The following thesis, entitled, "a comprehensive literature study on the effect of cannabis use on cognition and aggressiveness, including a small study to explore these variables" is submitted for the M.Med. degree at the University of Cape Town, South Africa.

by

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The USA studies.

The North African studies.

The Greek studies.

Complications in measuring the effect of cannabis on cognition:

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(b) The time lapse between smoking cannabis and testing for cognitive deficit.

(c) Experienced vs. naive users of cannabis.

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SUMMARY

Twenty seven consecutive black male patients who were admitted as acute admissions to FEH were examined in this thesis.

The following demographic information characterized the sample group.

a) Age.

Bimodal distribution with peaks at 21-25 years and 31-35 years. Five patients were older than 35 years.

b) Marital Status

In the sample, 59.2% were single, 11.1% married and 29.6% the marital status was unknown.

c) Number of Children

In the sample, 75% did not know how many children they had. Numbers ranged from no children (14.3%) to 2 children (7.1% of the sample).

d) Employment Status

In the sample 81.1% were unemployed

e) Level of Schooling

In one third of cases, level of schooling was unknown. Most men did reach secondary level of education.

The men were divided into 5 groups depending on:

a) The written history which accompanied each patient
b) History on presentation
c) Physical examination
d) Laboratory testing of blood and wine samples

The sample was distributed as follows:

Group	Number of Patients
THC+\LFT-	5
THC-\LFT+	9
THC-\LFT-	7
THC+\LFT+	2
VDRL+	4
Total	**27**

Tests used to examine for cognitive function:

These tests had to be simple, practical and suitable for a population with no formal education and had been tested for reliability and validity in the literature.

a) The perceptuo-motor pencil tapping test (page 153). This test was done on admission and a few days later as follows:

Group	Time Interval Between the Two Attempts (in days)
THC+\LFT-	X = 3, R = 2-4
THC-\LFT+	X = 3.2, R = 2-4
THC+\LFT+	X = 2
THC-\LFT-	X= 3.7, R = 2-6
. VDRL+	X = 3

b) The Coursi block tapping test using the WAIS digit sequence (page 154).

This test was done on admission and a few days later as follows:

Group	Time Interval Between the Two Attempts (In days)	
THC+\LFT-	X = 3.6,	R = 2-5
THC-\LFT+	X = 3.9	R = 2-5
THC-\LFT-	X = 3.4	R = 2-6
THC+\LFT+	X = 3.5	R = 2-5
VDRL+	X = 4	R = 3-5

c) Immediate and delayed recall of a group of common familiar objects based on the Satz et al (1976) and Dornbush (1973) model.

This test was done on admission and a few days later as follows:

Group	Time Interval Between the Two Attempts (In days)	
THC+\LFT-	X = 6.4,	R = 2-8
THC-\LFT+	X = 5	R = 3-7
THC-\LFT-	X = 4.1	R = 3-6
THC+\LFT+	X = 1.5	R = 0-3
VDRL+	X = 4.3	R = 0-7

d) Test for reproductive memory based on the Graham Kendall memory for design test (page 166).

The test was done on admission and a few days later as follows:

Group	Time Interval Between the Two Attempts (In days)	
THC+\LFT-	X = 3.6	R = 2-5
THC-\LFT+	X = 3.9	R = 2-5
THC-\LFT-	X = 3.4	R = 2-6
THC+\LFT+	X = 3.5	R =2-5
VDRL+	X = 4.5	R = 4-5

The above tests were done on admission and a few days later to rule out any effects of intoxication.

Retesting at a later interval (such as 6 weeks later as in the Swartz et al 1989 study) was not done as most patients were discharged from hospital as follows:

Group	Average Length of Stay in Hospital (in days)	Range in Length of Stay in Hospital (in days)
THC+\LFT-	13	7-23
THC-\LFT+	13	10-16
THC-\LFT-	17	7-32
THC+\LFT+	14	12-30
VDRL+	14	-

The reason for the brief hospital stay was due to the pressure on beds.

Follow up for re-testing in the community was not possible as the patients came from outlying rural areas.

Aggression was a common presenting feature in the sample group. The concept of aggression could not be further explored because:

a) There is no universal instrument to measure aggression

b) All patients came from outlying rural areas and the initially reported aggression was no longer evident on admission to FEH due to the delays in transporting the patients from the site of initial presentation to FEH.

INTRODUCTION

Cannabis sativa Linn., the plant from which cannabinoids are derived is thought to have originated from the Caspian Sea region and then spread with human migration.

Cannabis has been used as a medicine from at least 2737 BC and was only removed from the USA pharmacopoeia in 1942. Its use as an anti-emetic following chemotherapy was advocated up until 1992.

Cannabis remains one of the most widely abused drugs in the world. In the USA, an estimated 67,7 million Americans (33,4% of the population) have used cannabis at least once in their lifetime (Kaufman et al 1992).

South Africa has a long history of cannabis use. Initially it was used in a highly structured, ritualized setting amongst the indigenous people. In the present time, the social restraints on cannabis use have largely disappeared and it has emerged as a drug of abuse.

Cannabis use can present with a variety of syndromes which will be examined in the present thesis. Of particular significance is the role of cannabis in producing either short term and\or long term cognitive disturbances and the possible link between cannabis use and subsequent aggression.

Both of these factors will be examined in the present work.

Similarly the use of alcohol has changed in the black population. McAllister (1986) recorded in his research work that the Xhosa people in the Eastern Cape had a very ritualized approach to the use of traditionally brewed beer and the consumption of alcohol was governed by a well understood, ordered and accepted set of rules.

However, by the turn of the century, research workers in the E. Cape were reporting on the use of spirits (especially brandy) and that consumption, freed from the social restraints governing the use of alcohol, had resulted in alcohol becoming a drug of abuse.

Earlier evidence suggests that alcohol abuse amongst the Xhosa was established at the time of the frontier wars, as recorded by the artist W. Langschmidt in 1850 (see frontispiece).

The present sample represents 27 consecutive black male acute admissions to Fort England Hospital, a 400 bed mental institution in Grahamstown, E. Cape. This hospital drains a large area stretching from East London through to the Transkei.

The 27 subjects examined in the present study were all subjected to a variety of psychoprojective tests on admission and a few days later.

Urine and blood tests as well as patient history and physical examination was used to consign the men to 5 groups, namely:

1. THC+\LFT- (Use of cannabis alone detected)
2. THC-\LFT+ (Use of alcohol alone detected)
3. THC-\LFT- (Control group, no toxins detected)
4. THC+\LFT+ (Use of both cannabis and alcohol detected)
5. VDRL+ (Patients positive for neurosyphilis)

In the final analysis of the results, the toxin abusing sub-groups were combined (referred to as group 7) and those patients with neurosyphilis were excluded.

Two physical signs noted in the cannabis users were:

a) Burn marks on the palms of the hands from use of a bottle top Cannabis pipe (fig. 11).

b) An area of hypopigmentation on the lower lip, presumed to represent the damage caused by the heat generated from burning cannabis.

Both results and a conclusion are presented in this study.

KEY:

The following abbreviations have been used in this study:

1.	THC	Delta 9 Tetrahydro-cannabinol.
2.	EMIT	Enzyme multiplied immunoassay technique.
3.	STM	Short term memory.
4.	LTM	Long term memory.
5.	BVRT	Benton visual retention test.
6.	ALT	Serum alanine aminotransferase.
7.	AST	Serum asparate amintransferase.
8.	GGT	Gamma glutamyl transpeptidase.
9.	ALP	Alkaline phosphatase.
10.	FEH	Fort England Hospital, Grahamstown, E. Cape.
11.	MFD	Graham Kendall memory for design test.

Frontispiece: Canteen scene during the frontier wars, 1850.
Artist: W. Langschmidt
Provence: W. Fehr collection, the Castle, Cape Town, S. Africa.

ACKNOWLEDGMENTS

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5. Dr. D. Wilson, Department of Psychiatry, University of Cape Town.

BOTANICAL HISTORY OF CANNABIS, ITS EARLY USE IN SOUTH AFRICA AND ITS EARLY MEDICAL USE

The cannabis plant, Cannabis sativa Linn. (Fig.1) was classified by Linnaeus in 1753 (Du Toit 1980). The latin name Cannabis is derived from the Assyrian word "Kunnapu" = a way to produce smoke (Maykut 1985).

La Marck classified the Indian plant as C. indica but later research has shown it does not merit the status of a distinct species, but is rather a sub-species of C. sativa. The two sub-species recognised and the wild and cultivated varieties are:

C. sativa spp. sativa (fibre type)
wild var. spontanea
cult var. sativa

C. sativa spp. indica (drug type)
wild var. Kafiristanica
cult var. indica

The division into 2 sub-species each with 2 varieties is supported by cannabinoid analysis of the plants which has indicated that at least 5 phenotypes exist (Gill et al 1970. Vree et al 1971, Merkus 1971, Gill 1971, Small et al 1973, Small et al 1973).

Small et al (1973) and Fairburn et al (1974) have demonstrated that plants with a high THC content have been grown in temperate climates and the view that tropical or sub-tropical climates are required for high production of THC is erroneous.

C. sativa Linn. is thought to have originated in the semi-desert regions of South and East of the Caspian Sea and then spread to the Himalayas and then through out Asia. (Du Toit 1980, Johnson et al 1990).

Fig. 1 The Cannabis plant, Cannabis sativa Linn.

(from a herbaruim specimen, Albany Museum, Grahamstown, E.Cape, South Africa.

The spread of Cannabis sativa is associated wit the spread of human settlement. Early trading between India and Africa resulted in the spread of Cannabis to the African continent. Arab traders had moved into the interior of the African continent via the river systems at the start of the sixteenth century (Fagan 1965). At the same time there was migration of black people southwards and by the time of the white settlement in the Cape, cannabis was in common use among the indigenous populations (Du Toit 1980, Mkhize 1989).

The earliest treatise on Cannabis use in South Africa was by Dr Armstrong, district Surgeon, Craddock, E. Cape in 1855 (Du Toit 1980). He described the use of Cannabis amongst the local population and noted its intoxicating affect. He reported Cannabis was usually mixed with tobacco and smoked.

The first full study of Cannabis use in South Africa was conducted between 1908 and 1912 by C. Bourhill. His M.D thesis was entitled, "the smoking of dagga amongst the native races of Southern Africa and the resultant evils".

Seventy percent of Cannabis in South Africa is grown in a rectangle formed by latitudes and longitudes 28 ° and 30° which includes most of Swaziland and part of the Transkei. Most of the rest is grown in N. Natal and Zululand (Ben-Arie 1984).

Newspaper reports of recent Cannabis use in the East Cape appear in appendix 1.

Medical Use of Cannabis

The earliest known medical use of Cannabis was 2737 BC when it was listed in the Chineese pharmacopoeia of Emperor shen Nung (Talbott et al 1969, Du Toit 1980, Johnson et al 1990).

In India, the stimulating and euphoric properties of Cannabis were recognized and recorded in the Atharua Veda (2000 - 1400 BC) (Du Toit 1980).

In the seventeenth century, Cannabis was planted in the colonies of North America (Rubin 1971).

Its medicinal properties were recognised and over 100 medical reports were published in the nineteenth century recommending the use of Cannabis derivatives (Talbott et al 1969). Cannabis was only removed from the USA Pharmacopoeia in 1942 (Du Toit 1980).

Therapeutic use of Cannabis has been reported in this century. Table 1 lists the reported therapeutic uses of Cannabis.

THERAPEUTIC USE	AUTHOR(S)
Anorexia	Zinberg 1974
Epilepsy	Carlini and Cunha 1981
Rheumatism, asthma,	Noys et al 1975
pain	Jain et al 1981
Nausea induced by chemotherapy	Relman 1982
	Abood et al 1992

Table 1: Modern therapeutic uses of Cannabis

BIOCHEMISTRY AND EXCRETION OF CANNABINOIDS

1. BIOCHEMISTRY AND METABOLISM OF CANNABINOIDS

Over 421 different compounds have been isolated from Cannabis (ARF\ WHO report 1981, Maykut 1985).

The Cannabinoids are carboxylic acids with 21 Carbon atoms. 61 natural cannabinoids unique to **C. sativa** have been identified (Megersee, Turner et al 1980, Maykut 1985, Mason et al 1985, Harvey et al 1990, Abood et al 1992).

Wickler (1970) classified the canabinoids as psychotomimetic drugs. Only THC is known to be psychoactive and is present in high amounts in the plant, usually 1 - 5 % by weight (Ellis et al 1985). All parts of the plant contain psychoactive cannabinoids with the highest concentration being in the flowering tops (Abood et al 1992, Talbott et al 1969). The cannabinoids form part of the plant's resin that is produced as a protective agent against the harmful effects of the sun (Talbott et al 1969).

THC has a basic structure of 3 rings, terpenoid, pyran and aromatic (fig 2, Maykut 1985). THC was first synthesized by Mechoulam et al (1965).

Two other derivatives of THC are known to be:

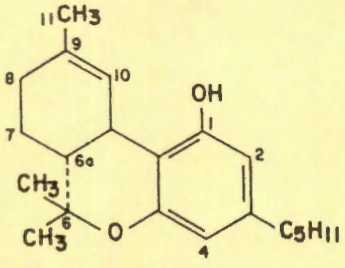
Psychoactive:

1/ The isomer of Delta 9 THC = Delta 8 THC

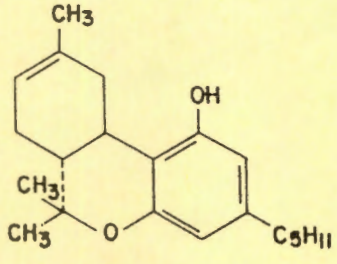
67 - 75 % as potent as delta 9 THC. It is a degradation product of THC and is not present in fresh cannabis.

2/ The propyl homologue of THC, delta 9 tetrahydro-cannabivarin (delta 9 THCV), 25 % as potent as THC. This is found in fresh cannabis but only in small amounts. (Gaonis et al 1964, Hively et al 1966, Gilman et al 1985).

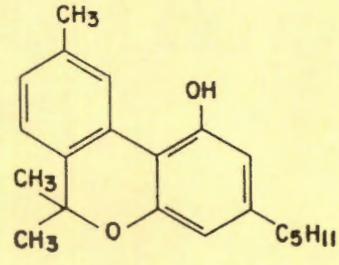
Another degradative product, Cannabinol (CBN) may be psychoactive. It is found in fresh Cannabis (Lindgren 1981).



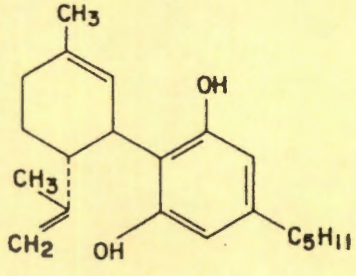
Δ^9 Tetrahydrocannabinol (Δ^9THC)



Δ^8 Tetrahydrocannabinol (Δ^8 THC)



Cannabinol (CBN)



Cannabidiol (CBD)

Fig . 2 THC Structure (after Maykut 1985).

Cannabidiol (CBD) is another major cannabinoid found in Cannabis but it is not psychoactive in humans (Lindgren 1981, Ohlsson et al 1986, Harvey et al 1990).

When cannabis is smoked, the natural 2 and 4 carboxylic acids of THC are decarboxylated to form THC. Other than de-carboxylation reactions, there seems to be little interconversion or isomerization of the cannabinoids during pyrolysis. The ARF\ WHO report (1981) noted that pyrolysis of Cannabis produces hundreds of compounds that make up the vapour and particulate phase of the smoke. The vapour contains nitrogen oxides, CO, HCN, Nitrosamines and other toxic materials. The particulate phase contains carcinogens including phenols, cresols and polynuclear aromatic hydrocarbons.

Estimates of total THC survival during pyrolysis range from 32 (Mikes et al 1971) to 50 % (Gaoni et al 1966, WHO/ ARF report 1981, Maykut 1985, Johnson et al 1990) to a maximum of 62% (Fehr 1972).

Systematic bioavailability of THC administered by smoking has been reported to be 18 ± 6 %.

Maykut (1985) and Abood et al (1992) have pointed out that the bioavailability of THC is also dependent on the smoking technique and the time the smoke is held in the lungs. THC is rapidly absorbed from the lungs (ARF/ WHO report 1981).

Peak THC plasma concentration develops very quickly after smoking Cannabis and then falls to + 10% of the peak concentration within the first hour (Johnson et al 1990, ARF/ WHO report 1981). After a single smoke of Cannabis, THC can be detected for up to 20 hours in the blood (Hunt et al 1980).

Subjective effects of Cannabis reach their peak between 20 and 40 minutes after smoking and usually last 4 hours (Weil et al 1965, Abel 1975, ARF/ Who Report 1981, Cocchetto et al 1981, Perez - Reyes et al 1981, Hollister et al 1981, Perez - Reyes et al 1982, Maykut 1985).

The potency of a preparation delivered by smoking is up to three times that of an equivalent amount injested orally because of the more rapid absorption from the lungs, avoidance of first pass metabolism and the enhanced release of THC from the pyrolysis of the THC acid (Ishbell et al 1967). Oral injection leads to a slow absorption (about 3 hours) but results in a longer duration of effect (Lemberger et al 1972).

In blood, THC is almost (97%) completely bound to plasma proteins alpha and beta, lipoproteins and albumin (Paton 1975, Maykut 1985). THC is rapidly distributed from the central compartment to peripheral tissues with high lipid content. This includes the salivary glands, spleen, adrenals, brain, liver, kidney and reproductive organs (Maykut 1985, Gill 1976, Margolis et al 1980, Deahl 1991). There is poor penetration of the blood brain barrier with less than 1 % THC entering the brain (Johnson et al 1990).

Nahas et al (1981) have demonstrated that with chronic smoking of Cannabis, there is fat and liver accumulation of THC. Rolfe et al (1993) noted that Cannabinoids, being highly lipophilic; accumulate in body fat leading to a long THC half life in Chronic users.

THC is metabolized in the liver through a process of hydroxylations (fig . 3, Negrete 1973, Mason et al 1985, Maykut 1985, Abood et al 1993). Fig .4 is a summary of this process.

Ohlsson et al (1986) noted that THC is a high clearance drug with a very large volume of distribution and is eliminated slowly from the body. Mirin and Weiss (1983) noted that THC remains in fatty tissue for up to two to three weeks.

Cridland et al (1983) assumed that excretion followed first order kinetics. They estimated THC half life to be three to four days (R = 1 - 10 days), However in chronic cannabis users, the metabolizing enzymes may be induced such that a shorted half life is seen (Johnson et al 1990).

Lindgren (1981) in his experiment with 9 heavy users of Cannabis (ie used cannabis more than once a day) and 9 light users of cannabis (ie. used cannabis less than once a month) found no statistical difference in the plasma levels of THC between the two groups. Perhaps the reason why he failed to demonstrate a shorter half life of THC in chronic users was because his experimental group was too small and the amount of THC used was insufficient to cause stimulation of the liver enzymes.

Hansten (1979) proposed that the metabolizing enzymes are inhibited by the use of neuroleptics in the subjects and Negrete (1973) noted that in impaired liver function there may be stronger and longer lasting cannabis intoxications. This observation may be of direct importance in subjects who abuse both cannabis an alcohol simultaneously. Ishbell (1971) demonstrated that if cannabis is given in sufficient doses (200 - 250 microgram\ kg), it invariably produces a psychotic state. However in those individuals who are simultaneously abusing alcohol in addition to cannabis, smaller concentrations of cannabis resulted in a psychotic state.

Table 2 lists the time lapse between last use of Cannabis and consistent negative urine results.

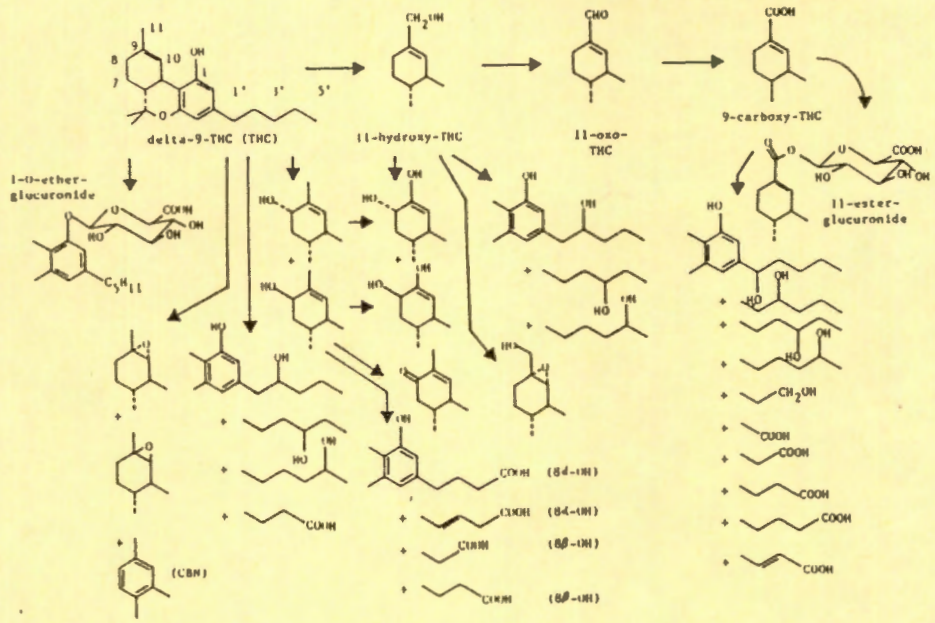


Fig . 3 Known human metabolites of THC (Mason et al 1985 p. 619).

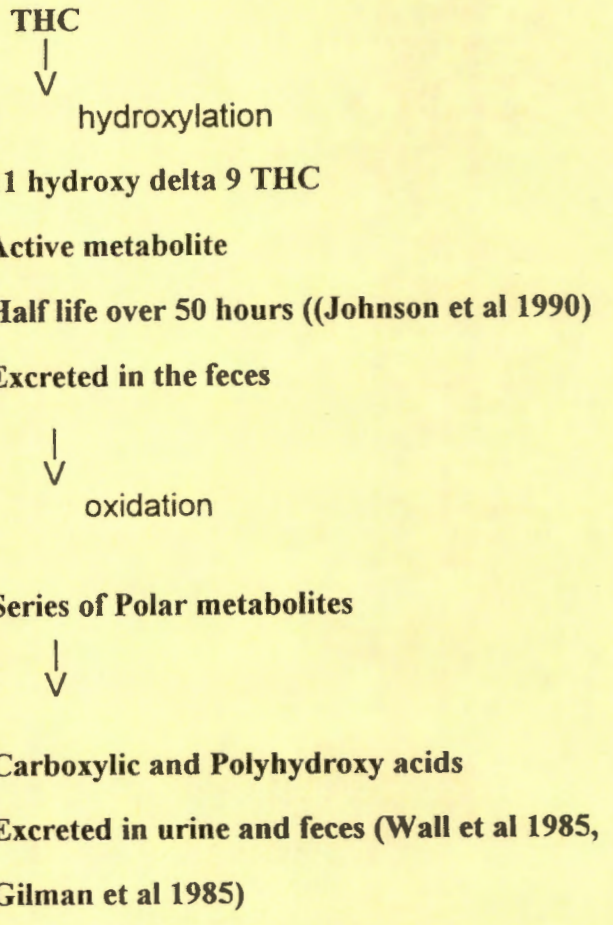


Fig. 4 Metabolism of THC in the liver through a series of hydroxylation reactions.

TIME LAPSE	AUTHORS
3 days	Hollister et al 1980.
Over 1 week	Lemberger et al 1971
14 - 36 days	Dackis et al 1982
Up to 30 days	Hunt et al 1980
	Ng et al 1990
	Mathers et al 1992
Several weeks	Ellis et al 1985

Table . 2 Time lapse between last exposure to cannabis and negative THC results.

2. POTENCY OF CANNABIS

Cannabis potency is a factor of soil, climate, cultivation, and the harvesting, and curing process. Potency is also dependent on whether the mixture contains leaves, stalks, shoots or flowers (Abel 1977, Paris et al 1980, Johnson et al 1990).

Rolfe et al (1993) recorded that there is a decrease in THC content when the Cannabis plant is grown in cool climates. This hypothesis was not supported by Small et al (1973) and Fairburn et al (1974).

Weil et al (1968) noted that the potency of Cannabis can vary by a factor of 2000.

The ARF/ WHO report (1981) and Tennant et al (1972) commented on the high frequency of Cannabis induced psychosis observed in North Africa and India and it was felt that one possible explanation was cannabis from these areas had a high THC content. Talbott et al (1969) noted the potency of Cannabis in Vietnam was twice that available in USA but Deahl (1991) has now reported a new high potency seedless variety of Cannabis (sinsemilla) which is available in USA.

Field (1980) noted the South African cannabis ranks among the more potent variants of the plant in terms of its THC content. He examined cannabis from the kokstad district of Transkei, the Pongola district of Natal and the Tzaneen district of the Transvaal. The Transkei cannabis had the highest THC content in South Africa.

Solomons et al (1990) found the potency of South African cannabis to be 20 to 30 times greater than the potency of the USA cannabis.

Rottanburg et al (1982, 1983) recorded that the South African cannabis lacks cannabidiol and this may account for the psych-toxicity of South African cannabis in that cannabidiol may protect users in other countries from becoming psychotic following the use of cannabis.

3. URINARY EXCRETION OF THE METABOLICS OF CANNABIS

The major psychoactive compound of cannabis is THC (Johansson 1989, Johansson et al 1990) and over 99 % of this is metabolized prior to excretion (Mason et al 1985). About 80 % of THC is eliminated in the feces an 20 % is eliminated in urine (Meggersee). There are a large number of urinary metabolites and the major metabolite of THC is 11 - nor - delta - 9 - THC - carboxylic acid or a combination of :

11 hydroxy delta 9 THC

8, beta - hydroxyl, delta 9 THC

8, beta - 11 - hydroxy - delta 9 THC

(Ellis et al 1985, Johansson 19\989, Meggersee).

Urinary excretion patterns of cannabinoids vary greatly between subjects (Meggersee) an even differ for an individual at different times.

Clearance rate of the metabolites is limited by a slow deep compartment return of sequestered THC.

Excretion is also related to hydration of the subject, kidney function, and the subject's prior exposure to Cannabis (Mason et al 1985).

Upon abrupt cessation of cannabis use, there is initially a rapid period of clearance followed by a period of relatively prolonged persistence and slowed clearance. Johansson et al (1990) gave 19 mg 14 C - THC to a sample of four people and collected urine for up to 120 hours. They found that the major part of the radio-active dose (54%) was excreted in the 0 - 8 hours fraction after smoking.

LENGTH OF TIME THAT CANNABIS METABOLITES ARE DETECTABLE IN THE URINE

The urinary excretory half life of cannabinoid metabolites is function of whether the subject is a naive or chronic user of cannabis.

In naive smokers, urinary metabolites are detectable for 4 to 10 days after the last use of cannabis (Johansson et al 1990, Mason et al 1985, Meggersee).
Johansson (1989) used 13 males who were heavy cannabis users and examined the urinary metabolites of THC after cannabis use. He discovered that the half life range was 0,8 to 9,8 days with the average being 3,0 + 2,3 days.

Ellis et al (1985) also looked at urinary excretory patterns in chronic users of cannabis. They had a sample size of 86 people who had used cannabis on average for 8,9 years. Cannabis was the only drug of abuse used in 60,5% of the sample and 55,8% of the sample used cannabis and one other drug of abuse. Ellis et al reported a biphasic excretory pattern, the first phase of which showed rapid excretion of THC metabolites and followed by a slower phase of excretion. They found it took up to 46 days to reach the first negative result. 60,6% of the sample had THC positive urinary results 21 days after last cannabis use, 32,7% had positive results 30 days after last use, and 5 subjects who had used cannabis for over 12 years still had positive urinary results 50 days after last use.

In summary, chronic users of cannabis have positive results from day 9 up to day 50 after last cannabis use.

Table 3 summarises these findings.

Tests used to detect the metabolites of Cannabis in urine.

The most commonly used method to detect cannabinoids in urine is EMIT (enzyme - multiplied immuno assay techniques), a semi-quantative enzyme immuno assay kit with a 95% confidence limit for detecting the major metabolite of the THC, 11- nor - delta 9 - carboxylic acid at concentrations greater than 50 micrograms\ ml (Rodgers et al 1978, O'Connor et al 1981). EMIT also detects :

11 hydroxy delta 9 THC

8 beta hydroxy delta 9 THC

8 beta - 11 - hydroxyl - delta 9 THC

(Rottanburg et al 1982, Cridland et al 1983, Ellis et al 1985, Johansson et al 1990, Mathers et al 1991, Mathers et al 1992).

A cut off point of 25 ng\ ml is used , ie results below this are regarded as negative.

Table 4 is used to interpret the EMIT results.

Figure 5 depicts in a graphical manner how EMIT operates.

Necessary precautions to observe when performing the EMIT test

(a) Time lapse between initial admission to hospital and the collection of urine.

This time lapse should be as short as possible. Mathers et al (1991) obtained urine from patients within 72 hours of admission., and Onyango et al (1986) obtained urine within 48 hours of admission.

THC POSTIVE URINE RESULTS	AUTHOR (S)
detected up to	
9, 8 days	Johansson (1989)
20 days	Mason et al (1985)
36 days	Meggersee
50 days	Ellis et al (1985)

Table . 3: Detection of THC Metabolites in the urine of chronic cannabis users after the cessation of cannabis use.

Amount of THC metabolites detected using standard calibration curve from EMIT assay	Interpretation
less than 20 - ng\ ml	Negative
20 - 50 ng\ ml	Suggests person is using Cannabis
50 - 100 ng \ml	Diagnostic that person is using cannabis
Greater than 150 ng\ ml	Associated with psychosis

Table . 4 : Interpretation of EMIT results.

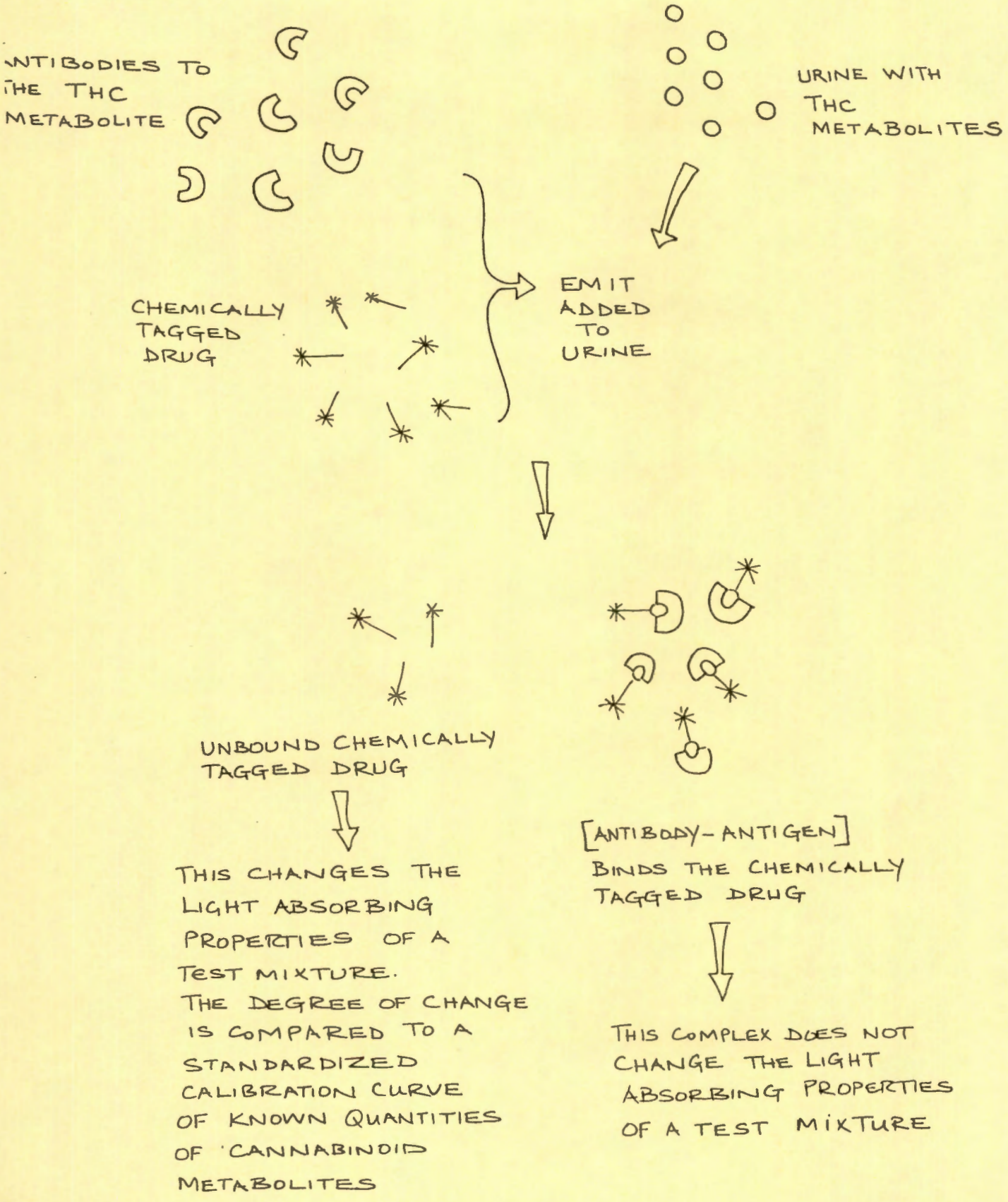


Fig. 5 The EMIT system in graphical form

(b) Temperature at which urine sample is stored. It is recommended that samples are placed in a refrigerator on collection and should be stored at - 20° c if not analysed within 48 hours of collection.

(c) Drugs which can interfere with the EMIT assay.

Certain drugs and compounds can give false positive and false negative results. These are listed in tables 5 and 6.

It is possible to have a false positive urinary THC result as a result of passive inhalation of cannabis smoke. Factors which need to be considered are :

(a) Amount of side stream smoke released.

(b) Concentration of THC in the smoke.

(c) Distance between the smoker and non-smoker.

(d) Length of time person is exposed to smoke.

(e) Type and size of enclosure.

(f) Amount of ventilation during exposure.

It is possible to record a concentration greater than 25 ng\ ml THC in the urine of passive smokers but any positive result quickly reverts to negative.
False negative results are possible if the subjects consumes excessive water prior to giving a urine sample. The resultant urine is diluted and a result of less that 25 ng\ ml urinary THC may be recorded.

False negative results have proven to be more of a problem than false positive results. One survey (Solomons et al 1990) recorded 2,9 % false positive results and 18 % false negative results, ie under-estimation of urinary cannabinoids is more likely than an over-estimation.

Interpretation of the Urinary cannabinoid results.

There is no reliable method for predicting the degree of impairment in the individual from the urinary cannabinoid concentrations (Mason et al 1985) although Table 4 gives an approximation in interpretation.

Compounds which could result in a false negative reading in the EMIT assay for urinary THC metabolites.
Vitamin C
Bilirubin
Creatinine
Ethanol
Glucose
Protein

Table . 5 **Compounds which could result in a false negative result when when testing urine with the EMIT assay. (leass than 10% chance these compounds result in a false negative reading).**

Amitriptyline	Fluphenazine
Amoxil	Haloperidol
Ampicillin	Imipramine
Antabuse	Maprotyline
	Methyldopa
Caffeine	Orphenadrine
Carbamazepine	Oxazepam
Chloramphenicol	Perphenazine
Clomipramine	Phenytoin
Codeine	Trazadone
Desipramine	Trimipramine
Diazepam	

Table . 6 **Drugs that can result in a false positive result in the EMIT assay for urinary THC metabolites.**

Impairment is difficult to predict because of the highly variable excretory patterns of the urinary cannabinoids seen in individuals. Excretion is a function of hydration of the individual. In a dehydrated individual, high urinary cannabinoids may be detected but no cannabis induced psychological effects are present. Therefore high urinary THC concentrations may indicate recent cannabis intake but they cannot be used to indicate the presence of any effects of impairment. Ellis et al (1995) have pointed out that because of the large individual variability, a positive THC result may reflect use within the past few hours, days or weeks.

Johnsson et al (1990) noted that in addition, urinary cannabinoid levels give no reliable clue as to the total amount of pharmacologically active cannabis in the body at that time. Blood or plasma are the only specimens that can be used to correlate experimentally determined THC concentrations, and resultant effects because they are the only easily obtainable specimens that can be analyzed to provide concentrations of cannabinoids that are potentially relatable to the concentrations of psychoactive cannabinoids at the active sites in the CNS. However the correlation between THC plasma concentration after smoking and subjective self reported psychological effects is not strong (Mason et al 1985).

Ellis et al (1985) found that body weight or height\ weight index were of no predictive value in determining cannabinoid excretion patterns.

CONCLUSION

The EMIT assay is the most commonly used technique to detect cannabinoid metabolites in the urine. Both false positive and false negative results are possible.

Concentrations of cannabinoids metabolites recorded in the urine have no predictive value as to the individual's clinical presentation. A test result of over 25 ng\ ml indicates that the individual has recently used cannabis.

THE THC RECEPTOR IN THE BRAIN

The strict structure - activity relationship for the cannabinoids was for many years the only evidence to support the existence of a cannabinoid receptor. The development of novel potent analogs has played a major role in the characterization and cloning of cannabinoid receptors (Howlett et al 1986, Matsuda et al 1990). One such analog CP55940 was developed by Melvin and Johnson (1986). Howlett et al (1986) worked with cell membranes from :

(a) N18 TG2 neuroblastoma cells

(b) NG108 - 15 neuroblastoma X glioma hybrid cells.

They reported that the psychoactive cannabinoids inhibited adenyl-cyclase activity in these cells. These two cell lines are known to contain opioid receptors and muscarinic acetyl choline receptors but the effects of the cannabinoids are not inhibited when antagonists are used to block both the opioid and muscaranic acetyl choline receptors.

Amino - alkyl-indole analogs are known to compete for the cannabinoid binding sites (Pacheco et al 1991). One particular amino alkyl indole WIN - 55212, has been shown to share a common site of action with the cannabinoids (Eisenstat et al 1990).

Autoradiographic studies have demonstrated a heterogenous distribution of cannabinoid binding sites in the brain. Most sites were located in the hippocampus, cerebellum and basal ganglia. The role of the hippocampus in memory dysfunction will be discussed in this thesis.

Less abundant sites were located in the cerebral cortex and corpus striatum (Kerkenham et al 1990, 1991).

Kaufman et al (1992) have postulated that there may be an endogenous substance in humans that resembles the cannabinoids.

THE ROLE OF CANNABIS IN PRODUCING STRUCTURAL AND FUNCTIONAL DAMAGE TO THE BRAIN

Introduction :

It is difficult to evaluate the precise role of Cannabis in producing structural and functional damage to the brain because of the large number of variables operating. For instance, cannabis may not be the only drug of abuse used by the individual. Alcohol is often used together with cannabis (Grant et al 1979). Also many factors in the individual's life style have to be considered such as nutritional status and exposure to head trauma as a result of falls, assaults, and overdoses with resultant anoxia (Wert et al 1986).

Structural changes

1. Macroscopic changes :

CT brain scans in cannabis users have reported :

(a) No atrophy (Fink 1976, Karacan et al 1976, Co et al 1977, Kuehnle et al 1977, ARF/WHO report 1981).

(b) Possible atrophy (Kolansky et al 1972).

(c) Atrophy (Campbell et al 1971).

In the Campbell et al (1971) study, cerebral atrophy was demonstrated in 10 individuals who had smoked cannabis for 3 to 11 years. In addition, all 10 individuals were polysubstance abusers and 3 of the 10 had had a head injury.

2. Microscopic and biochemical changes.

Synaptic alterations in the septum, hippocampus and amygdala have been described . These include widened synaptic clefts, clumping of vesicles in the pre-synaptic nerve ending and disruption of the rough endoplasmic reticulum. (Health et al 1980, Maykut 1985).

Maykut (1985) also mentioned that Cannabis may cause damage to the septal area and such individuals are prone to violence when smoking Cannabis.

Mc Issac et al (1971) and Drew et al (1974) have demonstrated the preferential concentration of THC in the hippocampal region.

Kourron et al (1978) found that when primates were exposed to moderate to heavy doses of cannabis, there were persistent (7 - 8 months post exposure) EEG changes in the septal area.

The studies of Fehr et al (1976, 1979) and Radouco-Thomas et al (1976) looked at the effects of chronic cannabis exposure in rats. Their studies indicated decreased learning ability in the rats and it was thought this was due to changes in the hippocampus. The acetyl-choline system was postulated to have been disrupted by cannabis. Cannabis is thought to decrease the release and turn over of AC in the hippocampus (Knudson et al 1984). The anticholinergic hypothesis has noted the many behavioural and pharmacological similarities between cannabis and anticholinergic drugs and this has led to the suggestion that cannabis exerts its effect on the hippocampus via a cholinergic mechanism. It is known that the main hippocampal afferents are cholinergic (Shute et al 1967). This model explains why THC, hippocampectomy and anticholinergic drugs all impair the retention of new information (Drew et al 1974, Paton 1975, Scoville et al 1957, Carlton et al 1965, Meissner 1966, Safer et al 1971, Abel 1971, Miller et al 1972). It is known that digit span memory is impaired when an individual is exposed to cannabis and scopolamine (Tinklenberg et al 1970, Safer et al 1971, Dornbush 1971) and this observation has been explored using the Corsi board in the present thesis. Even though the hippocampus is involved with the aquisition of new memory, it is not thought to be the storage site for such memories (Drew et al 1974). Drew et al (1972) reported that there was confabulation in cannabis subjects and felt this was reminiscent of the cognitive deterioration seen in alcoholic dementia which is characterized by lesions in the hippocampus and mamillary bodies (Barbizet 1963).

Schuster (1990) noted that cannabis is toxic to the cells of the hippocampus and noted that the toxic alterations in the hippocampal neurons induced by THC are similar to those observed in ageing.

It should be noted that the complexity of the limbic forebrain\ limbic midbrain system with its many reciprocating subconnections within the brain stem complicates the finding of the precise locus of Cannabinoid action.

In addition to the effect of THC on the cholinergic neurotransmitter system, Gardner et al (1988, 1990) using the Lewis Strain of rats, found that THC augments intra-cranial electrical self stimulation in the median forebrain bundle and also enhances pre-synaptic basal dopamine efflux in the nucleus accumbens and pre-frontal cortex. This finding has only been recorded in the Lewis Strain of rats.

In addition to the effect of cannabis on the cholinergic neurotransmitter system in the hippocampus, Lipparini et al (1969) have demonstrated that THC abolished hippocampal alpha rhythm and Hockman et al (1971) found THC induced spindling and high amplitude slow wave activity in recordings obtained from the hippocampus.

Kaufman (1992) reported that cannabis is toxic to the cells of the hippocampus.

Milner (1971) did not work with subjects who abused cannabis but with brain damaged individuals. He noted that in subjects with a right temporal lobectomy which involved the hippocampal region, there was a marked deficit in the short term memory of the subject.

Dornbush (1973) conceptualized STM as being a complex of 3 stages (fig : 6). He postulated that cannabis has a direct effect on the storage procedure in that because of decreased attention in cannabis smokers, storage of information does not occur because of inadequate rehearsing. This hypothesis is supported by Dittrich (1973) (fig : 7). Diltrich noted that the larger the dose of cannabis and the longer the interval between aquisition of information and its retrieval, the greater the decay of the stored information.

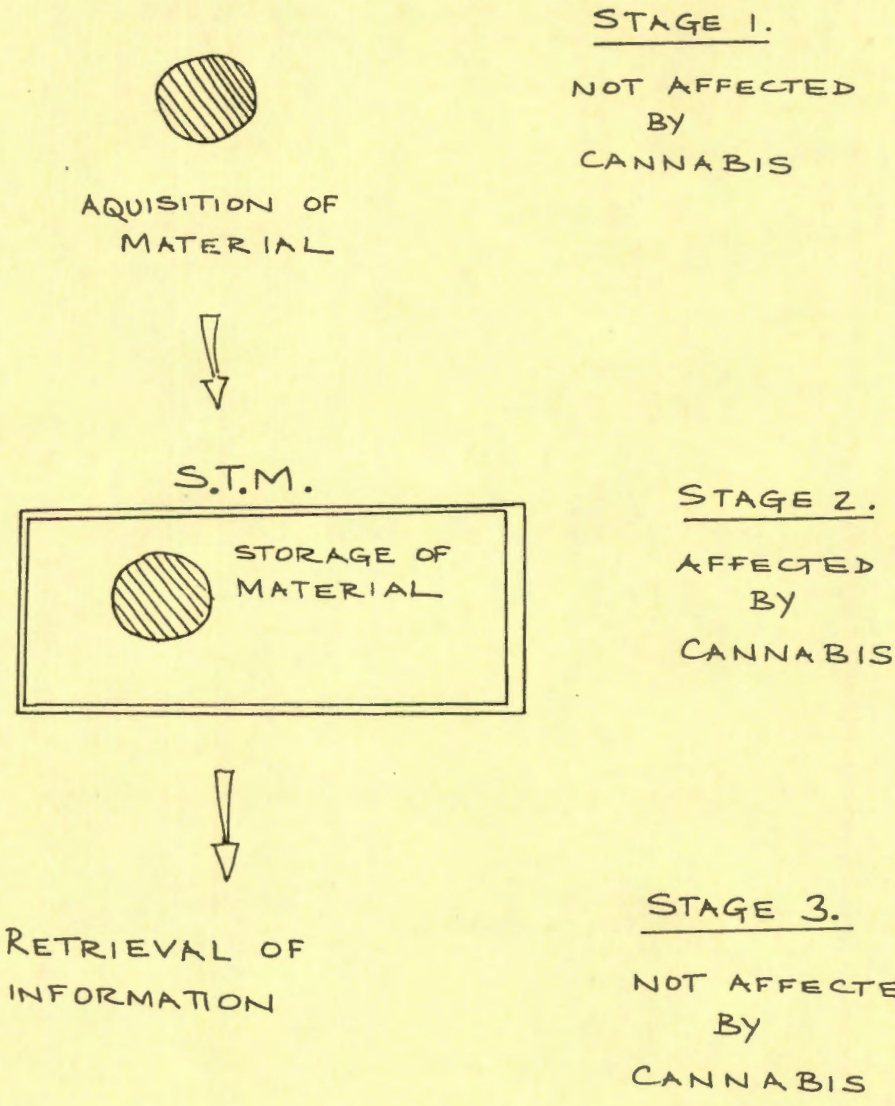


FIG. 6 : STM as conceptualized by Dornbush (1973).

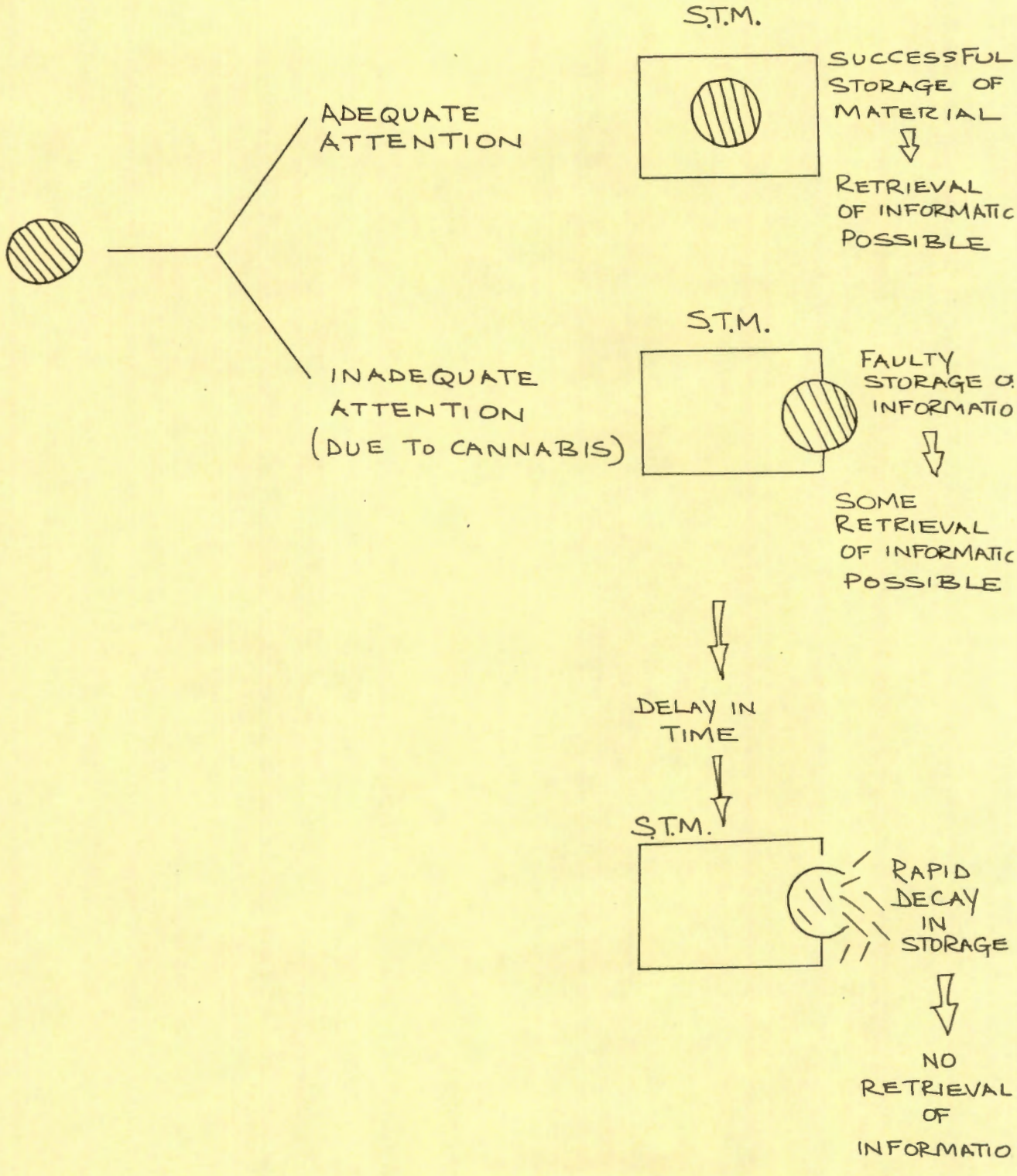


FIG. 7: **Dittrich's (1973) hypothesis that in Cannabis smokers there is inadequate attention and hence inadequate rehearsal of new information and a STM deficit**

Dornbush (1974) and Darley et al (1977) supported the model proposed by Dittrich (1973) that cannabis causes a faulty storage of material. If material is learnt prior to cannabis exposure, Darley et al (1977) demonstrated that such material is equally well retrieved when the subject is exposed to cannabis or a placebo.

Fig . 8 demonstrates the proposed sites of action of cannabis on the cognitive process.

Abel (1971), Drew et al (1974) and Maykut (1985) all supported the hypothesis that the main action of cannabis on memory function was by inhibiting the flow of information from STM to LTM. Maykut (1985) proposed that the faulty transfer process was due to synaptic cleft alteration in the memory traces between the STM and LTM.

In contrast, Weil et al (1969) and Low (1973) proposed that cannabis affects the retrieval mechanisms in both STM and LTM.

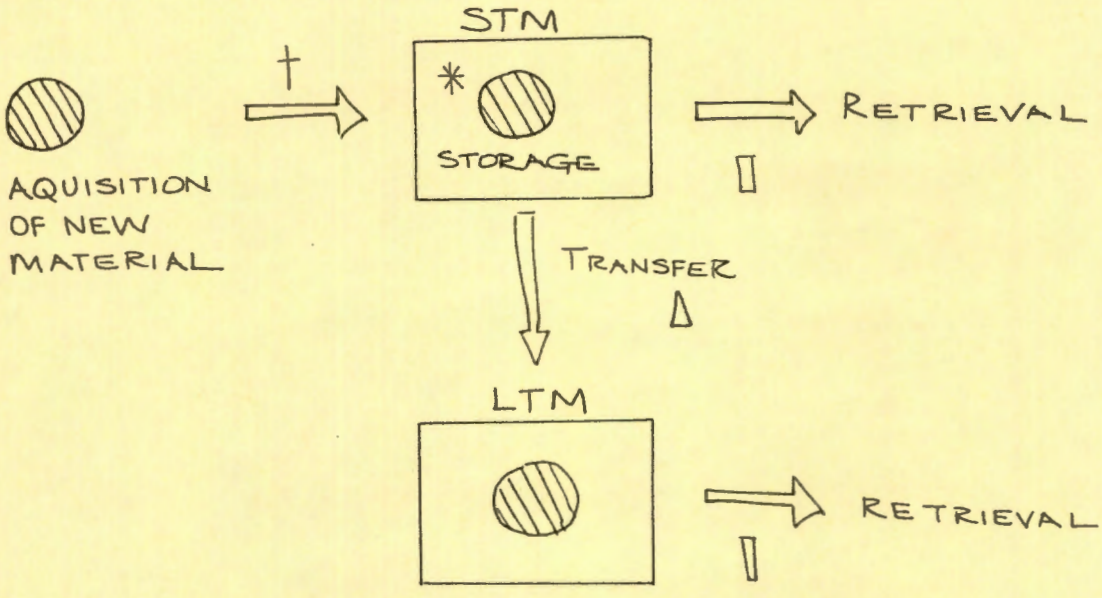
Tinklenberg et al (1973) and Paton (1973) proposed that cannabis alters the intial coding of new information through a process of sensory disinhibition which results in perceptual flooding and hence faulty strorage of new information.

Rosenkraz et al (1971) demonstrated that there was a consistent severe loss of brain protein and RNA in the brain tissue of rats exposed to chronic long term cannabis use. Kolansky et al (1972) postulated that the same changes may be present in humans.

Physiological changes seen with cannabis use

1/ EEG changes:

Studies have demonstrated long term residual abnormalities in the EEG tracings from the cortex and hippocampus of cats (Baratt et al 1972), rats (Fehr et al 1976, 1979) and monkeys (Heath 1976) who had been exposed to chronic long term cannabis use. Maykut (1985) noted that in humans exposed to an oral dose of 210 mg\ day THC, there were alterations in the observed EEG sleep trace with a decrease in REM and an



key THE PROPOSED SITES OF ACTION OF CANNABIS WHICH RESULT IN COGNITIVE DISTURBANCE

* DARLEY ET AL (1977)

Δ ABEL (1971), DREW ET AL (1974), MAYKUT (1985).

▯ WEIL ET AL (1969), LOW ET AL (1973)

† TINKLENBERG ET AL (1973), PATON (1973).

FIG. 8 : The different sites of action of cannabis on the cognitive process.

increase in non-REM sleep. Mehndiratta et al (1975) recorded insomnia in one third of all cannabis users.

Campbell (1971) reported marked abnormalities in the EEG from the temporal lobe region of a group of patients who had a cannabis induced psychosis.

2/ Cerebral blood flow (CBF) changes

CBF is closely coupled with brain function. It is known that significant CBF changes are caused by benzodiazepines, caffeine and ethyl alcohol (Mathew et al 1989).

Mathew et al (1986) looked at CBF in 17 chronic cannabis users who had smoked six cannabis cigarettes a week for over six months. Using the ^{133} Xenon inhalation technique, they were unable to detect any CBF changes in the cannabis users. However this technique measures predominantly cortical perfusion and not subcortical perfusion. Also the amount of THC is not specified and 6 cannabis cigarettes per week may have been too small a dose to detect any changes in CBF. The study size may also have been too small to have detected subtle changes to CBF.

Mathew et al (1989) repeated their experiments, this time the experimental group used 10 cannabis cigarettes a week for three years. They detected an increased CBF to the right and left frontal regions and left temporal regions when the experimental group was exposed to "one high potency cannabis cigarette", but overall there is a lower resting CBF in chronic cannabis users compared to a control group. It is thought that this lower resting CBF is associated with the reported cognitive dysfunction in cannabis users and the temporary increase in CBF to certain brain regions when exposed to cannabis results in the observed euphoria and decreased anxiety associated with cannabis use.

3/ Glucose utilization defects.

Primate studies have revealed a glucose utilization defect in cannabis smokers (Ames et al 1979).

Conclusion

The exact role of cannabis in causing structural and functional damage to the brain has been difficult to assess because of the variables involved.

The tentative conclusions conclusions are :

1/ Possible structural changes :

(a) global cerebral atrophy.

(b) Widened synaptic clefts, clumping of vesicles in the pre-synaptic nerve endings and disruption of RER in the septal, hippocampal and amygdala regions of the limbic system.

2/ Possible functional changes :

(a) Decrease release and turnover of AC in the hippocampal region resulting in disturbance of memory.

(b) loss of brain proteins and RNA.

(c) Changes in the EEG patterns in the hippocampal area.

(d) lower resting CBF which is thought to reflect on cognitive dysfunction.

(e) glucose utilization defects.

DEMOGRAPHIC DATA ON CANNABIS USERS.

Table 7 summarizes the demographic data on cannabis users.

The emerging profile is that cannabis users are :

1/ Male

2/ Young

3/ Single

4/ No children

5/ Poorly educated

6/ Poor work record or unemployed

7/ A possible history of delinquent behaviour

8/ Homeless

9/ Come from a disturbed family background

10/ Started using cannabis when a teenager

11/ Use of cannabis over many years

Table . 7 Demographic data on Cannabis users.

Personal details	**References**
1/ Vast majority of users are male	Mathers et al 1992
	Mehndiratta et al 1975
	Rolfe et al 1993
2/ Age :	
Young	Onyango et al 1986
	Solomons et al 1990
15 - 50 years (Average = 39)	Soueif 1975
16 - 60 years	Mathers et al 1992
18 - 37 years	Wig et al 1977
23 years (R = 17 - 52)	Rottanburg et al 1982
24, 5 years (R = 15 - 35)	Varma et al 1988
29, 5	Rolfe et al 1993
Under 35	Onyango et al 1986
Under 40	Carney et al 1984
3/ Marital status	
Single	Solomons et al 1990
	Soueif 1975
Majority single	Varma et al 1988
4/ Number of children	
Nil	Solomons et al 1990
	References
5/ Level of education	
Poorly educated	Solomons et al (1990)
25 % had no formal education	Rolfe et al 1993
12 % had std 10 education	Low 1973
60, 6 % illiterate	Soueif 1975
80 % illiterate	Mehndiratta et al 1975

6/ Work record

Poor	Mehndiratta et al 1975
Less than 5 % had jobs	Rolfe et al 1993
	Solomons et al 1990
Unemployed	Peck et al 1986
	Onyango et al 1986
High unemployment	Hammer et al 1985

Criminal Record

1/ History of delinquency	Kendall et al (?)

Social History

1/ Homeless	Onyango et al 1986
2/ Family disturbance	Mehndiratta et al 1975

Cannabis History

1/ Age at which cannabis use was

Started

14 years	Ben Arie 1984
15 years	Louw 1973
< 17 years	Botha et al 1981
17 years (R = 10 - 28)	Mathers et al 1992
< 20 years	Mehndiratta et al 1975

2/ Length of time that Cannabis had been used

70 % of sample > 2 years	Ng et al 1990
> 4 years	Mehndiratta et al 1975
50 % of sample > 5 years	Ng et al 1990
5 - 30 years	Soueif 1975
9, 4 years (R = 1 - 25 years)	Mathers et al 1972
10 years	Botha et al 1981
15 years	Wig et al 1977

3/ Dependent on Cannabis alone

21 % white sample	Ben Arie 1984
41 % coloured sample	Ben Arie 1984
30 % white sample	Levin 1974

4/ Dependent on Cannabis and other drugs

68 % of the white sample	Levin 1974

5/ Amount of Cannabis used

60 % of sample smoking Cannabis > 1 x day	Soueif 1975

6/ Cannabis use and the psychiatric population

Drug related admissions 8,3 %	Ohaeri et al 1993
Prevalence of Cannabis use in the psychiatric population 17, 4 %	Onyango et al 1986
33 % daily users	Nga et al 1990
66 % weekly users	Nga et al 1990
47 % men, 24 % women in general psychiatric unit had drug related problems	Brady et al 1991
30,8 % of admissions THC positive	Rolfe et al 1993
Drug of abuse on admission Cannabis in 77 % of cases.	Ohaeri et al 1993

12/ High frequency of simultaneous use of other drugs

13/ High prevalence of a concurrent mental disorder

Yamaguchi et al (1985) in their longitudinal study found that many young people stopped using cannabis once they had established families of their own, ie the socialization into an adult role resulted in the cessation of cannabis use due to the theory of role incompatibility. Kandel et al (1989) have pointed out that in those individuals who experience a delay in establishing an adult role (for example through unemployment) have a higher probability of continuing cannabis use.

Hamner et al (1990) have found that in those individuals who remained unemployed, there was a high probability of continued cannabis use.

Sullivan (1993) studied the characteristics of repeat users of a psychiatric emergency service and found that such individuals were most likely to be young separated or divorced, black unemployed males with a diagnosis of schizophrenia, personality disorder or substance abuse.

PREVIOUS STUDIES OF CANNABIS USE IN SOUTH AFRICAN BLACKS

One of the most importance studies on the use of cannabis in South African was done by Du Toit between 1972 and 1974 and published in 1980. He concentrated on urban and rural blacks in Natal but also looked at cannabis use in the coloured, Indian and white population.

Du Toit had 457 rural blacks in his sample, 94,7 % of whom were male. Use of drugs besides cannabis and alcohol was almost non existent. 51,6 % of the sample used both drugs concurrently, the alcohol being mainly consumed over the weekend.

Table 8 summarizes the data collected on rural blacks and Table 9 lists the reasons given by rural blacks for smoking cannabis. Of interest is reference to the Rastafari movement in that the term "Rasta" in the E Cape has come to mean a person who smokes cannabis. A common reason given for smoking cannabis in the present study is

Table . 8 :

Rural Blacks in Du Toit's survey		No = 457 Age 10 - 90 years
Social	No	%
Married	177	38,9
Single	278	61,1
Educational		
No formal Ed	145	32,5 %
Up to std 6	114	25 %
Up to std 10	5	0,8 %
Cannabis history		
Age of 1st use	9 - 45	x = 18,7
Age	No	% sample started Regular use
13 - 15	75	16,3 %
16 - 19	172	37,9 %
20 - 29	130	28,4 %
Introduced to cannabis by a relative		18,4 %
Introduced to cannabis by friends		58,8 %
First experience in a group setting		82,1 %
First experience alone		12,7 %
Length cannabis use	1 - 77 years	x = 11, 7 years
Quantity	2,7 zols\ day	6,8 days\ week

Cannabis increases concentration.
Cannabis decreases one's worries.
Cannabis increase's one's physical endurance.
Cannabis promotes general good health.
Cannabis increase's one's happiness.
It is patriotic to smoke cannabis.
Cannabis cures "idliso" (ie being poisoned in the traditional way).
Cannabis is used to attract the ancestral spirits.

Table. 9. Reasons given for smoking Cannabis in Du Toit's survey (1980) of Rural black people

that the subject is a "Rasta". Hickling et al (1994) have articulated what Rastafarianism is, ie a cult and a political movement which speaks for the needs of the black underclass in Jamaica. They believe the true home of blacks is Ethiopia and that god was re-incarnated in Haile Selassie. They do not believe in violence, follow a vegetarian diet and use no other drugs except cannabis. No individual in the present sample who claimed to be a "Rasta" was able to formulate the beliefs of the movement.

Solomons et al (1990) looked at 110 consecutive black men who were admitted to hospital with acute psychiatric symptoms. The average age was 28,2 years, 81 % were single and 83 % had no children. Most were poorly educated with the average subject reaching a standard 4 education. Only 5 % had matriculated and 7 % had no formal education. 69 % of the sample were unemployed. 31 % of the sample were diagnosed as having a cannabis induced psychosis.

Using the brief psychiatric rating scale (BPRS), they found that whereas 25 % of the sample were assessed as being extremely disturbed on admission, only 7 % were still disturbed 7 days later. 27 % of the sample admitted to using cannabis in the month preceding admission and 40 % had used alcohol in the month preceding admission. The average length of stay in hospital was 27 days and 72 % were discharged within one month of admission.

Meursing et al (1989) administered a self report questionnaire to a random sample of 1135 students, aged 11 to 27 years old in Lesotho, South Africa. The majority of the sample (62 %) were female. 3 % admitted to cannabis "sometimes" or "daily" and 3 % admitted to cannabis "once". Almost all the cannabis smokers were male.

Mkhize (1989) looked at 70 people from Swaziland, South Africa to discover their reasons for smoking cannabis. The reasons included:

1/ Loss of socio-cultural norms.

2/ A belief that cannabis enhances concentration

3/ A means of coping with anger.

4/ A means of enjoying the sense of being powerful and in control, flaunting authority figures.

Mkhize felt that the pervading sense of futility and powerlessness was crucial to the initiation and continuation of cannabis use. This hypothesis is supported by Gerard et al (1955) who found that the subject used drugs to cope with overwhelming anxiety in anticipation of adult roles in the absence of adequate preparation, role models and prospects.

Table 10 summarizes the work done on the South African black population.

Author	Sex	Population	Age	Size of sample	Cannabis use
		Group			
Bourhill (1913)	Male	Admission to a	20 - 60	627	40%
		Psychiatric -			
		Hospital			
Du Toit (1980)	947%	General -	10 - 90	457	60%
	Male	population			
Meursing et	62%	Students	11 - 22	1135	3 % some-
al (1989)	Females				times used
					cannabis, 3 %
					had used
					cannabis
					once.
Solomons et	Male	Admission to a	Average	110	31 % cannabis
al (1990)		Psychiatric -	= 28,2		psychosis,
		Hospital			45 % history
					of cannabis
					abuse.

Table . 10 :

Summary of work done on the use of Cannabis in the black South African population.

THE CULTIVATION OF CANNABIS PLANTS

Two subjects in the present survey grew cannabis primarily for their own use. All other subjects purchased their cannabis from a dealer.

One subject grew his cannabis from seed planted in old tins containing a rich mixture of soil and cow manure. The seedlings were then planted out when they had attained a certain size.

The other subject obtained seedlings from a friend. These were planted out using a lot of cow dung as manure. The seedlings required frequent watering but not on a daily basis. He waited until the plants had reached 1,5 m. in height and then he harvested the leaves and dried them over a primus stove.

METHODS USED TO SMOKE CANNABIS IN SOUTH AFRICA.

There are many pipe forms and diverse ways of inhaling cannabis smoke. The most comprehensive descriptions of the various cannabis pipes in use in South Africa appears in the study of Du Toit (1980). **Fig. 9** is a drawing done by one subject in this study. He was a single man in his early 20's. He described how he and his friends used a large potato to make a cannabis pipe. This pipe form was not described by Du Toit (1980).

Cannabis in the East Cape is usually sold in small quantities for the private use of the purchaser **(fig. 10).** The crude cannabis mixture often contains seeds and this impedes the smooth burning of the cannabis. Consequently, users often grow one long finger-nail in order to facilitate the quick removal of seeds from the crude mixture prior to smoking **(fig. 11).**

Most often the cannabis was mixed with tobacco prior to smoking. Du Toit (1980) lists two reasons for this practise:

a) Economy

b) The belief that the smoking of pure cannabis causes madness and\ or foot ulcers of the type called "impehlwa".

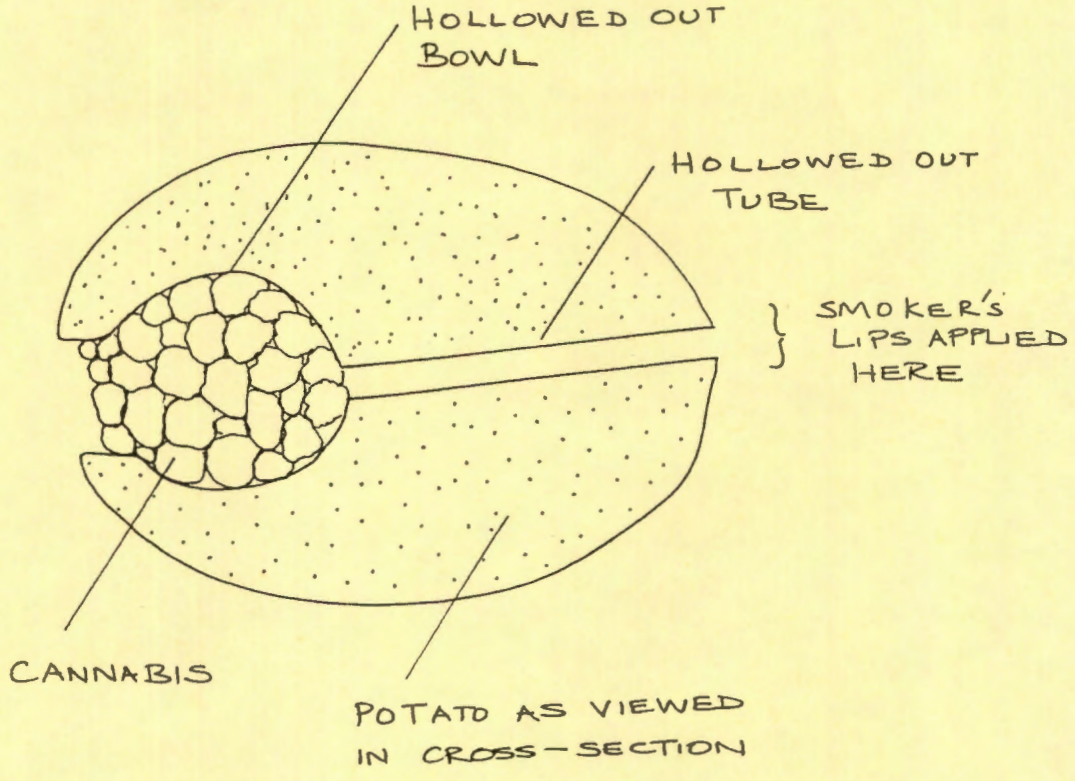


Fig. 9 : The potato cannabis pipe.

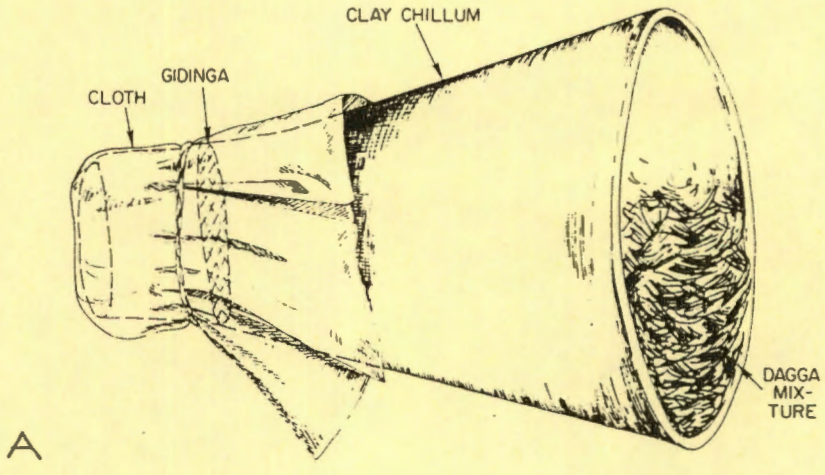
Fig. 10 : **Recent purchase of Cannabis found in the possession of a patient admitted to Fort England Hospital. The cannabis in the packet was a crude preparation of flowering tops, leaves seeds and stems.**

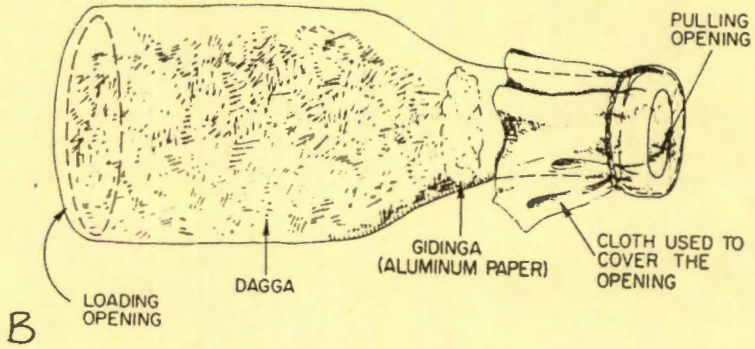
Du Toit (1980) mentioned that blacks buy small amounts of Cannabis at a time, often buying one "zol" at a time or a handful (as featured in the photo) which is enough to make 15 "zols" and represents a week's purchase.

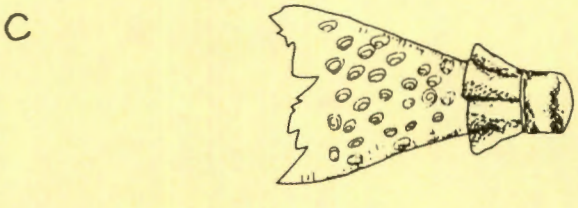
Fig . 11. Hand of a Cannabis user demonstrating the long finger-nail to facilitate the removal of seeds from the crude Cannabis mixture. This particular subject had a THC level of 660 ng\ ml and an AST\ ALT ratio of 2:1. Du Toit (1980) mentioned that many blacks in his survey believed that smoking pure cannabis (ie without tobacco) caused insanity and that the seeds of Cannabis were responsible for causing insanity.

Fig. 12 is from Du Toit's survey and illustrates the most common "pipe" in use in the East Cape.

The "zol" is also in common use, ie. Cannabis and tobacco are rolled together using commercial cigarette papers or brown wrapping paper. After the "zol" is rolled, it is greased with butter, sunflower oil or saliva to make it burn more slowly and evenly.







A kind of "pipe" currently in use among urban African youths. A filter called a "gidinga" is used and the mouth opening is covered with a cloth called a "saafi" which prevents ash from entering the mouth.

Fig. 12. Some Cannabis pipes from the Du Toit (1980) survey

CANNABIS INDUCED SYNDROMES.

The DSM IV lists the following syndromes :

1/ Cannabis dependence.

2/ Cannabis abuse.

3/ Cannabis intoxication.

4/ Cannabis intoxication delirium.

5/ Cannabis induced psychotic disorder with delusions.

6/ Cannabis induced psychotic disorder with hallucinations.

7/ Cannabis induced anxiety disorder.

8/ Substance withdrawal delirium.

The following three syndromes will be considered :

1/ Cannabis intoxication.

2/ Cannabis withdrawal delirium.

3/ Cannabis induced psychotic disorder.

Cannabis Intoxication

Intoxication can be examined in a variety of ways :

1/ Noted physiological response to cannabis.

2/ Noted psychological response to cannabis.

3/ Noted behavioural response to cannabis.

Three models of intoxication have emerged from the examined literature :

1/ Dose - response model.

2/ The phases of intoxication model.

3/ The acute vs chronic use model.

It is also recognised that the individuals response to cannabis intoxication is influenced by a variety of factors which include the individual's personality, pre-existing mental illness, cultural factors, expectations of the user, environmental factors and external incentives offered to the user.

Noted physiological responses to cannabis.

The following systems have been noted to be affected by cannabis :

1. Nervous System

(a) Central nervous system.

(i) Level of consciousness.

The ARF\ WHO report (1981) noted that at high doses cannabis can induce a stuperous state. The same conclusion was reached by Ishbell et al (1967), Thacore et al (1976) and Ashton (1987).

(ii) Hypothalamic axis.

An increase in appetite has been noted (Abel 1982). Also hypothermia has been associated with high doses of cannabis (Ishbell et al 1967, Thacore et al 1976, Ashton 1987).

(iii) Brain Stem.

The following eye signs have been noted :

Ptosis (Ishbell et al 1967, Gilman et al 1985, Ashton 1987,).

Pupillary constriction (Maykut 1985).

Photophobia (Ishbell et al 1967, Gilman et al 1985, Ashton 1987).

(b) Automic nervous system.

The following anticholinergic effects have been noted with cannabis use :

Increased thirst (Abel 1982)

Dry mouth (Abel 1982)

Constipation (Ishbell et al 1967, Gilman et al 1985, Ashton 1987)

2. Cardiovascular system

The following effects have been noted with cannabis use :

(a) bradycardia with high doses of cannabis (Ishbell et al 1967, Thacore et al 1976, Ashton 1987)

(b) Tachycardia (Ishbell et al 1967, Talbott et al 1969, Maykut 1985, Abood et al 1992)

(c) Raised blood pressure (Ishbell et al 1967)

(d) Orthostatic hypotension when cannabis is used in high doses (Ishbell et al 1967, Thacore et al 1976, Ashton 1987, Abood et al 1992)

(e) cold extremities (Ishbell et al 1967, Thacore et al 1976, Ashton 1987)

(f) Dilation of conjunctival blood vessels (Abood et al 1992)

3. Respiratory system

(a) Dyspnoea (Talbott et al 1969)

(b) Irritation of bronchial mucosa (Marray 1985)

Johnson et al (1990) noted that cannabis can aggravate chronic lung disease such as emphysema and that cannabis could be carcinogenic to lung tissue because of the high content of polyaromatic hydrocarbons.

(c) Bronchodilation (Ishbell et al 1967, Thacore et al 1976, Ashton 1987)

4. Muscular - skeletal system

(a) hypomobility following high doses of cannabis (ARF\ WHO report 1981)

(b) Ataxia following high doses of cannabis (Ishbell et al 1967, ARF\ WHO report 1981, Gilman et al 1985, Ashton 1987).

(c) Manneristic behaviour\ Posturing

Rashid et al (1991) looked at 15 subjects, he noted 20 % presented with manneristic behaviour

5. Reproductive system and immune system

A decrease in testosterone levels (Kolodmy et al 1974), decreased spermatogenesis (Margolis et al 1980) and decreased libido (Maykut 1985) have been reported following the chronic use of cannabis.

Abood et al (1992) felt that there may be some alterations in the reproductive system, immune system and respiratory system following chronic long term use of cannabis, but they concluded, "however convincing evidence has yet to emerge that cannabis is solely responsible for any alterations that have been observed in these organ systems".

Noted Psychological responses to cannabis

The psychological responses to cannabis depends on many variables which include dose of cannabis, the smoking technique, prior experience with the drug, concomitant use of other drugs, individual's expectation, whether cannabis is consumed in a group setting or alone, whether cannabis is consumed in a hostile atmosphere or not and whether the individual has a past psychiatric history (Abood et al 1992).

A review of the literature identifies three categories of response :

1. Affective response
2. Perceptual response
3. Cognitive disturbance

Table 11 summarizes the psychological responses to cannabis.

1. The affective response.

(a) Anxiety

Onyango et al (1986) looked at a sample of 25 patients admitted to a psychiatric hospital in inner London and noted that in those patients whose urine was positive for cannabis, the features of anxiety, conceptual disorganization and grandiosity were especially prevalent.

(b) Fear\ Panic

The ARF\ WHO report (1981) noted that acute panic states were the most commonly observed short term adverse psychological effect following cannabis use.

Weil (1970) reported that in the panic state, cannabis users can believe they are dying or loosing their minds and that such states can be terminated by "simple reassurance" from medical staff. He felt that medication or hospitalization was contra-indicated except in cases of extreme agitation.

Table. 11 The psychological responses to Cannabis.

1. AFFECTIVE RESPONSE	AUTHOR (S)
Anxiety	Onyango et al 1986
	Johnson et al 1990
	Mathew et al 1989
	Maykut 1985
	Rashid et al 1991
	Talbott et al 1969
	Levin 1974
Fear\ Panic	Du Toit 1980
	ARF\ WHO Report 1981
	Talbott et al 1969
	Rashid et al 1991
Euphoria\ hypomania	Rottanburg et al 1982
	Abood et al 1992
	Rashid et al 1991
	Mathew et al 1989
	Johnson et al 1990
	Christov 1965
Grandiosity	Negrete 1973
	Onyango et al 1986
	Rashid et al 1991
Laughter	Du Toit 1980

Melancholy\ Dysphoria	Talbott et al 1969 Negrete 1973 Levin 1974 Johnson et al 1990 Shiling et al 1980 Rashid et al 1991
Anger\ Aggression	This has been examined in detail in a separate section of this thesis.
Apathy	Kolansky et al 1972

2. <u>PERCEPTUAL DISTURBANCES</u>

Delusions :	Johnson et al 1990 Onyango et al 1986 Talbott et al 1969 Negrete 1973 Abood et al 1992 Rashid et al 1991 ARF\ WHO report 1981 Maykut 1985
Depersonalization	Weil 1970 Talbott et al 1969 Negrete 1973 Keshaven et al 1986 Maykut 1985 Mathew et al 1989 Johnson et al 1990 Dittrich et al 1973

Derealizations	Ishbell 1967
	Negrete 1973
	Keshaven et al 1986
	Johnson et al 1990
	Weil 1970
Auditory hallucinations	Ishbell 1967
	Christov 1965
	Talbott et al 1969
	Onyango et al 1986
	Johnson et al 1990
	Rashid et al 1991
	Du Toit 1980
Visual hallucinations	Du Toit 1980
	Johnson et al 1990
	Onyango et al 1986
	Negrete 1973
	Ishbell 1967

3. COGNITIVE DISTURBANCES

Confusion\ Drowsiness	Talbott et al 1969
	Mathew et al 1989
	Rashid et al 1991
	Kolansky et al 1972
Cognitive Retardation	ARF\ WHO report 1981
	Kolansky et al 1972

Altered time sense	Negrete 1973
	Johnson et al 1990
	Mathew et al 1989
	ARF\ WHO report 1981
Decreased attention	ARF\ WHO Report 1981
Memory disturbances	Maykut 1985
	Mathew et al 1989
	Onyango et al 1986
	Negrete 1973
	Rashid et al 1991

Negrete et al (1973) felt that panic states, together with depression and depersonalization reactions are a function of individual psychological factors and environmental cues rather than an intrinsic property of cannabis use.

(c) Euphoria\ hypomania

Abood et al (1992) have noted all the variables which need to be considered in assessing the individual's response to cannabis but they felt there are some behavioural effects which are observed regardless of all the possible variables. One such response is initial euphoria when smoking cannabis. Ishbell (1967) expressed a similar view point.

(d) Grandiosity

Rashid et al (1991) looked at a sample of 15 psychiatric patients and they noted 73 % presented with grandiosity following cannabis use.

(e) Melancholy\ Dysphoria

Weil (1970) reported that Depressive reactions were mainly seen in obsessive compulsive individuals who were ambivalent about using cannabis.

(f) Anger\ Aggression

The complex inter-relationship between cannabis use and subsequent aggression has been examined in a separate section of this thesis.

2. The perceptual disturbances

The phenomenon of a cannabis induced psychosis has been examined in a separate section of this thesis.

(a) Delusions

Johnson et al (1990) have noted that at concentrations of over 250 micrograms\ kg THC, the emergence of psychotic phenomena becomes more likely. Apprehension, suspiciousness, and morbid preoccupation herald the emergence of confusion, delusions and hallucinations.

Christov (1965) looked at 140 patients admitted to a Moroccan mental hospital and he felt that the content of the delusions was determined by local cultural traits.

The ARF\ WHO report (1981) noted that the setting alone does not explain the occurrence of the observed delusions.

Kolansky et al (1972) had a small sample of 13 people and noted that paranoid delusions were frequent in those who were "heavy cannabis smokers".

Weil (1970) felt that depersonalization was more likely to occur in vulnerable individuals who smoked cannabis. Ishbell (1967) noted that depersonalization only occurred with large doses of THC, together with auditory and visual hallucinations.

Usually depersonalization is short lived but Keshaven et al (1986) reported a case study of a 20 year old male whose sense of depersonalization lasted 10 months after last smoking cannabis. They also reported on another case study of a 24 year old male who had been cannabis free for one year but presented with a six month history of depersonalization. They noted "cannabis is known to be excreted over several weeks but this does not explain the symptoms spanning almost a year and the possibility of a residual neurotoxic effect of cannabis has to be evoked".

(b) Auditory hallucinations

Rashid et al (1991) in their sample of 15 patients noted their 66,6 % exhibited hallucinatory behaviour after smoking cannabis.

3. Cognitive disturbances

This has been examined in detail in a separate section of this Thesis.

Negrete (1973) noted poverty of ideation and concrete thinking in cannabis smokers. The ARF\ WHO report (1981) found decreased concept formation and decreased learning in subjects who used high doses of cannabis.

In most cases, the duration of measurable memory disturbances is a matter of hours after smoking cannabis but there may be some vulnerable individuals who have more long lasting cognitive disturbances.

Noted behavioural changes following cannabis use

Motor excitement (Du Toit 980), decreased co-ordination with decreased reaction time (ARF\ WHO report 1981, Maykut 1985, Johnson et al 1990) and lethargy (Christov 1965, Mathew et al 1989) have all been noted in cannabis users.

The three models of Cannabis intoxication

1. The dose - response model of cannabis intoxication.

This model attempts to demonstrate that the observed physiological, psychological and behavioural responses to cannabis are a function of the THC dose. Ishbell et al (1967) noted that the acute psychomimetic effects of cannabis are dose related.

Johnson et al (1990) divided dosage into two categories :

(a) low dose of THC (under 50 micrograms\ kg).
There is a clear but not linear relationship between dose and observed effect.

(b) High dose of THC (over 250 micrograms\ kg).
At this dose, psychotic features present following cannabis use.

The ARF\ WHO report (1981) refer to the dose\ response model as a "biphasic pattern of response".

This biphasic pattern of response to cannabis dose has been supported with animal studies on rodents, dogs and monkeys (ARF\ WHO report 1981).

Johnson et al (1990) felt that the psychological sequalae were not as closely related to dosage as were the physical sequalae of cannabis use.

Table 12 summarizes the features of the dose - response model.

Table. 12 The Dose\ Response model of Cannabis use

Low doses of THC (less than 50 micrograms\ kg)

1. Non Specific

The behavioural effect of low doses of Cannabis are relatively non specific and show extensive overlap with the effects of amphetamines, opiates, hypnosedatives and alcohol (ARF\ WHO report 1981)

2. Psychological

Mild ego decompensation (Kolansky et al 1972)

Minimal perceptual and cognitive dysfunction (Rhea et al 1971)

3. Physiological

(a) Decreased reaction time : (Kvalseth 1977), Rhea et al (1971) did not confirm that low doses of cannabis affected reaction time.

(b) Decreased co-ordination (Kvalseth 1977)

(c) Increased sensitivity to auditory and tactile sensations (ARF\ WHO report 1981)

4. Pharmacological

Mutual enhancement with the effects of amphetamines or opiates (ARF\ WHO report 1981)

5. Behavioural

Hyperactivity (ARF\ WHO report 1981)

High doses of THC (over 250 micrograms\ kg)

1. Physiological

(a) Stupor (ARF\ WHO report 1981, Johnson et al 1990)

(b) Hypomobility (ARF\ WHO report 1981)

(c) Ataxia (ARF\ WHO report 1981)

(d) Decreased auditory and visual reaction time (Rhea et al 1971)

(e) Loss of weight (ARF\ WHO report 1981)

2. Psychological

(a) Decreased insight (Abood et al 1992)

(b) Depersonalization (Abood et al 1992)

(c) Psychosis

(d) Decreased in STM (Rhea et al 1971)

(e) Acute panic (Abood et al 1992)

(f) Paranoid ideation (Abood et al 1992)

2. The phases of intoxication model.

Abood et al (1992) erected a model of cannabis intoxication which recognized three distinct phases :

(a) Initial euphoria

(b) Drowsiness with sedation, followed by a distortion in time, hearing and vision.

There may be illusions and hallucinations.

(c) Cognitive disturbances, slowed reaction time, overt aggression.

3. The acute -chronic use model of cannabis use.

This model proposes that the effects observed in the individual depend on the time exposure to cannabis, ie whether the individual is a naive smoker or chronic smoker of cannabis.

Maykut (1985) observed the following in naive smokers :

(a) altered time sense

(b) memory dysfunction

(c) decreased concentration

(d) increased anxiety

(e) Alteration in time sense

(f) Paranoid ideation

Noyes et al (1975) noted that naive smokers have presented with acute anxiety and transient reality distortion, mild paranoia or a delirium.

Abel (1977) noted that chronic cannabis users tend to be more hostile and rebellious in their attitudes than do naive users of cannabis.

The following have been described in chronic cannabis users :

(a) Confusion and paranoia (Kolansky et al 1972)

(b) residual neurotoxic effects (Keshaven et al 1986)

(c) amotivational syndrome. This was described in middle class, highly motivated American college students who had had little more than experimental exposure to cannabis. The features described include :

Apathy
Childlike thinking
Impaired memory
Loss of interest in achievements
disorganization of life style
Dullness
Impaired judgement
Loss of interest in personal appearance
(McGlothin et al 1968, Negrete 1973, Johnson et al 1990, Abood et al 1992)

Samples of people from a more representative sample of the population have been unable to replicate the earlier studies. (Campbell 1976, Sutz et al 1976, Abood et al 1992)

However Kolansky et al (1972) and Levin (1974) felt the amotivational syndrome existed. Levin reported that 26,1 % of his sample of 448 white males fulfilled the criteria for the amotivational syndrome.

(d) Chronic users reported that the effects of cannabis are easily suppressed. Weil et al (1968) reported that chronic users of cannabis did better on some tests when under the influence of cannabis and that chronic users do not show the same degree of impairment compared to naive subjects.

Factors which determine the individual's response to cannabis

The observed effects following cannabis use depend on a combination of specific drug effects and many variables which are summarized in fig. 13. (Kolansky et al 1972)

1. Cultural effects :

Abood et al (1972) mentioned the role of the individual's culture in shaping the observed response to cannabis.

Table 13 summarizes the role of one's culture in defining the resultant expected experience following use of cannabis.

Rubin (1975) also commented on the role of culture in defining the subjective experience reported following cannabis use. He noted that the reported behaviour varied from aggression, agitation and delinquent behaviour to passivity and conviviality. He noted that, "most differences observed are likely to be determined by factors other than the pharmacological action of the drug".

This view point was supported by Bowman (1973)

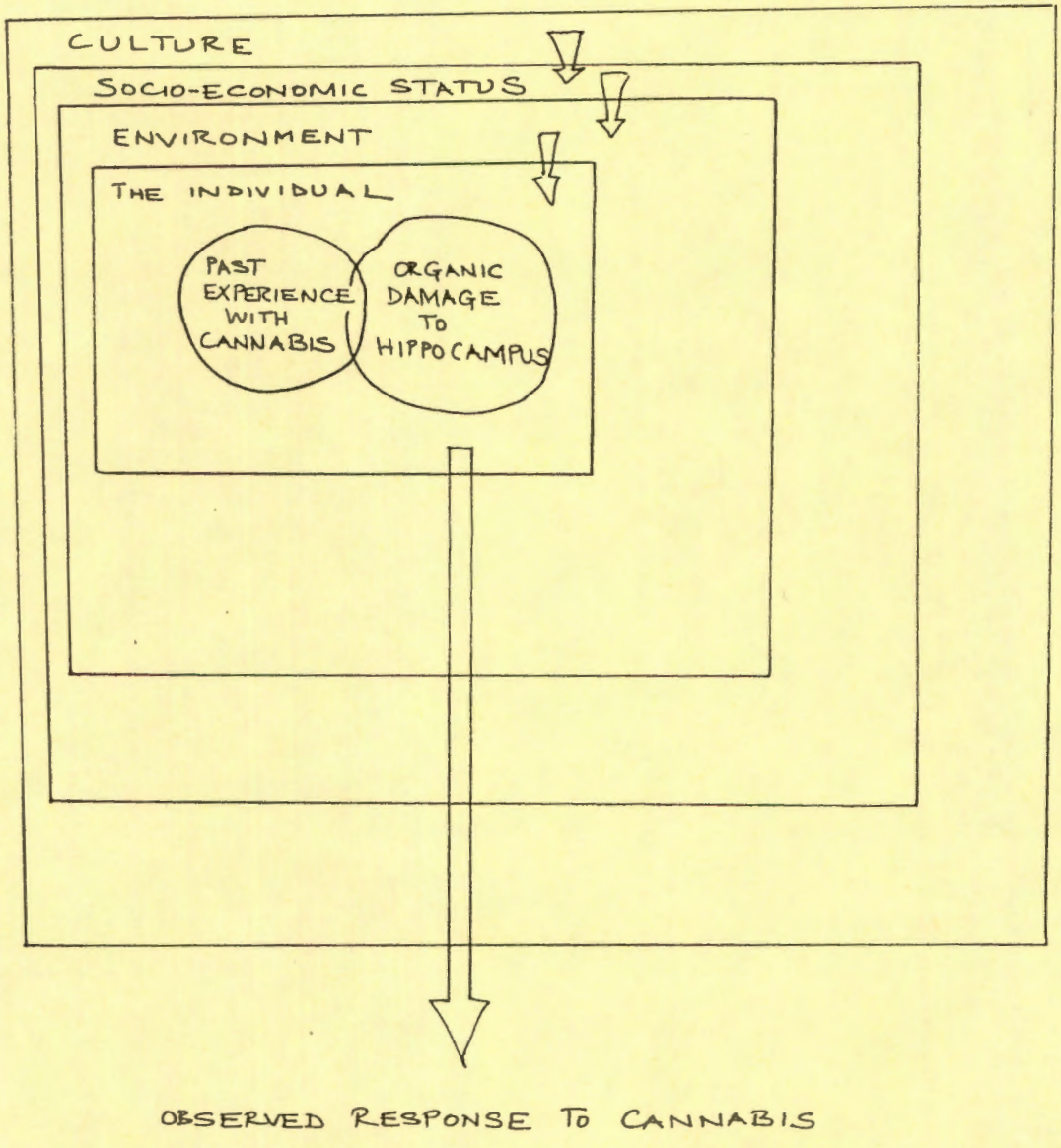


Fig. 13 **The individual response to cannabis use depends on a variety of factors found in the culture, environment and intra-psychic process of the individual.**

CULTURE	BELIEF	AUTHOR (S)
Egyptian	Cannabis will increase sexual potency	Soueif (1967)
Indian	Cannabis alleviates hunger	Chopra et al (1957)
Moroccan	Cannabis increases personal endurance	Bell (1972)
	in the face of physical hardship	
North American	Cannabis counter-acted the alienating	Negrete (1973)
	effects of modern society. It results in	
	feeling more relaxed, allows the	
	individual to express themselves more	
	freely	

Table. 13 Different culture beliefs shape the individual's response to cannabis

2. Personality of the user :

This factor has been recognised as being important in the observed effects of cannabis (Allenluck et al 1942, Talbott et al 1969, Negrete 1973, ARF\ WHO report 1981, Johnson et al 1990).

Hochman et al (1973) examined the personality profiles of chronic cannabis users who had failed to complete their schooling education and who lived in suburban areas. They found such individuals :

(a) were areligious

(b) had had early sexual experiences.

(c) were more rebellious, independent, reckless and anti-authoritarian

Similarly, Krug et al (1974) found cannabis users to be :

(a) more domineering

(b) more impulsive

(c) more socially uninhibited

(d) unconventional

3. Expectations of the user

Negrete (1973) noted that the novice smoker of cannabis had to learn from more experienced smokers how to smoke effectively and how to recognize the effects of cannabis and how to define such effects as pleasurable.

4. Pre-existing psychiatric illness

The existence of a pre-existing psychiatric illness is known to influence the individual's response to cannabis (Negrete 1973, Abood et al 1992).

Naditch (1974) noted that pre-existing psychopathology may predispose some sensitive individuals to adverse psychological reactions, Boyd et al (1984) noted that in those individuals with an underlying affective disorder, there was an increased risk of developing psychiatric symptoms after the use of cannabis.

5. Factors relating to the environment

Talbott et al (1969) noted that "environmental stressors may potentiate, exaggerate or otherwise effect the symptoms of cannabis intoxication". A similar view point was expressed by Negrete (1973) and by the ARF\ WHO report (1981).

Abel (1977) noted that if Cannabis was smoked in a situation not considered to be threatening or aggressive laden, then the user would be unlikely to react in an aggressive function.

6. External incentives

The ARF\ WHO report (1981) noted that the motivation for cannabis users to perform well in psychological tests can be enhanced by incentives such as money and this enhancement can decrease some of the cannabis effects.

2. <u>Cannabis withdrawal delirium</u>

The earliest report of a cannabis withdrawal delirium was reported in nine Indian soldiers who were deprived of cannabis when their garrison was moved to an isolated out-post where no cannabis was available (Fraser 1949). For the first few days following abrupt cannabis withdrawal, the soldiers presented with no symptoms. There was then an increase in irritability which escalated into violent outbursts which subsided after 48 to 72 hours, only to re-emerge as a violent out burst with psychotic features which lasted up to 4 weeks and then a spontaneous remission.

Jones et al (1983), in a survey of the literature, noted that frequent users of cannabis reported sudden onset of irritability, restlessness, insomnia and perspiration after cessation of regular cannabis use. Jones et al looked at 53 male volunteers all of whom were between the ages of 21 and 31 years old and who smoked cannabis at least twice a week for the past 5 years. These volunteers were given 10 - 30 mg THC every 3-4 hours for 21 days. Sudden cessation of cannabis use in this group resulted in :

mood changes

disturbed sleep with insomnia

restlessness with hyperactivity

irritability

hand tremors

anorexia with weight loss

Increased sweating with an increased temperature

nausea

Their work further reported that both subjective and objective changes as listed above were decreased when the subjects were given cannabis again.

Wallace (1978) also reported an increase in "psychic discomfort" when cannabis is stopped. He noted there was a peak disturbance 4 days after stopping cannabis which then subsided and disappeared by the tenth day.

Insomnia as part of the withdrawal delirium was also noted by Alterman et al 1980 and Brady et al 1991.

Rohr et al (1989) also supported the idea of a cannabis withdrawal syndrome.

Frederick's study (1980) demonstrated that when animals are deprived of cannabis, there was an increasing restlessness, tooth bearing and increased eye contact.

Kaymakcalan (1973) used IV THC in monkeys and demonstrated significant withdrawal effects. However his work is open to question as the observed effects were not unequivocally reversed when the monkeys were re-exposed to THC.

Beardsley et al (1986) did similar work with monkeys. They found that abrupt withdrawal of THC resulted in a disruption of schedule controlled behaviour and this could be reversed by the re-introduction of THC.

Other authors believe that there is no characteristic cannabis withdrawal syndrome (Ishbell et al 1970, Lemanna 1981, Keshaven et al 1986, Abood et al 1992).

McMillan et al (1971) showed that administration of increasingly larger doses of THC to dogs and pigeons resulted in the development of tolerance yet no withdrawal syndrome.

Abood et al (1992) stated, "chronic heavy use of cannabis does not result in a withdrawal delirium with severe symptomology. Psychological dependence is more probable than physical dependence".

3. Cannabis induced psychotic disorder

Introduction :

The DSM IV currently recognises two psychotic disorders linked to cannabis use :

(a) Cannabis induced psychotic disorder with delusions.

(b) Cannabis induced psychotic disorder with hallucinations.

Psychosis associated with cannabis use has been known for over 100 years (Tunving 1985).

Moreau de Tours (1845) described, "acute psychotic reactions, generally lasting a few hours, but occasionally as long as a week, its main features include paranoid ideation, illusions, hallucinations, depersonalization, confusion, restlessness and excitement. There can be delirium, disorientation and clouding of consciousness".

The Indian Hemp Commission of 1893 (Mehndiratta et al 1975) estimated that cannabis was a factor in 7 to13 % of all admissions to mental institutions. Tien et al (1990) looked at 4994 individuals who had used cannabis. They reported that 11,4 % (N= 507) individuals had experienced at least one psychotic episode and that daily use of cannabis was associated with a 30 % increased risk for the onset of a psychotic

episode, without daily use of cannabis, the risk of a resultant psychotic episode is "much less likely".

Solomons et al (1990) reported that 31% of their sample of 110 black South African men who presented with acute psychiatric symptoms had a diagnosis of cannabis induced psychosis.

Many workers have found support for the unique entity of a cannabis induced psychosis. (Marihuana 1969, Carney et al 1984, Thornicroft 1990, Mathers et al 1991, Mathers et al 1992).

Marihuana (1969) concluded that the syndrome has a central core of symptoms and the condition is self limiting, recovery is complete and symptoms to not re-occur unless there is further exposure to cannabis.

Mathers et al (1991) looked at a sample size of 908 hospitalised patients, 34.5% of whom used cannabis and they found, "a highly significant association between urine samples positive for cannabis and an initial diagnosis of psychosis".

In contrast, many researchers felt that even though pharmacological studies have provided strong evidence that use of amphetamines, cannabis, alcohol and other psychoactive drugs can induce delusions and hallucinations (Tien et al 1990), there was either no unique entity of a cannabis induced psychosis or alternatively it was a rarely observed phenomenon seen in certain predisposed individuals who had an underlying functional illness.

Negrete (1973) felt that individual psychotherapy and environmental setting dictated the observed response to cannabis use, rather than a unique psychomimetic property of THC. Campbell (1971) proposed a similar line of reasoning in that he found those individuals who developed a cannabis induced pyschosis had pathological EEG traces with excess theta waves.

Ohaeri et al (1993) reported that when a subject presented with cannabis induced psychosis, follow up with a diagnosis of schizophrenia, "could be made for most cases of cannabis users". Ohaeri et al added that, "the impression of cannabis being a major aetiological factor in psychosis is so strongly rooted among health workers in the north [of Nigeria] that one senior doctor said that from his experience the majority of schizophrenic symptoms among male suffers were associated with abuse of cannabis. In practise, when all admissions in his centre for 1989 were reviewed, only 13 % were reported to have used cannabis".

The problem with this conclusion is that no urine testing was done to validate whether the subject had used cannabis or not.

Spenser (1987) worked for several years in Australia and did not observe a single case of cannabis induced psychosis. He did however suggest that the controversy which arises as to whether cannabis induced psychosis exits or not is associated with variance of the THC content of the cannabis plant.

Stringaris (1972) concluded that the existence of , "cannabis induced psychosis has not been proven but such a psychosis must be presumed".

Tennant et al (1972) looked at 36000 men, 46 % of whom reported, "some use " of cannabis. They observed 18 cases of a cannabis induced psychosis and 85 cases of a psychotic illness when alcohol and cannabis were used together. However it appears that the dose of cannabis used together with the THC content and the degree of regularity of use are all important variables which regulate whether a cannabis induced psychosis is manifested or not.

Weil (1970) felt that psychiatric intervention in psychosis would result in a prolongation of the psychotic episode and that such a psychosis is the result of a re-inforcement from staff following an admission to a psychiatric unit.

He felt that the observed cannabis psychosis was the result of a medical mishandling of the more benign pathological intoxication state.

Identified variables which are thought to play a role in the manifestation of a cannabis induced psychosis.

Fig . 14 summarized the important variables.

(a) Personality of the cannabis user :

Spenser (1970) looked at 12 young males who had been admitted to hospital because of severe behavioural disorder following the use of cannabis. All were under 25 years old and had smoked cannabis every day for several years. He went on to describe the resultant cannabis induced psychosis but added that the study of the individuals pre-morbid personality would have helped to clarify why these men presented with an organic psychosis.

Talbott et al (1969) looked at a total of 35000 American soldiers in Vietnam. They identified 12 cases of cannabis induced psychosis. Of the cases, 2 had a premorbid history of personality disorder (not specified).

Lishman (1978) felt that the personality structure was an important determinant in the manifestation of a cannabis induced psychosis, together with the circumstances under which cannabis is used and the individual expectations accompanying drug use. Negrete (1973) was of the same opinion.

No author has linked a specific personality profile with the development of a cannabis induced psychosis. Gersten (1980) believed that at high doses, cannabis can cause significant ego disruption. Usually the individual is able to reconstitute rapidly as cannabis is eliminated from the system. However in those individuals who have a pre-existing ego deficit, they may not reconstitute as expected and present with a psychiatric picture when exposed to cannabis.

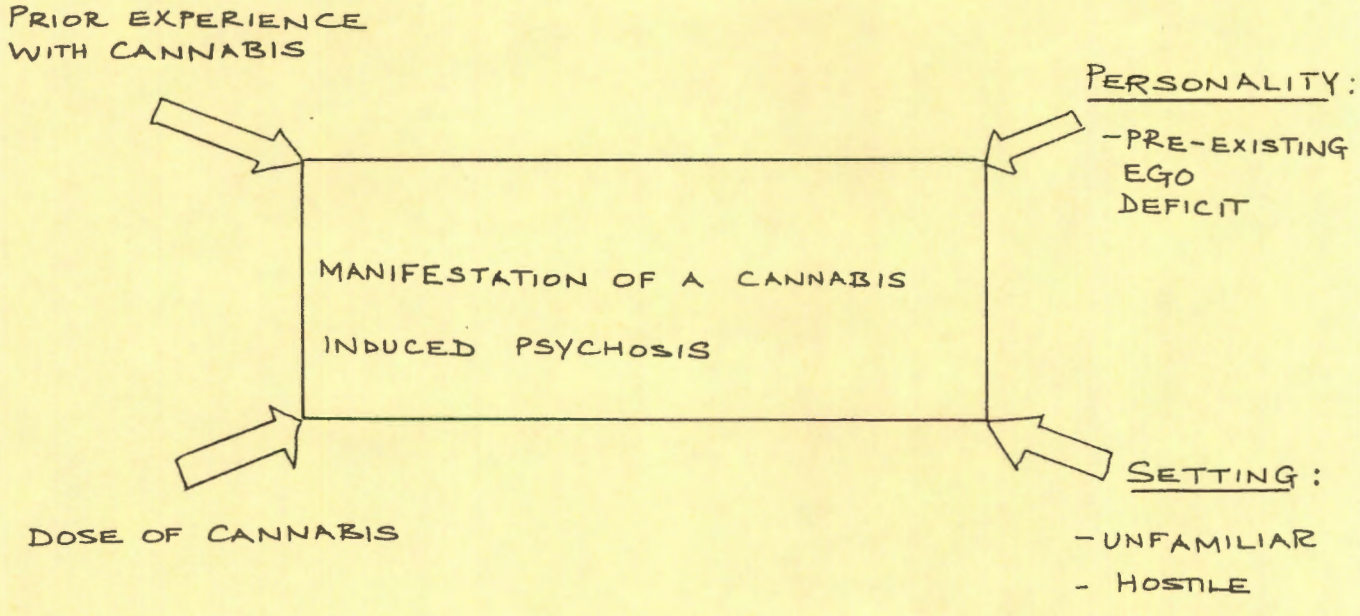


Fig. 14 **Identified variables which are thought to play a role in the manifestation of a cannabis induced psychosis.**

(b) The setting in which cannabis is used :

Negrete (1973) believed that the symptoms observed following cannabis use were influenced by psychological and environmental factors. He assumed that paranoid reactions occurred in settings which were unfamiliar to the users and that the reactions observed were not so much as due to the pharmacological effects of cannabis but rather due to cannabis acting as a precipitant in a specific set.

Talbott et al (1969) also believed the environmental setting was important in the manifestation of a cannabis induced psychosis in that, "the environmental stressors may potentiate, exaggerate or otherwise affect the symptoms".

(c) Cannabis dose :

Thornicroft (1990), noted "there is widespread agreement that high doses of cannabis precede acute organic toxic reactions".

The same conclusion was reached by Palsson et al (1982) who found that the "extensive consumption" of cannabis resulted in a short lived psychosis.

Johnson et al (1990) noted that with absorption of over 250 micro-gms\ kg THC delivered by smoking, then , "the appearance of psychotic phenomena becomes more likely". Johnson et al (1990) also noted that at lower doses of cannabis, a psychosis can result as part of an idiosyncratic reaction.

Ishbell (1967) noted that "THC is a psychomimetic drug and its psychomimetic effects are dependent on dose".

The work of Tennant and Groesbeck (1972) looked at 720 cannabis using USA soldiers. They suggested that under 12 gms of cannabis a month was only associated with minor respiratory ailments, whereas up to "30 gms of cannabis in a short space of time" was associated with an acute toxic reaction and up to 600 gms a month produced a chronic intoxicated state. They were also aware that the more potent preparations of cannabis, "precipitate a more severe and rapid reaction".

Other workers have supported the conclusion of Tennant and Groesbeck (Ishbell et al 1967, Talbott et al 1969, Tart 1970).

(d) Prior exposure to cannabis.

Negrete (1973) noted that certain psychotic features occur more frequently in the early stages of cannabis usage when the individual has not yet learnt to understand and predict the course of intoxication.

In summary, it appears that in naive cannabis users, with pre-existing ego deficits, using a sufficient dose of cannabis in an unfamiliar or hostile setting, they can present with a cannabis induced psychosis. The absence of these variables may explain why some authors have failed to identify cannabis induced psychosis.

Characteristics of the studied population

In studies which have looked at a cannabis induced psychosis, the following aetiological factors were considered :

(a) Sex of the subject :

All but one study used male subjects. The implication was that cannabis use was more prevalent in males.

Ohaeri et al (1993) looked at male patients admitted to a Nigerian psychiatric unit and felt that, "drug abuse cases consist predominantly of young males from a low socio-economic status and exhibit schizophrenic-like symptoms".

Sample size ranged from 12 males in Spenser's work (1970) to 36,000 USA soldiers serving in West Germany, 46 % of whom had smoked cannabis on at least one occasion and 16 % smoked cannabis at least three times a week (Tennant et al 1972).

The largest sample size consisted of 350,000 USA soldiers present on active duty in Vietnam from 1967 to 1968, 30 % of whom had used cannabis at least once (Talbott et al 1969).

(b) Age of subjects.

Most subjects examined were young, although Mathers et al (1991, 1992) did consider people who were aged 60 years.

Table 14 lists the age range of subjects examined. Age may have a direct relevance on whether a psychotic episode is manifested after cannabis use or not. Age may influence the development of ego strengths and prior experience with cannabis. It may therefore be that psychotic episodes are more readily observed in young males.

(c) Socio-economic Status.

Ohaeri et al (1993) in the Nigerian study noted that those individuals who presented with a cannabis induced psychosis came from a lower socio-economic status.

(d) Occupation.

Most studies did not record the occupation of the subjects who experienced a cannabis induced psychosis. Only two occupational categories were listed :

(i) Soldiers (Talbott et al 1969, Tennant et al 1972, Thornicroft 1990).

(ii) Unskilled workers (Solomons et al 1990).

Research indicated that young men of low socio-economic status are more likely to present with a cannabis induced psychosis. Solomons et al (1990) further added that such individuals were childless, urban dwelling, poorly educated, often unemployed and with a history of concurrent alcohol abuse.

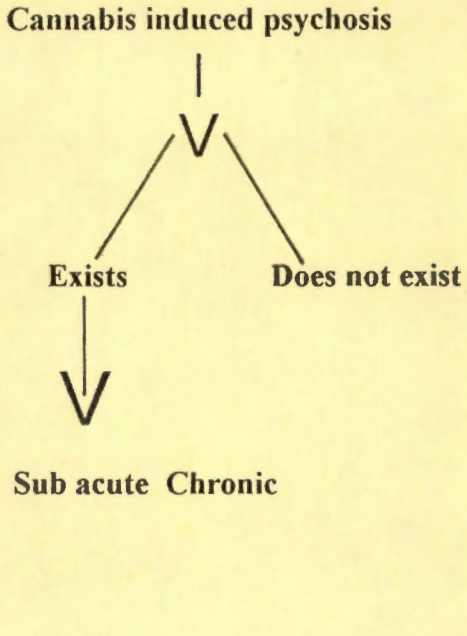
Various classifications of cannabis induced psychosis

Fig . 15 summarizes the various classifications of a cannabis induced psychosis.

Many researchers have disputed the existence of such an entity arising de novo. It is felt that the cannabis induced psychosis is only seen in vulnerable individuals with an underlying undiagnosed functional illness (Talbott et al 1969, Thornicroft 1990).

AGE (IN YEARS)	AUTHOR(S)
16 - 60	Mathers et al 1991, 1992
18 - 32	Rashid et al 1991
18 - 49	Tien et al 1990, Solomons et al 1990
23 (R = 17 - 52)	Rottenburg et al 1990
Under 25	Spencer 1970

Table . 14 : Age range of men who exhibited a cannabis induced psychosis.



1. Arising de novo
2. Exposing a previously latent functional psychosis
3. Precipitating a relapse of a known pre-existing functional psychosis

main manifestation of the entity is :

1. Paranoid
2. Schizophreniform
3. Manic
4. Organic

Fig . 15 The various classifications of a cannabis induced psychosis

Thornicroft (1990) stated that the entity of cannabis induced psychosis was "not warranted on phenomenological grounds". However the work of Thacore et al (1976) has demonstrated the phenomenological distinction between a cannabis induced psychosis and a functional psychosis. In addition, Thornicroft has ignored the rapid resolution of the cannabis induced psychosis which usually resolves within seven days.

Andreasson et al (1987) followed 45,570 Swedish men for 15 years. 9,4 % had used cannabis and 1,7 % were "high consumers" of cannabis. The relative risk of schizophrenia for such high consumers of cannabis was twice that compared to people who had never used cannabis ie the presentation of a cannabis induced psychosis is a label for an underlying functional psychosis.

Stefanis (1978) found that cannabis users were four times more likely to have underlying schizophrenia.

Other workers have felt that an established functional psychosis may lead to an increased risk of cannabis use because of the anticholinergic properties of cannabis.

The various view points of the inter-connections between cannabis and psychosis have been summarized by Benabud 1957, Chopra et al 1957, Ames 1958, Talbott et al 1969, Colbach 1970, Kemp 1970, Grossman 1969, Chopra 1971, Stringaris 1972, Spencer1971, Davidson et al 1972, Harding et al 1973, Breakey et al 1974, Rottanburg et al 1982, Palsson et al 1982, Thornicroft 1990, Rolfe et al 1993.

There appears to be less evidence for the existence of a chronic psychotic state as a result of cannabis use (Spenser 1970, Winkler 1970).

Spenser (1970) described a chronic form of cannabis induced psychosis as :

(a) persistent amnesia for the onset of the illness

(b) Flattening of affect

(c) Thought disorder / (d) Perceived as being odd and\ or suspicious.

Spenser felt the chronic form persisted for "an indefinite time".

Tennant et al (1972) also reported on a chronic psychotic state in cannabis users "similar to a schizophrenic reaction in predisposed individuals".

Negrete (1973) believed that a chronic psychotic state following prolonged use of cannabis existed. Chopra et al (1974) felt that the chronic psychotic form was particularly likely to occur in third world countries but added that the distinction between this category and schizophrenia was not clear.

Behaviour prior to the onset of a cannabis induced psychosis

Several researchers have reported that individuals increase their cannabis use prior to the onset of a drug induced psychotic episode (Bernhardson et al 1972, Palsson et al 1982, Thornicroft 1990). Palsson et al (1982) noted that the intensifications of cannabis abuse was over a period of weeks to months prior to the onset of the observed psychotic episode.

The features of the cannabis induced psychosis

Table 15 and Table 16 summarize the described features of a cannabis induced psychosis.

In length, the reported psychotic episode appears to be short lived, usually about seven days.

Table 15 records the Reported features of a psychotic episode. The most often reported features are :

(a) Confusion with cognitive dysfunction

(b) hypomania

(c) Aggression

(d) Paranoid delusions

(e) hallucinations

SYMPTOM	AUTHOR(S)
Sudden onset after smoking cannabis	Spenser 1970
	Tennant et al 1972
	Palsson et al 1982
Decreased sleep	Spenser 1970, Palsson et al
	1972, Negrete 1988
GENERAL :	
Dishevelled appearance	Gersten 1980
Blunted	Gersten 1980
Manneristic	Rashid etal 1991
Increased psychomotor acitivity	Spenser 1970, Gersten 1980
Circumstantial speech	Gersten 1980
AFFECT AND MOOD	
Labile, elevated affect	Spenser 1970
	Talbott et al 1969, Harding et
	al 1973, Rottenburg et al 1982
	Thornicroft 1990
	Rashid et al 1991
Anxiety	Talbott et al 1969, Thornicroft
	1972, Tennant et al 1972,
	Negrete 1973
	Palsson et al 1982
Panic	Thacore 1972, Negrete 1973
	Thacore and Shuklar 1976
Fear	Talbott et al 1969
Suspicion	Talbott et al 1969
Aggression	Spenser 1970
	Bernhardson et al 1972
	Thacore et Shuklar 1976
	Palsson et al 1982
	Rashid et al 1991
	Rolfe et al 1993
DEPRESSION	Talbott et al 1967, Davidson et
	al 1972
	Negrete 1973,
	Palsson et al 1982
THOUGHT PROCESS	
Pressure of thought	Talbott et al 1969,
	Spenser 1970
Thought fragmentation	Spenser 1970,Thornicroft 1990
	Rolfe 1993
PERCEPTUAL DISORDER	
Derealization	Ames 1958, Talbott et al 1969,
	Tennant et al 1972,
	Negrete 1973
Paranoid delusions	Talbott et al 1969, Spenser
	1970, Tennant et al 1972,
	Thacore 1972, Negrete 1973,
	ARF\ WHO report 1981,
	Palsson et al 1982, Thornicroft
	1990, Rashid et al 1991, Rolfe
	et al 1993
(CONTINUED .....)	

Table . 15 (continued)

(CONTINUED .....)	
Hallucinations	Talbott et al 1969, Weil 1970,
	Tart 1970, Keller et al 1971,
	Thacore 1972, Tennant et al
	1972, Palsson et al 1982,
	Thornicroft 1990, Rashid et al
	1991, Rolfe et al 1993
COGNITION :	
Poor concentration	Talbott et al 1969,
	Thornicroft 1990
Confusion, disorientation	Talbott et al 1969, Weil 1970,
	Tennant et al 1972,
	ARF\ WHO report 1981,
	Palsson et al 1982,
	Thornicroft 1990,
	Rashid et al 1991
Amnesia for the episode	Spenser 1970

Table . 15 : Reported features of a cannabis induced psychotic disorder.

LENGTH OF PSYCHOTIC EPISODE (DAYS	AUTHORS
NON SPECIFIC :	
Rapid resolution	Carney et al (1984)
Symptoms remit rapidly	Mathers et al 1982
Short lasting	Thacore 1972
Acute, short lived	Weil 1970, Mayer 1975
Few days	Chopra et al 1974
few days to four weeks	ARF\ WHO report 1981
few weeks	Gersten 1980
SPECIFIC	
three days	Carney et al 1984, Tennant et al 1972
four + days	Talbott et al 1969
five days	Rashid et al 1991
seven days	Rottanburg et al 1982, Palsson et al 1982,
	Solomons et al 1990, Rolfe et al 1993
14 days	Tennant et al 1972
15 days	Negrete 1973

Table . 16 : The reported length of a cannabis induced psychotic episode in hospitalized patients treated with neuroleptics.

Solomons et al (1990) examined 110 consecutive black South African men admitted to hospital with acute psychiatric symptoms. They felt that the diagnosis of a cannabis induced psychosis could only be made when all three of the following criteria were met :

(a) The patient had a history of recent cannabis use or the patient's urine tested positive for cannabinoids or both.

(b) The patient was psychotic or had been psychotic shortly before admission to hospital, ie evidence of :

formal thought disorder

hallucinations

delusions

behavioural disturbances

lack of insight

(c) During hospitalization the patient responded reasonably rapidly to treatment with clear evidence of return to pre-episode personality function.

Furthermore, Solomons et al (1990) did not view a cannabis induced psychosis as a single clinical entity but rather a group of disorders whose main clinical presentation was :

(a) **Maniform** :

Agitated, restless, pressure of speech, grandiose, circumstantial, flight of ideas. There was a decreased need for sleep and over activity in a purposeless manner.

(b) **Paranoid form** :

(c) **Schizophreniform** :

Blunted, withdrawn, poverty of ideation, poverty of volition, psychomotor retardation, bizarre somatic delusions or other delusions.

(d) **Organic form**

Clouding or fluctuating level of consciousness, disorienatation. Cognitive deficits evident.

Solomons et al reported on the following frequency of presentation of the different forms of cannabis induced psychosis :

	Number of cases	%
Schizophreniform	13	41,9
Maniform	8	25,8
Paranoid	5	16,1
Organic	5	16,1

	Total : 31	

Solomons et al did consider the concurrent use of alcohol with cannabis in their sample. 32,3 % had consumed alcohol together with cannabis whereas 45,2 % of the sample had consumed no other drug besides cannabis.

In contrast, Rottanburg et al (1982) felt that the most common presentation in heavy cannabis users was a psychotic illness characterized by marked hypomanic features.

Edwards (1963) and Abel (1982) felt that there was no unique set of psychotic symptoms following the use of cannabis and the term, "cannabis induced psychosis could not be justified".

Thacore et Shukler (1976) felt there were considerable differences in the clinical features of a cannabis induced psychosis and paranoid schizophrenia and felt that the former was characterized by more bizarre and violent behaviour, a greater affective component and less thought disorder compared to paranoid schizophrenia.

The concurrent use of other drugs together with Cannabis

A commonly used argument against the existence of a unique entity of a cannabis induced psychosis is that the effects observed may have been in response to the concurrent use of drugs by the patient.

Tennant et al (1972) looked at a sample size of 36,000 USA soldiers serving in West Germany, 46 % of whom had smoked cannabis on at least one occasion and 16 % smoked cannabis more than three times a week. When cannabis samples were analyzed, 3 % were found to be contaminated with cocaine, opiates, spices, shoe polish and feces. They also mentioned that 112 observed psychotic reactions were associated with the concurrent use of cannabis, amphetamines and alcohol.

In all, only 18 cases recorded in their sample size presented with a psychotic episode due to cannabis use alone, whereas 85 psychotic episodes were due to concurrent use of alcohol and cannabis.

Conclusion

Most researchers felt that the existence of the entity cannabis induced psychosis is merited on phenomological grounds. Its presentation depends on many factors which include dose of cannabis used, the users familiarity with the drug, personality of the user and the setting in which cannabis is used.

There are less convincing arguments for the existence of a chronic form of cannabis induced psychosis.

Many workers have felt that cannabis induced psychosis is a rare entity (Onyango et al 1986) but Solomons et al (1990) reported that 31 % of their sample of acute admissions presented with a cannabis induced psychosis. Similarly, Rottanburg et al (1982) noted in their sample of 117 acute admissions, 30 % had a diagnosis of cannabis induced psychosis.

THE CONCURRENT USE OF CANNABIS AND ALCOHOL

Introduction

It has been reported in the literature that the concurrent use of cannabis and alcohol is common in Western countries (Manno et al 1970).

Galletly et al (1993) looked at 121 patients admitted to a psychiatric hospital in Adelaide, South Australia. Urine samples were obtained within two hours of admission. In 85 patients (70,2 %) only one drug was detected in the urine. In 31 samples (25,6 %) drugs were present which had not been reported by the patient.

In 12 samples (9,9 %), alcohol and cannabis was present in the urine. The authors concluded that there was, "considerable discrepancy" between the patients self report of recent drug intake and the results of urine drug screens. Many patients would admit to recent alcohol intake but not to cannabis. They reported the drug screen provided clinically useful information that was not obtained at interviews in 25,6 % of the sample.

Mehndiratta et al (1975) mentioned that by comparison in the East, it is uncommon for cannabis to be used concurrently with alcohol or any other drug because the use of cannabis has been ritualized and traditionally accepted but this sanction does not extend to alcohol. In their sample of 50 cannabis users, no subject used alcohol on a "regular basis".

Concurrent use of cannabis and alcohol in South Africa

Bourhill (1913) conducted the first full length study of cannabis use in South Africa. His sample size was 627 male patients. He noted, "many dagga smokers are also heavy drinkers and it is almost impossible to differentiate how much of the insanity in a given case is due to alcohol anD how much to dagga" (page 2 & 3 Bourhill, 1913).

Du Toit (1980) did not support that there was widespread concurrent use of alcohol and cannabis. He concluded, "urban blacks are not party to the polydrug phenomenon which is emerging world wide" (Du Toit 1980, p. 195).

The black male subjects in his survey who smoked cannabis gave the following reasons for not using alcohol simultaneously :

" alcohol has a bad taste"

" alcohol numbs the senses"

" alcohol produces a head-ache and hang-over"

" alcohol slows a person down"

Of the sample who did use alcohol concurrently with cannabis, most alcohol was of the traditionally brewed type and its consumption was based on cultural grounds. The use of alcoholic spirits was uncommon but was positively linked to the educational level of the individual.

Concurrent use of cannabis and alcohol in Scandanavia

In contrast to the South African experience, Hammer et al (1985) have reported that, "cannabis use is clearly associated with high alcohol consumption".

THE EFFECT OF CANNABIS ON COGNITION

Introduction

Controversy exists as to whether cannabis use results in a cognitive deficit in the user (Satz et al 1976, National institute on drug abuse, Marijuana and health 1980, Varma 1988).

The possible connection between cannabis use and cognitive deficit remains a complex interaction because of the multiplicity of variables which will be examined in this Section.

It is also important to establish whether there was any evidence of cannabis intoxication, delirium, psychotic disorder or anxiety disorder at the time of testing. All these states could influence the results of any attempt to measure cognition (Wert et al 1986).

Early research work on the effects of cannabis on cognition

Over 80 % of the published research on chronic cerebral effects of cannabis has been conducted since 1970 (Wert et al 1986).

In 1892, the Indian Hemp Drugs Commission examined the, "physical, mental and moral effects of cannabis use" (Wert et al 1986). The Commission interviewed 1193 individuals and reviewed the records of all the judicial proceedings for the previous 20 years in which cannabis was thought to have been used by the alleged offenders. The Commission also looked at 222 individuals whose admission to a mental institution in 1892 was though to have been linked to the recent use of cannabis.

The Commission concluded that the "moderate" use of cannabis produced no cognitive deficit, whilst "excessive" use may have caused a cognitive deficit. However, the Commission failed to define what was meant by "moderate" and "excessive" use of cannabis and also failed to define how cognitive deficit was measured and whether any cognitive deficit was of a temporary or permanent nature.

The next major report was also completed in India by Chopra et al (1939). A total of 1238 cannabis smokers were examined. They concluded that "moderate" use of cannabis caused no cognitive deficit, but "excessive" use lead to impairment. The problems associated with this survey was that the effects of poor nutrition on cognitive performance was not considered. Also 2,5 % of the sample had syphilis and the population examined were of low socio-economic status such that cognitive deficits would be hard to detect.

Varma et al (1988) made a detailed study of cognitive function in 26 long term heavy Indian cannabis users following 12 weeks of abstinence. The battery used contained 10 different domains and the conclusion was that cannabis did cause a selective and significant impairment in STM in addition to poor performance in perceptuo motor function.

The first USA report on the effect of cannabis on cognitive functioning was done by the Mayor's committee in 1943 (Wert et al 1986). They looked at 72 prison inmates, 48 of whom were cannabis users. Their conclusion was that cannabis did not appear to cause any cognitive deficit. The La Guardia report (1944) and Williams et al (1946) did not support the conclusion of the Mayor's committee. These two research teams reported that there was impaired intellectual functioning in cannabis smokers.

One problem with many early North American studies which failed to detect any cognitive deficits in cannabis smokers was that the experimental groups were college students who were occasional light users and therefore did not represent cannabis users overall (Deahl 1991).

In conclusion, studies conducted between 1960 and the 1980's on cognitive impairment in long term cannabis users showed inconsistencies (Soueif 1967, Soueif 1971, Soueif 1975, Agarwal et al 1975, Satz et al 1976, Soueif 1976, Wig et al 1977, Fletcher et al 1977, Ray et al 1978, Mendhratta et al 1978, Fletcher et al 1978, Schaefer et al 1981).

Table 17 summarises the different population groups which have been surveyed for possible cognitive impairment following the use of cannabis.

COUNTRY	AUTHOR(S)
Jamaica	NIMH 1972, Bowman 1973, Rubin 1975
INDIA	Agarwal et al 1975, Wig et al 1977,
	Ray et al 1978, Mendhratta et al 1978,
	Varma et al 1988,
GREECE	Stefanis et al 1977
EGYPT	Soueif 1967, Soueif 1971, Soueif 1975,
	Soueif 1976, Fletcher et al 1977
USA	Wig et al 1977, Wert et al 1986,
	Schwartz et al 1989
COSTA RICA	Satz et al 1976, Page et al 1988
NORTH AFRICA	Christov 1965, Negrete 1973

Table . 17 : The different population groups which have been surveyed for possible cognitive impairment following the use of cannabis.

West et al (1986) have pointed out that often people in countries outside the USA consume cannabis with a higher content of THC. Also other factors such as poor nutrition, low socio-economic status and the concurrent use of other substances to enhance the effects of cannabis all result in a bias of finding neurological deficits in the samples surveyed. West et al have also pointed out that cross culture studies often use tests developed in the USA which have not been standardized for other culture groups.

The Jamaican Studies

The Jamaican project (Rubin et al 1975) looked at chronic long term use of cannabis. In all, 19 different neuropsychological tests were used. The study used 30 subjects and 30 controls. Subjects had a history of regular cannabis smoking of 8 cannabis cigarettes\ day for 7 - 37 years. However the amount of THC consumed was not stated.

The results of the survey failed to demonstrate any major differences in neuropsychological functioning between the controls and the subjects.

A serious flaw of the study was that no attempt had been made to standardize the neuropsychological test battery on a group of Jamiacan residents prior to the study. Also of note is that the study had virtually no measure of STM deficit.

Furthermore, the study was flawed in that a multivariate analysis of the results was not used.

Bowman (1973) similarly looked at the effect of chronic, heavy, daily use of cannabis in Jamaican men who came from the lower social classes. Heavy use of cannabis was a term not defined but the experimental groups had all used cannabis for more than 10 years. The battery of tests used by Bowman have been used to demonstrate impairment in individuals who abuse alcohol or other substances known to cause organic damage to the brain.

His work likewise failed to show any differences in memory function between the subject and control group. However, as in the case of the Jamaican project (Rubin et al 1975), Bowman's neuropsychological battery was not standardized for the Jamaican population and also by using subjects from the lower socio-economic classes, it would be difficult to detect any cognitive dysfunction in the experimental group.

The Costa Rican studies.

Satz et al (1976) standardized their neuropsychological tests on their test subjects in Costa Rica. They used the Williams Memory Scale (1968) and the Benton visual retention test (Benton 1963). They used 41 chronic cannabis users and 41 controls. Their definition of chronic cannabis user was up to and in excess of 8 cannabis cigarettes a day for 10 years. THC content was not measured.

Satz et al (1976) concluded that, "chronic marijuana use is not associated with permanant or irreversible impairment in higher functioning". This conclusion was supported by (Mendelson et al 1972, Grant et al 1973 and Knights 1975).

Page et al (1988) conducted a follow up study of the work of Satz et al (1976) and re-tested 27 of the original 41 experimental group and 30 of the original controls. They found that the experimental group had a decreased capacity for sustained attention and significant impairment of STM in 3 of the 7 neuropsychological tests that had been standardized for the population.

The Indian Studies.

Several investigators (Agarwal et al 1975, Wig et al 1977, Mendhratta et al 1978, Ray et al 1978) have found that cannabis is associated with abnormal Bender-Gestalt and Weschler memory scale scores in Indian subjects. The problem with these studies is that they had absent or poorly matched controls, inadequate consideration of the pre-morbid variables, unreliable ascertainment of the duration and severity of cannabis or other drug use and the use of culturally inappropriate psychometric tests that had not been adequately validated on the sample population.

The study of Varma et al (1988) consisted of an experimental group of 26 heavy users of cannabis with daily intake of 150 mg of THC at least twenty times each month for 5 years, and a control group of 26 individuals.

They noted that the large majority of cannabis users in India came from the main stream of society because social sanctions against cannabis smoking were not as pronounced as in the West.

Varma et al (1988) used a battery of 13 tests. 3 tests specifically looked at a measure of intelligence, all of which had been standardized on the Indian population, namely the WAIS-R, Bhatia short scale and Raven's standard progressive matrices. Users were hospitalized for 12 hours prior to testing to minimize the risk of acute effects of cannabis compounding the results.

Varma et al (1988) found that the experimental and control group did not differ significantly on any of the various sub-tests of memory.

The authors then developed their own tool to measure memory function in 10 different areas and found no significant differences between the experimental and control group. The only differences noted pertained to perceptuo-motor tasks.

This work therefore failed to support the earlier work of Agarwal et al (1975) who used the Weschler memory scale, the Benton visual memory test and the Bhatia battery of intelligence in 40 cannabis users. Agarwal et al (1975) felt that there was cognitive impairment in cannabis users but their work had no control group.

Negrete (1973) made mention of Indian Studies of individuals who had a "heavy, chronic consumption" of cannabis and "have as a common denominator a severe deterioration of higher cognitive functioning". Negrete did not elaborate on the above conclusion.

The Egyptian Studies.

Several investigators (Soueif 1967, 1971, 1975, 1976, Fletcher 1977) found that cannabis use in Egypt was associated with abnormal Bender-Gestalt tests and Weschler memory scale scores.

Soueif (1976) studies 1700 Egyptian cannabis users and controls using a wide range of psychological tests. He found that cannabis users performed significantly more poorly on 10 of the 16 measures used but the differences noted were small.

Wert et al (1986) found that place of residence (urban vs rural) and degree of literacy affected the test scores at least as much as cannabis use.

The USA Studies.

Schwartz et al (1989) looked at a group of white middle class adolescents with a medium age of 16 years, all of whom had an I.Q. between 90 and 125 and had no history of chronic alcohol intoxication and all of whom had at least 8 years of formal education. There were 10 experimental subjects and 17 controls.

A total of 7 neuropsychological tests were used, which included tests of STM. Testing was done between day 2 and 5 following hospital admission to dissipate any obvious short term effect of cannabis intoxication on cognition.

The group was then tested 6 weeks later after cannabis abstinance was checked by bi-weekly urine testing.

They found the experimental group committed more errors on the Benton visual retention test (BVRT) and also the experimental group did not improve statistically across time on any of the memory tests which raised the possibility of long lasting cognitive deficits in cannabis users.

This work supported the earlier findings of Wig and Varma (1977).

Wert et al (1986) have pointed out that, "the majority of studies have found no clinically significant differences between groups of cannabis users and controls on commonly accepted neurological and psychological measures of cerebral function". They pointed out that this finding was all the more surprizing given the number of variables such as, "polydrug abuse, low motivation and acute effects which bias the results towards finding impairment in cannabis using subjects".

The North Africa Studies.

Christov (1965) examined 140 cases that had been admitted to a Morocan mental hospital following the use of cannabis. The symptoms on admission included behavioral disturbances, impaired sensorium, disturbed thought process, and impaired intellectual function comprising of poor concentration, memory and comprehension. However Christov concluded that he was uncertain whether the observed cognitive deficits were the result of cannabis use per sec or, "merely a reflection of the attitudes consciously adopted within a frame of reference of a new philosophy of life".

Negrete (1973) mentioned that publications from North Africa which dealt with, "heavy, chronic consumption" of cannabis and "have as a common denominator a severe deterioration in higher cognitive functioning".

The Greek Studies.

Stefanis et al (1977) looked at 47 Greek cannabis users and 41 controls. They found 4 significant differences on the WAIS subtests and concluded that cannabis was responsible for the cognitive deficits in the experimental group.

Complications in measuring the effect of cannabis on cognition.

Many variables must be considered when an attempt is made to measure the effect of cannabis on cognition. Variables reported in the literature are summarized in Table 18 and are discussed in detail below.

(a) THC dose.

The potency of cannabis can vary by a factor of 2000 (Weil et al 1968, Paton 1975). Mason et al (1985) have noted that above a certain threshold dose, increasing doses of THC produced a linear dose - dependent decrease in mental and physical performance. This is supported by an article in the Lancet (1989), Levin (1974), Dornbush (1973), Ray et al (1978), Wert et al (1986).

Wert et al (1986) noted that there is no standardized amounts of THC in street samples. Self report of frequency of drug use is often suspect and therefore light to moderate users, especially if use has been short term, would be unlikely to demonstrate impairment and so their presence in a sample could serve to statistically mask impairment in heavier users.

Satz et al (1976) noted that many of the early studies on the effect of cannabis on cognition failed to control the dosage level of THC.

VARIABLE	AUTHOR(S)
THC Dosage	Dornbush 1973, Levin 1974, Satz et al 1976, Ray et al 1978, ARF/ WHO report 1981, Mason 1985, Weil et al 1986, Wert et al 1986, Lancet 1989.
Time lapse between smoking cannabis and test for cognitive deficit	Weil et al 1968, Hollister 1971, ARF/ WHO report 1981.
Experienced\ naive users of cannabis	Caldwell et al 1969, Weir et al 1968, Marks et al 1989, Abood et al 1992.
Concurrent use of alcohol	Stone 1970, Manno et al 1971, Wert et al 1986, Marks et al 1989, Deahl 1991, Abood et al 1992.
Concurrent use of other drugs (excluding alcohol)	Campbell et al 1971, Kolansky et al 1971, Kolansky et al 1975, Heath 1973, Wert et al 1986, Deahl 1991.
Motivation of the subjects.	ARF/ WHO report 1981, Wert et al 1986.
Variables with the individual subject	Deahl 1991, Soueif 1976, Ray et al 1978, ARF/ WHO report 1981, Wert et al 1986, Lancet 1989, Johnson et al 1990.
Nutritional factors	Wert et al 1986, Deahl 1991.
The use of psychiatric patients in cognitive studies	Satz et al 1976, Deahl 1991.
Setting in which cannabis is smoked	Weil et al 1968, Abood et al 1992.

Table 18 : Identified variables which need to be considered when investigating the effect of cannabis on cognition.

The ARF\ WHO report (1981) noted that animal studies with rodents, dogs and monkeys had revealed a biphasic dose effect of cannabis. This biphasic pattern has been described in humans. Higher doses of cannabis may cause greater cognitive deficits but this observation is influenced by the subject's degree of prior exposure to cannabis.

(b) The time lapse between smoking cannabis and testing for cognitive deficit.
This needs to be considered such that there is no cannabis intoxication, delirium or withdrawal delirium or a cannabis induced psychotic disorder at the time of testing for a cognitive deficit.

The ARF\ WHO report (1981) noted that in most studies, the cognitive deficits noted occur only within a few hours of smoking cannabis but also suggest that there may be a more lasting effect of cannabis on the transfer of information from STM to LTM.

Reviews of Weil et al (1968) and Hollister (1971) suggest that cannabis may have an immediate depressing effect on some cognitive or attentional tasks but such defects are of a temporary nature.

(c) Experienced vs naive users of cannabis.
Weil et al (1968), Caldwell et al (1969), Dornbusch (1973) and Marks et al (1989) noted that naive users of cannabis performed worse on cognitive tests compared to experienced users.

Abood et al (1992) felt that experienced users had developed some kind of compensation which enabled them to perform better on cognitive tests.

(d) The concurrent use of alcohol.

Abood et al (1992) noted that cognitive impairment noted in cannabis users was more marked if there was concurrent use of alcohol. This is supported by the work of (Manno et al (1971), Wert et al (1986), Deahl (1991).

Marks et al (1989) looked at the effect of 3 levels of cannabis use combined with 3 levels of alcohol consumed. They found evidence of marked cognitive deterioration when cannabis was combined with alcohol use. The authors also found cross tolerance between cannabis and alcohol use in that there is a resistance in heavy cannabis users to consume concurrent large doses of alcohol. A similar conclusion was reached by Stone (1970).

(e) The concurrent use of other drugs (excluding alcohol)

Many previous studies have reported on the role of cannabis in producing irreversible cognitive damage but these studies were flawed both in terms of design and methodology. One factor which was not controlled was the concurrent use of other drugs.

In the Campbell et al (1971) study all 10 reported cases had used LSD in addition to cannabis and 9 cases had also used amphetamines, barbiturates, heroin or morphine.

Wert et al (1986) pointed out that in many cases opium and datura had been used concurrently with cannabis and this made interpretation of results difficult.

A similar conclusion was reached by Deahl (1991).

(f) Motivation of the subjects.

Motivation of the test subject is thought to influence the test results (ARF\ WHO report 1981). Wert et al (1986) noted that many drug users may be poorly motivated and so exhibit minimal co-operation during testing and so produce spuriously low test results.

(g) Variables within the individual subjects.

Little is known about individual vulnerability to cannabis (Deahl 1991). Some factors which have been identified and are thought to be important are:

(i) Intelligence of the subject.

The Lancet (1989) noted that individuals with learning disabilities and those with borderline or low IQ may be more susceptible to cannabis induced STM deficits. The ARF\ WHO report (1981) is not in agreement with this and felt that impaired cognitive deficit was more likely to be recognized in University students than in agricultural labourers or in other groups for whom intellectual tasks were not important.

(ii) Access to formalized education.

Ray et al (1978) and Wert et al (1986) noted that the degree of literacy in subjects was found to effect the test scores at least as much as cannabis use.

(iii) Socio-economic status and cultural background of the subjects.

The ARF\ WHO report (1981) felt that socio-economic factors as well as cultural factors influence the identification of adverse effects of cannabis, especially those related to emotional and cognitive function.

(iv) Ethnic variation.

The ARF\ WHO report (1981) noted that, "another item that requires exploration is the possibility of ethnic variation in drug response which has not yet been studied systematically with respect to cannabis".

(v) Urban vs rural populations.

Wert et al (1986) commented on the Egyptian study of Soueif (1976) and felt that factors such as place of residence affected the test scores at least as much as cannabis use.

Ray et al (1978) came to the same conclusion.

(vi) Individual psychic vulnerabilities.

The ARF\ WHO report (1981) felt that the adverse effects experienced in users of cannabis, including cognitive deficits were a factor of :

(a) Cannabis dose.

(b) Individual psychic vulnerability

(c) Individual physical vulnerability

(d) The Social\ cultural matrix in which cannabis is consumed.

Their conclusion was that any cognitive deficit that was observed in cannabis users was "more likely to be determined by factors other than the pharmacological action of the drug".

The same conclusion was reached by Johnson et al (1990).

(h) Nutritional factors

Deahl (1991) noted that a variety of pre-morbid factors may be over-represented in drug users and as such may influence the results of cognitive testing. Such factors include the nutritional status of the subject.

Wert et al (1986) came to the same conclusion.

(i) The use of psychiatric patients in cognitive studies:

Deahl (1991) noted that the effects of cannabis on healthy subjects may differ from those in individuals with a co-existing mental illness or brain damage.

Satz et al (1976) noted that many of the early studies which claimed that cannabis caused severe and irreversible brain damage were, "grossly marred" in terms of design and methodology and one bias was the use of psychiatric patients in the early studies who would not be representative of the general population of chronic cannabis users.

(j) Setting in which cannabis is smoked.

Wert et al (1986) have recorded that the setting is an important variable in influencing the response to cannabis. Abood et al (1992) came to the same conclusion.

Evidence for cognitive deficits in users of cannabis.

(1) Temporary cognitive deficits

Table 19 lists the reviews that have suggested cannabis may have an immediate depressing effect on some cognitive or attentional tasks but these effects are not severe and persist from 3 weeks after the last use of cannabis up to 6 weeks (Swartz et al 1989, Lancet 1987).

Table 20 summarizes the various tests used in the detection of cognitive deficits.

(2) Permanent cognitive deficits

In general, it is thought that permanent cognitive deficits may arise from cannabis use after exposure to high doses over a prolonged period.

Many of the early studies (Campbell et al 1971, Kolansky et al 1971, Heath 1973, Kolansky et al 1975) were flawed in tems of design and methodology. It has proven difficult to control all the variables listed earlier and as such it is difficult to attribute any observed cognitive deficit to be due solely to the use of cannabis.

AUTHOR(S)	DATE
Williams et al	1946
Weil et al	1968
Talbot et al	1969
Weil et Zinberg	1969
Abel	1971
Rhea et al	1971
Kolansky et al	1972
Tennant et al	1972
Dittrich et al	1973
Dornbusch	1973
Negrete	1973
Dornbusch	1974
Levin	1974
Aggarwal et al	1975
Venkoba et al	1975
Soueif	1976
Tinklenberg et al	1976
Kvalseth	1977
Mendhiratta et al	1979
Sethi et al	1981
Knudsen et al	1984
Page et al	1988
Varma et al	1988
Swartz et al	1989
Marks et al	1989
Rashid et al	1991

Table 19: **The reviews that have suggested cannabis causes an immediate depressing effect on some cognitive or attentional task.**

Author	Date	Psychological test
Swartz et al	1989	BVRT
Agarwal et al Stefanis et al Wig et al Swartz et al	1975 1977 1977 1989	Weschler memory scale
Agarwal et al Wig et al Soueif	1975 1977 1976	Bender gestalt test
Page et al	1988	Selective reminding test of Bushka
Page et al	1988	Continuous performance test of Buchsbaum and Sostek
Dornbush Safer et al Soueif	1971 1971 1976	Digit memory scan
Agarwal et al	1975	Bhatia battery of intelligence
Rhea et al	1971	Consonant Trigram test

Table 20: Reported temporary cognitive deficits and the psychological tests used.

Evidence for no cognitive damage in users of cannabis

(1) Temporary cognitive deficits:

Many researchers have stated that even when variables are controlled as far as is possible, there is insufficient evidence to suggest any temporary cognitive deficit. (Darley et al 1977, Varma et al 1988).

Tests used to demonstrate no temporary cognitive deficits in cannabis users are summarized in Table 21.

Varma et al (1988) looked at memory function in 10 different areas and they concluded, "it appears that the differences, if any, between users and non-users in terms of cognitive function pertain to perceptuo-motor tasks".

(2) Permanent cognitive deficits:

Many researchers have failed to find any evidence of permanent cognitive deficits in chronic long term cannabis smokers (NIMH Jamaican study 1972, Bowman 1973, Ray et al 1978, Schaeffer et al 1981, Varma et al 1988, Abood et al 1992).

Satz et al (1976) recorded that their sample group who smoked in excess of 8 cannabis cigarettes a day for over 10 years, there was no cognitive deficits and they concluded, "thus on the basis of these studies, one might conclude, with caution, that chronic marijuana use is not associated with permanent or irreversible impairment in higher brain functions or intelligence".

The ARF/ WHO report (1981) noted that, "most studies which have compared performance of chronic users with controls in neuropsychological tests have failed to elicit significant differences in cognitive functioning".

TEST	AUTHORS
Wais (R)	Varma et al 1988
Bhatia's short scale if memory	Varma et al 1988
Ravens progressive matrices	Varma et al 1988
Attention and concentration:	
(i) Digits backwards	Ray et al 1978
(ii) Serial addition of 3's	
(iii) Serial subtraction of 3's	
(iv) Colour cancellation test	
Visuo- motor co-ordination	

Table 21: Tests used to demonstrate no temporary cognitive defects in cannabis users.

Bowman's (1973) Jamaican study used subjects who had been "heavy daily consumers" for over 10 years. He could find no evidence of permanent cognitive deficit in the experimental group.

Varma et al (1968) looked at the use of long term heavy cannabis use in Indian subjects who used a daily intake of 150 mg, THC at least 20 times a month for 5 years. They found no significant difference between the experimental and control group on the WAIS-R. Bhatia short scale and Raven's standard progressive matrices. The deficits which were recognized by Varma et al (1988) related to the individual's personal, social and vocational functioning.

Ray et al (1978) examined the effects of cannabis on cognitive functioning. They used a series of tests (Table 21) and concluded there was no difference between the experimental and control group on attention, concentration, visuo-motor co-ordination and memory function (except in one sub-test). Their conclusion was that there was no significant association between long term heavy cannabis use and cognitive dysfunction.

Abood et al (1992) concluded that even though there is no conclusive evidence for chronic psycho-pathology, it is premature to conclude there is none.

General conclusion regarding the effect of cannabis on cognitive function

Fig 16: Summarizes the variables examined when considering the effect of cannabis on cognition.

Little evidence has been advanced which demonstrated that there is long term cognitive damage following the exclusive use of cannabis in healthy individuals.

The study of Schwartz et al (1989) was the first adequately controlled work on the effects of cannabis on memory function. They attempted to control the listed variables as far as was possible and they believed there were cognitive deficits in the. experimental group which remained for up to 6 weeks after the last use of cannabis.

Experimental design

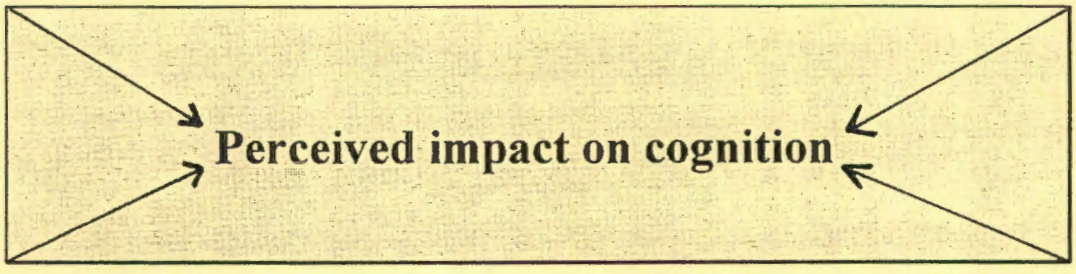
1/ Method was to measure cognition.

2/ Standardization of test used.

3/ Time lapse between last cannabis use and time of testing.

4/ Degree of individual motivation to participate in the tests.

Setting in which drug (s) taken



Drugs

1/ Cannabis dose.

2/ Period for which cannabis is used.

3/ Concurrent use of other drugs

Individual characteristics

1/ Experimental vs. naive smokers.

2/ I.Q.

3/ Educational level.

4/ Socio - economic status.

5/ Ethnicity.

6/ State of physical health.

7/ Past psychiatric history.

Fig 16: Variables examined in considering the effect of cannabis on cognition.

Wert et al (1986) felt that there may be some cognitive deficits following the long term use of cannabis but that the individual adapted and overcame the deficit through a process of relearning. They also noted, "whilst the vast majority of cannabis using subjects are not impaired, there may be a very small number of users who are vulnerable to cannabis producing impairment". Wert et al (1986) also raised the possibility of the currently used tests being too insensitive to detect cognitive damage. They suggested that prospective studies would test the hypothesis of differential vulnerability in cannabis users.

The ARF/ WHO report (1981) stated that, "the overall conclusion from a review of the literature is hampered by a general inadequacy of reported data, especially in the clinical studies which have often been characterized by poor sample size and selection, poor or no differentiation between intoxication, withdrawal and residual change and an absence of before and after longitudinal studies of regular users"

In conclusion, the possibility remains that cannabis may cause cognitive deficits in the short term at least but there is inadequate evidence at presence to suggest that the deficits observed are long lasting.

RESEARCH INTO THE POSSIBLE RELATIONSHIP BETWEEN CANNABIS USE AND RESULTANT AGGRESSIVENESS

(1) Introduction

The possible relationship between cannabis use and resultant cognitive deficit has been explored. It was pointed out that many variables need to be considered and the same applies when the inter-relationship between cannabis use and resultant aggressiveness is examined.

Abel et al (1977) noted that, "one of the most controversial issues in all of psychopharmacology is the nature of the relationship between cannabis and violence". He proposed 4 possible kinds of relationship:

(1) Cannabis is a major cause of aggression.

(2) An underlying predisposition towards violence may be precipitated by cannabis.

(3) There is no connection between cannabis and resultant violence.

(4) Cannabis reduces the likelihood of violence occurring in pre-disposed individuals.

It also needs to be established whether any observed increase in aggressiveness is a specific effect related to THC or a nonspecific result of repeated exposure to a noxious stimuli.

Abel et al (1977) noted that specific neural mechanisms lying within the limbic system are involved in aggressive behaviour. Campbell et al (1971) reported on the marked abnormality in the EEG recorded from the temporal lobe region of a group of patients suffering from a cannabis induced psychosis and suggested that increased activity in the temporal lobe may set off neural impulses in those areas of the brain that underlie feelings and behavior involved in aggression.

2. The variables that need to be considered when examining the connection between cannabis use and resultant aggression.

Table 22 summarizes the variables which have been considered in the literature.

(a) The dose

Nahas (1973), Salzman et al (1976) and Abel (1977) have all referred to the THC dose as a factor in causing aggression.

Salzman et al (176) noted that at low THC doses, the effect induced in subjects may be mild disinhibition whereas higher doses result in the potential for aggressiveness in certain settings.

A similar finding was reported by Abel (1977) who also felt that at lower doses of THC, environmental variables are important in determining the degree of aggressiveness displayed whereas at higher doses, such environmental cues are of less importance.

Nahas (1973) added that at very high doses of cannabis, the over all effect would be sedation regardless of all the other variables operating.

(b) Biphasic response to THC

The biphasic response to THC refers to the ability of THC to cause stimulation and\ or depression in a subject. This response was reported by Garriott et al (1968).

Salzman et al (1976) have similarly noted that in animal studies, the biphasic response to a singe dose of THC has been noted. Initially there is a phase of excitement followed by a period of depression.

(c) Development of tolerance to the effects of Cannabis

Harris (1971) noted that naive cannabis smokers may exhibit aggressive behaviour following the use of cannabis but in experienced smokers, aggressiveness is less common.

VARIABLE	AUTHOR
Dose response	Nahas 1973, Salzman et al 1976, Abel 1977, Abood et al 1992
Biphasic response to THC	Garriott et al 1968, Salzman et al 1976, Abel 1977
Development of tolerance to the effects of THC	Harris 1971, Abood et al 1992
The setting	Jones 1971, Nahas 1973, Salzman et al 1976, Abel 1977, Abood et al 1992
Species specific response	Bose et al 1964, Carlini et al 1966, Santos et al 1966, Grunfeld 1969, Sheckel et al 1969, Gershon 1970, Grinspoon 1971, Alves et al 1973
Underlying psychiatric illness	Alterman et al 1982, Yesavage et al 1983, Knudsen et al 1984, Regier et al 1984, Convit et al 1988, Gallander et al 1988, Ananth et al 1989, Regier et al 1990, Bartels et al 1991, Minkoff et al 1991, Lehman 1992, Sanguineti 1993
Concurrent use of cannabis and alcohol	Johnson et al 1990
Individual vulnerability to psychotoxic effects of cannabis	Abood et al 1992

Table 22: Variables that need to be considered when examining the relationship between cannabis use and resultant aggression.

(d) The setting in which cannabis is consumed

The setting in which cannabis is consumed is generally considered to affect how the subject behaves. Abel (1977) and Salzman (1976) noted that if cannabis is smoked in a situation not considered to be threatening, then the subject would be unlikely to react in an aggressive manner. Salzman (1976) noted that cannabis may produce different effects when taken in a social group or when taken in isolation. Jones (1971) commented that cannabis, when smoked by the subject on his own, resulted in a state of slight drowsiness with relaxation. However, in a group setting, no sedation was seen, rather an euphoric mood was evident.

Nahas (1973) noted that, "overt aggressive behaviour requires the absorption of enough active material and also an unfavourable setting".

(e) The species specific response

Animal studies have noted a variable response to cannabis in producing an aggressive response (Scheckel et al 1969, Gershon 1970, Grinspoon 1971).

Bose et al (1964), Carlini et al (1966) and Alves et al (1973) noted an increase in aggressive behaviour in dogs and rats exposed to cannabis whereas Santos et al (1966) and Grunfeld et al (1969) noted a decrease in aggression when mice and the Rhesus monkey were exposed to cannabis.

Luthra et al (1976) worked with rats and questioned whether aggressiveness is a specific effect of cannabis inhalation or a non specific result of repeated exposure to a noxious stimuli. They exposed rats to smoke from cannabinoid free cannabis and noted no development of aggressiveness which tends to support that view that there is a specific drug effect.

(f) Underlying psychiatric illness in the subject

Minkoff et al (1991) noted that substance abuse is the most common co-morbid complication among severely mentally ill persons.

Regier et al (1984, 1990) research indicated that people with schizophrenia have a 10,1 times greater rate of concurrent alcohol use disorder and a 7,6 times greater rate of other drug use disorder compared to those who do not have schizophrenia.

Galander et al (1988), Ananth et al (1989) and Lehman (1992) found that over one third of patients in an outpatient setting and over one half of those in an inpatient facility have a concurrent substance abuse problem. Alcohol, cannabis and cocaine were the drugs most commonly used.

An increase in hostility and assaultativeness in psychiatric patients who abused toxins was noted by Alterman et al (1982), Bartels et al (1991), Convit et al (1988), Yesavage et al (1983), Knudsen et al (1984).

Knudsen et al (1984) examined schizophrenic patients who abused cannabis. They found the cannabis aggravated the patients functional illness and resulted in confusion, impaired memory, and impulsive behaviour. In one case, the patient became violently aggressive after using cannabis and presented with persecutory delusions.

Sanguineti (1993) noted that in those patients with an affective disorder and cannabis use, higher scores were obtained on hostility and depression sub scales compared to a control group of patients.

It appears therefore that in those individuals with an underlying psychiatric illness and cannabis use, there is a greater possibility of aggressive behaviour being exhibited after cannabis use compared to a control group when there is no such underlying psychiatric illness.

(g) Concurrent use of alcohol and cannabis

Johnsson et al (1990) noted that when alcohol is consumed with cannabis, the two drugs act together in increasing the chance of possible aggression.

3. Demographic and personal characteristics which have been considered in the actiology of aggressive behaviour.

The following were considered:

(a) Age, race, sex and socio-economic status of the cannabis user.

On the whole, there were no connections between these variables and the emergence of aggression, except Davis (1991) felt that assaultative patients were more likely to come from a low socio-economic status.

(b) Adaptive ego defenses.

Saltzman et al (1976) felt that in those individuals who were experienced users of cannabis and had a well developed healthy obsessional character style, then the development of aggression following the use of cannabis is unlikely since adaptive ego defenses are mobilized in the face of some aggression inducing threat.

Naditch (1974) felt that in vulnerable individuals, the use of cannabis could overwhelm the ego defenses leading to a variety of emotional responses which included aggression.

(c) Personality type and the development of aggression following the use of cannabis.

It is generally accepted that those individuals who have a pre-morbid anti-social personality structure will have a greater probability of expressing aggression following the use of cannabis (Oshaughnessy 1838, Marcovitz et al 1944, Salzman et al 1976, Abel 1977, Carrey et al 1984).

Mehndiratta et al (1975) whilst accepting the above, did add a note of caution that in the absence of well controlled prospective studies, it is very difficult to be sure whether cannabis per sec produces social disturbances or previously disturbed personalities opt more often for cannabis.

Saltzman et al (1976) noted that in those individuals with an anti-social personality structure and in the presence of a strong stumulus in a non supportive environment, then there may well be aggressive behaviour following the use of cannabis.

4. Anecdotal evidence linking cannabis use with aggression.

Kaplan (1969), Goode (1970) and Grinspoon (1971) reported on anecdotal evidence which linked cannabis with aggression.

Stringaris (1972) collected anecdotal material from the near East and noted that cannabis use is "often accompanied by restlessness and vagabondage".
Similar reports are available from North Afica (Bouquet 1951) and West Africa (Lambo 1965). These reports suggest that chronic users of cannabis tend to be more hostile in their attitudes compared to light users of cannabis.

Such reports are of limited value as there has been no standardization in method and no attempt to control the multiple variables.

5. Animal studies showing the variable effects of cannabis on aggression levels.

Table 23 summarizes some research into the effect of cannabis on aggression in a variety of animals.

Salzman et al (1976) and Abel (1977) felt that the variable response was due to the biphasic activity of THC, a dose response , the development of tolerance with repeated dosing and a species specific response.

The ARF\ WHO report (1981) noted that observed behavioural changes only emerged months after continual cannabis administration.

Luthra et al (1976) noted that rats exhibited an increase in aggressive behaviour when exposed to cannabis, but when exposed to smoke from cannabinoid free cannabis, there was no development of aggressiveness which tends to support the view that there is a specific drug effect.

Studies which demonstrate:	Author(s)
Decreased aggression when exposed to cannabis	
(a) Mice	Santos et al 1966, Grunfeld et al 1969
(b) Rhesus monkey	Grunfeld et al 1969
Increased aggression when exposed to cannabis	
(a) Dogs	Bose et al 1964, ARF/ WHO report 1981,
(b) Rats	Carlini et al 1966, Alves et al 1973, Luthra et al 1976, ARF/ WHO report 1981,
(c) Monkey	ARF/ WHO report 1981

Table 23: Animal studies which demonstrate the variable effect of cannabis on aggression levels.

Abel (1977) commented on the additive effect a stress (eg food deprivation, cold, pain, sleep deprivation) had when combined with exposure to cannabis. This resulted in an increase in aggression in animals compared to animals that were not stressed in a similar manner.

In summary, it appears that certain experimental animals do exhibit an increase in aggression when exposed to cannabis.

This effect is due to cannabinoid content of the cannabis. The observed increase in aggression is exaggerated if the cannabis is combined with some stressor.

6. Research which supports a connection between cannabis use and aggression.

Tunving (1985) quoted the 1893 report from British Guyana where a doctor described the state of cannabis intoxication, "he moves incessantly, waving his arms, throwing himself from one side to the other, running up and down, crying and singing. It may be associated with violent behaviour. Sometimes he refuses to eat, sometimes he gets an intense hunger. The states may change rapidly and very soon he will recover and seem quite normal again".

Salzman et al (1976) in reviewing many of the early reports have disputed the correlation between cannabis use and subsequent aggressive behaviour because the reports were anecdotal in nature. The same criticism applies to the work of Palsson et al (1982). They looked at 11 subjects who abused cannabis and reported that 7 of the 11 presented with aggressive behaviour.

Tart (1970) attempted to quantify his work by administering a lengthy questionnaire to experienced cannabis users. He asked them to rate how they felt and behaved when intoxicated. 77% said they had never displayed aggressive behaviour, 22 % said they had on rare occasions and 1 % admitted to aggressive behaviour whilst intoxicated.

Table 24 summarizes the many papers which support the hypothesis that cannabis use results in subsequent aggression.

AUTHOR (S)	DATE
Marcovitz et al	1944
Cristov	1965
Spencer	1970
Tart	1970
Halikas et al	1971
Kolansky et al	1972
Nahas	1973
Thacore et al	1973
Fisher et al	1974
Mehndiratta et al	1975
Jones et al	1976
Salmon et al	1976
Salzman et al	1976
Thacore et al	1976
Abel	1977
Valzelli	1978
Pallson et al	1982
Knudsen et al	1984
Onyango et al	1986
Ghodsa	1986
Solomons et al	1990
Rashid et al	1991
Rolfe et al	1993

Table 24: **Examination of the relationship between cannabis use and resultant aggression : research which supports that such a relationship exists.**

Some researchers have drawn the distinction between aggressive feelings which may be of an intermittent or continuous nature following cannabis use and overt aggression behaviour. Halikas et al (1971) reported that 43% of their sample of cannabis users admitted to "occasional aggressive feelings", but did not exhibit overt aggressive behaviour.

53% of the sample reported that only once or alternatively they had never experienced aggressive feelings following the use of cannabis. Fisher and Stecker (1974) looked at 530 cannabis users. Only 22 reported feeling more anger whilst under the influence of cannabis.

Ghodse (1986) found that up to 10% of cannabis users may be at risk of developing an acute cannabis psychosis which results in aggressive outbursts and the need for enforced admission to hospital.

Rashid et al (1991) looked at 15 subjects and 10 controls. The subjects used only cannabis. A brief psychiatric rating scale was used and they reported that 80% of the sample presented with excitement and hostility. However, the quantity of cannabis consumed was not reported.

Rolfe et al (1993) and Jones et al (1976) reported that, "occasionally, very frequent cannabis users have a sudden onset of irritability, restlessness, and insomnia following the use of cannabis".

In summary, although there have been many reports on the link between cannabis use and subsequent aggression, the work is largely anecdotal or the work consists of poorly controlled trials characterized by loosely defined terms and the lack of a standard measurement of aggression.

Mehndiratta et al (1975) felt that "in the absence of a well controlled prospective study, it is very difficult to be sure whether cannabis per sec produces overt aggression or whether previously disturbed personalities opt more often for this drug".

With reference to those researchers who did find a correlation between cannabis use and resultant aggression, not all individuals presented with aggression following cannabis use.

Ghodse (1986) reported 10% and Rashid et al (1991) reported 80% of their sample presented with post use cannabis aggression. Likewise, Palsson et al (1982) reported that 63% of their sample presented with aggression. The small sample size and the tools used to measure aggression may have exaggerated the findings but it appears that in certain vulnerable individuals, in the presence of certain settings, aggression is a possible outcome to cannabis consumption.

7. Research which does not support a connection between cannabis use and subsequent aggression.

Table 25 summarizes the research work which indicates there is no correlation between cannabis use and subsequent aggression.

There is difficulty in evaluating the literature because of the lack of standardization and the use of different scales to measure aggression.

Little attempt was made to examine compounding variables such as the concurrent use of other drugs, education and socio-economic status. The evidence presented is therefore largely of an anecdotal nature.

Hollister et al (1968) used the Clyde mood scale and found that there was a decrease in aggressiveness following the use of cannabis but the observed result may be a dose related phenomenon.

AUTHORS	DATE
Hollister et al	1968
Bloom	1972
Tennant et al	1972
Tinklenberg	1974
Salzman et al	1976
Johnson et al	1990
Abood et al	1992

Table 25: **Examination of the relationship between cannabis use and resultant aggression : research which does not support such a relationship.**

Tinklenberg (1974) felt, "there is no convincing evidence that the pharmacological properties of cannabis incite or enhance human aggression". He felt that many other variables could explain the observed aggression noted in some individuals who smoked cannabis.

The Salzman et al (1976) study found a decrease in hostile feelings in a group of 60 male volunteers is invalidated since 30 out of the 60 volunteers only smoked cannabis once a week and the research was done in a clinical setting.

Conclusion

It appears that there may be a group of vulnerable individuals who, when exposed to a sufficient amount of cannabis in a hostile, threatening environment, can react in an aggressive manner following the use of cannabis. The situation is aggravated by the concurrent use of other drugs such as alcohol and the user's perceived expectation of the effect of cannabis.

The problem is whether cannabis per sec has a specific aggression inducing property or whether it acts as a general disinhibitor of impulse control. The work of Abel (1977) does suggest that cannabis does indeed have a specific aggression inducing effect. This is also supported by the hypothesis that cannabis acts on the limbic system which is involved in the expression of aggression.

THE USE OF CANNABIS IN THE PSYCHIATRIC POPULATION

The importance of identifying substance abuse in the psychiatric setting critically affects the diagnosis (Elangovan et al 1991), treatment (Bowers et al 1990) and planning phases of the mentally ill. Failure to detect substance abuse results in misdiagnosis, over treatment of psychiatric syndromes (Ananth et al 1989) and neglect of appropriated interventions such as detoxification and substance abuse education (Drake et al 1993). Other problems identified in the psychiatric population who abuse drugs are:

(a) Premature discharges against medical advise (Muller et al 1989)

(b) A more severe course of illness (Alterman et al 1982)

(c) Hostility and assaultativeness (Alterman et al 1982, Bartels et al 1991, Convit et al 1988).

Mathers et al (1991) looked at all acute admissions presenting with psychotic symptoms to two hospitals in England for a period of 1 year. Urine was tested for the presence of THC and the research group found 34,5% of patients had urine positive for cannabis. However only 9% admitted to the use of cannabis during the week preceding admission. The researches also pointed out that cannabis users were significantly younger than non users (28,4 years old and 39,7 years old respectively) and that users were predominantly male. A similar finding was reported by Cuffel et al (1993).

Mathers et al (1991) concluded that there was "a highly significant association between urine results positive for cannabis and initial diagnosis of psychosis" and suggested that urine testing for THC is a good practice in young psychiatric patients. Safer (1987) came to the same conclusion.

Zuckerman et al (1989) also reported urine analysis had revealed a higher incidence of cannabis use than is disclosed by self report.

Wilkens et al (1991) examined 56 male psychiatric patients who were admitted to hospital. They were asked about abuse of drugs and signs of intoxication on admission were recorded. No structured interview was used. Table 26 records the results. Fifteen of the patients with a positive THC urine result denied substance abuse in the week prior to admission.

In 23 out of the 35 patients who had urine positive for THC, the doctors did not identify that the patient was using cannabis. It was felt that drug tolerance in the chronic user tends to confound the assessment since tolerance can mask the outward signs of acute intoxication.

Barber et al (1987) pointed out that such factors as depression, IQ, fatigue and the need for approval all influence self report of substance abuse.

Solomons et al (1990) working with 110 black man admitted to a South African psychiatric hospital noted that 31% of the sample had a diagnosis of cannabis induced psychosis but few admitted to using cannabis prior to hospital admission. They concluded that, "urinary THC results were more valuable in diagnosing a cannabis induced psychosis than a history of previous cannabis use"

Similarly, Ben-Arie (1984) found that two-thirds of young psychotic coloured men admitted to hospital had urine positive for THC and in one third of cases, this level was considered high.

Rottanberg et al (1982) found that 59,8% of male black psychotic admissions had urine positive for THC.

In contrast, Martin et al (1998) found that self report is a valid measure of recent use of cannabis. Also, Elangovan et al (1991) looked at a random sample of 200 patients presenting to a psychiatric emergency service in USA.

Diagnosed Illness of the patients	No. of patients	No. of patients who had THC positive urine results	% of sample who had THC positive urine.
Schizophrenia	25	9	36
Affective disorder	10	3	30
Substance abuse	13	4	31
Post traumatic Stress disorder	2	1	50
Personality disorder	2	1	50

Table 26: **The results of Wilkins et al (1991) survey of 56 male psychiatric patients admitted to hospital.**

They used a structured clinical interview and also obtained urine samples from the patients. Of the sample, 24% tested positive for THC. They found the structured clinical interview correctly identified those individuals using cannabis and the toxicology screening, although helpful, did not increase diagnostic sensitivity.

Gersten (1980) and Elangovan et al (1991) have also pointed out that cannabis can pose a risk for individuals who are predisposed to develop a psychiatric illness. Negrete (1986), Andreasson et al (1987) and Mathers et al (1991) have all noted that a cannabis induced psychosis may precede a functional psychosis by years, ie the presentation of a cannabis induced psychosis is a marker for the subsequent development of a functional psychosis.

Rover (1990) found that those individuals who smoke cannabis were 5 times more likely to be schizophrenic, 4 times more likely to have an affective illness and 8 times more likely to have an anti-social personality disorder. Similarly, Mueser et al (1990) found the rate of co-morbid diagnosis of schizophrenia and substance abuse ranged from 15,4 to 64,7%.

Cuffel et al (1993) noted that substance abuse is the most prevalent co-morbid psychiatric condition associated with schizophrenia. Furthermore, those schizophrenics who abused toxins were more likely to present with increased hostility, increased non-compliance with medication and increased management problems in the community.

Breakey et al (1974), Tsuang et al (1982) and Kovasnay et al (1993) noted that in those schizophrenics who abuse toxins, there is an earlier onset of the functional illness.

Andreasson et al (1989) have reported that schizophrenics who abuse cannabis have a more abrupt onset of illness compared to those schizophrenics who do not use cannabis.

Rohr et al (1989) noted that cannabis can exacerbate a pre-existing affective disorder previously controlled on neuroleptic medication.

It is known that cannabis is an anti-parkinsonian agent (Thornicroft 1990) and people on neuroleptic medication may use cannabis in an attempt to diminish the extra pyramidal side effects of neuroleptic medication.

THE SAMPLE GROUP

A total of 27 consecutive acute black male admissions to Fort England mental hospital, Grahamstown, E Cape were used in the present study.

Tables 27, 28, 29, and 30 record personal details of the sample group.

Table 27 records the age distribution of the sample group. There is a bimodel distribution with peaks being at ages 21 - 25 years and 31 -35 years. Only 5 patients in the sample were over the age of 35 years. The distribution of the different age groups is recorded in Table 27. The age group 21 - 25 years is equally distributed between the three groups of those who abuse cannabis or alcohol or neither toxin. The older age group 31 -35 years is not as evenly distributed between the groups and 3 subjects in this age group had neurosyphilis.

Fig. 17 records the age distribution in Du Toit's (1980) sample. Most men in his sample were in the age range 20 - 30 years. Table 7 records the age distribution in previous research projects.

Rottanberg et al (1982) recorded the mean age in their sample group as 23 years with a range of 17 to 52 years.

Solomons et al (1990) looked at 110 consecutive black men admitted to hospital with acute psychotic symptoms and their average age was 28, 2 years with a range of 18 years to 49 years.

Varma et al (1988) recorded the mean age in his sample as 24,5 years with a range of 15 years to 35 years. Similarly Rolfe et al (1993) recorded an average age of 29,5 years in their sample group.

Age Range (in years)	Number	%
21 - 25	9	35,7
26 - 30	3	10,7
31 - 35	9	32,1
36 - 40	5	17,8
41 - 45	-	-
46 - 50	1	3,6
TOTAL	**27**	
GROUP	**AGE GROUP 21-25**	**AGE GROUP 31-35**
THC+\LFT+	-	-
THC+\LFT-	3	3
THC-\LFT+	4	2
THC-\LFT-	3	1
VDRL+	-	3

Table 27: **The age range of black male patients in the Fort England hospital sample.**

Marital Status	Number	%
Single	16	59,2
Married	3	11,1
Unknown	8	29,6
Number of children		
0	4	14,3
1	1	3,6
2	2	7,1
Unknown	20	75
Employment Status		
Employed	1	3,6
Unemployed	23	82.1
Unknown	3	14,3

	MARITAL STATUS		
SUBDIVISION	SINGLE	MARRIED	UNKNOWN
THC+\ LFT -	4	0	1
THC -\ LFT+	7	1	1
THC -\ LFT -	2	0	5
THC+\ LFT+	1	1	0
VDRL+	2	1	1

	% OF KNOWN MEN SINGLE	
Subdivision	Within the Subdivision	Within the total sample
THC+\ LFT -	80	14, 8
THC -\ LFT+	77, 8	25, 9
THC -\ LFT -	28, 6	7, 4
THC+\ LFT+	50	3, 7
VDRL+	50	3, 7

Table 28: The marital status, number of children and employment status of the black male patients in the Fort England hospital sample.

Standard of schooling	Number	%
Unknown	9	32,1
1	2	7,1
2	2	7,1
3	2	7,1
4	4	14,3
5	2	7,1
6	1	3,6
7	1	3,6
8	4	14,3
9	1	3,6
10	-	-

	STANDARD										
GROUP	1	2	3	4	5	6	7	8	9	10	UNKNOWN
THC+\ LFT -	1	-	1		1	-	-	2	-	-	0
THC -\ LFT+	-	1	1	2	-	-	-	2	1	-	2
THC -\ LFT-	-	-	-	1	1	1	1	-	-		3
THC+\ LFT+	-	1	-	1	-	-	-		-	-	0
VDRL+	1	-	-	-	-	-	-	-	-		3

Table 29: Standard of education attained by the sample group at Fort England Hospital.

Number of previous admissions	Number	%
Unknown	18	66,7
1	6	22,2
2	1	3,7
3	-	-
4	-	-
5	1	3,7
> 5	1	3,7
TOTAL	27	

Table 30: **Number of previous admissions to a Mental Hospital in the present Fort England hospital sample.**

Fig. 17

Black males using cannabis (Du Toit study 1980) N= 457 rural blacks

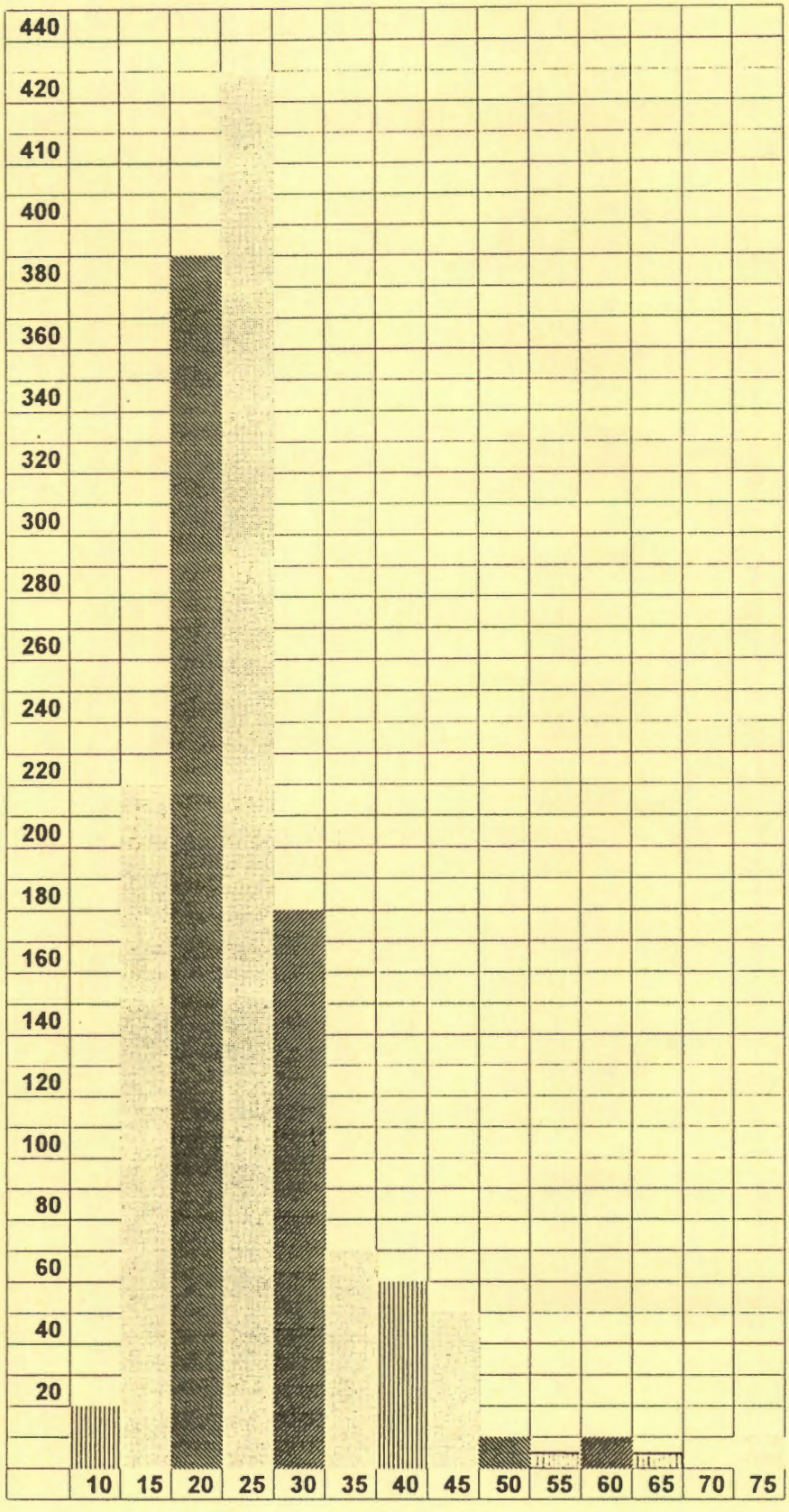


Table 28 records the marital status, number of children and employment status of the Fort England hospital sample.

It is seen that the majority of men (59,2%) were single. Only 11,1% were known to be married whereas the marital status of over one quarter (29,6%) of the sample could not be established.

Within the sub-divisions, 80% of cannabis smokers were single, and an almost equal percentage (77,8%) used alcohol alone. Only 28,6% of the control group were known to be single and 50% of the group who abused both cannabis an alcohol were single.

Soueif (1975), Varma et al (1988), and Solomons et al (1990) similarly found that cannabis users tended to be unmarried men. In Du Toit's study (1980), 61,1% of the cannabis using sample were single.

Three quarters of the men in the sample did not know how many children they had. This was because most men in the sample were single and did not have stable relationships. Only a few men knew the number of children they had fathered. In most cases the men claimed paternity for a single child. In Solomons et al (1990) study, 83% of the men had no children.

The majority (82,1%) of the present sample were unemployed. Only one man was known to be employed and in 3 cases the employment status was not known. In the cannabis smoking sub-group 4 men were unemployed and the status of the fifth man was unknown. Likewise, Solomons et al (1990) recorded that the majority of the men in their sample were unemployed. Rolfe et al (1993) recorded that less than 5% of their cannabis using sample were employed and Hammer et al (1985) refer to "high unemployment" in their cannabis group.

The highest standard of schooling attained is recorded in Table 29. In nearly one third of the cases, the standard of education achieved was not known. Most men in the sample did not reach a secondary school level of education and no-one in the sample had a tertiary education.

Du Toit (1980) recorded that one third of his sample of cannabis users had no formal education and only 25% attained standard 6 and 0,8% reached Standard 10.

Similarly Solomons et al (1991) noted that the men in his sample were "poorly educated" and Louw (1973) reported only 12% of his sample had a secondary level of education.

Rolfe et al (1993), Soueif (1975) and Mehndiratta et al (1975) have all recorded the poor level of education attained by cannabis smokers.

The importance of considering the educational level of the sample groups is because Ray et al (1978) and Wert et al (1986) noted that the degree of literacy effects test scores as much as cannabis use. Therefore any differences in the test scores could be on the basis of degree of formal education rather than cannabis use.

Examination of Table 29 does not reveal any particular educational trend in the different experimental groups.

Tables 30 and 31 record the number of previous admissions to a mental institution. In over two-thirds of cases, it was not known how many previous admissions the subject had had.

Over one-fifth (22,2%) of cases had had one previous admission. Only a small proportion had had more than two previous admissions to a mental hospital.

In those subjects who had had a previous admission, the previous diagnosis was always Schizophrenia except in one case of a patient who had previously undiagnosed neurosyphilis and had a diagnosis of epilepsy. In those cases where it was recorded, the prescribed treatment was Modecate (Table 31). The diagnosis of Schizophrenia could not be confirmed in any of the subjects examined. Sullivan (1993) likewise noted that repeat users of Psychiatric Services were most likely to be young single, black, unemployed men with a diagnosis of Schizophrenia, personality disorder or substance abuse.

Table 32 records the length of stay in Fort England hospital. The average length of stay was two weeks with a rapid resolution of the presenting symptoms.

The ritual of cannabis smoking.

In most cases in the present sample, cannabis was mixed with tobacco and then smoked in the form of a cigarette (= zol). Alternative methods were used (see Fig. 9 and 12). An equal number smoked alone or in a group setting. In contrast, Du Toit (1980) reported the majority of black men in his sample (82,1%) smoked cannabis in a group setting. .

Reasons for smoking cannabis.

Table 33 records the reasons why men in the present sample smoked cannabis. Du Toit (1980, Table 9) likewise recorded that rural black men smoked cannabis to cope with their worries an increase their concentration.

GROUP	DIAGNOSIS	TREATMENT
THC+\ LFT -	Schizophrenia	Modecate 50 mg IMI monthly
	Schizophrenia	Modecate 50 mg IMI monthly
	Schizophrenia	-
THC - \ LFT+	-	Modecate 50 mg IMI monthly
	Schizophrenia	Chlorpromazine 200 mg PO TDS
	Schizophrenia	-
	-	Thioridazine
	Schizophrenia	-
	-	Modecate monthly
	Schizophrenia	-
THC - \ LFT -	Schizophrenia	-
	Schizophrenia	-
	Schizophrenia	Modecate 25 mg IMI monthly
	Schizophrenia	-
THC+\ LFT+	Schizophrenia	-
VDRL+	Epilepsy	Phenytoin 300 day

Table 31: Previous diagnosis an treatment of the Fort England Hospital sample.

GROUP	AVERAGE LENGTH OF STAY IN HOSPITAL (DAYS)	RANGE IN LENGTH OF STAY (IN DAYS)
THC+\ LFT -	13	7 - 23
THC - \ LFT+	13	10 - 16
THC - \ LFT -	17	7 - 32
VDRL+	14	-

Table 32: **Recorded length of stay in hospital for the Fort England Hospital sample.**

GROUP	REASON
THC+\ LFT-	To decrease worries
	To increase intelligence
	Smokes because of unemployment
THC+\ LFT+	To increase intelligence
	To prevent being assaulted

Table 33: Reasons given by the present sample for smoking cannabis.

METHODS USED

1. LIVER FUNCTION TESTS:

AST and ALT are present in high concentrations in the liver. ALT is formed in few organs and is therefore more specific for liver disease. In general, both ALT and AST are elevated with hepatic cirrhosis or metastases, ALT usually being more elevated than AST.

An increase in AST is seen in 40% of those who abuse alcohol and an elevated ALT is seen in 20% of those who abuse alcohol. A ratio AST/ALT of greater than 2 is indicative of alcohol abuse (Mead 1993).

GGT is usually elevated due to hepato-biliary and pancreatic disorders. Elevation of GGT is seen in over 90% of liver disease and therefore an elevated GGT is not specific for alcohol abuse but an elevated GGT is seen in over 80% of individuals who abuse alcohol (Mead 1993). Normal social drinking does not cause an elevation of GGT. However, after several weeks of persistent drinking, there is an increase in GGT levels and in binge drinkers there can be an excessive elevation of GGT within 18 hours of the binge episode (Mead 1993).

ALP is moderately raised in hepato cellular disease. IN the case of jaundice, the higher the ALP, the more likely the jaundice is due to obstructive jaundice rather than hepato cellular jaundice.

In the present sample, every man had blood taken for liver enzymes on the day of admission. The blood was stored in a fridge prior to sending it off to the laboratorium.

2. URINE THC SAMPLES

Urine was collected from the sample group on admission and stored in a refrigerator until it was sent off to the laboratorium.

Testing was done using the EMIT assay and the results interpreted as recorded in Table 4.

3. TEST FOR PERCEPTUO-MOTOR FUNCTIONING - THE PENCIL TAPPING TEST

It has been reported that perceptuo-motor functioning is impaired in those individuals under the influence of cannabis (Soueif 1975, Abood et al 1992).

One commonly used test of perceptuo-motor functioning is the pencil tapping test. The subject is simply required to tap a piece of paper with a pencil as many times as is possible in a 30 second interval. The total number of dots gives an estimation of motor activity and speed.

The 30 second interval was chosen so that performance on the tapping test would not generate reactive inhibition (ie muscle strain, fatigue, boredom). Hull (1952) noted that the more repetitive and homogenous a task is, the more reactive inhibition is bound to generate in a specified time limit.

The pencil tapping test has been used by Soueif 1975, Varma et al 1988, Mendhiratta et al 1988.

Researchers have shown cannabis users react more slowly on the pencil tapping test (Williams et al 1946, Kielholz et al 1973, Soueif 1975, Kvalseth 1977, Mendhiratta et al 1988, Varma et al 1988, Schwartz et al 1989, Deahl 1991).

Kvalseth (1977) has pointed out that perceptuo-motor performance is a function of both the individual's experience with cannabis and the dose of cannabis used.

Varma et al (1988) gave the following values for the pencil tapping test:
Cannabis users: 151,5 ± 25,40 dots in 30 seconds
Controls: 167, 76 5 ± 18,35
t value = 2,59, results significant at 0,05 level.

In contrast, the Canadian Commission of enquiry (1972, quoted in Soueif 1975) reported that cannabis has no effect on the tapping speed. However the time limit used by the Canadian Commission was one minute and this time interval could be expected to generate reactive inhibition.

The results for the pencil tapping test appear in Table 35. The first attempt at the pencil tapping test was done on admission and the second attempt was done a few days later to rule out any cannabis intoxication effects.

4. MEMORY TESTS

a) TEST FOR RETENTION OF NEW INFORMATION : DIGIT SPAN MEMORY

Reference has been made to the hypothesis that cannabis exerts its effect on the hippocampus via the cholinergic pathway and THC, hippocampectomy and anti-cholinergic drugs all impair the retention of new information such as digit span memory (Tinklenberg et al 1970, Dornbush et al 1971, Safer et al 1971). Satz et al 1976, mentioned that digit span is traditionally used to assess immediate recall in clinical practice. Similarly, Soueif (1975) used forwards and backwards in his research work on the effects of cannabis on cognition.

Corsi's block tapping test was described by Milner (1971), Dr Renzi (1977) and Lezak (1981) and Fig. 18 illustrates the Corsi board used in the present study. It is a non verbal spatially cued task.

GROUP	FIRST ATTEMPT	SECOND ATTEMPT	TIME INTERVAL BETWEEN THE TWO ATTEMPTS (IN DAYS)
THC+\ LFT-	128	-	-
	142	-	-
	128	151	4
	160	145	3
	118	150	2
AVERAGE	132,2	148,6	3
RANGE	118 - 150	145 - 151	2 - 4
THC -\ LFT+	144	-	-
	158	-	-
	152	-	-
	142	-	-
	129	136	3
	175	177	4
	166	176	4
	151	171	2
	172	136	3
AVERAGE	154,3	159,2	3,2
RANGE	129 - 175	136 - 176	2 - 4
THC -\ LFT-	126	-	-
	142	175	4
	144	156	4
	105	122	6
	131	144	2
	185	140	2
	129	131	4
AVERAGE	137,4	144,7	3,7
RANGE	105 - 185	122 - 175	2 - 6

Table 35: The Pencil tapping test. The numbers recorded represents the number if dots made by the subject in a 30 second interval.

GROUP	FIRST ATTEMPT	SECOND ATTEMPT	TIME INTERVAL BETWEEN THE TWO ATTEMPTS (IN DAYS)
THC+\ LFT+	175	162	2
	-	170	-
AVERAGE	175	166	2
RANGE	-	162 - 170	-
VDRL	160	144	3
	-	148	-
	-	123	-
AVERAGE	160	138,3	3
RANGE	-	123 - 148	-

Table 35: The pencil tapping test. The numbers recorded represent the number of dots made by the subject in a 30 second interval.

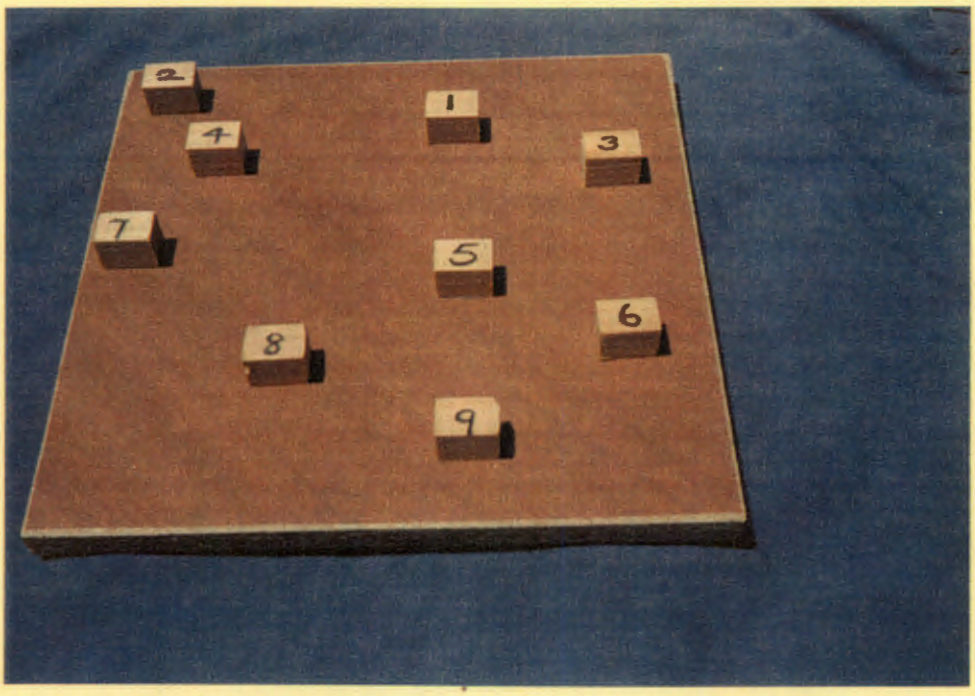


Fig18: The Corsi black as described by Milner (1971) and De Renzi (1977)

This is of importance in the present study because in 32,1% of the sample, the level of formal education was unknown, 42,7% of the sample only achieved a junior school education (up to Standard 5) and 25% achieved up to a Standard 9 education. (Table 29).

The digit sequence used was from the WAIS test and appears in Table 34. Soueif (1975) used the WAIS and found that when the digits forwards sequence was used, there was no statistical difference between users and controls but the digits backwards sequence differentiated at a high level of significance between cannabis users and the control group. Soueif also reported that cannabis users were inferior to the controls on the digits backwards sequence irrespective of literacy.

Mendhiratta et al (1988) also used the WAIS sequence of digits and reported that in their sample of cannabis users, there was impairment in recall of both digits forwards and backwards compared to the control group.

De Renzi (1977) described how the Corsi block tapping test was performed. The cubes were numbered so that the patient could not see the digits and strings of digits in length 2 to 9 cubes were tapped out by the examiner at 1 digit\ sec and the subject was then asked to tap out the same sequence immediately afterwards. Two series of digit sequences were always given at each length and the test discontinued when the subject failed on both trials of a given length.

The results on the Corsi board appear in Table 36 and 37.

b) IMMEDIATE AND DELAYED RECALL OF A GROUP OF COMMON, FAMILIAR OBJECTS.

In this test, a tray containing 8 familiar objects was displayed to the subjects on admission (Figs 19, 20). After it was established that each subject could correctly identify all 8 objects, the tray was removed and the subject asked to recall all 8 objects.

DIGITS FORWARDS	DIGITS BACKWARDS
6 - 8 - 2	2 - 4
6 - 9 - 4	6 - 8
6 - 4 - 3 - 9	6 - 2 - 9
7 - 2 - 8 - 6	4 - 1 - 5
4 - 2 - 7 - 3 - 1	3 - 2 - 7 - 9
7 - 5 - 8 - 3 - 6	4 - 9 - 6 - 8
6 - 1 - 9 - 4 - 7 - 3	1 - 5 - 2 - 8 - 6
3 - 9 - 2 - 4 - 8 - 7	6 - 1 - 8 - 4 - 3
5 - 9 - 1 - 7 - 4 - 2 - 8	6 - 3 - 9 - 4 - 1 - 8
4 - 1 - 7 - 9 - 3 - 8 - 6	7 - 2 - 4 - 8 - 5 - 6
5 - 8 - 1 - 9 - 2 - 6 - 4 - 7	8 - 1 - 2 - 9 - 3 - 6 - 5
3 - 8 - 2 - 9 - 5 - 1 - 7 - 4	4 - 7 - 3 - 9 - 1 - 2 - 8
2 - 7 - 5 - 8 - 6 - 2 - 5 - 8 - 4	9 - 4 - 3 - 7 - 6 - 2 - 5 - 8
7 - 1 - 3 - 9 - 4 - 2 - 5 - 6 - 8	7 - 2 - 8 - 1 - 9 - 6 - 5 - 3

Table 34: **The digit span forward and backwards used with the Corsi board (from the WAIS test).**

GROUP	FIRST ATTEMPT	SECOND ATTEMPT	TIME INTERVAL BETWEEN THE TWO ATTEMPTS (IN DAYS)
THC+\ LFT-	9	9	5
	4	4	4
	8	7	4
	5	7	3
	4	7	2
AVERAGE	6	6,8	3,6
RANGE	4 - 9	4 - 9	2 - 5
THC -\ LFT+	7	5	5
	2	6	4
	3	4	5
	7	7	6
	5	3	3
	7	5	4
	4	6	4
	6	6	2
	3	5	3
AVERAGE	4,9	5,2	3,9
RANGE	3 - 7	3 - 7	2 - 5
THC-\ LFT-	7	7	4
	3	5	4
	6	5	4
	4	8	6
	6	4	2
	6	6	2
	8	6	2
AVERAGE	5,7	5,8	3,4
RANGE	3 - 8	4 - 8	2 - 6

Table 36: **The Corsi block tapping test using the WAIS sequence of numbers. Digits forward to 3 consecutive errors. The first attempt was done on admission to hospital.**

GROUP	FIRST ATTEMPT	SECOND ATTEMPT	TIME INTERVAL BETWEEN THE TWO ATTEMPTS (IN DAYS)
THC+\ LFT+	5	5	2
	6	6	5
AVERAGE	5,5	5,5	3,5
RANGE	5 - 6	5 - 6	2 - 5
VDRL+	6	6	3
	2	6	5
	0	0	4
AVERAGE	2,7	4	4
RANGE	0 - 6	0 - 6	3 - 5

Table 36: **The Corsi block tapping trest using the WAIS sequence of numbers. Digits forwards to 3 consecutive errors. The first attempt was done on admission to hospital.**

GROUP	FIRST ATTEMPT	SECOND ATTEMPT	TIME INTERVAL BETWEEN THE TWO ATTEMPTS (IN DAYS)
THC+\ LFT-	7	2	5
	4	6	4
	7	9	4
	5	6	3
	8	7	2
AVERAGE	6,2	6,0	3,6
RANGE	4 - 8	2 - 9	2 - 5
THC -\ LFT+	7	7	5
	0	2	4
	2	2	5
	2	2	5
	2	5	3
	4	5	4
	2	2	4
	6	6	2
	5	5	3
AVERAGE	3,3	4	3,9
RANGE	0 - 7	2 - 7	2 - 5
THC-\ LFT-	2	3	4
	6	6	4
	6	6	4
	5	5	6
	4	5	2
	5	5	2
	2	6	2
AVERAGE	4,3	5,1	3,4
RANGE	2 - 6	3 - 6	2 - 6

Table 37: **The Corsi block tapping test using the WAIS sequence of numbers. Digits backwards to 3 consecutive errors. The first attempt was done on admission to hospital.**

GROUP	FIRST ATTEMPT	SECOND ATTEMPT	TIME INTERVAL BETWEEN THE TWO ATTEMPTS (IN DAYS)
THC+\ LFT+	3	2	2
	6	5	5
AVERAGE	4,5	3,5	3,5
RANGE	3 - 6	2 - 5	2 - 5
VDRL+	2	2	3
	5	2	3
	0	0	4
AVERAGE	2,3	1,3	4
RANGE	0 - 5	0 - 2	3 - 5

Table 37: **The Corsi block tapping test using the WAIS sequence of numbers. Digits backwards to 3 consecutive errors. The first attempt was done on admission to hospital.**

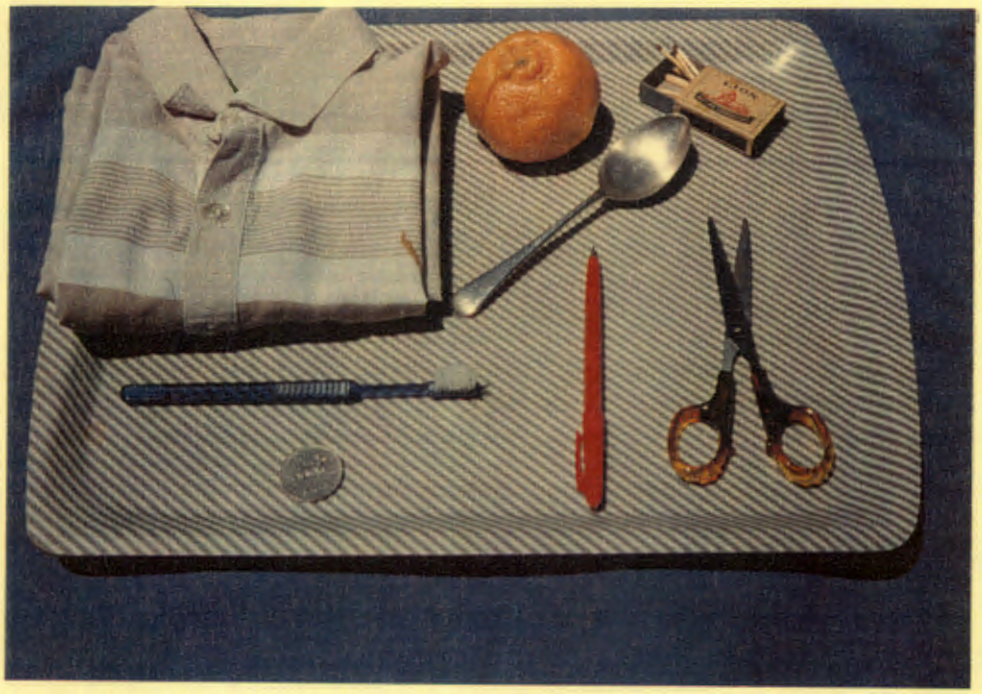


Fig. 19: **The tray of 8 familiar objects shown to the subject on admission. It was first established that the subject could identify all 8 objects and then he was required to immediately recall the objects when the tray was removed from sight. After a 5 minute delay, the subject was again requested to recall the 8 objects for a second time.**

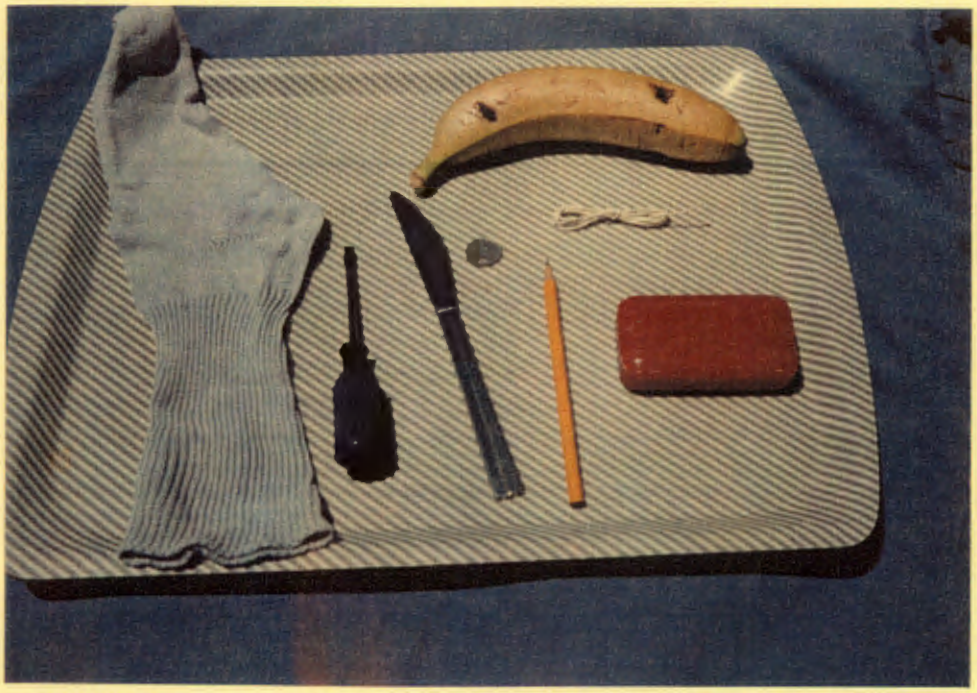


Fig. 20: **The tray of 8 familiar objects shown to the subject after a few days post admission. After it was established the subject could correctly identify each object, the tray was removed from sight and the subject was asked to recall the 8 objects. After a delay of 5 minutes, the subject was again asked to recall the 8 objects.**

If an object was not recalled spontaneously, the subject was given a clue. Failure to recall the object after a clue was given was recorded as an error in storage of information.

This test was then repeated after a 5 minute interval in which the subject was distracted by doing a simple jig-saw.

This test is based on the one used by Satz et al (1976) and Dornbush (1973).

Satz et al (1976) presented line drawings of familiar objects to the subjects, whereas Dornbush (1973) read out a list of familiar objects at the rate of one item\ second.

The results are recorded in Table 38.

c) TESTS OF REPRODUCTIVE MEMORY.

Several tests have been used to measure reproductive memory deficits in cannabis users. A deficit in these tests could be due to:

a) Decreased attention.

b) Decreased filtering of information.

c) Decreased encoding of information.

d) Decreased retrieval of information (Schwartz et al 1989).

Three commonly used tests are:

1) The Benton visual retention test. (BVRT - Benton 1959)

In this test, most cards had 3 geometrical designs of varying complexity which were shown to the subjects for varying periods of time (5 - 10 seconds) and then the subject was required to reproduce the design either immediately or after a delay of 15 seconds.

Schwartz et al (1989) found that cannabis dependent individuals committed more errors on the BVRT and that there was no improvement after a 6 week period which suggests

GROUP	IMMEDIATE RECALL ON ADMISSION	RECALL 5 MINS LATER	RETEST INTERVAL (IN DAYS)	IMMEDIATE RECALL	RECALL 5 MINS LATER
THC+\ LFT-	6	5	5	8	8
	4	1	4	7	6
	8	8	4	8	6
	5	5	3	6	6
	6	3	2	8	6
AVERAGE	5,8	4,4	3,6	7,4	6,4
RANGE	4 - 8	1 - 8	2 - 5	6 - 8	6 - 8
THC-\ LFT+	7	7	5	6	7
	3	0	4	7	5
	5	5	5	6	5
	5	5	5	7	6
	5	2	3	6	4
	3	4	4	7	3
	6	5	4	5	5
	6	3	2	5	4
	7	6	3	6	6
AVERAGE	5,2	4,1	3,9	6,1	5
RANGE	3 - 7	0 - 7	2 - 5	5 - 7	3 - 7
THC-\ LFT-	5	3	4	8	6
	5	5	4	7	6
	7	6	4	5	5
	7	7	6	5	5
	4	2	2	3	4
	4	3	2	5	5
	5	6	2	4	3
AVERAGE	5,3	4,6	3,4	5,3	4,1
RANGE	4 - 7	2 - 7	2 - 6	3 - 8	3 - 6

Table 38: **8 common object recall test. The subject was shown 8 common objects on admission and was then asked to recall the objects immediately and then 5 minutes later after being distracted by a jig-saw puzzle. A few days later the subject was re-tested using 8 different common objects.**

GROUP	IMMEDIATE RECALL ON ADMISSION	RECALL 5 MINS LATER	RETEST INTERVAL (IN DAYS)	IMMEDIATE RECALL	RECALL 5 MINS LATER
THC+\ LFT+	6	6	2	5	3
	6	3	5	6	0
AVERAGE	6	4,5	3,5	5,5	1,5
RANGE	6	3 - 6	2 - 5	5 - 6	0 - 3
VDRL+	6	4	3	7	6
	5	5	5	7	7
	0	0	4	0	0
AVERAGE	3,7	3	4	4,7	4,3
RANGE	0 - 6	0 - 5	3 - 5	0 - 7	0 - 7

Table 38: **The 8 common object recall test.**

a lingering impact on short term auditory and visual memory processes as well as spatial organization problems.

In contrast, Satz et al (1976) found no differences between the cannabis dependent group and a set of controls when each were administered the BVRT.

2. The Benton visual motor gestalt test (BVMG).

In this test, subjects are required to copy 6 designs, one at a time. The BVMG has been more frequently used that the BVRT in the study of STM deficits in cannabis users.

Many researchers have demonstrated an abnormal performance in the BVMG test when cómpleted by cannabis dependent individuals and compared to matched controls (Soueif 1967, Soueif 1971, Agarwal et al 1975, Soueif 1975, Soueif 1976, Fletcher et al 1977, Wig et al 1977, Mendhratta et al 1978, Ray et al 1978). However the work of Varma et al (1988) failed to find a difference in performance on the BVMG when cannabis dependence subjects were compared with controls.

3. The Graham Kendall memory for Designs (MFD).

This test consists of 15 geometrical designs of varying complexity and are shown one at a time to the subject for 5 seconds. Immediately after exposure, the subject is asked to draw what he has seen.

The MFD has been compared to the BVMG test and the two tests have the same sensitivity (Lezak 1981). Lezak has pointed out that impaired immediate memory is a common early symptom in what ultimately results in general intellectual deterioration.

The MFD has the advantage of an easy scoring system.

It was decided to adapt the MFD test in the present study as it had an easy scoring system, was simple to administer and did not require great effort on the part of the subject.

Figs. 21 and 22 illustrate the cards used in the present study. Two sets of cards were used to eliminate any residual memory from the first test.

Each subject was shown the first set of 5 cards on admission (Fig. 21). Each card was shown to the subject for 5 seconds. The subject was instructed to:

a) Remember the design.

b) Remember the colour of the design.

Immediately afterwards the subject was given a blank piece of paper and a box of crayons and asked to reproduce all 5 designs in their correct colours.

The subject was then distracted for 5 minutes by being asked to complete a simple jig-saw puzzle.

The subject was then asked to re-draw the 5 designs using the correct colours.

A different set of 5 cards was used a few days later (Fig. 22), and the test repeated.

One point was awarded for each correct design.
One point was awarded for each correct colour used.
A maximum score of 5 in each category indicated that the subject was able to correctly reproduce the design using the correct colour.

The results are recorded in Table 39.

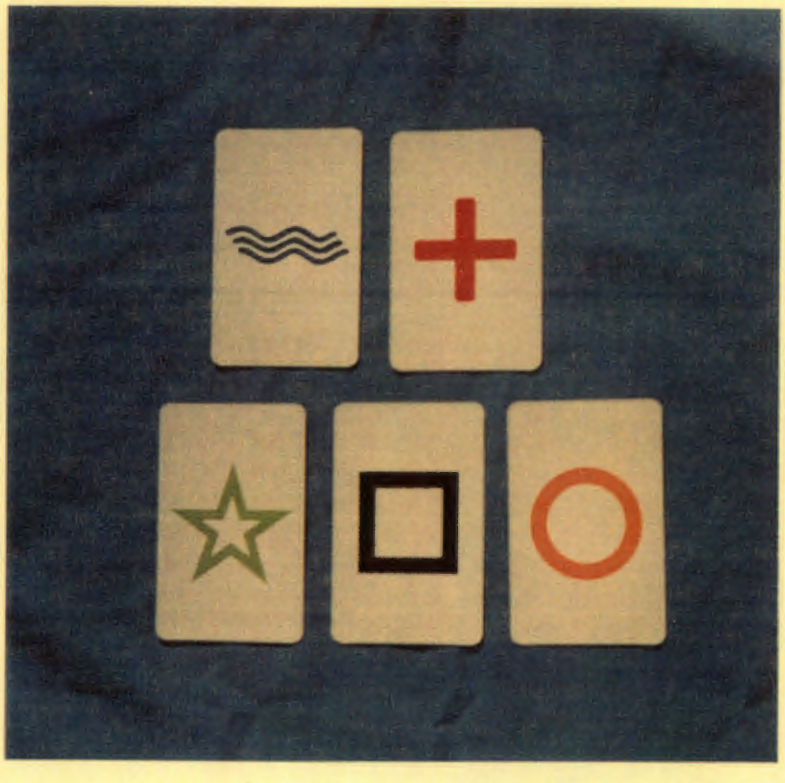


Fig. 21: **The above cards were shown on admission to the subject. Each card was shown for 5 seconds. The subject was instructed to remember both the design on the card and the colour of the design. The subject was asked to reproduce the designs immediately and then 5 minutes later during which time the subject was distracted by being asked to complete a simple jig-saw puzzle.**

Fig 22: **The above cards were shown to the subject a few days after admission. Each card was shown to the subject for 5 seconds. The subject was instructed to remember both the design on the card and the colour of the design. The subject was asked to reproduce the designs immediately and then 5 minutes later during which time the subject was distracted by being asked to complete a simple jig-saw puzzle.**

GROUP	ON ADMISSION				TIME INTERVAL (IN DAYS	REPEAT TEST			
	IMMEDIATE RECALL		5 MINUTES LATER			IMMEDIATE RECALL		5 MINUTES LATER	
	DESIGN	COLOUR	DESIGN	COLOUR		DESIGN	COLOUR	DESIGN	COLOUR
	5	5	5	3	5	3	2	3	2
THC+\LFT-	2	2	0	0	4	5	5	4	4
	3	3	2	2	4	5	5	5	5
	3	1	3	2	3	3	1	3	1
	4	5	4	5	2	4	2	4	2
AVERAGE	3,4	3,2	2,8	2,4	3, 6	4	3	3,8	2,8
RANGE	2-5	1-5	0-5	0-5	2-5	3-5	1-5	3-5	1-5
	5	2	5	2	5	5	5	5	5
THC-\LFT+	0	0	0	0	4	3	2	3	2
	3	1	2	0	5	2	0	2	0
	4	1	3	1	5	5	4	4	4
	3	1	3	1	3	0	0	0	0
	4	4	4	4	4	4	2	4	2
	2	1	2	1	4	2	0	1	0
	5	3	5	2	2	4	0	5	0
	2	1	2	0	3	1	0	0	0
AVERAGE	3,1	1,6	2,9	1,2	3, 9	2,9	1,4	2,7	1,4
RANGE	0-5	0-4	0-5	0-4	2-5	0-5	0-5	0-5	0-5
	1	1	0	0	4	2	2	1	1
	4	4	4	4	4	4	2	4	1
THC-\ LFT-	4	3	4	1	4	5	2	4	0
	3	3	4	3	6	3	0	3	0
	3	2	3	1	2	1	0	1	0
	3	1	3	0	2	5	1	5	0
	3	3	2	0	2	3	1	1	0
AVERAGE	3	2,4	2,6	1,3	3, 4	3,3	1,1	2,7	0,3
RANGE	1-4	1-4	0-4	0-4	2-6	1-5	0-2	1-5	0-1
THC+\LFT+	5	1	4	2	2	1	1	2	0
	1	1	1	1	5	2	0	2	0
AVERAGE	3	1	2,5	1,5	3, 5	1,5	0,5	2	0
RANGE	1-5	1	1-4	1-2	2-5	1-2	0-1	2	0
	4	4	4	4	3	2	2	2	2
VDRL+	4	4	4	2	5	0	0	0	0
	0	0	0	0	4	0	0	0	0

TABLE 39: The adapted MFD test used inthe present sample. One point was awarded for each correct design reproduced and one point awarded if the correct colour was used.

ASSIGNMENT OF THE MEN TO THE VARIOUS GROUPS.

Five groups were considered in this study:

GROUP	NUMBER IN EACH GROUP	
THC+\LFT-	5	
THC-\LFT+	9	
THC-\LFT-	7	
THC+\LFT+	2	
VDRL+	4	
	TOTAL	27

THC+ This indicates that a urine sample taken on admission had a reading greater than 25 ng\ ml using the EMIT system.

THC - This indicates that a urine sample taken on admission had a reading less than 25 ng\ ml using the EMIT system.

LFT+ This indicates that blood was taken on admission and analysis indicated raised liver enzymes. Raised GGT is not specific for recent alcohol consumption but a AST/ ALT ratio of greater than 2 is a good indicator of recent alcohol use.

LFT - This indicates that blood was taken on admission and analysis indicated normal levels of liver enzymes.

VDRL+ This indicates blood taken on admission was positive for RPR. This was automatically followed by a more specific TPHA test. A positive TPHA was in turn followed by a lumbar puncture to obtain cerebro-spinal fluid (C.S.F.) for serology. CSF positive for TPHA indicated neurosyphilis. Such a result was followed by standard treatment with IM penicillin.

The 27 subjects were not assigned to two groups "aggressive" and "non aggressive" because of the heterogeneity implied in this classification.

Muller (1997) noted that the presentation of violence in subjects may well be a reflection of the manner in which they were handled by staff rather than a reflection of any underlying pathology in the subject.

Powel et al (1994) also noted that the restrictive hospital environment may be a precipitator of violence in patients. This situational model to explain violence in psychiatric patients has been emplored by Bowers (1973), Endler et al (1976) and Seridan et al (1990).

All the patients in this study had come from outlying centres so that the situational variable could not be controlled.

Likewise, the other variables involved in the ultimate expression of aggression could not be controlled. It was more practical to consider history examination, blood and urine results in the assignment of a subject to a particular group.

On admission, the following sources of information were available:

1. Admission notes which accompanied the patient. These notes sometimes mentioned the recent use of alcohol or cannabis by the patient.

2. Admission history from the patient. Each patient was asked about his current use of alcohol and cannabis as part of the routine history taking.

3. Physical examination of each subject to note any signs of long term alcohol or cannabis use.

These include:

a) Cannabis use: (i) burn marks on the palms of both hands (see Fig.11) as a result of using a bottle pipe such as illustrated in Fig. 12(c). (ii) an area of depigmentation which is often seen on the lower lip of cannabis abusers. It is thought this is due to the high temperature which results from the ignition of cannabis.

b) Alcohol use: On examination the following were noted:

Palmar erythema

hepatomegaly

Spider naevi

Dupetran's contractures

4. Blood and urine samples from the patient on admission.

Based on the information from 1,2,3 and 4, a patient was assigned to one specific group. One doctor (J.S.) was responsible for 1,2,3 and 4 above whereas another doctor (NF) was responsible for doing the various perceptuo-motor and cognitive tests. This means at the time of testing, it was unknown to which group a patient had been consigned.

RESULTS

1. THC and LFT results

Table 40 records the THC and LFT results of the relevant groups in the present project. The present laboratory recorded normal values as follows:

a) THC less than 25 ng\ ml was recorded as a negative result.

b) AST range 0 - 40.

c) ALT range 0 - 53.

The men in the present study were assigned to one of the 5 subgroups based on:

a) Admission history accompanying patient.

b) History from patient.

c) Physical examination.

d) Blood and urine results.

In the THC+\ LFT - Subgroup, the average THC concentration in the urine on admission was 321,4 ng\ ml with a range of 80 to 664,5 ng\ ml. With reference to Table 4, a range of 20 - 50 ng\ ml suggests the person is using cannabis, 50 - 100 ng\ ml is diagnostic that the person is using cannabis and levels greater than 150 ng\ ml are associated with a Cannabis induced psychosis.

Only two men in the THC+\ LFT - Subgroup had a THC level less than 90 ng\ ml. The other three men presented with a range of 344,9 to 664,5.

In the subgroup THC+\ LFT+, the range in the THC concentrations was 28,1 to 801 ng\ ml.

In the Subgroup THC -\ LFT+, the average AST concentration was 61,4 with a range of 47 - 84 I.U. The average ALT concentration was 44,2 with a range of 27 - 67 I.U.

It was very difficult to establish an accurate alcohol history from the subjects. Also, there was often a few days delay between the acute presentation and admission to Fort England hospital. This was because of the delay in transport of the patients and the distances between the subject's home town and the hospital. Nearly one half of the men in the THC -\ LFT+ Subgroup were admitted on a Friday. This may reflect the delay in admission since most drinking was confined to the weekend with presentation during the weekend or to a local hospital on Monday and referral to Fort England hospital by Friday.

The THC+\ LFT - Subgroup was too small to draw any similar conclusions except to point out that 4 of the 5 subjects presented between a Monday and Wednesday, perhaps after a weekend of smoking cannabis.

In terms of the present random sample of 27 consecutive men who presented with acute symptoms to Fort England Mental Hospital, 7 had urine positive for cannabis (25,9% of sample). In previous research projects in South Africa, Rottanberg et al (1982) reported 59,8% of their sample had urine positive for cannabis, Ben Arie (1984) reported 66% of his sample of male coloured men had positive urine samples and Solomons et al (1970) reported 31% of his sample being positive for cannabis in the urine.

GROUP	THC	LFT	
	ng/ ml	AST	ALT
THC+\ LFT-	428		
	80		
	344, 9		
	89, 5		
	664, 5		
AVERAGE	321, 4		
RANGE	80 - 664,5		
THC-\ LFT+		54	56
		84	52
		72	46
		66	39
		67	28
		49	45
		60	61
		47	27
		54	44
AVERAGE		61,4	44,2
RANGE		47 -	27 -
RANGE		84	61
THC+	801	72	25
LFT+	28, 1	58	48
AVERAGE	-	65	36,5
RANGE	28,1 - 801	58 - 72	25 - 48

TABLE 40: THC and LFT results from the 5 groups in the Fort England hospital sample.

Wilkins et al (1991) reported 35,3% of their sample was THC postive and Mathers et al (1991) reported 34,5% of their sample had urine positive for THC.

2. PRESENTING SYMPTOMS IN THE VARIOUS SUBGROUPS.

a) THC+\ LFT - Subgroup

The results appear in Table 41 as well as in Tables 31 and 32.

In all cases, the only presenting symptom mentioned in the admission papers was aggression. In three cases, the subject had assaulted someone and in one case property had been destroyed.

In two cases, the admission papers mentioned the subjects had smoked cannabis and two other subjects denied the use of cannabis but subsequent urine testing revealed levels of 82 and 428,5 ng/ ml respectively.

The average length of stay in hospital for this sub-group was 12,4 days with a range of 7 to 23 days.

By comparison, Rashid et al (1991) recorded that 80% of their cannabis using sample presented with hostility and Polsson et al (1982) found 63,6% of their sample presented with aggression following cannabis use.

The present subgroup does not fulfill the criteria of a cannabis induced psychosis as described in Table 15 and by Solomons et al (1990).

Table 15 does mention aggression associated with cannabis use and Table 24 lists the research groups who have found a relationship between cannabis use and resultant aggressive behaviour.

SUBJECT	PRESENTING HISTORY (FROM ADMISSION PAPERS)	CANNABIS HISTORY (TAKEN ON ADMISSION)	PERIOD IN HOSPITAL (IN DAYS)	PAST PSYCHIATRIC HISTORY
1	Described by family as dangerous. Threatening to kill everyone. Has assaulted people.	Subject denied cannabis. Urine THC 428,5	23	-
2	Very aggressive	Subject denied cannabis. Urine THC 82.	7	A previous admission to one psychiatric hospital. 2 previous admissions to Fort England hospital. Previously diagnosed as schizophrenic
3	Known to abuse cannabis. Very aggressive, assaulted father.	Smokes cannabis every day. Smokes alone. Smokes a cannabis bottle pipe. Burn marks on both palms. Urine THC 344,9	9	-
4	Known to smoke cannabis becomes violent and aggressive. Has assaulted people and destroyed property.	Smokes cannabis daily. Does not count number of zols he smokes. Prefers not to mix cannabis with tobacco. Smokes with friends. Urine THC 89,5.	-	1 previous admission to a mental hospital. On Modecate. Diagnosed as schizophrenic
6	Speaking nonsense, wandering, aggressive.	Smokes cannabis daily. Does not mix cannabis with tobacco. Smokes alone. Smokes to take away his worries. Urine THC 664,6.	23	One previous admission to a mental hospital. Diagnosed as schizophrenic

Table 41: Presenting symptoms, cannabis history, length of stay in hospital and previous hospitalisations in the THC+\ LFT- sub-group.

Abel (1977) has suggested that cannabis has a specific aggression inducing effect by acting on the limbic system. Both McIssac et al (1971) and Drew et al (1974) have demonstrated the preferential concentration of THC in the hippocampal region and Maykut (1985) noted THC causes damage to the septum.

Abood et al (1992) erected a 3 phase model of cannabis intoxication and the last phase was characterized by overt aggression. The implication of this model is that aggression will only be observed as a presenting symptom if the cannabis using subject has passed through the two preceding phases of:

a) initial euphoria

b) drowsiness with sedation, distortions in time, hearing and vision

Abood et al (1992) also proposed an alternative way of examining the link between cannabis use and aggression. They proposed that the individual's culture shapes the observed response to cannabis.

David (1991) felt it was rather the subject's socio-economic status rather that his culture which determined the observed response to cannabis. He observed that those individuals who came from a low socio-economic status presented with aggression following cannabis use.

Abel (1977) proposed that it was neither the culture or the socio-economic status of the subject but rather environmental cues which determined the observed response to cannabis. If the environmental setting was non-threatening, then the subject was unlikely to react in a threatening manner.

Harris (1971) observed that the most important determinant in deciding the response to cannabis use was the past experience with the drug, experienced users did not present with aggression.

Abel (1977) did not support this proposal. He found that chronic users of cannabis were more hostile and rebellious compared to naive users.

The dose of cannabis used has also to be considered when examining the observed response. Field (1980) has noted the South African cannabis ranks among the more potent variants of the plant in terms of THC content and he further mentioned the Transkei cannabis had the highest THC content in the whole of South Africa.

Fig. 13 summarizes the diverse variables which are thought to shape the observed response to cannabis use.

There is little information available to comment on the socio-economic status of the THC+\ LFT - Subgroup except to observe that 80% of the sample were single, all were unemployed and only two had achieved a Secondary level of education. Three of the sample had a known past psychiatric history.

No information was available on the setting in which cannabis was smoked.

In conclusion, all of the men in the THC+\ LFT - Subgroup presented with aggression and settled rapidly in hospital.

b) <u>THC -\ LFT+ Subgroup</u>.

The results appear in Table 42 as well as in Tables 31 and 32. In contrast to the THC+\ LFT - Subgroup, there were psychotic features mentioned in the THC -\ LFT+ Subgroup which included:

visual, tactile, auditory hallucinations, Delusions.

There was also evidence of restlessness, aggressiveness and excessive talking. Insomnia and poor personal hygiene was also mentioned.

SUBJECT	PRESENTING HISTORY (FROM ADMISSION PAPERS)	PERIOD IN HOSPITAL (DAYS)	PAST PSYCHIATRIC HISTORY
1	Known to abuse alcohol. Restless wandering, talkative, auditory, tactile and visual hallucinations.	15	2 previous admissions to Fort England hospital. Diagnosed as schizophrenic, on Modecate.
2	Known to abuse alcohol. Restless, wandering, talkative.	-	-
3	Known to abuse alcohol. Deluded and suicidal.	10	2 previous admissions to Fort England hospital.
4	Known to abuse alcohol. Aggressive, not sleeping. Auditory hallucinations.	13	One previous admission to Fort England hospital.
5	Known to abuse alcohol. Undressing in public, not sleeping, talkative, destroying property. Believes he is bewitched.	-	One previous admission, diagnosed as a schizophrenic.
6	Aggressive. Known to abuse alcohol.	16	One previous admission.
7	Known to abuse alcohol. Aggressive, talkative, violent,not sleeping, not eating, wandering. Poor personal hygiene.	-	One previous admission.
8	Known to abuse alcohol. Aggressive, restless, talking nonsense, wandering. Believes he is bewitched.	11	One previous admission, diagnosed as schizophrenic, on Modecate IM.
9	Known to abuse alcohol. Violent, assaultative, talkative, restless, deluded.	-	One previous admission. Diagnosed as schizophrenic.

Table 42: **Presenting symptoms, past psychiatric history and length of stay in hospital for the THC-\ LFT+ sub-group.**

In eight cases it was known that there had been at least one previous admission to a mental hospital and the diagnosis was invariably Schizophrenia. It is interesting to note that in all previous admissions, the use of alcohol was not inquired into and blood had never been taken for liver enzyme evaluation.

In the present study, the previous diagnosis of Schizophrenia could not be confirmed in any of the cases. Also, the rapid recovery period (range 10 to 16 days) argues against a Schizophrenic illness.

c) THC -\ LFT - Subgroup:

The results appear in Table 43 as well as in Tables 31 and 32.

The present Subgroup, similar to the THC-\ LFT+ Subgroup, presented with many psychotic features.

These included:

Withdrawn, isolated behaviour, speaking to self.

Mannerisms.

Wandering aimlessly around, sometimes naked.

Self neglect.

Persecutory delusions.

No hallucinations were mentioned.

Four of the seven subjects had previously been diagnosed as Schizophrenic and one subject was known to be on IM Modecate.

This Subgroup took the longest to settle, with a range of 7 to 32 days in hospital.

In three subjects, a presenting complaint was violent, aggressive behaviour. Mention has been made of a concurrent diagnosis of substance abuse and a functional illness and

Subject	Presenting history from (admission papers).	Period in hospital (in days).	Past psychiatric history.
1	Talking nonsense, aggressive roaming the streets, restless.	7	Known schizophrenic. 11 previous admissions to a hospital.
2	Aggressive, assaulting children, roaming.	12	One previous admission.
3	Undergoing treatment with a traditional healer. Traditional healer identified Subject needed to be seen by Western doctors. Thin, neglected, confused, suspicious. Believes that there is a problem with his heart, keeps on stopping because someone has poisoned him.	-	-
4	Violent, assaultive, withdrawn, ? Mental retardation.	-	Previous admission to a mental hospital. Diagnosed as schizophrenia.
5	Wandering around naked in public.	-	Previous admissions to a mental hospital. Diagnosed as schizophrenic.
6	Wandering around, speaking to self, withdrawn, unable to answer questions, self neglect.	32	-
7	Hitting cars, excitable, flight of ideas, mannerisms, gesticulating.	-	Previous admission to a mental hospital. Diagnosed as schizophrenic.

Table 43: Presenting symptoms, past psychiatric history and length of stay in hospital for the THC-\ LFT- sub-group.

in such people with a co-morbid diagnosis, there is increased hostility and assaultativeness (Alterman et al 1982, Bartels et al 1991, Convit et al 1988). Mathers et al (1991) reported that 34,5% of their sample had a co-morbid diagnosis of functional illness with substance abuse.

Similarly Wilkins et al (1991) demonstrated that 36% of their sample of Schizophrenic patients had concurrent substance abuse problems.

A substance abuse history was taken but all the subjects in this Subgroup denied recent use of alcohol and cannabis. Mathers et al (1991) pointed out that only 9% of their group of subjects admitted to substance abuse prior to admission and Zuckerman et al (1989) reported urine analysis had revealed a higher incidence of cannabis use than was disclosed by self report.

In the present Subgroup urine and blood analysis was negative for THC and alcohol.

It could be argued that the resultant negative findings were due to the delay between last drug abuse and obtaining a urine an blood sample. However physical examination of the subjects failed to reveal any signs associated with cannabis or alcohol abuse. Also this Subgroup presented with the longest time in hospital, 7 to 32 days.

The accuracy of the diagnosis of Schizophrenia was not explored. A brief reactive psychosis or a major depressive illness with psychotic features are two commonly missed diagnoses.

d) <u>THC+\ LFT+ Subgroup</u>.

The results for this Subgroup appear in Tables 44, 31, and 33.

Subject	Presenting history (from admission papers).	Period in hospital (in days).	Past psychiatric history.
1	Violent in the community. Admits to cannabis use on a daily basis. Restless, shouting, smelt of alcohol on admission. THC 801,8 AST 72 ALT 25	14	Considered to be epileptic.
2	Wandering, assaulting people. Admits to cannabis Had cannabis in his possession. Admits to alcohol three days prior to admission, often drunk. THC 28,1 AST 58 ALT 48	-	Known to mental hospital since 1984. Previous admissions. Diagnosed as schizophrenic.

Table 44: **Presenting symptoms, past psychiatric history and length of stay in hospital for he THC+\ LFT+ sub-group.**

Only 2 subjects in the sample qualified for this Subgroup. Both admitted to extensive alcohol and cannabis use prior to admission and one subject smelt of alcohol when he was admitted to hospital.
One subject had a long past psychiatric history and had previously been diagnosed as being Schizophrenic.

Both subjects had been violent prior to admission. Johnsson et al (1990) noted that when subjects use both alcohol and cannabis concurrently, there is an increased chance of aggressive behaviour. The present sample is too small to confirm this or to draw comparisons with the THC+\ LFT - Subgroup.

Du Toit (1980) reported that concurrent use of cannabis and alcohol was not common in South African black males. He also pointed out that most alcohol consumed was of the traditional home-brew variety. The current work suggests that there is a changing social pattern in South Africa in that the phenomenon of concurrent use of cannabis and alcohol is becoming more prevalent in black South African males and also the use of traditional home-brew beers is being replaced by the consumption of commercial alcoholic spirits (commonly brandy).

VDRL+ Subgroup.

The results for this Subgroup appears in Tables 45, 31 and 32.

All 4 men in this Subgroup presented with violent, aggressive behaviour, both assaulting people and destroying property. All men gave a vague history of alcohol or cannabis use but physical examination and lab results did not support current use of toxins.

All 4 men had a lumbar puncture following the positive blood TPHA result. In all 4 cases, the CSF was reactive ie: the men had a diagnosis of neurosyphilis. In one case, the subject was presenting with seizures.

Subject	Presenting history (from admission papers).	Lab results.	Past psychiatric history.	Length of stay in hospital (in days).
1	Violent, assaulting people, destroying property. Not able to give a history on admission.	RPR 1: 64 CSF reactive AST 51 ALT 16 THC negative	Diagnosed as having epilepsy and was on anticonvulsants.	-
2	Wandering,arguementative, aggressive, destroying property, isolating self, neglect of self, neglecting his children. Initially denied any use of cannabis and then admitted to cannabis over one month prior to admission.	RPR 1:8 TPHA positive CSF reactive AST 22 ALT 10 THC 20,6	Nil	-
3	Aggressive, admits to alcohol in the past, no cannabis.	RPR 1:2 TPHA positive CSF reactive THC 19,2 AST 29 ALT 9	Previous admision to a mental hospital. Previously in jail as a member of "Bender 28".	16
4	Aggressive,destroying property, undressing in public. Vague past alcohol history. Denies cannabis.	RPR 1:64 TPHA positive CSF reactive THC negative AST 22 ALT 19	Nil	-

Table 45: Presenting symptoms, past psychotic history, lab results and length of stay in hospital for the VDRL+ sub-group.

One subject (number 3) was a member of a prison gang (bender) known as the "28" gang. Such gang members participate in sexual activity with other prisoners and take the penetrative role in anal intercourse. The recipients are known as the "26" gang.

All 4 subjects were treated with IM Penicillin whilst in hospital.

RESULTS

The results were first analysed using the statistical package SPLUS which generated a graphical box plot.

Following this, two further statistical tests were used. Both tests were non-parametrical because of the small sample size and the non normality of the data.

The tests analysed the differences between categories and also the differences between the initial and repeat test scores. The 2 tests used were:

1. Kruskal-Wallis test

   This test is used to test the equality of means,

   i.e. $H_0 : E(X) = E(Y)$

   $H_1 : E(X) \neq E(Y)$

   This test was used to test whether the mean of the control group (THC-\LFT- and referred to as group 3) is equal to the mean of the toxin abusing groups (a combination of THC+\LFT-, THC-\LFT+ and THC+\LFT+ and referred to as group 7).

2. Wilcoxon Test

The Wilcoxon test is used to test the equality of means,

i.e. $H_0 : E(X) = E(Y)$

$H_1 : E(X) \neq E(Y)$

This test will be used to test whether the mean of the initial scores is equal to the mean of the repeat test scores. Thus, the set of initial scores is paired with the set of repeat scores. This test is therefore used for related samples.

Both tests return a p value. A p value between 0 and 0,05 is considered significant. Values of less than 0,02 suggest significance but do not provide strong evidence to reject the null hypothesis.

The Pencil Tapping Test

The results as recorded in table 35 were analyzed using the statistical package SPLUS and the generated graphical analysis appears in fig. 34.

No clear trend emerges. The control group (3,1 and 3,2) showed no superiority over the other groups.

The group of individuals who had neurosyphilis was next excluded and the toxin using group (group 7) was compared to the control group (group 3). Fig. 35 displays the resultant box plot.

The results were next analyzed using the Kruskal-Wallis rank sum test:

X^2 = 1,5286 (df = 1)

p value = 0,2163

This result suggests that the toxin abusing group performs the pencil tapping test as well as the control group.

Further analysis demonstrated no change in score between the first and second attempt at the pencil tapping test. The differences obtained in the initial and repeat test scores were analyzed using the Wilcoxon signed rank sum test.

Z value = - 0,8793

p value = 0,3792

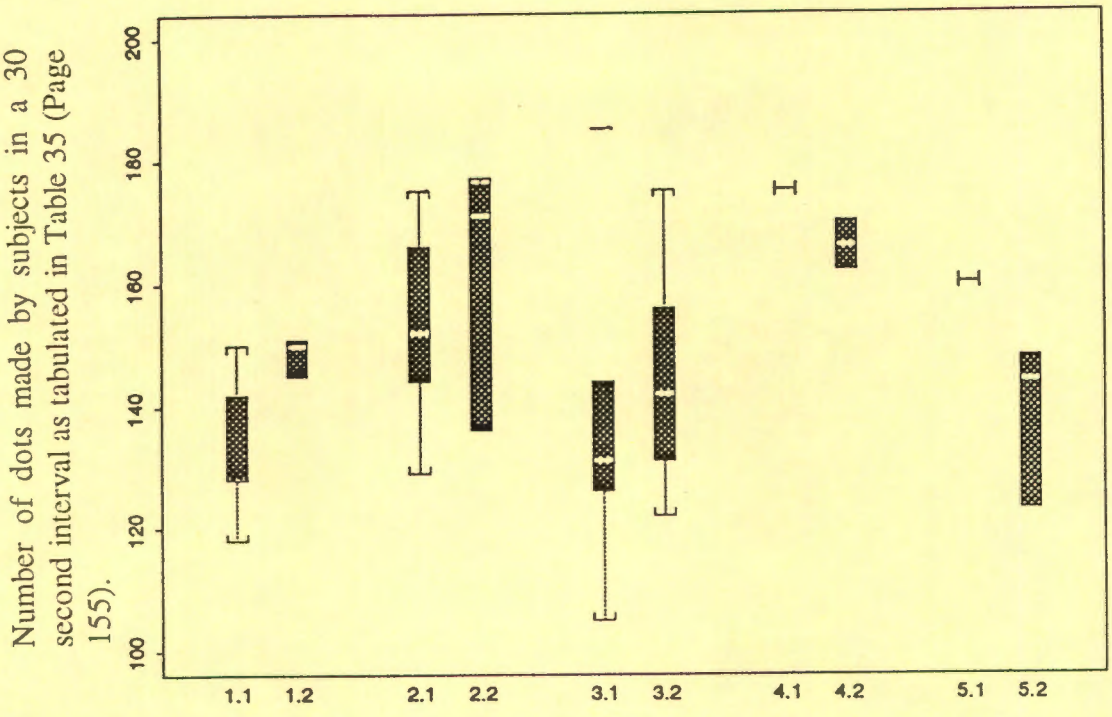


Fig. 34: The results from the pencil tapping test. The data from table 35 was analysed using the statistical package SPLUS which generated the above box graph.

KEY: Groups	First attempt	Second attempt
THC+\LFT-	1,1	1,2
THC-\LFT+	2,1	2,2
THC-\LFT-	3,1	3,2
THC+\LFT+	4,1	4,2
VDRL+	5,1	5,2

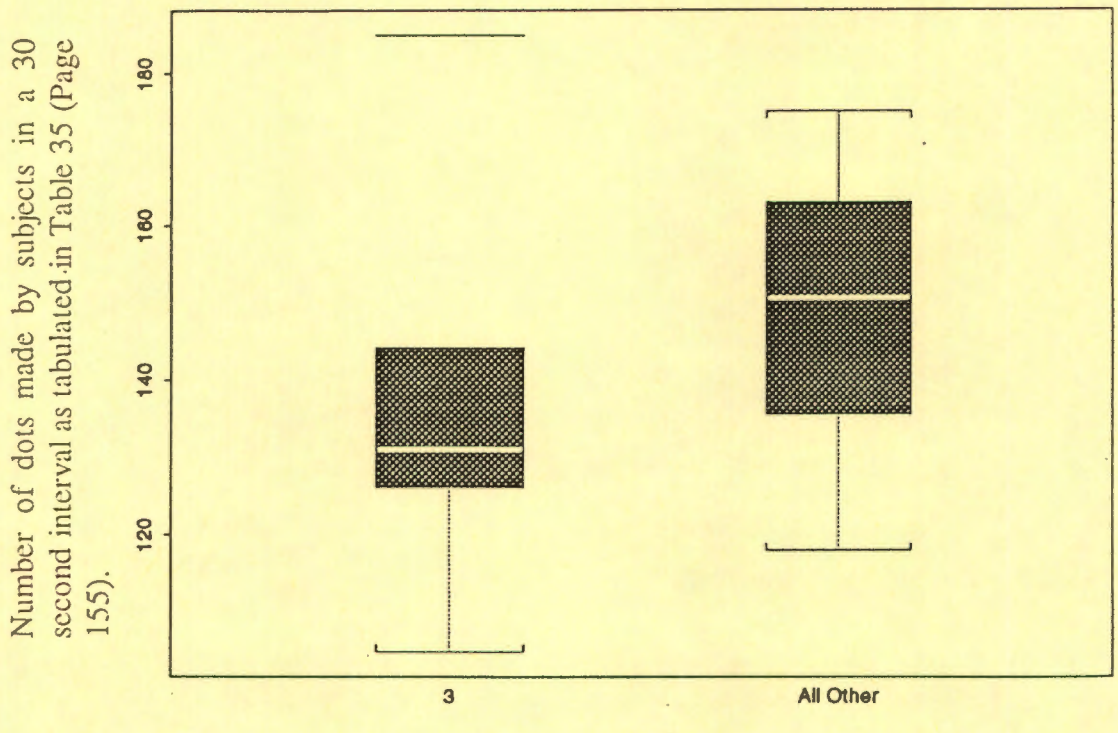


Fig. 35: Comparison of results in the pencil tapping test between the control group (3) and all other groups which have been collapsed into one group (all other).

Fig. 36 represents the delay plot in the pencil tapping test. It was necessary to discover if the length of the lag is a factor in the change of performance. For instance, it may be assumed that performance increases as a linear function of time.

Fig. 36 demonstrated no clear trend emerging, i.e. the length of delay does not appear to be a significant influence in the change in performance. A subject who waited 2 days to repeat the test performs as well as a subject who waited 5 days to repeat the test.

Previous workers using the pencil tapping test as a function of perceptuo-motor functioning demonstrated that cannabis users performed less well in this task compared to a control group, (Williams et al 1946, Kielholz et al 1973, Soueif 1975, Kvalseth 1977, Mendhiratta et al 1988, Varma et al 1988, Schwartz et al 1989, Deahl 1991, Abood et al 1992).

A comparison of the results obtained by Varma et al (1988) and the present study appear in table 47. The FEH control group demonstrate a wider range of scores than those recorded by Varma et al (1988) in that the present study recorded scores well below the minimum score recorded by Varma et al (1988). By contrast, the scores of the cannabis users in both studies is the same.

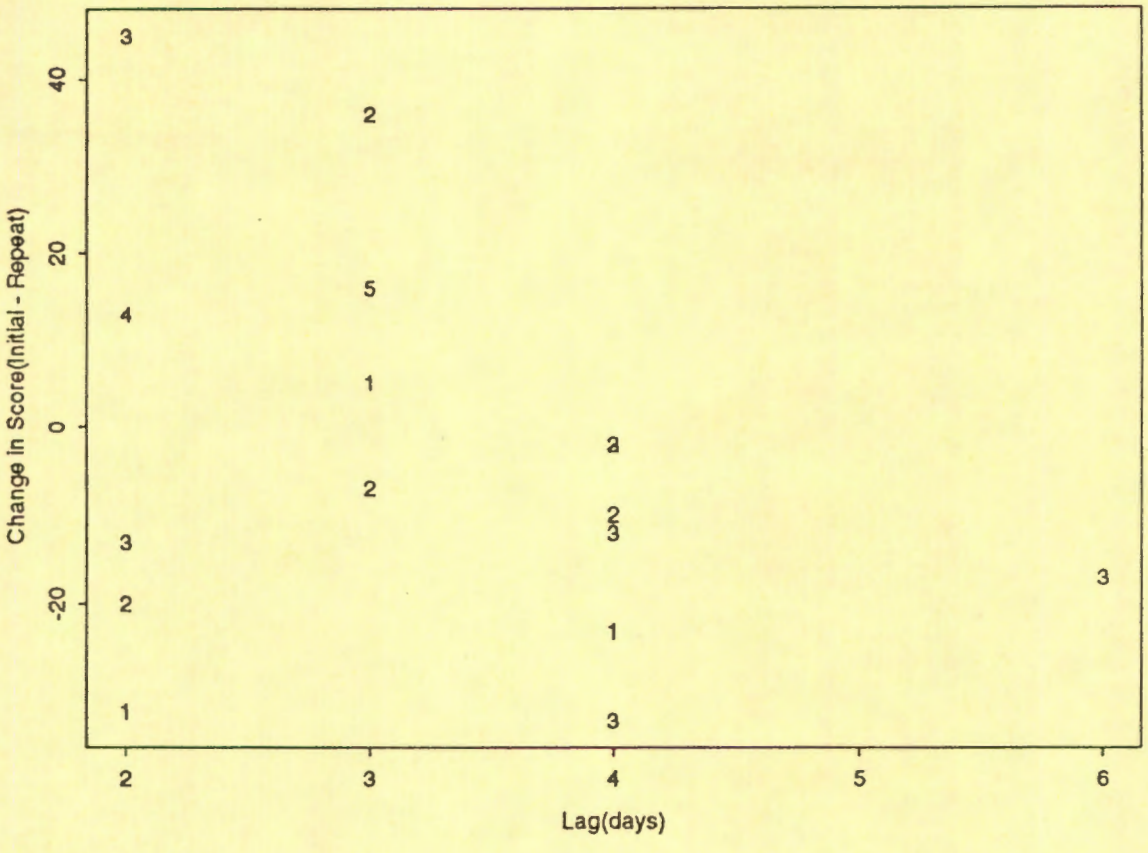


Fig. 36: Delay plot of the pencil tapping test. The lag for each subject is plotted on the x axis and the change in score is plotted on the y axis. The plot is used to determine trends in performance as a function of lag.

Group	Pencil tapping score (30 sec. interval)		
	Varma et al (1988)	Fort England hospital study	
		First attempt	Second attempt
Cannabis users	151,5 ± 25,40	133,2 (R=118-150)	148,6 (R=145-151)
Controls	167,76±18,35	134,4 (R=105-185)	144,7 (R=122-175)

Table 47: Comparison of the pencil tapping scores for a 30 second interval from the work of Varma et al (1988) and the present work.

The Canadian commission of enquiry (1972, quoted in Soueif 1975) likewise reported cannabis use does not influence the pencil tapping score.

Weil et al (1968) and Abood et al (1992) offered an explanation for this result. Both groups noted that on some tests, cannabis users demonstrated a superior performance compared to a control group and explained this in terms of over compensation by the cannabis users.

Conclusion

The pencil tapping test is a measure of perceptuo-motor skill and the present study has failed to demonstrate that users of cannabis and\or alcohol perform less well compared to a control group.

Results for the Corsi board digit span memory test.

The results are recorded in tables 36 and 37 as well as in figs. 37, 38, 39 and 40.

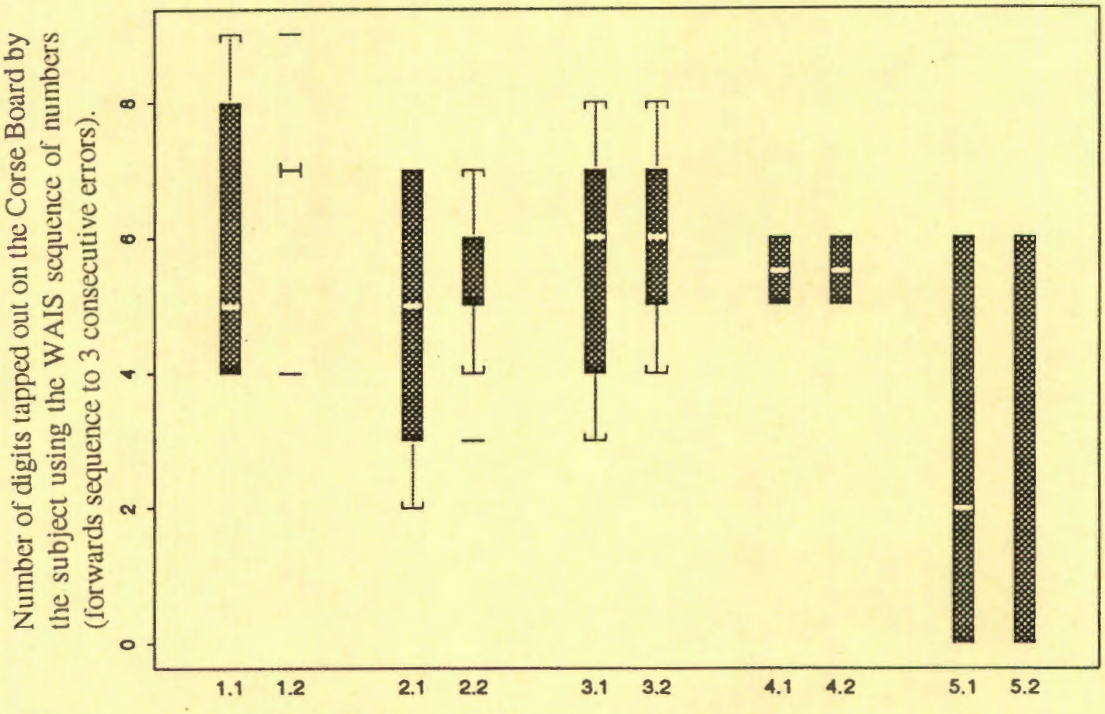
Results from tables 36 and 37 were analyzed using the statistical package SPLUS and the generated graphical analyses are represented in figs. 37, 38, 39 and 40.

Fig. 37 indicated that no differences emerged between the control group (3,1 and 3,2) performance and the performance of the other 4 groups. The results were then analyzed using the Wilcoxon test to see if there was a difference between the initial and repeat test results.

Z value	=	0,8834
p value	=	0,3770

This result suggests that the subjects' performance on admission was the same as when retested a few days later.

Fig. 38 compares the control group (3) to the other 4 groups collapsed into one group (all other). Again there appears to be no difference between the performance of the control group and the experimental groups.



KEY: Groups	First Attempt	Second Attempt
THC+\LFT-	1,1	1,2
THC-\LFT+	2,1	2,2
THC-\LFT-	3,1	3,2
THC+\LFT+	4,1	4,2
VDRL+	5,1	5,2

Figure 37

Box plot of the results for the digits forwards sequence using the Corsi board. The data was analyzed using the statistical package SPLUS.

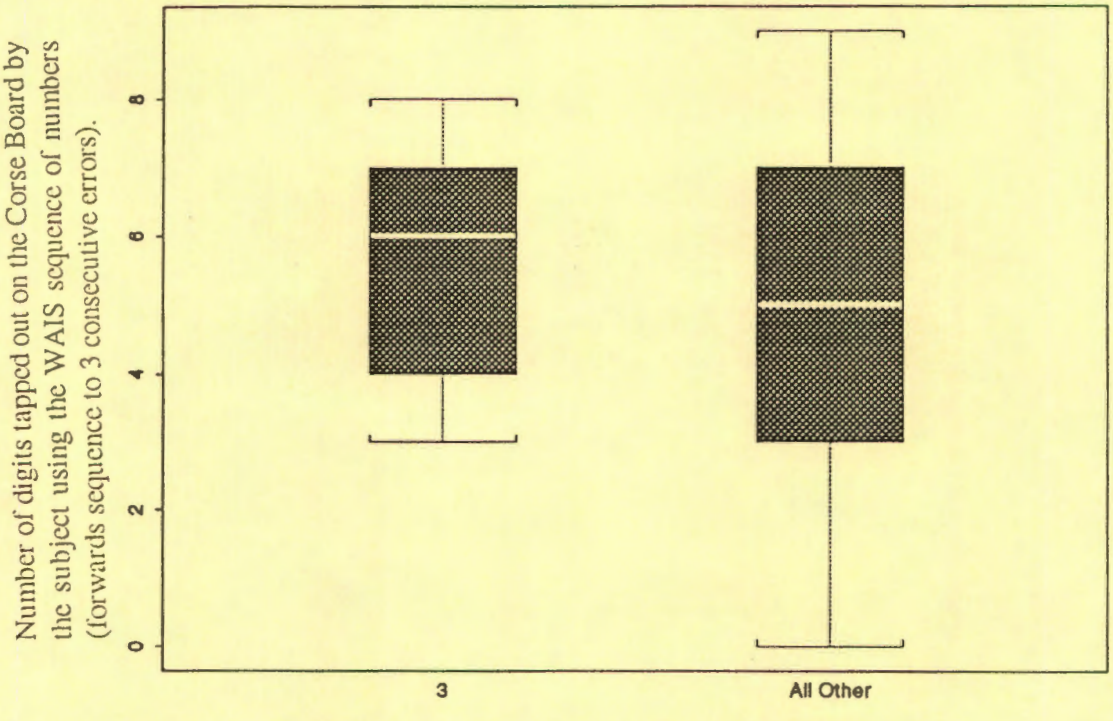


Fig. 38: Box plot of the results for digit forwards sequence using the Corsi board. The control group (3) has been compared to the other 4 groups collapsed into one group (all other).

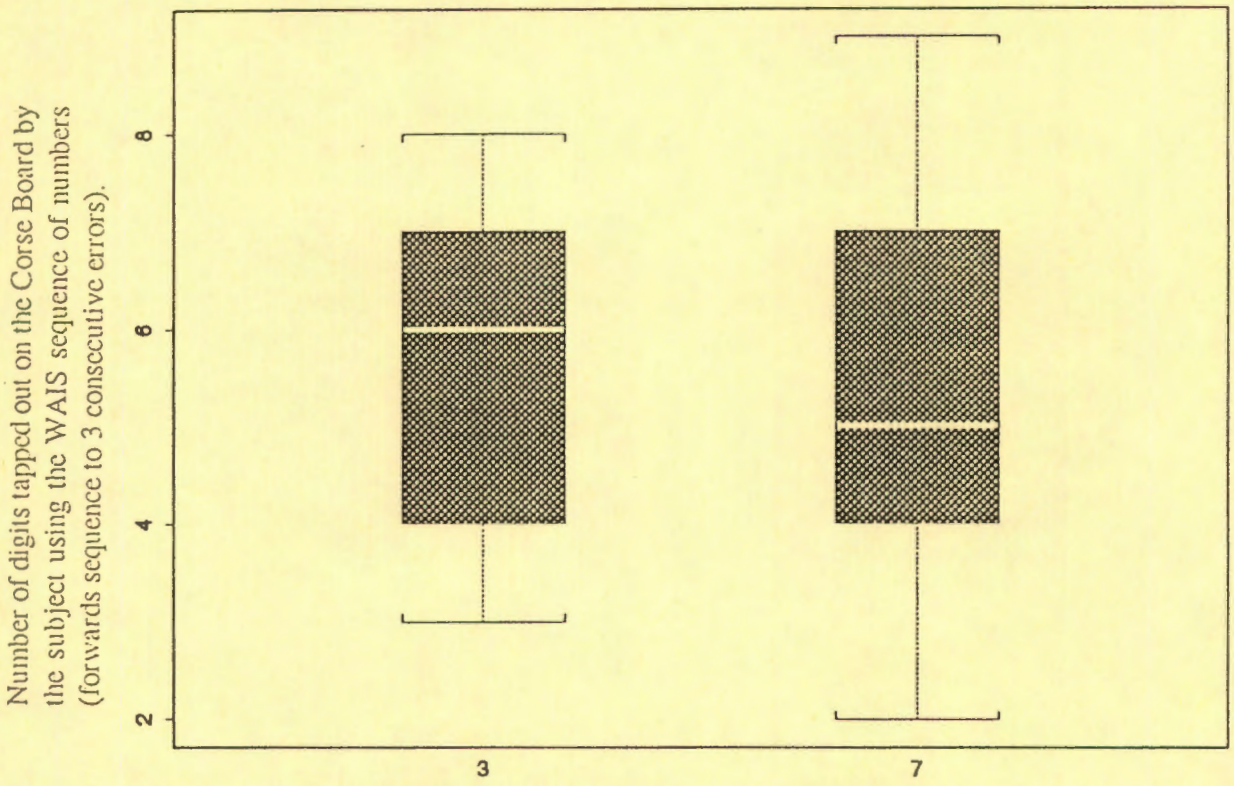


Fig. 39: Box plot comparing the scores for digits forwards on the Corsi board in the control group (3) and the toxin abusing group (7).

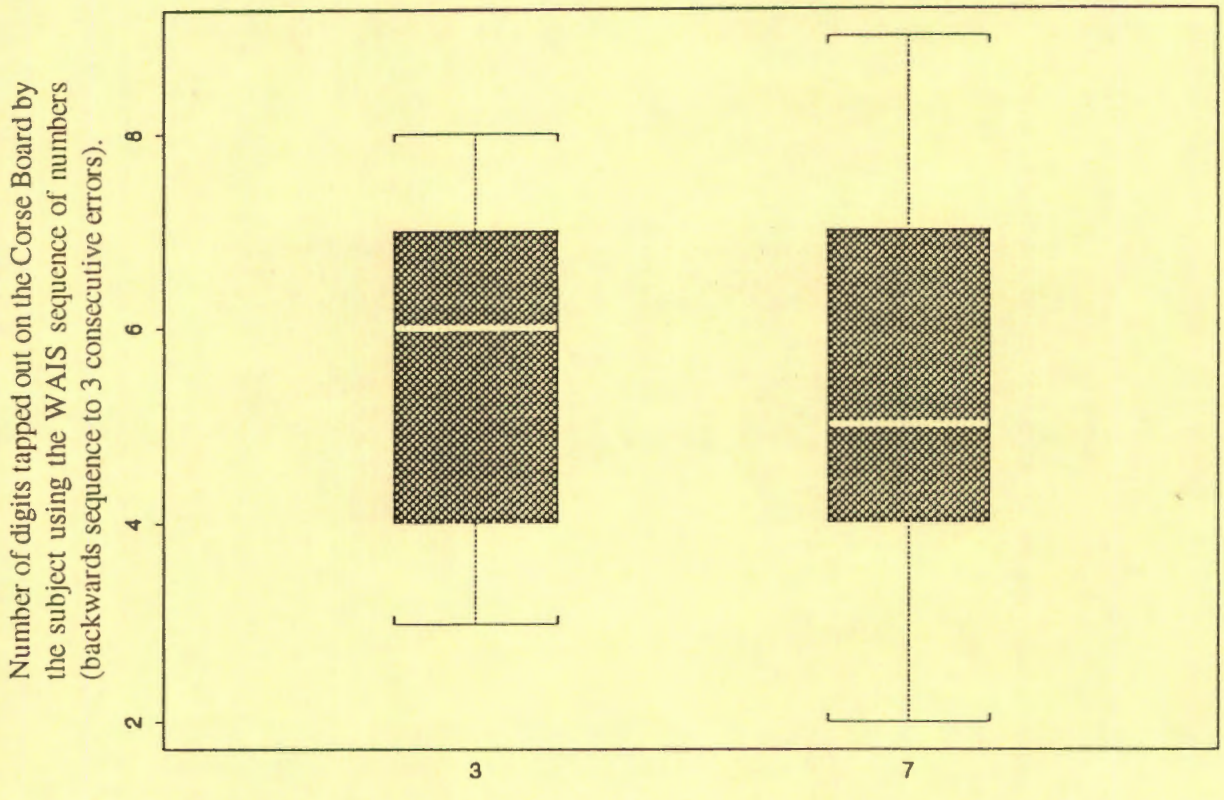


Fig. 40: Box plot comparing the digits backwards performance of a control group (3) with the toxin abusing group (7).

The results suggest the toxin abusing group performs as well as the control group in this task.

Groups 3 (control) and 7 (toxin abuse) were then compared and the box plot appears in fig. 39. Again no differences emerged. When the Kruskal-Wallis test was applied to the data, the results were:

X^2 = 0,2573 (df = 1)

p value = 0,6119

which again supports the conclusion that the toxin abuse group performs as well as the control group in the digits forwards test using the Corsi board.

Fig. 40 is the box plot for the digits backwards test using the Corsi board. When the data was analyzed using the Kruskal-Wallis test the results were:

X^2 = 0,0415 (df = 1)

p value = 0,8386

These results confirm that the toxin abusing groups perform as well as the control group in this test.

Tinklenberg et al (1970), Safer et al (1971), Dornbusch (1971) and Mendhiratta et al (1988) all found that in cannabis users there was impairment in digit span memory, both for digits forwards and backwards.

Soueif (1975) found that cannabis users performed as well as the controls on the digits forwards sequence but performed significantly less well on the digits backwards sequence.

Hollister (1971) and Weil et al (1968) felt that cognitive deficits, if any, in cannabis users would be of a temporary nature and so predicted that non-intoxicated cannabis users would perform as well as a control group in any cognitive test.

Bowman (1973) worked with Jamaican cannabis users who came from a low socio-economic status and he felt that in this group, any cognitive deficit would be hard to detect.

In the present sample, the patients all came from a low socio-economic status with little formal education and were predominantly unemployed.

Conclusion:

The digits forwards and backwards sequence using the Corsi board has failed to demonstrate any differences in performance between cannabis users and the other groups.

The world literature gives conflicting results. It has been postulated that in those individuals from a low socio-economic status and who smoke cannabis it would be difficult to detect any cognitive deficit when compared to a matched control.

Results for the immediate and delayed recall of a group of 8 familiar objects

The data from table 38 was analyzed using the statistical package SPLUS and the generated graphical analyses appear in figs. 41, 42, 43 and 44.

It appears that the 4 experimental groups perform as well as the control group. Furthermore, recall after a 5 minute interval with a distraction task showed no impairment in recall. When the test was repeated a few days later using a different set of 8 objects all groups performed as well as when first tested.

Fig. 43 is a delay plot which examines if there are changes in performance due to the size of the lag. Fig. 43 demonstrates that no pattern of change as a function of the lag. This means that there is no difference in performance when tested initially and a few days later. Statistical analysis of the data using the Wilcoxon test to test for a difference in the repeat and initial recall of 8 objects gave the values:

Z value = - 1,7407

p value = 0,0817

i.e. subjects performed equally well initially compared to their performance a few days later.

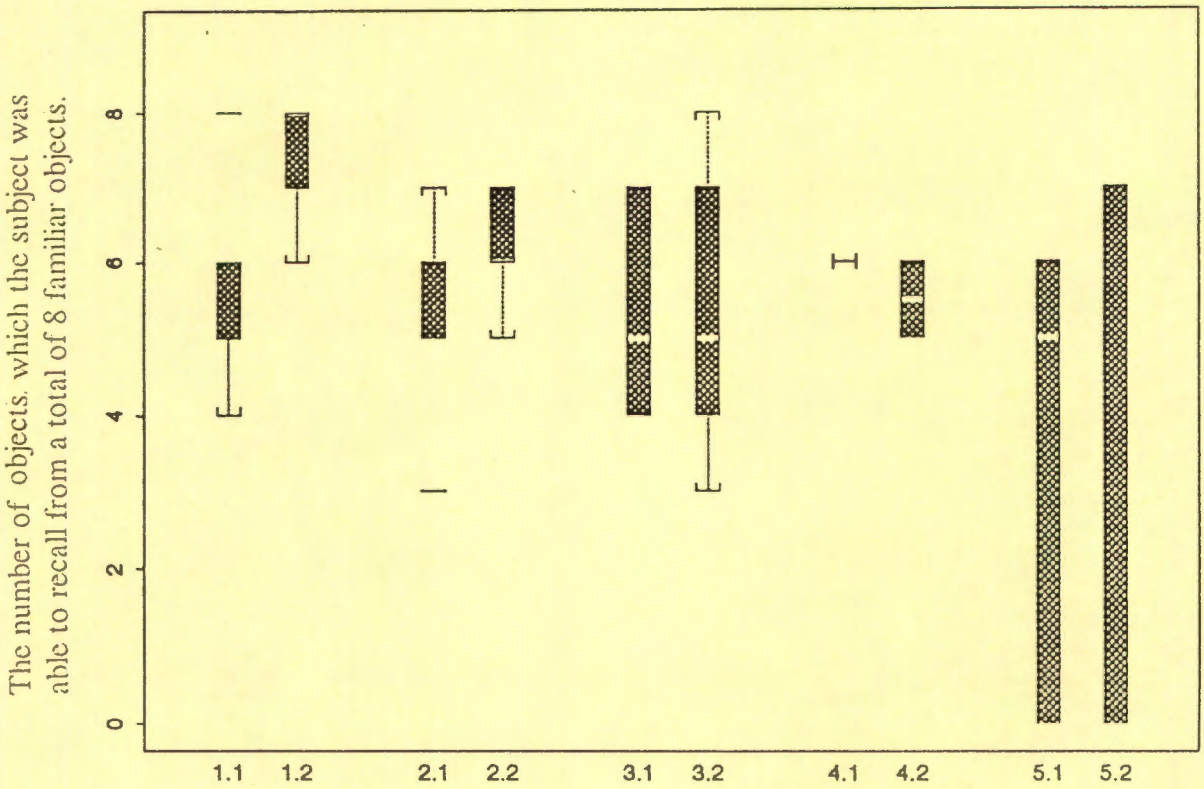


Figure 41

Immediate and delayed recall of a group of 8 familiar objects. The data was analyzed using the statistical package SPLUS.

KEY: Groups	First Attempt (on admission)	Second Attempt (a few days after admission)	Mean number of days (and range) between first and second attempt
THC+\LFT-	1,1	1,2	$\bar{x}$ = 3,6 R = 2-5
THC-\LFT+	2,1	2,2	$\bar{x}$ = 3,9 R = 2-5
THC-\LFT-	3,1	3,2	$\bar{x}$ = 3,4 R = 2-6
THC+\LFT+	4,1	4,2	$\bar{x}$ = 3,5 R = 2-5
VDRL+	5,1	5,2	$\bar{x}$ = 4,0 R = 3-5

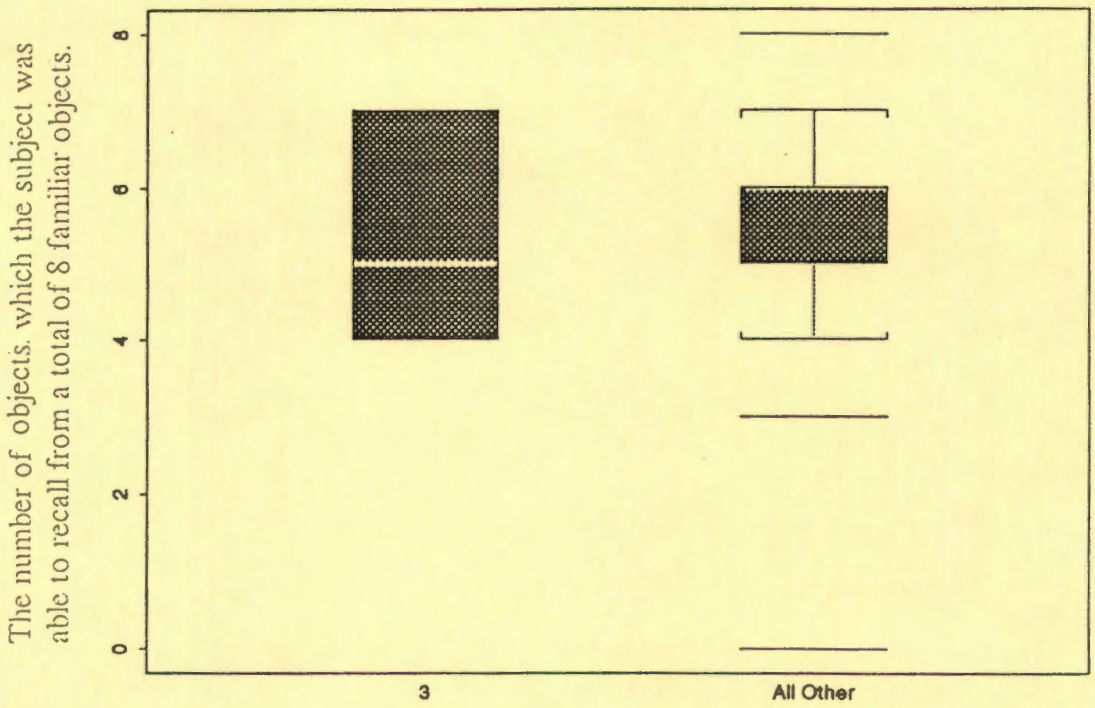


Fig. 42: Recall of 8 familiar objects by the control group (3) and all the other groups collapsed into one group (all other).

The box graph indicates that all experimental groups performed as well as the control group in recalling 8 familiar objects.

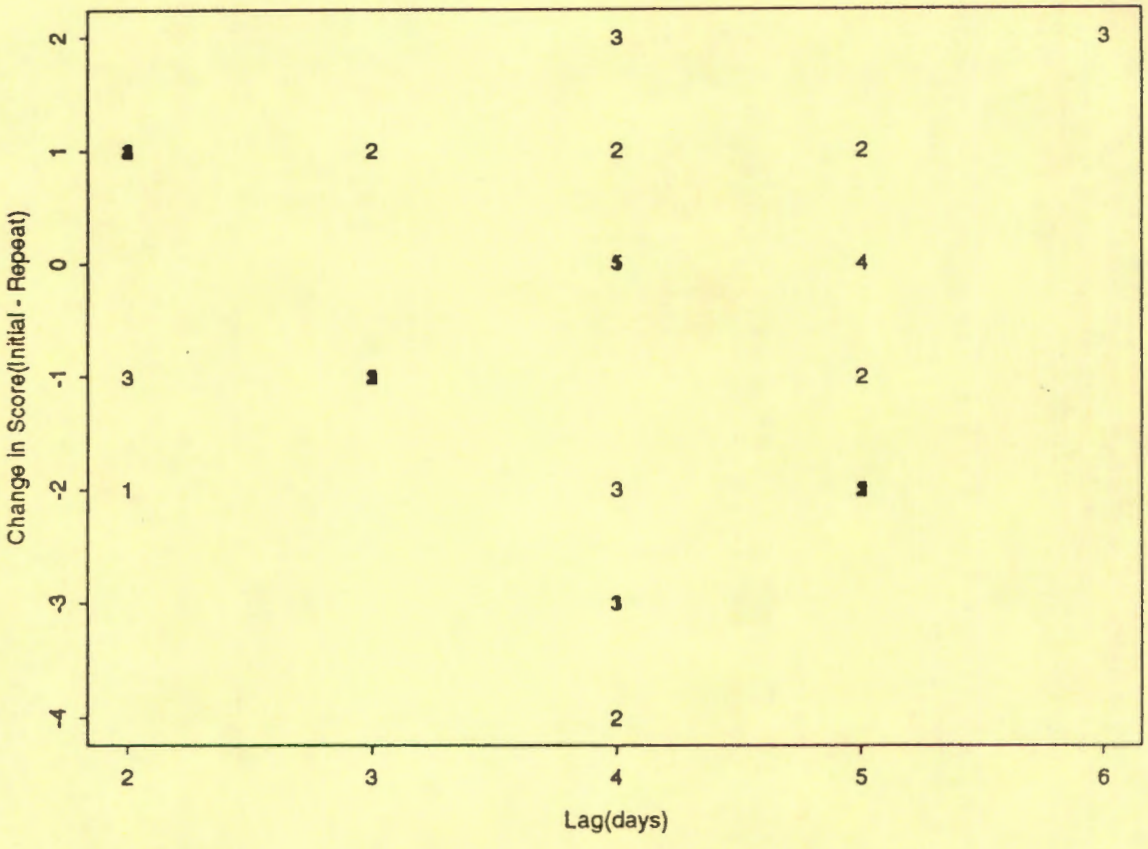


Fig. 43: The delay plot which examines if there are changes in performance in recalling 8 familiar objects due to the size of the lag.

The lag for each of the subjects is plotted on the x axis and the change in score is plotted on the y axis.

The plot looks at trends in performance as a function of lag. The present data demonstrates that the subjects perform as well initially as they do a few days later.

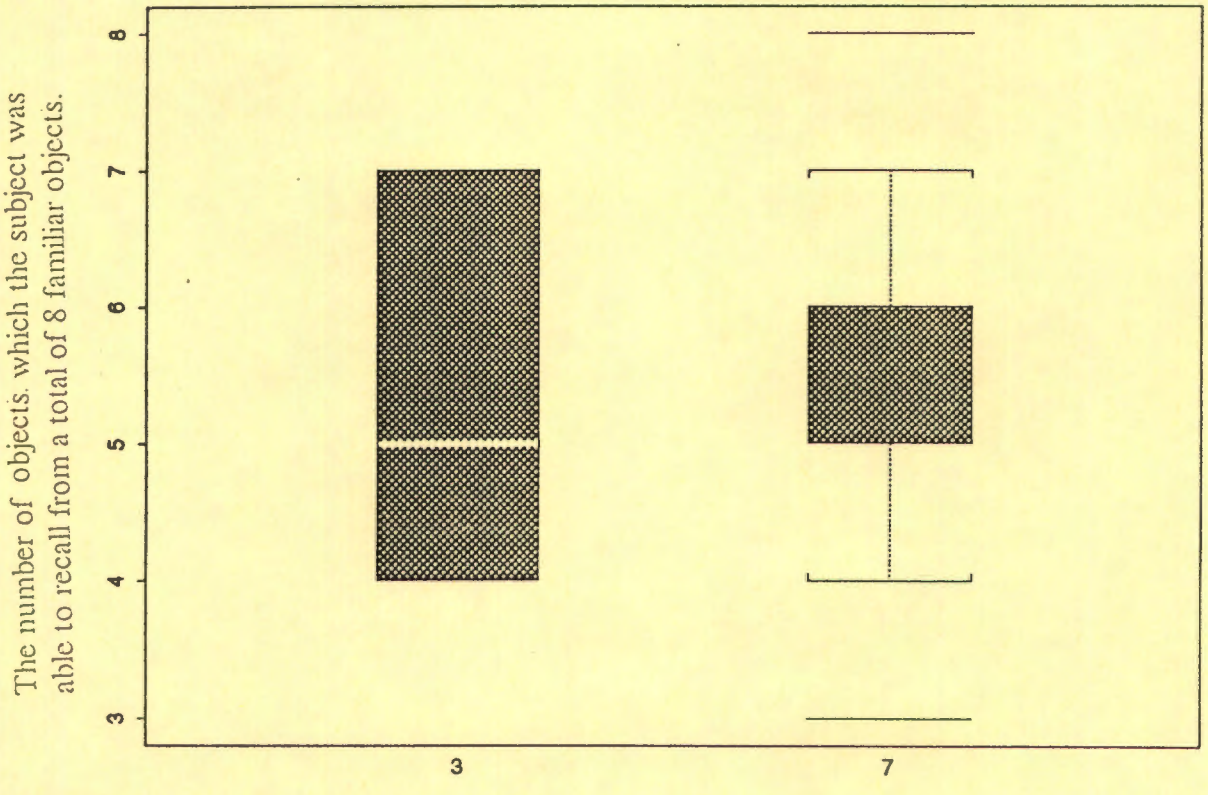


Fig. 44: Comparison plot between the control group (3) and the toxin abusing group (7).

The results indicate that the toxin abusing group performs as well as the control group in recalling 8 common objects both initially and after a lag period.

Fig. 44 is a comparison plot between the control group (3) and the toxin abusing group (7). When the Kruskal-Wallis test was performed on the data, the results were:

X^2 = 0,3015 (df = 1)

p value = 0,5829

i.e. the toxin abusing group could recall 8 common objects as well as a control group.

Dornbush (1974) presented his group of subjects with 8 lists consisting of 10 common objects. The objects were presented by a pre-recorded auditory tape at the rate of 1 object/sec. At the end of each list, the subject was given 1 minute to recall the items on the preceding list. Following the 8 lists, all subjects were given a distraction task of 50 minutes and then asked to recall as many objects as possible from the 8 lists. He found that in the cannabis using group, recall of information was impaired.

In contrast, Satz et al (1976) used 41 chronic cannabis users and 41 matched controls.

A total of 17 neuropsychological tests were used, one of which was the subject was shown a card with 9 line drawings of common objects. After a 10 minute delay, the subject was asked to recall the objects.

Satz et al found no significant difference between the experimental and control groups in object recall.

Therefore, the present set of results support the work of Satz et al (1976), that is object recall is not affected by cannabis use.

Results of the test for reproductive memory

The present test was an adaptation of the Graham Kendall memory for design test (MFD).

Other tests of reproductive memory (e.g. BVRT) have indicated that cannabis dependant individuals commit more errors in these tests compared to a control group.

Schwartz et al (1989) have suggested that the observed memory deficit may be long lasting in cannabis users.

The results from table 39 were analyzed using the statistical package SPLUS and the generated graphical analyses appear in figs. 45, 46, 47 and 48.

Fig. 45 indicates that there is no overall difference in performance between the control group (3) and the 4 experimental groups.

When the data was analyzed to see if there was a statistical difference between the initial and repeat tests using the Wilcoxon test, the following values were obtained:

Z value = 0,4305

p value = 0,6668

i.e. subjects performed as well a few days later compared to their initial performance on admission.

Fig. 48 is a comparison plot comparing the performance of the control group (3) with the toxin abusing group (7). It does not appear that the toxin abusing group performs less well than the control group. This is confirmed by the Kruskal-Wallis test which gave values:

X^2 = 0,1435 (df = 1)

p value = 0,7408

In terms of comparing the various groups in their ability to reproduce geometric shape vs. correct colour, fig. 46 indicates that groups 2 (THC-\LFT+) and 3 (THC-\ LFT-) reproduce shape better than colour but this result is not seen as statistically significant.

In fig. 47 all experimental groups have been collapsed into one group (all other) and compared to the control group (3). Again the box graph indicated that the experimental group did not differ in performance compared to the control group.

Conclusion:

The present adaptation of the MFD test has failed to demonstrate any significant differences in reproductive memory between the control group and the 4 experimental groups.

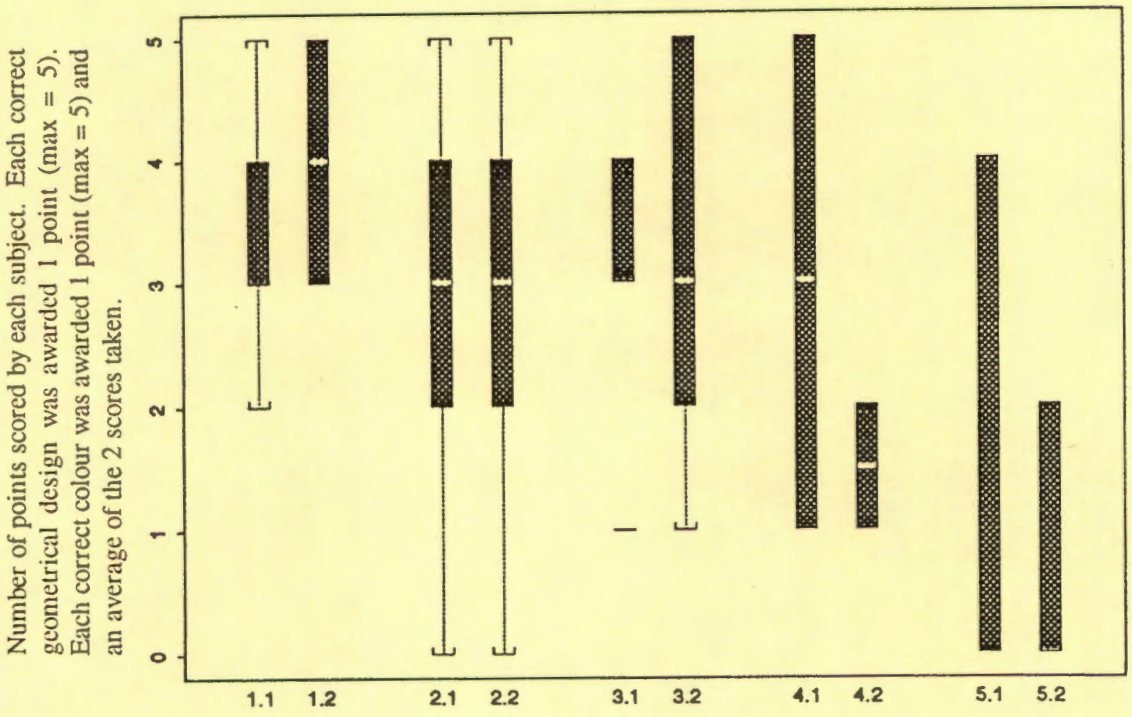


Figure 45

Box graph of results from the adapted MFD test showing the results from the first attempt (X,1) and the second attempt (X, 2) a few days later. The data was analyzed using the statistical package SPLUS.

The graph does not show any significant changes in performance over time or between the different categories.

KEY: Groups	First Attempt (on admission)	Second Attempt (a few days after admission)	Mean number of days (and range) between first and second attempt
THC+\LFT-	1,1	1,2	$\bar{x}$ = 3,6 R = 2-5
THC-\LFT+	2,1	2,2	$\bar{x}$ = 3,9 R = 2-5
THC-\LFT-	3,1	3,2	$\bar{x}$ = 3,4 R = 2-5
THC+\LFT+	4,1	4,2	$\bar{x}$ = 3,5 R = 2-5
VDRL+	5,1	5,2	$\bar{x}$ = 4,5 R = 4-5

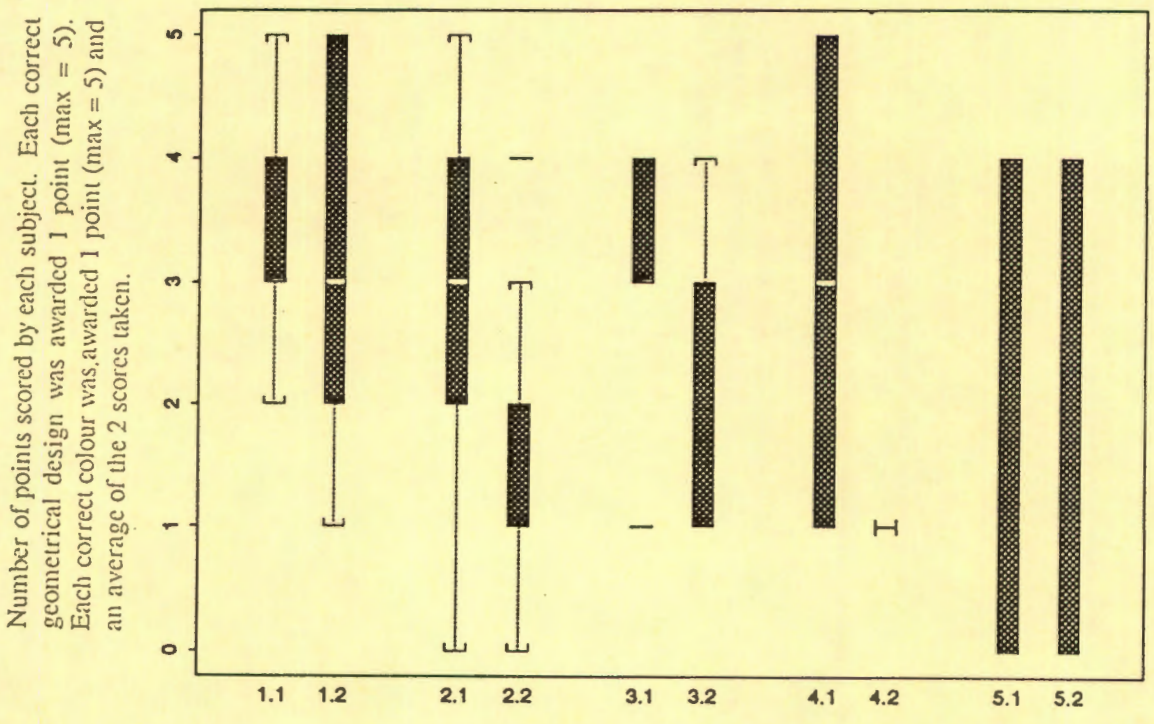


Figure 46

Results form the adaptation of the MFD test to discover if some groups are better at reproducing shape or colour of the geometric designs.

The data was analysed using the statistical package SPLUS which generated the above box graph. The results indicate that group 2 (THC-\LFT+) and group 3 (THC-\LFT-) reproduce shape better than colour but this result is not statistically significant.

KEY: Groups	First Attempt (on admission)	Second Attempt (a few days after admission)	Mean number of days (and range) between first and second attempt
THC+\LFT-	1,1	1,2	$\bar{x}$ = 3,6 R = 2-5
THC-\LFT+	2,1	2,2	$\bar{x}$ = 3,9 R = 2-5
THC-\LFT-	3,1	3,2	$\bar{x}$ = 3,4 R = 2-6
THC+\LFT+	4,1	4,2	$\bar{x}$ = 3,5 R = 2-5
VDRL+	5,1	5,2	$\bar{x}$ = 4,5 R = 4-5

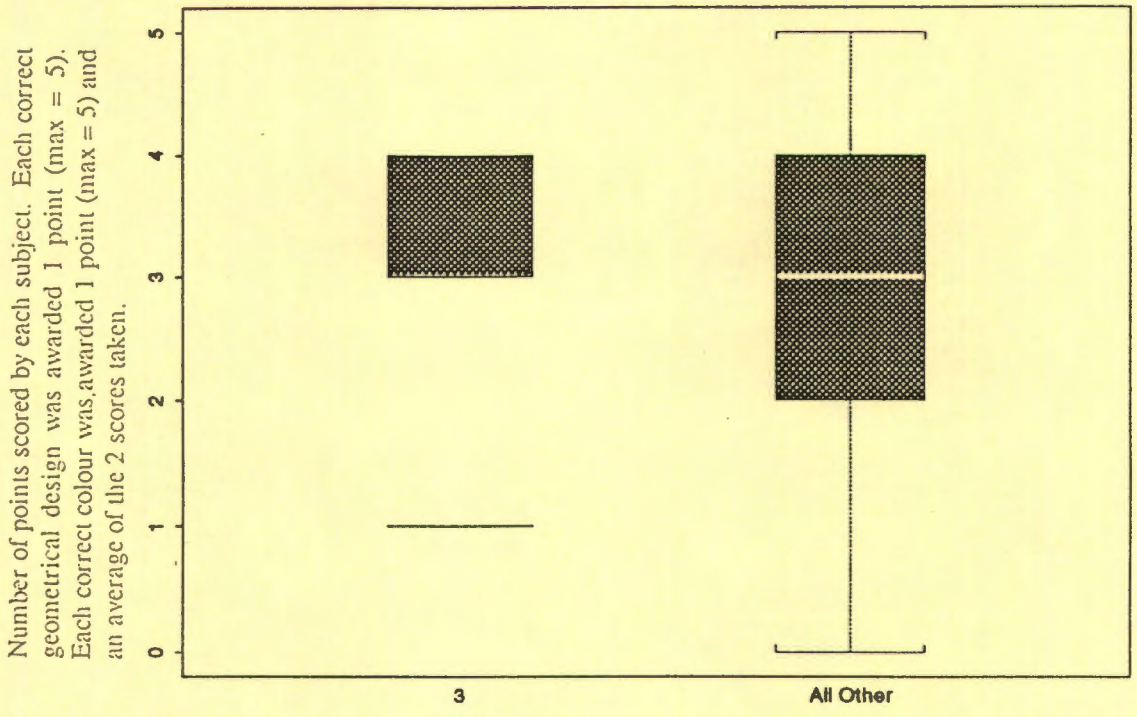


Fig. 47: The results from the adaptation of the MFD test. The 4 experimental groups have been collapsed into one group (all other) and compared to the control group (3).

The box graph indicates that the experimental groups (all other) did not differ in performance compared to the control group (3).

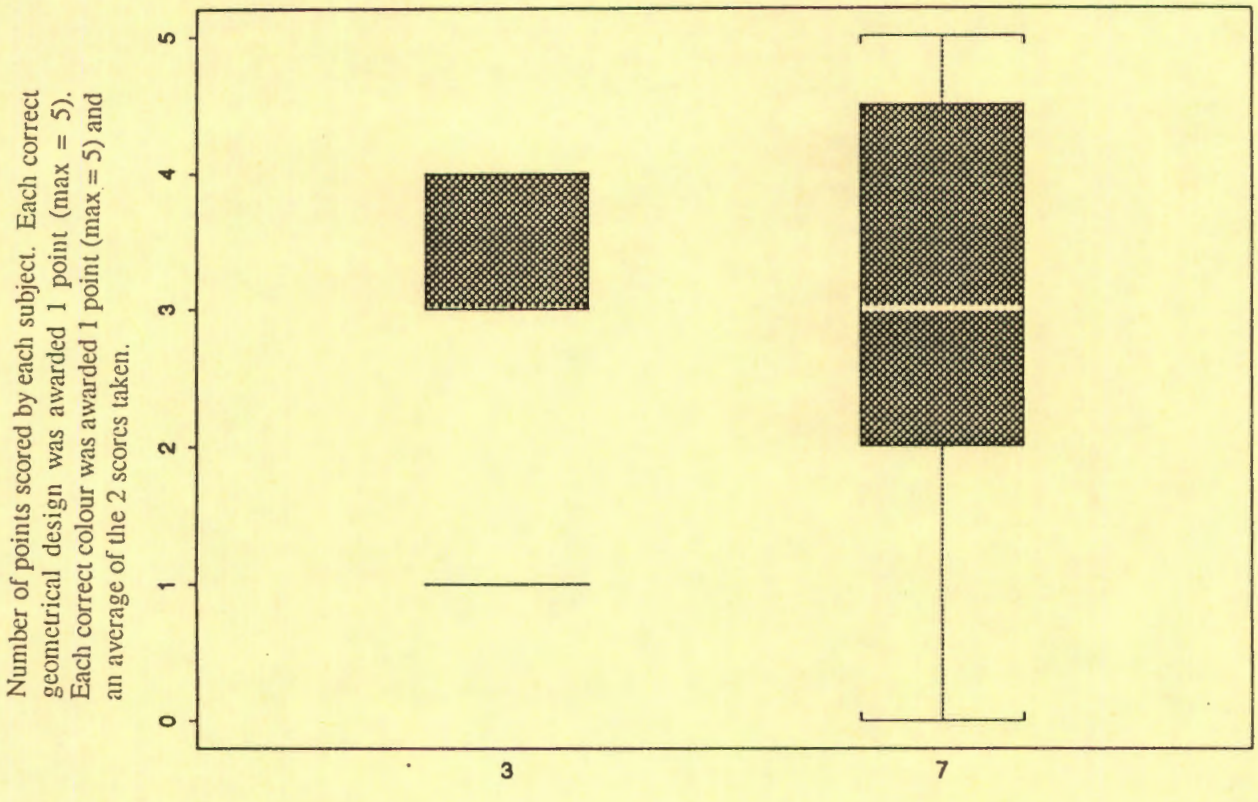


Fig. 48: Comparison plot of the adapted MFD test comparing the control group (3) with the toxin abusing group (7).

Statistical analysis demonstrated that the toxin abusing group do as well in this test as the control group.

DISCUSSION

There has been considerable debate in the literature as to whether cannabis does or does not produce cognitive deficits in the user. Satz et al (1976) noted that, "despite more than 4 decades of marijuana research, considerable controversy still exists concerning the acute and/or chronic effects of this drug on human adaptive functions, particularly on cognition, attention and personality."

The topic is complex because of the many variables which need to be considered which includes the concurrent use of other drugs such as alcohol.

One test of perceptuo-motor skills and three memory tests were used in the present study conducted on 27 consecutive male admissions to the acute ward at Fort England Hospital, Grahamstown, E. Cape.

The results were analyzed using the statistical package SPLUS which generated box graphs and in addition 2 non para-metric tests were used:

a) The Kruskal-Wallis test

b) The Wilcoxon test

These 2 tests were chosen because of the small sample size and the non normality of the data

The statistical analysis failed to demonstrate any differences in performance between the drug using groups and the control group. There are a number of explanations for this besides the assumption that cannabis has no lasting effect on cognition.

These include:

1) Dose of cannabis and/or alcohol was too small to interfere with the cognitive process.

2) Dose of cannabis and/or alcohol was sufficient to interfere with cognition but the time lapse between the initial intake of toxin and admission to hospital was so great that no short term effects were evident. Many patients in this sample came considerable distances from the Transkei.

3) All men in this sample had limited formal education and all were unemployed except one. All men came from a low socio-economic status so detection of any cognitive deficit would be difficult.

4) The small sample size may not have enabled any differences in performance to be detected.

5) The tests used were not sensitive enough to detect cognitive changes.

6) Subjects who abuse toxins could have learnt compensatory techniques in order to perform as well as those subjects who did not abuse toxins.

7) The control group could have been non-representative and so differences in cognitive capacity could not be detected.

Likewise, the role of cannabis in producing an aggressive response is not clear. It appears that many variables need to be considered such as dose of cannabis, prior experience of the user with cannabis, concurrent use of other drugs and the setting in which the cannabis is consumed.

In all likelihood, cannabis may cause some dis-inhibition in vulnerable individuals and in the correct setting this could manifest as aggression.

A common presenting feature of patients to Fort England Hospital was extreme aggression following use of cannabis. This appeared to be a short lived emotive state and the aggression usually disappeared together with any psychotic features. Mention has been made of the distances travelled by patients to reach Fort England Hospital and often the transient states of aggression and psychosis had disappeared prior to admission.

Due to the variables discussed and the fact that no satisfactory standardized measure of aggression is available, constructing a study designed to examine a direct relationship between cannabis use and resultant aggression in a South African psychiatric hospital setting is and will be a formidable task.

APPENDIX 1

Record dagga haul near Q'town

QUEENSTOWN Narcotics Bureau police have seized what is believed to be the biggest dagga haul in the country.

The dagga, with an estimated street value of R11,2m, was found in a routine check on the Queenstown-Cathcart road last night.

Investigating officer Frikkie Smith and Sergeant Tank Hattingh made the find when they stopped a 30-ton truck at 10pm and found the interior packed to the roof with 453 black refuse bags of dagga, a police spokesman said.

The dagga was later established to weigh 11,2 tons with an estimated street value of R11,27m. The spokesman said it was believed to be the biggest dagga haul ever in South Africa.

The driver has been detained for questioning and the truck impounded.

● The find is the third biggest in the Cape in the last 18 months. In a massive haul in April, 1992, a provincial traffic officer who stopped a furniture removal van on the N1 between Hanover and Colesberg discovered it contained 511 mealie bags of dagga with a street value of between R8m and R10m.

This find was thought by police to be the biggest seizure of dagga in South Africa.

In June this year two men were arrested in Cape Town with a R7m shipment of the drug from Transkei.

Weekend Post 2.10.1993

PE the distribution point for drugs in East Cape

By KATHY PATON

DRUG DEALERS are using Port Elizabeth as a central distribution point for their products in the Eastern Cape, says PE Narcotics Bureau head Major Willie O'Connell.

He said a total of 54 832 Mandrax tablets — worth R20 each — had been confiscated in the city since the beginning of this year.

This was a marked increase from the 43 176 tablets recovered last year.

In Cape Town last week a man carrying 5 000 Mandrax tablets was arrested at D F Malan Airport shortly before he was to fly to PE.

The drugs were discovered in a package in his hand luggage as it was X-rayed.

Major O'Connell said although less dagga had been confiscated in PE than last year, more was seized by police in other Eastern Cape areas.

In 1992, 16,2 tons of dagga — selling at R1 a gram — was found in PE, but only 8,4 tons had been recovered this year.

However, when the dagga seized in PE, East London, Queenstown, Middleburg and other towns in the region was combined, the figure shot up to 56,8 tons.

Sanab detectives had also seized 43 units of LSD in PE in the past year. LSD sold for between R25 and R30 a microdot, which made this a significant haul.

"PE is the only big city from the Western Cape down through the Eastern Cape and inland," Major O'Connell said.

"The drugs come through to PE and are then distributed to George, Oudtshoorn, Graaff-Reinet, East London and other centres. PE is the central point of distribution.

"It's difficult to say if the problem has become worse because there is no way to tell how much went through previously."

He said cocaine — which sells for between R250 and R350 a gram — was used mainly at private parties.

"A gram or two makes eight blades, which is usually gone within minutes.

"It is mainly used by wealthier people as the price puts it beyond the reach of the middle or lower class drug users."

● Police are investigating a number of cases involving escort agencies which are allegedly operating illegally within the city.

Major O'Connell said there were a number of cases pending involving unlicensed agencies. Several people had been arrested.

"A number of these agencies work from private homes and flats and most of them are unlicensed," he said.

"A couple are legitimate, but most are fly-by-night operations that close down after a short time."

Weekend Post 20.11.1993

Mandrax, dagga is confiscated

MEMBERS of the South African Narcotics Bureau team have been busy this week. Dagga and mandrax turned up in Fort Beaufort and two other hauls were made on the N2.

On Tuesday, Sergeant Manie van Dalen led a team who stopped a white ldv with registration CAJ 5278 on the N2. It was found to contain 133kg of dagga (value: R133 000) which was confiscated.

Two men, aged 25 and 30 were arrested. The vehicle was found to have been stolen in Addo last month.

Three hours later, also on N2, a bus travelling from Transkei to Cape Town was stopped. The luggage was searched and SANAB personnel turned up three suitcases containing 32kg of dagga (street value: R32 000).

It was confiscated but no arrests were made.

Next day Sergeant Ronald Vogel and Sergeant Chrisjan Elbrug with Sergeant Neil Kilian, working on information received, discovered a white Toyota Hilux, with XR registration, in a garage in Fort Beaufort.

The vehicle, which contained 41kg of dagga (value: R41 000), belongs to a Port Elizabeth man who had taken it into a garage in Port Elizabeth for repairs.
vehicle plus the possession of dagga is being investigated. An arrest is expected shortly.

Also in Fort Beaufort a man, 25, was arrested for possession of four mandrax tablets (value: R80). He was due to appear in court yesterday.

Grocott's mail 22.11.1993

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