# Effects of Long-Term Cannabis Use on Selective Attention: An Event-Related Potential Study

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SOLOWIJ, N., P. T. MICHIE AND A. M. FOX. Effects of long-term cannabis use on selective attention: An event-related potential study. PHARMACOL BIOCHEM BEHAV 40(3) 683-688, 1991. — Brain event-related potentials (ERPs) were recorded from nine long-term cannabis users during a complex auditory selective attention task and compared with nine nonuser controls. Stimuli consisted of a random sequence of tones varying in location, pitch and duration. Subjects were instructed to respond to long-duration tones of a particular pitch and location. Cannabis users' task performance was significantly worse than controls. The most striking difference between the ERPs of the two groups was in the greatly enhanced early processing negativity in the user group to short-duration stimuli which matched the target on location only. This is indicative of users engaging in unnecessary pitch processing and thus having difficulty in setting up an accurate focus of attention and in filtering out irrelevant information. The data suggest a dysfunction in the allocation of attentional resources and stimulus evaluation strategies. These results imply that long-term cannabis use may impair the ability to efficiently process information.

Cannabis Long-

Long-term effects Event-related potentials

ntials Cognitive functioning

Selective attention

ALTHOUGH numerous studies have reported the acute effects of cannabis on psychomotor and cognitive performance, relatively few studies have investigated cognitive functioning in chronic users. Of those that have, most were done more than a decade ago and produced contradictory results, due in part to the gross measures used and to methodological difficulties. Despite the lack of consistent evidence for cognitive impairment in chronic users, there remains considerable controversy over this issue. Reports in the clinical literature consistently describe mental deterioration associated with chronic use of cannabis, particularly in the form of attentional dysfunction, memory problems and disturbances of concentration and judgement (5,10).

The fact that, acutely, cannabis impairs the ability to perform complex functions requiring attention and mental coordination (e.g., driving) is well documented (10). The question as to whether chronic use of cannabis leads to any long-term impairment remains unresolved. In the past, researchers have relied upon the use of psychometric tests to assess the presence of dysfunction. While some studies did find significant differences between cannabis users and controls on a number of cognitive tests, these could variously be attributed to acute intoxication (21), lack of prestandardization of test batteries for the rural subject populations used (18), or the unrepresentative populations tested (20). Many studies have been unable to replicate the findings (1,10).

Of the more recently published studies, one examined regular and heavy cannabis users in India who were first evaluated in the early 1970s and then retested with similar instruments ten years later (6). Compared to the controls, users demonstrated a significant performance decrement on a number of tests measuring short-term memory, reaction time and visuomotor performance. The authors report these findings in terms of "impairment of cognitive functions associated with long-term heavy cannabis use." Neurological assessment techniques have also been employed to investigate this issue. One recent evaluation of regional cerebral blood flow demonstrated globally reduced resting levels in chronic users, which was interpreted as "most likely the consequence of the dysfunction of the central nervous system accompanying chronic cannabis use" (22). The conclusions drawn from each of these types of studies, however, provide little information as to the nature of any specific deficits associated with long-term use of cannabis.

One reason for the equivocal nature of results from past studies may be that the tests used are insufficiently sensitive to detect subtle dysfunction of specific cognitive processes. There has been relatively little use of quantitative measures derived from experimental cognitive psychology in any studies of chronic drug-related deficits. The advent of a number of sensitive new techniques based on modern theories of cognition and information processing permit the simultaneous assessment of electrophysiology, cognition and behaviour and the detection of even subtle dysfunction in specific stages of information processing. These involve recording brain event-related potentials (ERPs) while subjects are engaged in a cognitive task. The present study employed such techniques to address the question of the existence and nature of attentional deficits in long-term cannabis users.

The focus of current ERP and cognitive research has been to

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identify ERP components as markers of specific stages of information processing. The amplitude and latency of ERP components are thought to reflect the nature, timing and duration of these processes. ERP studies of selective attention have primarily utilised the "cocktail party" paradigm, in which multiple channels of auditory stimuli are presented to the subject at rapid rates. While the subject's task is to attend to one channel only, ERPs elicited by stimuli from every channel are recorded, and differences between attended-channel ERPs and unattendedchannel ERPs constitute the attention effect. This is seen as a broad negativity in the ERP waveform, termed "processing negativity" or PN (3,8). If, in addition, a response to a particular stimulus in the attended channel is required, the ERP waveform to that stimulus will show a large positive component, generally referred to as the P300 complex. The P300 is elicited by taskrelevant, infrequently occurring stimuli (2,16). Its amplitude reflects the allocation of attentional resources for stimulus evaluation processes (4,16). It is these two components that are of particular relevance in the present study.

ERPs were recorded during a complex multidimensional auditory selective attention task, based on a paradigm developed by Hansen and Hillyard (3), involving tones that vary on the dimensions of location, pitch and duration. There exists a wealth of normative data on the ERP patterns elicited by this paradigm, and it has been used to investigate information processing among other groups suspected of deficient attentional mechanisms, for example, schizophrenics (7). The paradigm is useful for studying hierarchical models of information processing by manipulating the difficulty of discrimination of each dimension. In this case, the duration discrimination was the most difficult, followed by pitch and then location. This enables the subject, whose task is to selectively attend to a particular combination of these dimensions, to rapidly reject half of the stimuli from further analysis on the basis of location. Use of this paradigm will determine whether chronic cannabis users engage in a less efficient mode of processing than do controls.

#### METHOD

#### Subjects

Cannabis users were recruited from the general community by advertising in the newsletter of NORML (National Organization for the Reform of Marijuana Laws) and by word of mouth. Control subjects consisted of friends and associates of the experimenters and respondents to an advertisement at a student employment centre on a university campus. All subjects were paid for their participation. The data reported below is based on the results from nine cannabis users and nine matched nonuser controls.

Subjects were initially screened in a telephone interview. The criterion for inclusion in the user group was a minimum of three years of regular use of cannabis. This was defined as using cannabis at least twice a week on average over the last three years. Subjects were asked specific questions relating to their general health, and any respondents with a history of fits, febrile, neurological or psychiatric illnesses, multiple concussions or periods of unconsciousness were excluded from testing.

Subjects on any prescribed medication other than antibiotics were excluded from the sample. Subjects were screened for alcohol consumption with the following criteria for inclusion in the sample: less than 28 standard drinks per week on average for males and less than 14 for females, based on the National Health and Medical Research Council (9) guidelines for levels of "safe" drinking. Further criteria for inclusion were no more than one month of continuous drinking above these levels in the last three years and no more than six months ever of drinking above these levels. Subjects were screened for other drug use and rejected on the basis of a history of any regular substance use (defined as greater than or equal to once a month) or any subject having used any other drug in the month prior to testing.

The final sample consisted of six male and three female cannabis users, aged 19–40 (mean 29.4 years, SD=8.47). These were matched on age (to within two years), sex and years of education with nine nonuser controls, aged 21–41 (mean 29.5 years, SD=7.76). Within each group, eight subjects were righthanded and one left-handed, as determined by the Edinburgh Inventory (11). The average number of standard drinks per week consumed by the user group was 11.44, (SD=9.41), and by the control group, 5.67, (SD=5.68). Alcohol consumption in the two groups was not significantly different, F(1,16)=2.49, p<0.1343. All subjects had completed 13 years of school education and at least one year at tertiary level.

The mean of years of cannabis use in the user group was 11.2 years (SD=6.98, range 3-20 years), and the average level of use was 4.77 days per week (SD=1.85, range twice a week to daily use). The mean weekly consumption was 766 mg THC (SD=859, range 30-2400 mg/week), calculated as 15 mg THC per average cannabis cigarette. The longest period of abstinence from cannabis in the last three years ranged from 3-4 days to three months, mean 42 days (SD=27.76). Of the controls, three had never tried cannabis, two had tried it once or twice, and the remainder had used cannabis occasionally at parties between 3 and 7 years ago with the most experienced control having used 15 times in his entire life.

Following the telephone screen, an appointment was made for the test session (usually within the following week). Subjects were instructed to abstain from cannabis and alcohol for at least twelve hours prior to testing. The day before the test session, subjects were telephoned and reminded of these instructions and requested to provide a urine sample prior to going to bed. All subjects complied with this request.

#### Stimuli

Stimuli consisted of sequences of tone pips delivered randomly to the left or right ear via stereophonic headphones (TDH 49) at an intensity of 80 dB SPL. Half the tone pips presented to each ear were 1047 Hz, and the remainder were of a higher pitch at 1319 Hz (representing C6 and E6 on the musical scale). Tones at each ear/pitch combination occurred with equal probability (p=0.25). Within each ear/pitch combination, nineteen percent of the stimuli were 51 ms in duration (the standards), and six percent were 102 ms (the targets), both having a 10-ms rise and fall time. The stimuli were presented as a random sequence lasting 160 seconds per run with random interstimulus intervals of 200 to 500 ms. All aspects of stimulus delivery and randomisation were under computer control (Data General Nova 4/C), the only constraint placed on the randomisation procedure being that two target stimuli of the same type could not occur consecutively.

#### ERP Recording

Seven channels of electrophysiological data, six EEG and one EOG, were recorded using an electrode cap (Electro-cap International) and tin electrodes, respectively. The data was recorded using a Beckman Accutrace EEG machine with a time constant of 5 seconds and high-frequency cutoff of 30 Hz (3 dB down). Scalp electrodes were located over six lateral sites, F3, F4, C3,

C4, P3 and P4. The EOG channel monitored vertical and horizontal eye movement via electrodes taped above and on the outer canthus of the left eye. All scalp electrodes were referred to linked earlobes. A light-emitting diode one metre away from the subject at eye level was used as a fixation point. The ground electrode was located on the forehead. EEG and EOG channels were continuously digitised at 5.76 ms/point (175 Hz) for the duration of a run and stored on disk with stimulus and response markers for later analysis.

### Procedure

Upon arrival at the laboratory, subjects completed a consent form and deposited their urine sample from the previous evening in a freezer. They were requested to provide a second urine sample sometime during the test session. Urine samples were subsequently analysed to confirm that the subject was not in an acutely intoxicated state during testing. The criterion upon which this assertion was based was that the THC levels detected in the second sample were lower than those detected in the first.

Subjects participated in a single three-hour test session. All subjects completed a detailed drug history questionnaire and were tested for normal hearing by standard audiometric assessment. They were then trained on the selective attention task until they achieved the criterion level of performance of 50% hits and no more than 25% of responses being false alarms. The electrodes were then attached and the recording session commenced.

Subjects sat in an armchair in a darkened, sound-reduced room adjacent to the laboratory. They were instructed to attend to a particular location and pitch, and to respond as rapidly as possible to the long-duration tones by pressing a response button mounted on the arm of the chair. There were four attention conditions: respond to left low long, left high long, right low long or right high long. Each subject completed two runs of each attention condition, one with a right-hand response and one with a left-hand response. The order of attention conditions and responding hand was randomised among subjects and counterbalanced across groups.

#### Data Analysis

Button-press responses were classified as correct detections or "hits" if they occurred within a 200- to 1200-ms response window after an attended target stimulus. Reaction time was measured as the latency in ms of the button press from the onset of the attended target. An attended target not followed by a response within the response window was regarded as an error of omission or "miss." Button presses at other times were regarded as errors of commission or "false alarms." The number of hits as a ratio of the number of attended targets provided an estimate of the hit rate, while the false alarm rate was calculated as a ratio of the total number of nontargets. The signal detection measures, d' and  $\beta$ , were calculated using these estimates of hit and false alarm rate.

The digitised EEG data with stimulus and response markers were analysed on a VAX11/780 using a program that extracted overlapping epochs of 1050 ms including a 150-ms prestimulus baseline. All epochs containing EOG artefact greater than 64  $\mu$ V were rejected prior to averaging. Separate averages were created for hits and misses and for nontarget (standard) stimuli, excluding those that were followed by a false alarm response.

Following a procedure adopted by Hansen and Hillyard (3), stimuli were classified according to whether they matched (+) or did not match (-) the target of each run, on each of the

TABLE 1

MEAN TASK PERFORMANCE MEASURES OF REACTION TIME (RT), HIT RATE, FALSE ALARM RATE, d' AND  $\beta$  LEVELS OF CANNABIS USERS AND CONTROLS (WITH SD IN PARENTHESES)

<u> </u>	RT (ms)	Hit Rate (%)	False Alarms (%)	ď	β
Users	573.06	71.94	1.64	2.99	17.94
	(67.63)	(16.04)	(1.58)	(0.86)	(15.75)
Controls	536.96	86.72	0.32	4.34	44.54
	(79.25)	(12.79)	(0.29)	(1.02)	(38.42)

stimulus characteristics of location (L), pitch (P) and duration (D). Thus the attended target requiring a response would be denoted as L+P+D+, whereas a stimulus presented to the same location but of a different pitch and of short duration would be denoted as L+P-D-. Using this notation, all eight stimuli within a run could be classified as one of eight types: L+P+D+, L+P+D-, L+P-D+, L+P-D-, L-P+D+, L-P+D-, L-P-D+, L-P-D-. The targets were always the long-duration (D+) tones. Averages to the same stimulus type across high- and low-pitched stimuli and runs with leftand right-hand responses and sorted according to whether they were recorded from the hemisphere ipsilateral or contralateral to the stimulated ear.

#### RESULTS

## Behavioural Data

Task performance measures of reaction time, percent correct hits and false alarms, d' and  $\beta$  are depicted in Table 1. The mean reaction time for the user group was longer than that of the control group, but this difference failed to reach statistical significance, F(1,16)=1.08, p<0.31. Cannabis users had a significantly lower correct hit rate than controls, F(1,16)=4.67, p<0.0461. Users made significantly more false alarms than controls, F(1,16)=6.10, p<0.0251. Controls displayed greater acuity in target detection, measured by d', F(1,16)=9.12, p<0.0081, and there was a trend towards a greater degree of caution in responding by controls, as measured by  $\beta$ , F(1,16)=3.69, p<0.0727. Thus all behavioural measures, with the exception of reaction time, indicated that the performance of cannabis users on this selective attention task was significantly poorer than that of the controls.

#### ERP Data

The processes of selective attention were assessed by comparing the amplitudes of the various ERP components elicited by the four standard and four target stimuli distinguished on the basis of their location and pitch characteristics. These measures were subjected to a repeated-measures analysis of variance, with factors of group, stimulus, electrode site and hemisphere. Figure 1 depicts grand average ERPs to target (D+) stimuli at contralateral frontal, central and parietal scalp sites. The early part of the epoch reveals similar patterns of processing of the location dimension in both groups, with early separation of the L+ and L- traces at frontal and central sites. By about 200 ms, the L+P+ trace separates sharply from the L+P- trace in controls with a second negative peak (the N200) followed by a later positive complex. Both the N200 and the late positive complex

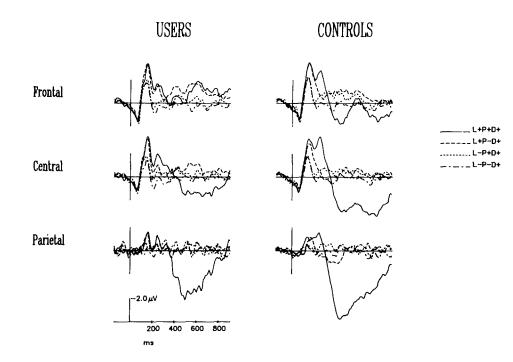


FIG. 1. Grand average ERPs to target stimuli at contralateral scalp sites.

appear to be greatly reduced in the cannabis user group.

Inspection of the L+P+ trace indicates substantial differences between the two groups in the amplitude of the positive peak between 300 and 900 ms, generally referred to as the P300. Measured as the mean amplitude between 300 and 900 ms, this component is smaller at all electrode sites in the user group compared to the control group, F(1,16) = 4.37, p < 0.0528. The lack of separation of the L+P+ and L+P- traces in the user group is due not only to the reduced N200 in the P+ ERP, but there is also evidence of an N200 (the negative peak between 200 and 300 ms) in the L+P- trace which is absent in the control group [mean amplitude between 250 and 275 ms: F(1,16) =4.36, p < 0.0532]. Although difficult to measure, inspection of the individual waveforms revealed eight of the nine users showing a clear N200 in their individual waveforms, while only 4 of the controls showed similar but small negative peaks to the L+P- stimulus. This pattern of results is indicative of unnecessary pitch processing in the user group, or an inability to reject pitch-irrelevant stimuli at an early stage of processing.

Figure 2 depicts grand average ERPs to short-duration (D-)stimuli at ipsilateral scalp sites. Early processing negativity (PN) is evident in both groups in the two ERPs to stimuli which matched the target on location (L+), indicating that cannabis users had no difficulty selecting or rejecting stimuli on the basis of location. However, with the processing of the pitch dimension, the controls show a large PN to L+P+ stimuli, while the user group fails to sustain this negativity between 200 and 300 ms at frontal and central sites, F(1,16) = 5.05, p < 0.0391. The most striking difference between the two groups is in the PN of the two L+P-ERPs, i.e., those elicited by stimuli at the same location but of a different pitch to the target. Relative to the L+P+ trace, the L+P- ERP shows an enhanced negativity in the user group in contrast to the positive shift apparent in the controls, particularly in the early 50- to 400-ms range, F(1,16) =4.58, p < 0.0481. This negativity is more pronounced in users in the ipsilateral hemisphere between 200 and 600 ms, F(1,16) =5.06, p < 0.0389. This pattern of results, with a smaller separation between the L+P+ and L+P- waves in the user group, is indicative of an inability to filter out stimuli on the basis of pitch attributes. Towards the end of the epoch, there were no significant differences between the two groups on the late component of PN.

#### DISCUSSION

Selective attention can be defined as those processes that allow some stimuli to be processed more rapidly and effectively than others. Early selection in the auditory system can occur as early as 60 to 80 ms poststimulus, as evidenced by the onset of processing negativity (PN). PN is elicited by all stimuli sharing the more salient properties of the relevant stimulus. Hierarchical models of information processing predict that easily discriminated features such as location are initially selected, followed by less discriminable features such as pitch. This process continues until all stimuli that do not share every attribute of the relevant stimulus are gradually filtered out and not accorded any further processing. The differences found between cannabis user and control groups in this study indicate that users may have some difficulty in setting up an accurate focus of attention and in filtering out irrelevant information.

Cannabis users displayed a similar pattern to controls in the early filtering of stimuli which did not match the targets on the dimension of location, as evidenced by the lack of PN to L-stimuli. However, both the presence of the N200 component in the L+P-D+ ERPs and the large PN elicited by L+P-D-stimuli imply that users were unable to effectively reject stimuli on the basis of pitch attributes.

The largest differences between users and controls were apparent in the early part of the PN component. According to Näätänen (8), this part of the PN reflects a matching process between the sensory information contained in the stimulus and an "attentional trace," an active voluntarily maintained neuronal representation of the physical features defining the stimuli that

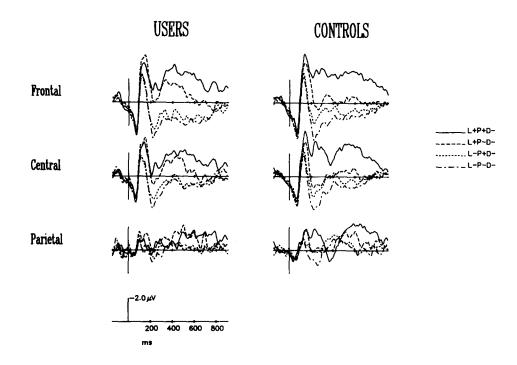


FIG. 2. Grand average ERPs to short-duration stimuli at ipsilateral scalp sites.

are the focus of attention. Thus it appears to be the process of the selection and setting up of the attentional trace that is impaired, rather than its maintenance or rehearsal, as would be reflected in the late component of PN according to Näätänen's theory. Further, the reduced P300 amplitude suggests a dysfunction in the allocation of attentional resources and stimulus evaluation strategies (4,16). P300 amplitude has consistently been found to be reduced in schizophrenics (7, 13, 14, 17, 23), among other psychiatric groups (13) and alcoholics (15,24). P300 amplitude has also been found to correlate with ratings of clinical symptoms of schizophrenia (14, 19, 23) and with performance on perceptual-motor tests in alcoholics and controls (12). The behavioural results of this study are important in demonstrating the value of examining the underlying mechanisms involved in processing information. Although users were no slower to respond than controls, their performance was significantly worse. It is not surprising, then, that tests measuring reaction time alone may fail to detect deficits in task performance. Taken together, these results imply that long-term cannabis use may impair the ability to efficiently process information.

At this stage, it is not possible to assess to what extent this deficit may be due to chronic buildup of THC and whether functioning would return to normal upon discontinuation of use. Further research is necessary to address this question and to examine the quantity and duration of use at which dysfunction is first manifest. The differences found in this relatively small diverse sample warrant further investigation of cognitive functioning in long-term cannabis users.

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