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Short communication

Neurocognitive functions of heavy cannabis using schizophrenia patients

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ABSTRACT

This current study assessed neurocognitive functioning in a carefully selected sample of schizophrenia patients with and without heavy cannabis use and healthy controls. All subjects were negative for any other substance use. Schizophrenia subjects had impaired neurocognitive functions across a wide range of tasks compared to healthy controls. Cannabis using schizophrenia patients had focused impairments on tasks of attention, and the findings suggest an impulsive pattern of response among these patients.

1. Introduction

The prevalence of substance abuse and dependence is elevated among schizophrenia patients [18], with cannabis being the most common illicit substance of abuse [14]. Though some negative effects of cannabis use among schizophrenia patients are established (poor adherence to medications, higher rates of relapse and hospitalizations [15,16], more severe positive symptoms [4,6,11]), the effects of cannabis use on cognitive functioning of schizophrenia patients is still unclear. While healthy subjects who report heavy cannabis use have cognitive impairments [20,21], findings among schizophrenia patients are heterogeneous; studies indicated impaired [10], similar [1,3], and better [7,13] cognitive performance in cannabis-using schizophrenia patients. A recent meta-analysis reports a paradoxical effect of cannabis use on cognitive functioning of schizophrenia patients [22]. However, only two of the analyzed studies consisted of patients without comorbid substance abuse. In addition, many of these studies included both schizophrenia and schizoaffective patients, despite reports proposing a different cognitive profile in the two patient populations [5]. The aim of this study was, therefore, to compare the cognitive functioning and clinical characteristics of a carefully selected sample of schizophrenia patients. We compared heavy cannabis using schizophrenia patients with no other substance use disorder with schizophrenia patients without a history of any substance use disorder. In order to determine particular differences in neurocognitive functioning among schizophrenia patients with and without cannabis use, we also compared the schizophrenia patients to healthy controls.

2. Subjects and methods

2.1. Sample

In the current study, we evaluated 28 schizophrenia outpatients who met DSM-IV-TR criteria for schizophrenia (age 18–45) and 15 healthy controls. Twelve of the patients met the DSM-IV-TR criteria for cannabis dependence (SCH+CAN), and 16 patients were negative for cannabis use (SCH-CAN). All groups were matched for age and gender. The SCH+CAN and SCH-CAN group were further matched for history of disease (age of onset of schizophrenia, time since diagnosed with schizophrenia, number of psychiatric hospitalizations), and use of medications (first generation and second generation antipsychotics, benzodiazepines, anticholinergic drugs).

Data regarding current and past substance abuse were collected through structured interviews and a detailed questionnaire that included questions on cannabis use (age of onset, frequency, last use) and use of other substances of abuse. Though self-report of cannabis has been shown to be reliable in a cohort of subjects with psychosis [12], additional information regarding past substance use was verified through patients' hospital and outpatient files and documented urine drug screenings.

Inclusion in the SCH+CAN group was based on common criteria for heavy cannabis previously reported [17,19] and required using cannabis at least five times per week during the previous 2 years. Further substance use, other than cannabis, was limited to less than five occasions during their lifetime (based on criteria from Jocker-Scherubl et al. [13]), none of these occasions being during

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the year prior to study entry. SCH-CAN subjects and healthy controls were negative for any substance abuse or dependence. They did not use any illicit substance on more than five occasions during their lifetime, and did not use these substances during the past year. All subjects were negative for current or past alcohol abuse or dependence. Subjects suffering from neurological disorders, mental retardation or color blindness were excluded from the study.

2.2. Clinical and functional assessment

All healthy controls were assessed by the Structured Clinical Interview for DSM-IV non-patient (SCID-NP).

Schizophrenia patients were clinically assessed using the Positive and Negative Symptoms Scale (PANSS), Scale for the Assessment of Negative Symptoms (SANS) and Clinical Global Impression (CGI). Functional assessment was conduced using the Global Assessment of Functioning (GAF) scale and two subscales of the Multinomah Community Ability Scale (MCAS; "adjustment to living" and "social competence").

2.3. Neurocognitive assessment

All participants performed a battery of neurocognitive tests using the Cambridge Neuropsychological Test Automated Battery (CANTAB). The tests performed were aimed at assessing general psychomotor abilities (Motor screening [MOT]), attention (Rapid visual information processing [RVIP]), visual memory (Pattern recognition memory [PRM]), spatial memory (Spatial recognition memory [SRM]), and executive functioning (Intra-extra dimensional set shift [IED]), Spatial working memory (SWM), Tower of London (CANTAB'S Stockings of Cambridge [ToL]). Tests were presented in semi-randomized manner.

2.4. Statistical analyses

First, schizophrenia patients were compared to healthy controls using independent samples *t*-tests (for parametric variables) and Chi^2 analyses (for non-parametric variables). Second, SCH+CAN and SCH-CAN were compared using similar statistical analyses.

3. Results

3.1. Schizophrenia patients and healthy controls

Several differences were found in the neurocognitive functioning of schizophrenia patients compared to healthy controls (as found earlier, for example, Braw et al., 2008 [2]).

Schizophrenia patients had impaired functioning across a wide range of tasks compared to healthy subjects: these include percent of correct answers on the PRM (81.84 ± 18.00 and 93.15 ± 5.32, respectively; $t[40] = -2.28$, $P < 0.05$) and SRM tasks (75.89 ± 14.97 and 85.00 ± 8.32, respectively; $t[40] = -2.11$, $P < 0.05$); suggesting impaired visual and spatial memory among the schizophrenia subjects. Significant differences were also found between schizophrenia subjects and healthy controls in the number of errors performed in the SWM task (25.78 ± 20.90 and 12.33 ± 14.83, respectively; $t[41] = 2.20$, $P < 0.05$) and the number of problems solved in minimal moves in the ToL task (8.21 ± 2.25 and 9.80 ± 1.93, respectively; $t[41] = -2.30$, $P < 0.05$) suggesting impaired executive functioning among the schizophrenia subjects.

3.2. SCH+CAN and SCH-CAN

No differences were found in PANSS, CGI and MCAS "adjustment to living" and "social competence" scores between the groups. Though no significant difference was found in SANS scores between the groups, there was a trend suggesting that SCH+CAN group suffered from less negative symptoms than controls ($t[25] = 1.87$, $P = 0.07$), and a significant difference was found in the asociality subtest ($t[25] = 3.12$, $P = 0.004$). Comparison of groups on GAF score revealed a significant difference ($t[26] = -2.16$, $P = 0.04$), with the SCH+CAN group having better functioning than the SCH-CAN group (47.58 [±11.56] vs 39.62 [±7.92] respectively).

These data are shown in Table 1.

Several significant differences were found in the cognitive tasks. Subjects in the SCH+CAN subjects responded to more non-target

Table 1
Clinical and functional scores of schizophrenia patients with (SCHI+CAN) and without (SCH-CAN) cannabis use.

	SCH + CAN ($n = 12$), mean (±SD)	SCH − CAN ($n = 16$), mean (±SD)	*P*
GAF	47.58 (±11.56)	39.62 (±7.92)	0.04[a]
MCAS adjustment to living subscale	11.73 (±3.13)	11.44 (±2.87)	0.81
MCAS social competence subscale	16.55 (±5.41)	13.62 (±4.72)	0.15
CGI	4.75 (±0.75)	4.75 (±0.78)	0.99
PANSS			
Total score	66.92 (±19.98)	66.56 (±20.98)	0.96
Positive subscale	14.33 (±6.51)	11.19 (±4.05)	0.13
Negative subscale	16.58 (±6.42)	18.38 (±7.65)	0.52
Psychopathology subscale	36.00 (±10.87)	37.00 (±13.91)	0.84
SANS – total score	31.73 (±18.29)	46.50 (±21.19)	0.07[b]
SANS – emotional flattening subscale	11.56 (±8.02)	15.62 (±8.52)	0.22
SANS – alogia subscale	3.64 (±3.30)	6.00 (±4.83)	0.17
SANS – apathy subscale	5.80 (±4.71)	6.38 (±5.02)	0.77
SANS – asociality subscale	7.82 (±6.71)	14.88 (±5.05)	0.004[c]
SANS – attention subscale	3.45 (±3.21)	3.62 (±4.27)	0.91

GAF: general assessment of functioning; MCAS: Multinomah Community Ability Scale; CGI: clinical global impression; PANSS: Positive and Negative Syndrome Scale; SANS: Scale for the Assessment of Negative Symptoms.

[a] $P < 0.05$.

[b] $P < 0.1$.

[c] $P < 0.01$.

Table 2
Neurocognitive test scores of schizophrenia patients with (SCHI + CAN) and without (SCH – CAN) cannabis use.

	SCH + CAN (n = 12), mean (±SD)	SCH – CAN (n = 16), mean (±SD)	P
MOT – response time (msec)	713.54 (±177.02)	854.01 (±244.93)	0.10
RVIP – Probability of hit (%)	87.42 (±5.16)	90.25 (±6.69)	0.23
RVIP – Probability of false alarm (%)	1.26 (±1.82)	0.16 (±0.29)	0.02[a]
PRM – Success (%)	86.11 (±16.22)	78.65 (±19.12)	0.29
SRM – Success (%)	72.92 (±14.37)	78.13 (±15.5)	0.37
SWM – Total errors	25.42 (±19.70)	27.00 (±23.20)	0.85
SWM – Within errors	1.67 (±1.97)	0.63 (±0.89)	0.07[b]
SWM – Between errors	1.83 (±2.21)	0.75 (±0.93)	0.84
SWM – Strategy	33.58 (±6.46)	32.69 (±7.38)	0.74
IED – Stages completed	8.85 (±0.79)	8.83 (±0.58)	0.72
IED – Total errors	25.33 (±19.36)	17.00 (±13.71)	0.24
ToL – Initial thinking time (msec)	4490 (±3123)	12995 (±12756)	0.04[a]
ToL – Subsequent thinking time (msec)	699 (±751)	1273 (±1297)	0.18
ToL – Problems solved in minimal moves	7.33 (±2.27)	8.88 (±2.06)	0.07[b]

MOT: motor test; RVIP: rapid visual information processing; PRM: pattern recognition; SRM: spatial recognition memory; SWM: spatial working memory; IED: intra-extra dimensional set shift; ToL: Towers of London (CANTAB's stocking of Cambridge).
[a] $P < 0.05$.
[b] $P < 0.1$.

sequences and had a higher probability of false alarm in the RVIP task (t[25] = −2.31, P = 0.02). SCH+CAN subjects had a lower initial thinking time (i.e., took less time until moving the first ball) in the ToL task (t[26] = 2.15, P = 0.04], but there was no difference in subsequent thinking time between the groups (t[26] = 1.37, P = 0.18]. A trend was found with subjects in the SCH+CAN group solving less problems in minimum moves in the ToL task (t[26] = 1.88, P = 0.07). A trend was also found in the SWM task; SCH+CAN subjects made more "within" errors (i.e. repeated responses to a box previously opened and shown to be empty earlier in the same search sequence) (t[26] = −1.89, P = 0.07). No significant differences were found in the IED test, though a ceiling effect was observed regarding the total number of steps completed; all but four participants acquired the maximal score of nine (completed all nine stages of the task). No significant differences were found in the SRM and PRM tests.

These results are presented in Table 2.

4. Discussion

Comparison of neurocognitive functioning of schizophrenia patients and healthy subjects are in line with previous reports showing impairment among schizophrenia patients across a wide range of tasks. These findings shed light on the specific differences found among the SCH+CAN and SCH-CAN groups.

Heavy cannabis-using schizophrenia patients detected less target sequences in the RVIP task (a continuous performance task [CPT]), representing a deficit in sustained attention. The optimal pattern of response in this task is to maximize sensitivity so that so that no targets are missed and such that no false alarms are committed. The higher probability of a false alarm in the cannabis-using schizophrenia patients may indicate that these subjects place a premium on speed rather than accuracy, thus impairing their detection of targets and their correction rejections. This conclusion is strengthened by the findings of shorter initial thinking time in the SCH+CAN group (i.e., subjects in this group took less time to move the first ball in the ToL task than those in the SCH-CAN group). Subjects in both groups were instructed and encouraged to plan their moves before actually enacting the solution to the problems in this task. As the overall functioning of SCH+CAN subjects on this task was not better, the rapid initial response cannot be explained by better overall processing of the task. These two findings may represent an impulsive pattern of response among subjects in the SCH+CAN group, which is in tune with previous reports on high impulsivity among cannabis-abusing schizophrenia patients [8]. Furthermore, subjects in this group tended to commit more errors on the SWM task, a finding of spatial memory, which has been previously reported to be associated with higher impulsivity scores [9]. As little is known about the dose-response effect of cannabis on cognitive functioning among schizophrenia patients, these findings may be specific to a sub-population of schizophrenia patients with heavy cannabis use. As these specific findings are different from those found when comparing schizophrenia patients and healthy controls, and as subjects for the SCH+CAN and SCH-CAN groups were matched for various sociodemographic and disease-related variables, these findings may be related particularly to cannabis use.

Though it is speculated that this pattern of neurocognitive functioning would interfere with subjects' ability to carry out complex mental manipulations and sustain a high level of functioning over time, subjects in the SCH+CAN generally had a higher level of functioning (as apparent by GAF scores) and did not differ from the SCH-CAN group in other functions (as evaluated by the MCAS). These findings are similar to those in previous reports indicating similar or better functioning among cannabis using schizophrenia patients. Possible explanations that have been proposed for this replicated finding include better premorbid functioning, a higher level of functioning required to continuously obtaining cannabis and the possible positive effects of cannabis on social and global functioning among schizophrenia patients. As groups were matched for sociodemographic and scholastic characteristics, this finding does not seem to be attributed to higher premorbid functioning. A longitudinal study is needed to fully assess this possibility.

There are several limitations to the current study. The exclusion of subjects with a history of non-cannabis substance use and non-schizophrenia psychotic disorders has limited the sample size

necessitating additional studies with a larger sample of subjects. As THC is regarded the major component of cannabis affecting psychotic and cognitive outcomes [10] and cannabidiol, another cannabis component, has been reported to have neuroprotective effects [23], the THC/cannabidiol ratio in the cannabis consumed may affect outcomes, though it was not possible to take this into account. Finally, since the study was cross-sectional, it is not possible to determine the causal relationship between neurocognitive functioning and heavy cannabis use among schizophrenia patients. These preliminary findings must be replicated with a larger sample of chronic cannabis using schizophrenia patients without comorbid substance use.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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