (Years of education completed)	< 11	6 (8.21%)	3 (4.10%)	0.8163	− 0.233	72
	12	9 (12.32%)	15 (20.54%)			
	13	11 (15.06%)	4 (5.47%)			
	14	10 (13.69%)	13 (17.8%)			
	15	6 (8.21%)	5 (6.84%)			
	16	22 (30.13%)	25 (34.24%)			
	17 +	9 (12.32%)	8 (10.95%)			
Times used Cannabis (lifetime)	0 (never used)	–	41 (56.16%)	2.2014e−43	31	72
	1 (1–5 times)	–	23 (31.5%)			
	2 (6–10 times)	–	9 (12.32%)			
	3 (11–100 times)	13 (17.8%)	–			
	4(101–999 times)	20 (27.39%)	–			
	5 (> 1000 times)	40 (54.79%)	–			
Age at first use of cannabis	1 (< = 14)	23 (31.5%)	–			
	2 (15–17)	32 (43.83%)	–			
	3 (18–20)	15 (20.54%)	–			
	4 (> = 21)	3 (4.10%)	–			
Mean Alcohol use (SD)		0.31 (0.51)	0.32 (0.55)	0.9489	− 0.064	72
Mean Tobacco use (SD)		0.24 (0.78)	0.15 (0.59)	0.4566	0.748	72

Age range = 22–36 years.

In the present study, we used graph-theoretical indices in cannabis users compared to healthy controls to identify changes in brain functional and structural connectivity and rich organization of structural and functional brain networks. intended to investigate. We also assessed the association between cannabis use time and network actions.

Materials and Methods

Subjects

This study included 146 subjects. All candidates contingent written informed consent. From this cohort (n = 1206, ages 22–36, 54 males), 109 met DSM-IV criteria for her cannabis dependence and had both rs-fMRI and DWI imaging data. Subjects with concurrent alcoholism, DSM-level anxiety and depression outliers (≥3 SD from the mean for all 1206 HCP subjects), and subjects with poor outlier image quality were excluded from this subgroup. 19. The final sample included 73 cannabis users. Matching groups based on demographic and lifestyle factors is recommended, so it is an important step to minimize the potential confounding effects of these factors11. Cannabis groups were matched by age, sex, education, BMI, alcohol and tobacco use using her MatchIt function in R ($p > 0.1$). Subject sociodemographic information is shown in Table 1.

Neuroimaging Data

Image data were acquired from each subject on a Siemens 3T scanner with a 32-channel coil at the University of Washington, as shown in Figure 26. 3D T1- and T2-weighted MR images were acquired at an isotropic resolution of 0.7 mm (FOV = 224 mm, matrix = 320, 256 slices). Diffusion-weighted images (DWI) were acquired isotropically at a high spatial resolution of 1.25 mm (TR/TE = 5520 ms/89.5 ms), using the high angular resolution diffusion imaging (HARDI) method, with 6 Shells with b = 1000, 2000, and 3000 s/mm2 with 270 q points distributed over three runs and three different shells. The rs-fMRI data were collected in two sessions, with EPI sequences (multiband coefficient = 8, TR/TE = 720 ms/33.1 ms, flip angle = 52°, FOV = 208 mm, spatial resolution = 2 in each session). 2 x 2mm). For rs-fMRI, participants were instructed to lie down with their eyes open, relax, look at a white cross on a dark background, think nothing, and not sleep.

Data Preprocessing

T1w images were minimally pre-processed for spatial distortion and motion correction and normalization in MNI space27. Diffusion-weighted images were also pre-

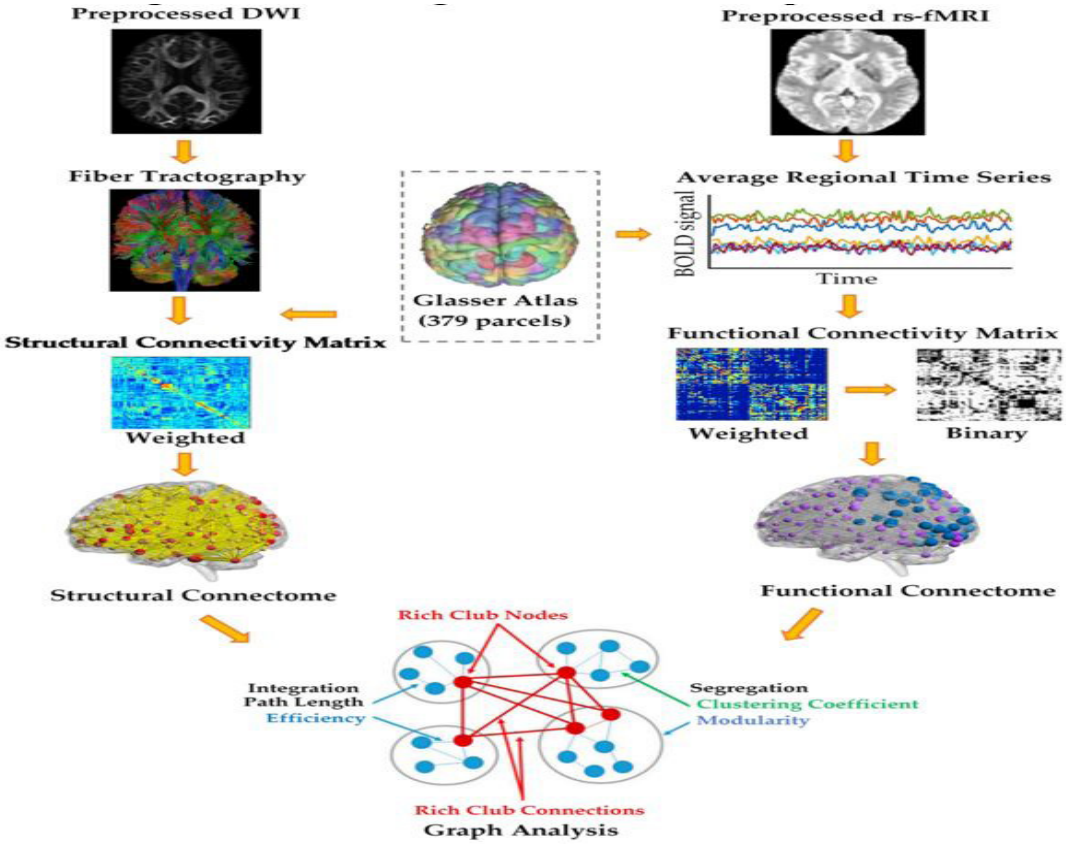

Figure 1: *A processing channel for brain structural and functional network analysis. We used fiber tractography and a subdivision scheme to construct the structural connectome for each individual. A functional connectome for each individual was also constructed by calculating the average time-course pairwise Pearson correlation coefficients of the 379 regions. Graph theory analyzes were then performed to examine the topological properties and abundant club organization of structural and functional brain networks in both healthy controls and cannabis users.*

processed for b0 intensity normalization, EPI distortion correction, eddy current and motion correction, and gradient non-linearity correction. All rs-fMRI data were used in 'CIFTI' format. H. Combination of cortical gray matter data modeled on the surface and subcortical gray matter data modeled on volumetric packets included in the image. All functional images were subjected to gradient equalization, EPI distortion correction, motion correction, registration of T1w scans, high-pass filtering with a cutoff of 2000 s for linear detrending, ICA-based de-noising for automatic artifact removal, Minimal preprocessing was done for bad images. Normalization of very low frequency and nonlinear components to MNI space. Details are described elsewhere28. The HCP preprocessing pipeline uses Independent Component Analysis (MELODIC, FSL-FIX) to remove artifacts and 'bad' components, as well as non-neuronal spatiotemporal components from 15 min of high-pass filtered rs-fMRI data. Did. To avoid removing interesting discrepancies from the data, a conservative, non-aggressive approach was still used in which a cutoff value of 2000 seconds was found to be better than 200 seconds in ICA-FIX29 . The rs-fMRI images were also cross-registered between subjects using the 'MSMall' algorithm30. This algorithm aligns functional networks to cortical functional maps using features derived from myelin, resting-state networks, and rs-fMRI visual field maps. Pipeline 30,31.

Network Construction

Glasser Atlas30 containing 360 regions (180 regions per hemisphere) was used to create functional and structural views of the brain. Since subcortical regions are often included in addiction studies, we used a modified version of this atlas containing 379 plots containing 19 subcortical regions. The subdivision scheme was based on changes in brain cortical architecture, function, connectivity and topography in 210 young healthy adults with HCP30. A structural connectivity matrix containing N × N elements representing normalized QA across regions was constructed for each participant. The optimal threshold was set to 0.1% of each person's maximum structural connectivity (the default threshold in DSI Studio).

We then calculated a weighted group structure matrix for each group by averaging the connectivity matrix elements for connections present in at least 75% of subjects23. In addition, a functional connectivity matrix for each individual was constructed by calculating the average time-course pairwise Pearson correlation coefficients of the 379 regions. We then thresholded the functional connectivity matrix using an optimal threshold of 0.2,27 retaining 20% of the strongest connections. The optimal threshold was determined based on a trade-off between density and overall efficiency36. The binary group function matrix for both groups was also calculated by averaging the individual matrices while retaining 20% of the strongest links. The overall procedure is shown in Figure 1.

Network Topological Properties

To examine the link between cannabis use and the structural and functional connectivity of the brain, the topological properties of both structural and functional networks at the individual and group level were analyzed using the Brain Connectivity Toolbox (BCT, http://www.brainconnectivitytoolbox.org/).http://www.brain-connectivity-toolbox.net/).

To characterize the network topology of the brain, metrics of network integration (characteristic path length, global efficiency and degree), separation (clustering coefficient and modularity), and small-worldness were calculated for each network. . Details of individual properties are shown on 37 and 10.

Rich-Club Organization

In addition, we examined the effects of cannabis on abundant club tissue in the brain using methods described in 23,24. For this purpose, unweighted Rich-Club coefficients were calculated for each group mean functional network. For each k in the range [1, the maximum degree in the network], the Rich-Crab coefficient φ(k) was defined as the ratio of the number of connections in the sub-graph defined by nodes of less than degree k. Computes the total number of possible connections in the sub-graph.

$$\phi^{w}(k) = \frac{w_k}{\sum_{l}^{E_k} w_l^{ranked}}$$

where Ek is the number of connections with a degree less than k, and Nk(Nk−1) is the total number of possible connections.

$$\phi(k) = \frac{2E_k}{N_k(N_k - 1)}$$

Following a similar procedure, a weighted rich-club coefficient φwk was computed for each group structural network. After ranking all weights of the structural network (w-ranked), φw(k) was computed as follows:

Where wk is the sum of the weights of links in the sub-graph of nodes with rank greater than k, and w-ranked is the vector of weights of all links in the structural network, ordered from highest to lowest weight. increase.

The normalized Rich-Club coefficients φnorm(k) of the structural and functional networks in each group were then calculated with respect to φrandom(k). It was computed as

the average rich club coefficient over 1000 random networks of the same size and similar connection distribution. We use 23 μm to test whether the rich clubs of the real network significantly exceed those of the null model $p < 0.05$. For structural and functional networks of cannabis users and healthy controls, φnorm(k) is greater than 1 and within k with $p < 0.05$ indicated the presence of abundant club nodes. In this study, we chose k levels such that 30% of the network nodes are identified as rich club nodes.

Statistical Analysis

Differences in global and local plot metrics between cannabis users and healthy controls were assessed using t-tests. In addition, we used node-level linear regression analysis to examine the relationship between cannabis users' structural/functional network measures (grade and clustering coefficients) and time of cannabis use (TUC). Results were presented using a range of statistical significance thresholds ($p < 0.05$, $p < 0.02$, $p < 0.01$, and $p < 0.005$). Mainly due to multiple corrections, the false discovery rate (FDR) was used, uncorrected and corrected for multiple comparisons. Comparisons can be overly conservative when dealing with large numbers of nodes.

Informed Consent

Informed consent was obtained from all subjects involved in the study.

Results

Graph Measures

As shown in Table 2, global network measures (global efficiency, characteristic path length, modularity, and small size) for either structural or functional networks between cannabis users and healthy controls No significant difference ($p > 0.05$) was found.

Figure 2 and Tables S1–S4 show significant differences ($p < 0.05$, $p < 0.02$, $p < 0.01$, and $p < 0.005$, uncorrected) in node degrees and clustering coefficients of structural and functional networks between groups. increase. As shown, the structural networks of cannabis users were less central ($p < 0.01$, unmodified). Several nodes in the left parieto-occipital region, including V3CD, showed increased structural grade in cannabis users compared with controls. In functional networks, the left anterior cranial cranium showed a significant reduction in grade ($p>0.005$, uncorrected) in cannabis users.

Cannabis users also showed higher regional segregation (clustering coefficient, $p<0.01$ uncorrected) within frontoparietal regions, including the premotor cortex, the anterior cranial cortex, and the inferior frontal cortex of the structural network. Several areas in the posterior visual cortex, including the ventral visual cortex and V3CD, showed lower clustering coefficients in cannabis users.

Functional networks in cannabis users were also characterized by increased clustering coefficients in the left inferior frontal cortex, ventral visual cortex, FST and TG dorsal regions. Compared with the control group, the cannabis group showed less regional functional segregation within the right hemisphere in the dorsolateral prefrontal cortex, parahippocampal cortex 2, and the ventral region of the diencephalon.

Overall, none of the above significant differences between cannabis users and healthy controls survived after FDR correction.

Rich-Club organization of structural and functional networks

Figure 3 and Tables S9, S10 show the spatial distribution of structurally and functionally abundant club nodes in both groups. As shown, the structure-rich clavate in both groups was mainly distributed in left bilateral frontal, temporal and occipital lobe regions and deep brain structures. Compared with controls, the structural networks of cannabis users showed higher and lower numbers of abundant club nodes within the superior and inferior temporal gyri, respectively.

Table 2: *Average values (mean ± SD) of structural and functional network properties for each group.*

Topological characteristic	Structural network					Functional network				
	Cannabis users	Healthy controls	p-value	t-statistic	df	Cannabis users	Healthy controls	p-value	t-statistic	df
Global efficiency	0.3185 ± 0.0215	0.3184 ± 0.0223	0.99	− 0.007	144	0.4864 ± 0.0292	0.4938 ± 0.0265	0.11	1.60	144
Characteristic path length	0.8234 ± 0.0652	0.8176 ± 0.0650	0.58	− 0.54	144	1.9604 ± 0.055	1.9538 ± 0.047	0.43	− 0.77	144
Modularity	0.3308 ± 0.0227	0.3222 ± 0.0280	0.05	− 2.03	144	0.2616 ± 0.0530	0.2697 ± 0.0459	0.33	0.97	144
Small-worldness	1.5792 ± 0.0928	1.5563 ± 0.1092	0.17	− 1.35	144	1.3042 ± 0.1939	1.3483 ± 0.1916	0.16	1.40	144
Degree	77.76 ± 5.21	78.53 ± 5.54	0.38	0.86	144	75.59 ± 1.43	75.59 ± 1.43	1	0	144
Clustering coefficient	0.2862 ± 0.02	0.2855 ± 0.0207	0.83	− 0.20	144	0.6257 ± 0.0183	0.6265 ± 0.0188	0.79	0.25	144

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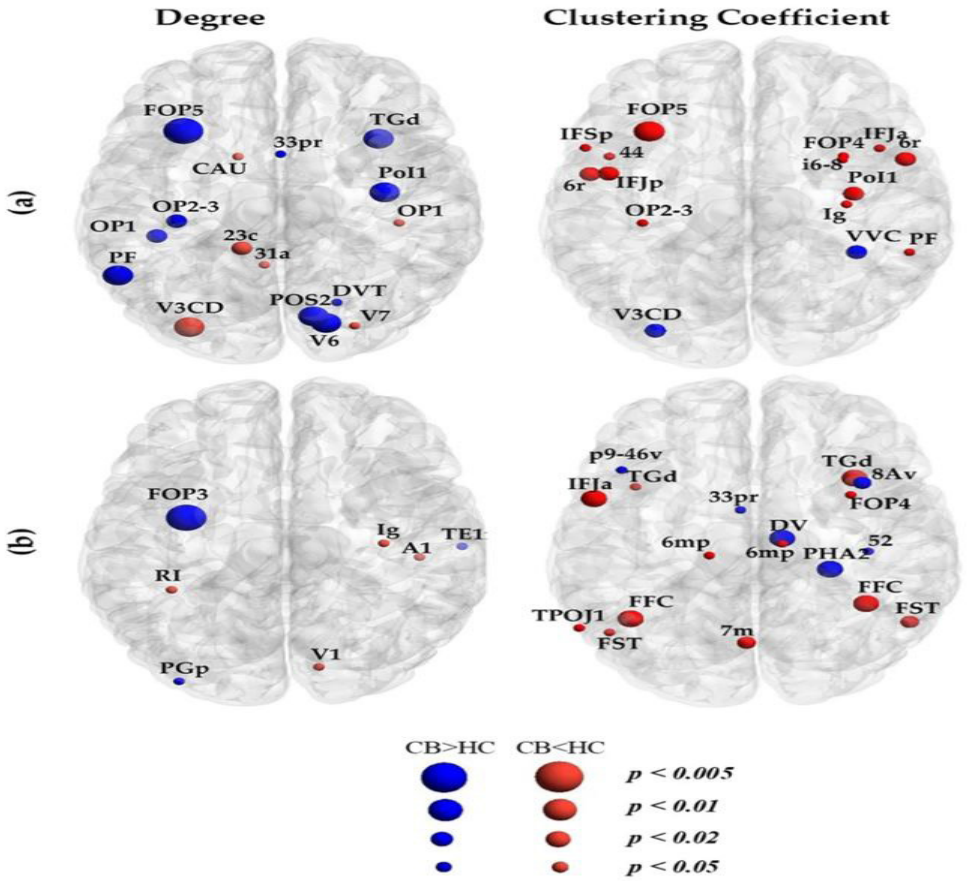

Figure 2: *Regions showing differences in degree and clustering coefficient between cannabis users and healthy controls in (a) structural networks and (b) functional networks. The color of nodes indicates significant increases (red) or decreases (blue) in degree and clustering coefficient for cannabis users (CB) compared to healthy controls (HC). The size of nodes represents between group differences with $p < 0.05$, $p < 0.02$, $p < 0.01$ and $p < 0.005$ (uncorrected) with larger nodes showing smaller p values.*

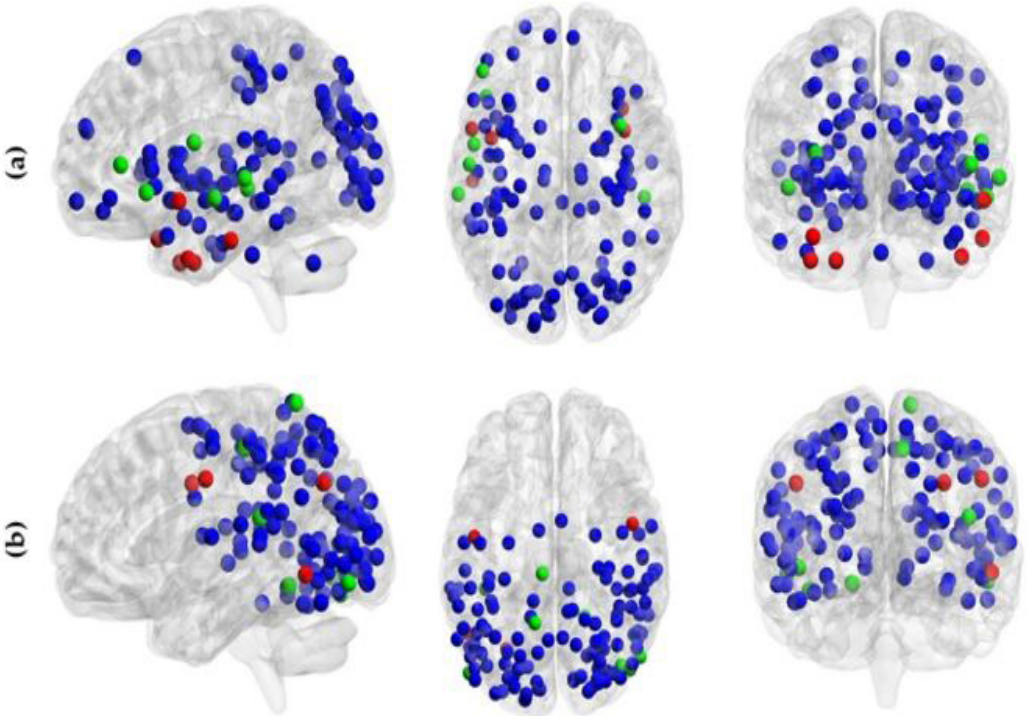

Figure 3: *Rich club organization of (a) structural networks and (b) functional networks for cannabis users and healthy controls. The common rich club nodes in two groups are shown in blue. Few rich club nodes were only found for healthy controls (in red) or cannabis users (in green).*

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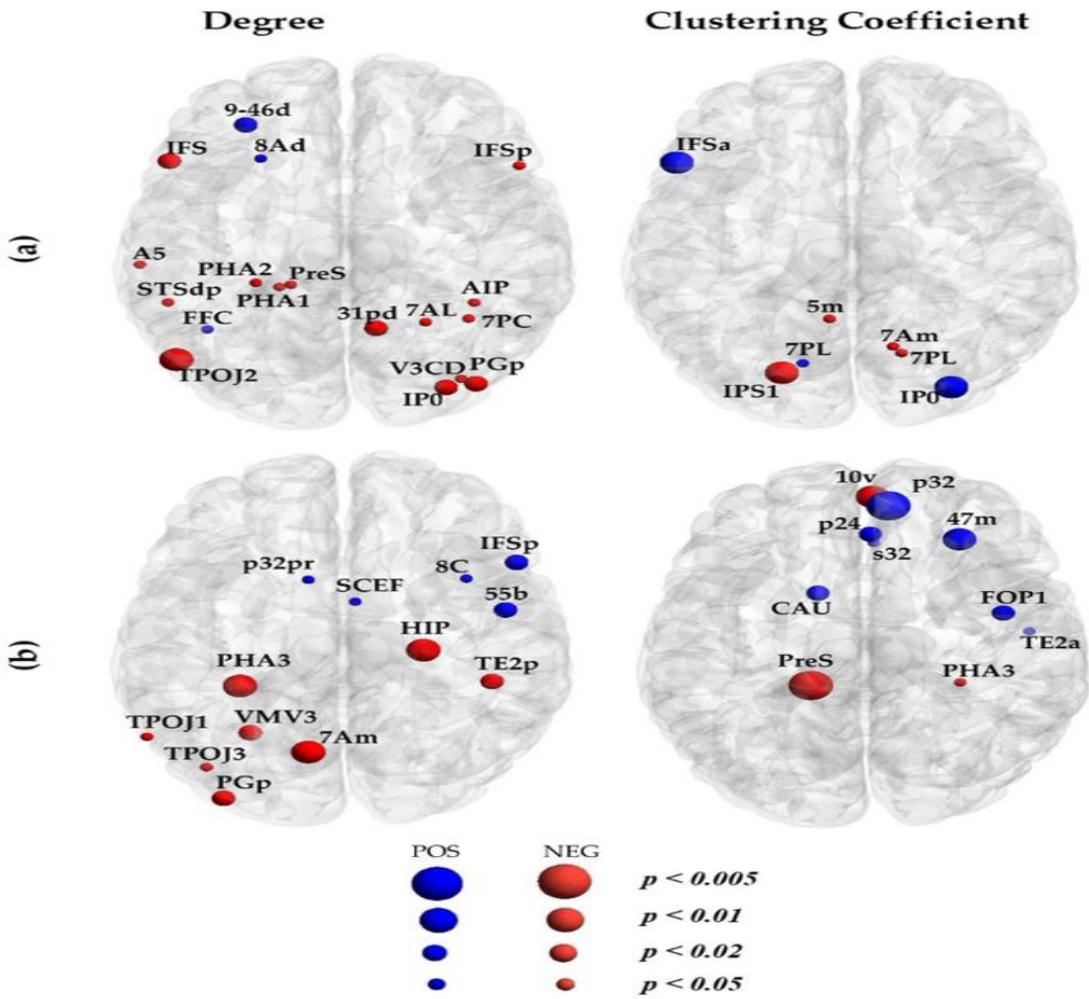

Figure 4: *Regions showing significant association with times used cannabis in (a) structural and (b) functional networks. Nodes in red and blue show a negative (NEG) and positive (POS) association with times used cannabis, respectively. The node size represents the significant level ($p < 0.05$, $p < 0.02$, $p < 0.01$ and $p < 0.005$, uncorrected) with larger nodes showing smaller p values. After FDR correction, only the PreS region was found to be statistically significant.*

Feature-rich club nodes were mainly located in the parietal and posterior regions of both groups, with minor differences. Cannabis users showed slightly fewer and more abundant club nodes within centrotemporal and parietal regions, respectively.

Post hoc Analysis

Figure 4 and Tables S5–S8 show regression results showing regions where plotted measures were significantly ($p < 0.05$, uncorrected) associated with TUC for structural (SN) and functional (FN) networks. In this figure, the nodes exhibit a rate of change in node degree (β coefficient) and a clustering coefficient higher than mean + 2SD with increasing TUC. In several regions of the posterior region, structural networks (within the bilateral frontal cortex, left parieto-parieto-occipital junction, right V3CD) and functional networks (within the left parahippocampal region, left ventral-medial). Visual field, left superior parietal cortex, left inferior parietal cortex, right hippocampus, right medial temporal cortex). Grades in several regions of the SN (in the left dorsolateral prefrontal cortex) and FN (in the right inferior frontal cortex, right premotor cortex) were positively correlated with TUC. Clustering coefficients of frontal and occipital multiple nodes were also positively correlated with TUC in functional and structural networks, respectively ($p < < 0.01$, uncorrected). The left interparietal sulcus region in the SN and the left anterior abutment, anterior cingulate gyrus and medial temporal cortex in the FN were found to be negatively associated with TUC ($p<0.01$, uncorrected). The left inferior frontal cortex and right intra-parietal area in the SN and the right orbital and pole-frontal cortex, right anterior cranial cortex and left tail in the FN showed opposite trends (Table S5). The above important associations between network measurements and TUC did not survive the FDR amendment. After FDR correction, only a significant association between grade and TUC within the presubiculum region persisted.

Discussion

Considering the fact that cannabis usage is very

common in the world, little is known about how marijuana could affect the brain. Using graph-theoretical analysis on a sizable sample of cannabis users and healthy controls, this study examined the relationship between cannabis use and brain structural and functional connectivity. Our findings revealed that: (1) cannabis users' brain structural and functional networks had a small world topology and a rich-club organisation, (2) there were no significant differences in global network measures between the groups, (3) cannabis users' regional integration and segregation of the structural and functional networks were significantly lower and higher, respectively, in comparison to healthy controls, and (4) there was a significant correlation between local measures of sativa use and global measures of sativa use. Collectively, the results demonstrated that cannabis users have altered regional characteristics of their brain's structural and functional networks. In line with earlier findings9,12,16, our findings revealed no appreciable differences between cannabis users and healthy controls in the overall network features of the structural and functional brain networks ($p > 0.05$, uncorrected). In keeping with earlier research38 on healthy persons, the small-world features of both structural and functional networks were also discovered to be comparable across the two groups.

The results revealed regional changes in structural networks associated with cannabis use, particularly in the cingulate cortex, dorsolateral, fronto/posterior tectum, fronto-medial cortex, insula, and temporal regions. . Altered structural connectivity observed in these regions may be related to regional changes in cortical gray matter thickness associated with substance use disorders and uneven distribution of cannabinoid receptors in the brain. There are 32,39,40,41,42. More isolated networks tend to have higher clustering coefficients,37 so increased clustering coefficients in some regions may indicate differences in the local processing power of these networks. 12. These different patterns of global and local indicators may reflect different sample characteristics in the study. This current data find abundant club nodes widely distributed in cortical and subcortical regions, consistent with previous findings. Structurally abundant club nodules were found predominantly in bilateral frontal, temporal, mid-occipital and deep brain structures in both groups, whereas functional networks were predominantly located in the parietal and posterior regions. rice field. Compared with controls, our results showed that the structural network of cannabis users had higher and lower numbers of Rich Crab nodes in the superior and inferior temporal gyri, respectively. This result contrasts with other studies16 that found no difference in the composition of structural networks between cannabis users and healthy controls in wealthy clubs. The results showed that most of the functional rich club nodes were located in the parietal and posterior regions of both groups, with slight differences in the number of rich club nodes. Compared with controls, cannabis users had slightly fewer and more centrotemporal and parietal horn knots, respectively. Only a few nodes in the back showed high levels of rich clubbing of the cannabis user's functional network. This domain has been reported to play an important role in habit formation in addictive behaviors44. These results suggest the possibility of an aberrant connectome associated with cannabis use.

This research findings also revealed a strong correlation between the number of lifetime cannabis users and the node degree/cluster coefficient of structural/functional networks. According to prior research41, the clustering coefficient of structural connectivity, a segregation measure, revealed a positive correlation between lifetime cannabis usage and the medial temporal cortex, as well as the dorsolateral prefrontal cortex in some cases. shown a bad correlation in the field of. In the prehippocampal region of the medial temporal cortex, we similarly discovered a negative association between local metrics (degree of structural network, clustering coefficient of functional network, and TUC). The medial temporal cortex, temporoparieto-occipital junction, and hippocampus were the areas with the greatest negative correlation between degree of functional network and length of cannabis usage. The hippocampus is one of the brain regions with the highest expression of CB1 receptors45. CB1-associated structural and functional alterations have been found to be common to this region in both humans and animal models16. However, positive associations between functional network clustering coefficients and TUC were mainly observed in the anterior cingulate cortex and medial prefrontal cortex. While some studies have reported no significant associations between duration of cannabis use, frequency of cannabis use, age of onset and adverse effects on brain networks, others have reported early onset of cannabis use or It has been suggested that prolonged prolongation can impair brain networks15,46. These discrepancies may be due to differences in self-reported values, differences in cannabis user populations in different studies, and differences in methodologies. Numerous restrictions apply to current research. The HCP database, which is a cross-cutting database, first, offers scant details on cannabis usage and addiction. Age of onset and other existing metrics are level-based and imprecise. Cannabis usage habits, whether daily or chronic, may cause changes in connection patterns. Second, he restricted the cross-sectional database to young adults between the ages of 22 and 36. To more accurately describe how connectivity patterns within the sample vary over time, longitudinal data are required. Last but not least, given that functional connectivity and rs-fMRI are

now generally believed to be temporally dynamic, dynamic connectivity analysis may help better uncover time-varying connectivity patterns linked to cannabis usage.

Conclusion

The current study looked into the relationship between cannabis usage and structural and functional connections in the brain. To find changes in brain connection related to cannabis use, a graph-theoretic analysis was done on whole-brain functional and structural networks of cannabis users and healthy controls. Both groups' brain networks revealed small-world characteristics. Our data also showed regional impacts on network segregation and integration metrics, with the insular, frontal opercular, and lateral/medial temporal cortices showing greater significance. The general characteristics of the brain networks are still present, though. A typical pattern was revealed by the rich-club analysis of the structural and functional networks, despite some slight discrepancies between the two groups. In some areas, such as the hippocampus and presubiculum, which have been found in prior research to have a high concentration of CB1-receptors, a negative correlation between cannabis usage frequency and regional structural and functional network measurements was discovered. Future research will look into how cannabis users' functional connection patterns develop over time.

Ethics Declarations

Competing Interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

1. Petker, T. et al. Cannabis Involvement and Neuropsychological Performance : Findings from the Human Connectome Project 1–9 (2019). https://doi.org/10.1503/jpn.180115.
2. Mercuri, K. et al. Episodic foresight deficits in regular, but not recreational, cannabis users. J. Psychopharmacol. 32(8), 876–882. https://doi.org/10.1177/0269881118776672 (2018).
3. Filbey, F. M. et al. Long-term effects of marijuana use on the brain. Proc. Natl. Acad. Sci. USA 111(47), 16913–16918. https://doi.org/10.1073/pnas.1415297111 (2014).
4. Chye, Y. et al. Cannabis, cannabinoids, and brain morphology: A review of the evidence. Biol. Psychiatry Cogn. Neurosci. Neuroimaging 1–9, 2020. https://doi.org/10.1016/j.bpsc.2020.07.009 (2020).
5. Tzilos, G. K. et al. Lack of hippocampal volume change in long-term heavy cannabis users. Am. J. Addict. 14(1), 64–72. https://doi.org/10.1080/10550490590899862 (2005).
6. Lorenzetti, V., Chye, Y., Silva, P., Solowij, N. & Roberts, C. A. Does regular cannabis use affect neuroanatomy ? An updated systematic review and meta-analysis of structural neuroimaging studies. Eur. Arch. Psychiatry Clin. Neurosci. https://doi.org/10.1007/s00406-019-00979-1 (2019).
7. Lorenzetti, V. et al. Gross morphological brain changes with chronic, heavy cannabis use. Br. J. Psychiatry 206(1), 77–78. https://doi.org/10.1192/bjp.bp.114.151407 (2015).
8. Filbey, F. M., McQueeny, T., Kadamangudi, S., Bice, C. & Ketcherside, A. Combined effects of marijuana and nicotine on memory performance and hippocampal volume. Behav. Brain Res. 293, 46–53. https://doi.org/10.1016/j.bbr.2015.07.029 (2015).
9. Chye, Y. et al. Alteration to hippocampal volume and shape confined to cannabis dependence: A multi-site study. Addict. Biol. 24(4), 822–834. https://doi.org/10.1111/adb.12652 (2019).
10. Bullmore, E. & Sporns, O. Complex brain networks: Graph theoretical analysis of structural and functional systems. Nat. Rev. Neurosci. 10(3), 186–198. https://doi.org/10.1038/nrn2575 (2009).
11. Manza, P., Tomasi, D. & Volkow, N. D. Subcortical local functional hyperconnectivity in cannabis dependence. Biol. Psychiatry Cogn. Neurosci. Neuroimaging 3(3), 285–293. https://doi.org/10.1016/j.bpsc.2017.11.004 (2018).
12. Kim, D. J. et al. Structural network topology revealed by white matter tractography in cannabis users: A graph theoretical analysis. Brain Connect. 1(6), 473–483. https://doi.org/10.1089/brain.2011.0053 (2011).
13. Lu, H. & Stein, E. A. Resting state functional connectivity: Its physiological basis and application in neuropharmacology. Neuropharmacology 84, 79–89 (2014).
14. Fornito, A., Zalesky, A. & Breakspear, M. The connectomics of brain disorders. Nat. Publ. Gr. 16(3), 159–172. https://doi.org/10.1038/nrn3901 (2015).
15. Zalesky, A. et al. Effect of long-term cannabis use on axonal fibre connectivity. Brain 135(7), 2245–2255. https://doi.org/10.1093/brain/aws136 (2012).
16. Kim, D. J. et al. Aberrant structural–functional coupling in adult cannabis users. Hum. Brain Mapp. 40(1), 252–261. https://doi.org/10.1002/hbm.24369 (2019).
17. Çelik, Z. Ç. et al. Structural connectivity in adolescent synthetic cannabinoid users with and without ADHD. Brain Imaging Behav. 14, 505–519 (2019).
18. Orr, J. M., Paschall, C. J. & Banich, M. T. Recreational marijuana use impacts white matter integrity and subcortical (but not cortical) morphometry. NeuroImage Clin. 12, 47–56. https://doi.org/10.1016/j.nicl.2016.06.006 (2016).
19. Manza, P., Shokri-Kojori, E. & Volkow, N. D. Reduced segregation between cognitive and emotional processes in cannabis dependence. Cereb. Cortex 30(2), 628–639. https://doi.org/10.1093/cercor/bhz113 (2020).
20. Van Hell, H. H. et al. Chronic effects of cannabis use on the human reward system : An fMRI study. Eur. Neuropsychopharmacol. 20(3), 153–163. https://doi.org/10.1016/j.euroneuro.2009.11.010 (2010).
21. Koenis, M. M. G. et al. Associations of cannabis use disorder with cognition, brain structure, and brain function in African Americans. Hum. Brain Mapp. 42, 1727–1741. https://doi.org/10.1002/hbm.25324 (2020).
22. Ramaekers, J. G., Mason, N. L., Toennes, S. W., Theunissen, E. L. & Amico, E. Functional brain connectomes reflect acute and chronic cannabis use. Sci. Rep. 12(1), 1–12. https://doi.org/10.1038/s41598-022-06509-9 (2022).
23. Van Den Heuvel, M. P. & Sporns, O. Rich-Club Organization of the Human Connectome, vol. 31 15775–15786 (2011). https://doi.org/10.1523/JNEUROSCI.3539-11.2011.
24. Van den Heuvel, M. P. & Sporns, O. An anatomical substrate for integration among functional networks in human cortex. J. Neurosci. 33(36), 14489–14500. https://doi.org/10.1523/JNEUROSCI.2128-13.2013 (2013).
25. Van Essen, D. C. et al. The human connectome project: A data acquisition perspective. Neuroimage 62(4), 2222–2231. https://doi.org/10.1016/j.neuroimage.2012.02.018 (2012).

26. Van Essen, D. C. et al. The WU-Minn human connectome project: An overview. Neuroimage 80, 62–79. https://doi.org/10.1016/j.neuroimage.2013.05.041 (2013).
27. Hodge, M. R. et al. ConnectomeDB-Sharing human brain connectivity data. Neuroimage 124, 1102–1107. https://doi.org/10.1016/j.neuroimage.2015.04.046 (2016).
28. Glasser, M. F. et al. The minimal preprocessing pipeline for the Human Connectome Project. Neuroimage https://doi.org/10.1016/j.neuroimage.2013.04.127 (2013).
29. Smith, S. M. et al. Resting-state fMRI in the Human Connectome Project. Neuroimage 80, 144–168. https://doi.org/10.1016/j.neuroimage.2013.05.039 (2013).
30. Glasser, M. F. et al. A multi-modal parcellation of human cerebral cortex. Nature 536(7615), 171–178. https://doi.org/10.1038/nature18933 (2016).
31. Robinson, E. C. et al. MSM: A new flexible framework for multimodal surface matching. Neuroimage 100, 414–426. https://doi.org/10.1016/j.neuroimage.2014.05.069 (2014).
32. Yeh, F. C., Wedeen, V. J. & Tseng, W. Y. I. Generalized q-sampling imaging. IEEE Trans. Med. Imaging 29(9), 1626–1635. https://doi.org/10.1109/TMI.2010.2045126 (2010).
33. Yeh, F. C., Verstynen, T. D., Wang, Y., Fernández-Miranda, J. C. & Tseng, W. Y. I. Deterministic diffusion fiber tracking improved by quantitative anisotropy. PLoS ONE 8(11), 1–16. https://doi.org/10.1371/journal.pone.0080713 (2013).
34. Yeh, F. et al. Differential tractography as a track-based biomarker for neuronal injury. Neuroimage 2019, 116131. https://doi.org/10.1016/j.neuroimage.2019.116131 (2019).
35. Yeh, F. C. et al. Automatic removal of false connections in diffusion MRI tractography using topology-informed pruning (TIP). Neurotherapeutics 16(1), 52–58. https://doi.org/10.1007/s13311-018-0663-y (2019).
36. Van den Heuvel, M. P. et al. Proportional thresholding in resting-state fMRI functional connectivity networks and consequences for patient-control connectome studies: Issues and recommendations. Neuroimage 152, 437–449. https://doi.org/10.1016/j.neuroimage.2017.02.005 (2017).
37. Rubinov, M. & Sporns, O. Complex network measures of brain connectivity: Uses and interpretations. Neuroimage 52(3), 1059–1069 (2010).
38. Hagmann, P. et al. Mapping the structural core of human cerebral cortex. PLoS Biol. 6(7), 1479–1493. https://doi.org/10.1371/journal.pbio.0060159 (2008).
39. Feil, J. et al. Addiction, compulsive drug seeking, and the role of frontostriatal mechanisms in regulating inhibitory control. Neurosci. Biobehav. Rev. 35(2), 248–275. https://doi.org/10.1016/j.neubiorev.2010.03.001 (2010).
40. Mackey, S. et al. Mega-analysis of gray matter volume in substance dependence: General and substance-specific regional effects. Am. J. Psychiatry 176(2), 119–128. https://doi.org/10.1176/appi.ajp.2018.17040415 (2019).
41. Harper, J. et al. The effects of alcohol and cannabis use on the cortical thickness of cognitive control and salience brain networks in emerging adulthood: A co-twin control study. Biol. Psychiatry 89(10), 1012–1022. https://doi.org/10.1016/j.biopsych.2021.01.006 (2021).
42. Bloomfield, M. A. P. et al. The neuropsychopharmacology of cannabis: A review of human imaging studies. Pharmacol. Ther. 195, 132–161 (2019).
43. Sporns, O. Contributions and challenges for network models in cognitive neuroscience. Nat. Neurosci. 17(5), 652–660. https://doi.org/10.1038/nn.3690 (2014).
44. Koob, G. F. & Volkow, N. D. Neurobiology of addiction: A neurocircuitry analysis. Lancet Psychiatry 3(8), 760–773. https://doi.org/10.1016/S2215-0366(16)00104-8 (2016).
45. Svíženská, I., Dubový, P. & Šulcová, A. Cannabinoid receptors 1 and 2 (CB1 and CB2), their distribution, ligands and functional involvement in nervous system structures - A short review. Pharmacol. Biochem. Behav. 90(4), 501–511. https://doi.org/10.1016/j.pbb.2008.05.010 (2008).
46. Solowij, N. et al. Cognitive functioning of long-term heavy cannabis users seeking treatment. JAMA 287(9), 1123–1132 (2015).