Cognition and Long-Term Use of Ganja (Cannabis)

Abstract. *Neuropsychological variables and urine cannabinoid metabolites were evaluated in ten subjects born, raised, and educated in the United States and having histories of heavy or prolonged use of cannabis. No impairment of cognitive function was found. Cannabinoid metabolites in excess of 50 nanograms per milliliter were present in the ten urine samples. The tetrahydrocannabinol content of cannabis exceeded 8.0 percent.*

Several studies have attempted to characterize the mental or cognitive functioning of persons with histories of heavy and prolonged use of ganja (cannabis). Generally, investigators have concluded that heavy and prolonged use has not led to impairment of mental and cognitive functions consistent with brain or cerebral dysfunction (*1–4*).

Although several studies have shown decrements in neuropsychological performance among those with brief or sporadic patterns of cannabis use here in the United States (*5–9*), comparable studies of prolonged heavy use in this country have not been performed. Thus, the only available literature is based on studies conducted in foreign countries (Jamaica, Greece, Egypt, and Costa Rica).

We had the opportunity to observe a group of long-term heavy users of ganja in both a Southern state and a Caribbean island. The ganja was used by this group for religious purposes and symbolized the sacrament of communion—"the Green Herb of the Bible." It was used, as we observed, even during the extensive neuropsychological evaluations that we completed, in a continuous and ritualistic manner throughout virtually all waking hours. Very large cigarettes (or "spliffs") and pipes, containing ganja mixed with tobacco, were regularly shared by members of the group (*10*).

We examined ten subjects (seven males and three females) ranging in age from 25 to 36 years. The mean number of years of education was 13.5 (all were born, raised, and educated in the United States), and all were Caucasian. None had any history of disease that could be related to central nervous system dysfunction. By their own report, they used between 2 and 4 ounces of the ganja-tobacco mixture per day, with a reported mean duration of use of 7.4 years (the time since joining this particular church). All subjects actively engaged in daily work, largely agricultural and business, and led active and spiritually oriented lives (*10*). It was not possible to collect control data in this environment, as all church members continuously smoked ganja. Thus, comparisons were made with the published standards and normative data for the psychometric instruments used.

Subjects in this study agreed to provide approximately 15 ml of fresh urine for enzyme immunoassay of cannabinoid metabolite content. Specimens were preserved with approximately 4 mg of sodium azide per 15 ml of urine that was collected. Urine samples for each of the ten individuals studied were obtained immediately before each subject began a series of selected neuropsychological tests designed to assess a broad range of cognitive functions.

A modified version of the Michigan Neuropsychological Test Sequence was used (*11–13*). Each subject was administered exactly the same group of tests in exactly the same order. General intellectual functioning was assessed on the basis of a prorated version of the *Wechsler Adult Intelligence Scale* (Table 1) (*14*). Additional neuropsychological tests included the following: *Benton Visual Retention Test* (administration C) (*15*), *Rey Auditory-Verbal Learning Test* (*16*), *Symbol-Digit Modalities Test* (*17*), *Hooper Visual Organization Test* (*18*), *Raven's Progressive Matrices Test* (*19*), and *Trailmaking Test* (forms A and B) (*20*). The following cognitive functions were assessed: language areas of function, nonlanguage areas of function, memory, complex multimodal learning, and general intellectual functioning. Auditory and visual memory functions included remote (years and months), recent (weeks, days, hours, minutes), and immediate events (within seconds).

An enzyme immunoassay method (Emit-d.a.u.) (*21*) was used to analyze urine samples. The assay is a semiquantitative immunochemical test designed to detect a level of at least 50 ng of 11-nor-Δ^9-tetrahydrocannabinol carboxylic acid per milliliter of urine with greater than 95 percent confidence. Each of the ten urine samples contained concentrations of cannabinoids at 50 ng/ml (one subject) or well above this level (nine subjects).

None of the neuropsychological test data indicated impairment of cognitive functioning. Language areas of function, nonlanguage areas of function, memory, complex multimodal learning, and general level of intellectual functioning were all completely unimpaired, compared with standardized-normative information available for each test (Table 1).

The mean IQ scores (Table 1) are all in the superior to very superior range of intellectual functioning, ranging from the upper 6.7 percent to the upper 2.2 percent of the population (*14*). Scores obtained on all of the other psychometric tests were also well within the normal range for age (*11–20*). There was nothing found in any of the ten subjects' protocols that might suggest impaired mental functioning due to brain or cerebral dysfunction resulting from heavy and prolonged use of ganja.

While several previous studies have reported transient cognitive impairment resulting from the acute effects of cannabis, primarily with respect to attention-concentration and visuomotor (hand-eye) coordination (*8, 9, 22, 23*), none of the studies involving prolonged and

Table 1. Summary of neuropsychological data (means ± standard deviations).

Test	Number correct	Scaled score
	Wechsler Adult Intelligence Scale	
Information	26.2 ± 3.12	16.5 ± 2.55
Arithmetic	15.2 ± 2.10	14.3 ± 1.95
Similarities	20.8 ± 2.30	14.2 ± 1.97
Digit symbol	69.6 ± 8.73	13.8 ± 2.49
Block design	42.7 ± 5.95	13.8 ± 2.39
Picture arrangement	29.1 ± 5.30	13.0 ± 2.98
Verbal IQ*	129.0 ± 10.87	
Performance IQ*	124.2 ± 13.07	
Full-scale IQ*	128.4 ± 10.36	
	Other instruments	
Benton	8.8 ± 1.02	
Rey	14.9 ± 0.32	
Symbol-digit	60.4 ± 10.25	
Hooper	28.7 ± 1.06	
Raven	35.2 ± 0.79	
Trailmaking (in seconds)		
Form A	28.8 ± 6.88†	
Form B	53.5 ± 15.28†	

*Prorated. †No errors.

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heavy use of ganja have shown any systematic decrements in mental abilities suggestive of impairment of brain or cerebral function and cognition (*1–4*).

We also included toxicologic verification of urinary cannabinoid metabolites, observed the inhalation of cannabis by all subjects studied, and analyzed samples of this cannabis for THC. Analysis of cannabis mixed with tobacco (by gas chromatography) yielded a Δ^9-THC content of 4.14 percent (half cannabis, half tobacco); thus the THC content of the pure cannabis exceeds 8.0 percent.

We observed no transient decrements in cognitive functioning that often accompany intermittent or sporadic use of cannabis. The development of tolerance to one or more of the constituents of cannabis may explain this phenomenon.

Although the obtained IQ scores were high, one could speculate that perhaps cannabis had produced a priori declines in IQ scores for all ten subjects, as well as scores on other neuropsychological measures. It was possible for us to obtain early school academic achievement test data on two of our subjects. These data included equivalent IQ conversion scores virtually identical to those we measured for those subjects. We realize that these conversion or equivalent IQ scores derived from early school achievement test data are not to be equated on a one-for-one basis with current scores. However, we do believe that IQ score ranges provide a reasonable degree of equivalency. These achievement test scores were obtained some 15 to 20 years earlier, long before either subject began the use of cannabis, by their report to us.

Finally, we stress the commitment of the ten subjects to their religious sect and way of life. They told us and others (*10*) that members of the church do not use substances (drugs, alcohol, or psychoactive herbs) other than ganja, and we observed them to maintain a regular diet consisting primarily of vegetables, fruit, and small amounts of meat. All ten subjects (as well as other members of the church) appear to be healthy and highly functional individuals adhering to a strict religious doctrine.

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Discharge Patterns of Hindlimb Motoneurons During Normal Cat Locomotion

Abstract. *Long-term recording from single lumbar motoneurons of intact cats revealed activation patterns fundamentally different from those seen in decerebrate preparations. In intact cats, motoneuron bursts showed marked rate modulation without initial doublets. Each unit's frequencygram generally resembled the envelope of the gross electromyogram simultaneously recorded from the corresponding muscle. Average and peak discharge rates increased for faster gaits. These findings suggest that, in cat locomotion, rate modulation is a more important contributor to force regulation than was previously thought.*

A prime objective in the field of motor control is to fully understand the relations between neuronal discharge patterns and movements. Comprehensive studies of the electrical and mechanical properties of hindlimb muscles and their motoneurons, the final output cells of the motor system, arose from the introduction of intracellular techniques (*1*) in anesthetized cat preparations (*2–8*). In contrast, until now, technical difficulties have made it impossible to investigate normal motoneuron firing patterns during locomotion. The only single-unit records obtained previously have come from unidentified motor axons in cut ventral root filaments of decerebrate cats induced to "walk" by being stimulated in the mesencephalic locomotor region of the brainstem (*9–11*).

Motoneurons in walking decerebrate cats typically fire in uniform bursts consisting of an initial doublet [a pair of spikes occurring within a brief interval, usually 3 to 10 msec (*10, 11*)] followed by a train of spikes that stabilize at a nearly constant "preferred discharge rate" (*9*) characteristic for each cell, which does not vary with treadmill speed, strength of stimulation, or duration of step cycle. Discovery of these motoneuron firing patterns had an important influence on current views of the neural control of locomotion (*4–6, 10–12*).

We have developed long-term recording methods in conscious, freely walking, intact cats (*13, 14*) in order to monitor the electrical activity of individual hindlimb motoneurons and to determine unitary axonal conduction velocity and muscle of destination. Records obtained from more than 100 motoneurons revealed striking differences from the characteristic decerebrate cat patterns.

Twelve cats trained to walk at several speeds on a motorized treadmill had electrodes and transducers implanted under deep pentobarbital anesthesia; they were allowed to recover for several days before recording sessions began. As many as a dozen fine, flexible, insulated wire electrodes (Fig. 1, A and B) were inserted in the fifth lumbar ventral root (L5 VR) through a small laminotomy, an approach recently shown successful for recording from afferent fibers (*15–19*). Root electrodes were of a modified "hatpin" design (*14, 20*): a recording surface was exposed by obliquely cutting a stiff, short iridium or platinum-iridium insulated wire (easily inserted into soft tissue), which was welded to a compliant gold lead (thereby allowing the electrode to "float"). Extracellular recordings from ventral root axons coursing out of the spinal canal were thus made in a

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