A CRITICAL REVIEW OF THE RESEARCH LITERATURE CONCERNING SOME BIOLOGICAL AND PSYCHOLOGICAL EFFECTS OF CANNABIS†

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INTRODUCTION

An electronic search of the published research literature through computerised on-line services, such as DIALOG Information Services, reveals that since the mid 1960's over 4000 papers, monographs and books on medical, psychological and social aspects of cannabis use and abuse have been published.[1] These studies cut across a wide range of disciplines including: the potential teratogenicity of Δ-9-tetrahydrocannabinol and related compounds (Cohen, 1986; Fried, 1989; Fried and O'Connell, 1987; Hill and Tennyson, 1986; Stern, 1981; Qazi, Mariano, Milman, Beller and Crombleholme, 1985); histopathology and functional occlusion of the pulmonary system (Henderson, Tennant and Guerry 1972; Tashkin, Shapiro, Ramanna, Taplin, Lee, and Harper, 1976; Tashkin, Shapiro, Lee, and Harper, 1976; Tennant, Guerry, and Henderson, 1980); cardiovascular changes (Aronow and Cassidy, 1974; Benowitz and Jones, 1975; Stimmel, 1979); possible permanent neurological effects (Campbell, Evans, Thomson, and Williams, 1971; Co, Goodwin, Gado, Mikhael, and Hill, 1977; Feinberg, Jones, Walker, Cavness, and Floyd, 1976; Fried, 1989; Grant, Rochford, Fleming, and Stunkard, 1973; Grant, Rochford, Fleming, and Stunkard, 1973; Hannerz and Hindmarsh, 1983; Heath, 1972; Heath, 1973; Heath, Fitzjarrell, Garey, and Myers, 1979; Kuehnle, Mendelson, Davis, and New, 1977; Tassinari, Amrosetto, Peraita-Adrados, and Gastaut, 1976); the likelihood of the existence of a psychological complex of behaviours and attitudes collectively referred to as the "amotivational syndrome" (Creason and Goldman 1981; McGlothlin and West, 1968; Smith, 1968; Weller, 1985); the possible effects on learning and behaviour (*DSM-III-R.*; Fabian and Fishkin, 1981; Fried, 1977; Johnston, O'Malley, and Bachman, 1986; Jones, 1975, 1980; Kolansky and Moore, 1971; McBay, 1986;

[1]Searches were conducted in two data bases: Medline (Index Medicus) and PsychInfo (Psychological Abstracts). The following inclusive 'or' statement was searched: MARIJUANA OR THC OR CANNABIS OR TETRAHYDROCANNABINOL. Medline produced 2253 'hits' and PsychInfo 1935. One can assume that there is some overlap, hence the approximation of over 4000.

Mullins, Vitola, and Abellera, 1974; Weller, 1985); and the possibility of a relationship between cannabis use and major psychiatric disorders (*DSM-III-R,* 1987; Andreasson, Allebeck, and Rydberg, 1989; Imade and Ebie, 1991; Lavik and Onstad, 1986; Meyer, 1975; Negrete, Knapp, Douglas, and Smith, 1986; Thacore and Shukla, 1976; Thornicroft, 1990; Tunving, 1985). Amongst these papers are a number of fairly thorough review articles and books which attempt an overview of most areas of cannabis research (Cohen, 1986; Hollister, 1988; Jones, 1980; Nahas, 1984; Nahas and Latour, 1992; Petersen, 1980).

Although the total volume of this literature is somewhat daunting at first glance, a sampling of the material soon reveals that much is repetitive and a relatively small number of papers are continually referred to by most authors. Therefore, this review will concentrate on a selective group of these articles (90+), which represent the core of this research, but in doing so, we proceed with a high degree of confidence in the representative nature of those papers chosen for review and critique. Nonetheless, no review can be assumed to be free of bias and this one is no exception. The quality of much of this literature reviewed, however, is confounded by the political and social debate surrounding illicit drug use in general and cannabis in particular. There seems to be few neutral parties in the debate and some reports barely hide the prejudices which drive for particular conclusions, no matter what the empirical data appears to indicate.

In commenting on the problems of research into the effects of cannabis on humans Jones (1980) states:

> This large and rapidly growing literature demonstrates that all relevant information on all effects of cannabis will probably never be available. Because of the nature of science, usually facts change as experience accumulates. As more people use any drug for more time, as analytic instruments become more sensitive, and as researchers ask more focused questions, new facts appear and the significance of older facts is continually revised (pp. 54-55).

And, we might add, the interpretation of these 'scientific facts' appears to change with the changing political climate.

Of course, this growth of knowledge and evolving interpretation of the empirical data can be seen in the alcohol and cigarette literature as well. Like these two licit drugs, the effects of cannabis must be taken in relation to its frequency of usage and hence dose rate. Thus, it is still an issue of debate whether the moderate use of alcohol, as claimed by some, is beneficial to cardiovascular health. However, there is little disagreement that intense, prolonged use of alcohol is deleterious to both physical and psychological well being. In the case of cannabis, on the other hand, no one appears to be able to define what constitutes heavy use and in field research of illicit users the results become highly uncertain because of the inability of scientists to ascertain actual dose rates and hence life-time intake of cannabinoids. This is due to the wide range of concentrations of THC and related compounds in smoked marijuana and differences of smoking habits from one individual to another. A 'fifth' of single-malt whisky at a given percent strength is a very precise amount of ethyl alcohol, but a kilogram of marijuana can vary widely in its content of bioactive and psychoactive compounds.

Further, when reading the scientific literature on the effects of cannabis, it is important to put the emerging evidence into perspective. Very often statements are made about the effects of its use which, when taken out of context, appear to be somewhat exaggerated in their supposed effect on human health. For example, infant birth weight is considered an important indicator of later rates of cognitive and psychological maturation and thus taken to be a significant risk-factor in the use of any drug by pregnant women. Some studies relate cannabis usage to reduced birth weight, but neglect to put this finding in the context of other, more commonly used substances such as tobacco, which cause even greater effects on birth weights of the infants of using mothers (Hill and Tennyson, 1986; Fried and O'Connell, 1987).

Behavioural studies also have attempted to address the issue of the relative effect of cannabis, as compared to other licit drugs such as alcohol, in performance tasks - particularly for its effect on driving an automobile. One of the more recent of these studies by Chesher *et al* (1985) concludes that "duration of impairment produced by all three drugs (cannabis was taken in two ways) at the doses used was very similar" (p. 624). A report issued in February, 1990 by the United States National Transportation Safety Board indicated that 12.8% of those involved in fatal truck accidents showed signs of cannabis ingestion in post mortem examination (cited in Nahas and Latour, 1992, p. 496). However, these published rates are usually confounded by multiple use of psychoactive substances in the majority of cases, particularly alcohol, which is believed to increase the deleterious effects on behaviour and judgement induced by cannabis alone. However, in an earlier and larger study drivers using cannabis *only* were involved in only 2.2% of recorded fatal accidents and Hollister (1988) concludes from the data that "at present, THC plays a relatively minor role in fatal traffic accidents as compared with alcohol" (p. 113). Apart from the direct neuropsychological effects of both drugs, the problems caused by alcohol and cannabis in relation to motor vehicle accidents, in particular, are more due to the methods and circumstances of their use by a minority of individuals rather than the fact that these substances both cause, in the main, reversible perceptuo-motor deficits.

As indicated in the opening remarks, this review of the effects of cannabis on humans will not attempt to be exhaustive and will be divided into two broad categories - physiological and psychological. The physiological classification will include discussions of effects on the cardio-pulmonary system, teratogenicity and the central nervous system. The psychological grouping, on the other hand, will discuss the relationship of cannabis use to social adjustment, driving behaviour, toxic psychoses and schizophrenia. Of course, the psychological and neurological are inextricably intertwined, but for heuristic purposes they will be kept separate, being cross-referenced only where necessary.

PHYSIOLOGICAL

Since most cannabis users smoke either marijuana or hashish, it is reasonable to examine the effect of smoking cannabis on the occurrence of lung disease. Nahas (1984) reminds us that smoking cannabis releases plant constituents such as tars, carbon monoxide, acids, aldehydes, pyrobenzenes and particulate irritant substances, so any toxilogical or pharmacological studies must consider these by-products of smoking in addition to the delta-9-THC content of the smoke, especially in the case of chronic use. The reader should also take note that many reporters on the effects of cannabis ingestion do not always make clear conceptual discriminations between the effects of smoke by-products (which are very similar to tobacco except for the presence or absence of nicotine or THC) and those specifically related to the pharmacology of THC. Of course, users primarily smoke cannabis, but it can also be ingested orally giving similar psychoactive effects. Thus, any reasonable discussion of the physiological effects of cannabis must take into account that it is illegally used primarily for its psychoactive properties and if THC were to be provided in an easily ingested rapid acting oral form, the problems due to smoking could be obviated.

When taken, delta-9-tetrahydrocannabinol rapidly disappears from the blood plasma and is taken up in fat where it remains with a half life decay rate of 5-7 days. This means that after a single dose of THC, less than 1% of the primary active ingredient remains in fatty tissue after approximately 35-50 days (Nahas, 1984). THC's oil solubility and thus high affinity for fatty tissue probably accounts for its attraction to neural tissue with its high lipid content in myelin and other components of the neurone. Herkenham *et al* (1990) used quantitative autoradiography to map the distribution of THC in mammalian brains in which they demonstrated that:

> ...in all species very dense binding was found in the globus pallidus, substantia nigra pars reticulata (SNr), and the molecular layers of the cerebellum and hippocampal dentate gyrus. Dense binding was also found in the cerebral cortex, other parts of the hippocampal formation, and striatum. In rat, rhesus monkey, and human, the SNr contained the highest level of binding. Neocortex in all species had moderate binding across fields, with peaks in superficial and deep layers. Very low and homogeneous binding characterised the thalamus and most of the brainstem, including all of the monoamine-containing cell groups, reticular formation, primary sensory, visceromotor and cranial motor nuclei, and the area postrema. The exceptions—hypothalamus, basal amygdala, central gray, nucleus of the solitary tract, and laminae I-III and X of the spinal cord—showed slightly higher but still sparse binding (p. 1935).

They conclude that the structure activity profile defined by the binding of the THC analogue used in the study is consistent with "the same receptor that mediates all of the behavioural and pharmacological effects of cannabinoids, ...including the subjective experience termed the human 'high'" (Herkenham *et al*, 1990, p. 1935). These binding sites are also consistent with THC's effects on loosening of associations, fragmentation of thought and short-term memory deficits. Further, dense bindings found in the basal ganglia and cerebellum suggest a role for cannabinoids in effecting motor control while involvement with the ventromedial striatum suggests connections to dopamine circuits. However, the expected

reinforcing properties usually associated with these dopamine pathways is difficult to demonstrate in the case of THC.

There are over 60 other cannabinoids and cannabidiols present in cannabis smoke, most of which have very little psychoactivity and do not bind to these same sites. The effect of these substances is largely unknown, nor is the level of psychoactivity for any THC remaining in fatty tissue on the days subsequent to the original ingestion known. Although, in the case of light to moderate cannabis users, THC can be detected in body fluids for approximately 30 days after the last consumption, it is quite difficult to detect perceptuo-motor effects this long after a given average single dose (1-3 mg THC in cannabis to be smoked). This is unlike alcohol where a clear dose/response curve is demonstrable in which effects of ethanol on behaviour and judgement can be demonstrated at blood levels below 0.05%. In their comparative study Chesher *et al* (1985) have estimated that a dose of cannabis originally containing 1 to 2 mg THC produced a decrement in performance on a battery of psychological tests which was approximately the same as that produced by alcohol at a concentration of 0.05% (at peak) (p. 627).

The results of this last study suggest that many of the behavioural studies to be examined later in this paper may be seriously flawed. The high dose rates of the typical chronic cannabis user recruited for these behavioural studies, when taken in the context of the relatively long half-life of THC, suggest that behavioural and psychological tests conducted on chronic users who are supposedly no longer using cannabis are, in fact, being carried out on individuals still highly intoxicated. If, as Chesher *et al* (1985) suggest, the ingestion of 1-2 mg of THC to be smoked is the equivalent, in a behavioural sense, of achieving a 0.05% blood alcohol, then typical dose rates of 150 mg per day (to be smoked) are the intoxication equivalent of drinking more than fifteen 10 oz schooners of standard beer per hour. Cannabis users at this level of consumption will still have very significant accumulations of THC in their fatty tissue, and hence a serum equivalent of more than 0.05% blood alcohol, several weeks after their last ingestion of cannabis. Thus, any studies conducted to examine the permanent effects of THC on behaviour for heavy cannabis users must be sure that their subject sample has not used any cannabis whatsoever for several months prior to examination.

Pulmonary Effects

There have been a number of anecdotal reports and uncontrolled clinical observations which link cannabis smoking to the risk of pulmonary pathology (Cohen, 1986). However, this evidence is much less conclusive than a controlled study of lung function tests carried out by Tashkin and colleagues (1980) in which 74 habitual cannabis smokers were compared to non-users. The results indicated no substantive difference between users and non-users but Cohen (1986) criticises these results as being skewed by the fact that all the participants were initially screened and those showing any respiratory pathology were removed from the study.

In addition, Tashkin *et al's* (1980) findings somewhat contradict their earlier (1976) report in which they conclude that very heavy marijuana smoking for 6 to 8 weeks appears to cause mild but significant airway obstruction.

Earlier studies of U.S. servicemen hashish smokers conducted by Henderson and Tennant (1972), however, make a more damaging case against cannabis in relation to lung disorders. These researchers found frequent and severe nose and throat inflammation often accompanied by X-ray findings which included sinusitis and lower airway diseases such as bronchitis and asthma. As part of these studies patients with chronic cough were subjected to bronchoscopy and biopsy of the epithelial lining of the posterior wall of the trachea. Microscopic examination of the biopsy samples revealed a number of cellular abnormalities which are associated with the later development of lung cancer and chronic obstructive pulmonary disease. These include the loss of cilia, basal epithelial cell proliferation and proliferation atypical cells.

The authors acknowledge that most of these men smoked tobacco along with hashish, but insist that the development of the abnormalities observed significantly pre-dates their usual appearance in those who are tobacco smokers only. The problem with ascribing these pathological changes to cannabis alone is obvious. The later attempts of Tennant and associates to disconfound tobacco effects from those of cannabis tended to show that either smoking tobacco alone or use of hashish on its own is less deleterious than combining the two (Tennant, Guerry, and Henderson, 1980). However, the sample size used in this later study was much too small to allow any clear-cut conclusions to be drawn. Cohen summarises these findings.

> Although not a single case of lung cancer has yet been attributed to chronic marijuana smoking in this country (U.S.), the possibility cannot be ignored that chronic, heavy marijuana smoking, like chronic tobacco smoking, may be a risk factor for the development of lung cancer and that the risks of developing lung cancer as the result of combined marijuana and tobacco smoking could be additive or even synergistic (parentheses mine) (Cohen, 1986, p. 156).

Finally, it should be borne in mind that cannabis produces similar carcinogenic 'tars' to that of tobacco, but in greater quantities than for an equal weight of tobacco, and the deep inhalation techniques employed by marijuana and hashish smokers tends to deposit that tar more deeply in the lungs. It has been calculated that 70% of the particulate matter is retained in the lungs and it thus can be assumed that in the case of cannabis this percentage is even greater (Jones, 1980). Again, in contrasting pulmonary effects of cannabis smoking with that of tobacco it should be recalled that most tobacco smokers are now using products which have been modified to reduce the 'tar' content and which are often filtered to that same end. Therefore, the comparison of illicit cannabis with legal, processed tobacco, in terms of health effects, is somewhat spurious.

Cardiovascular Effects

When cannabis is first smoked one of its most prominent immediate effects is tachycardia which tends to be proportional to the ingested dose (Stimmel, 1979). The rate increase varies from 50-100% of resting pulse with an accompanying decrease in orthostatic blood pressure. It was observed by Aronow and Cassidy that the consumption of one marijuana cigarette containing 19 mg of THC decreased exercise time until angina by 48% as compared to a marijuana placebo which only reduced time to angina by 9%. The authors of this study concluded that cannabis smoking increased myocardial oxygen demand while decreasing myocardial oxygen delivery (Aronow and Cassidy, 1974). Hollister (1988) concludes from these results that, although smoking is not recommended for anyone with angina, the shorter time until angina seen with cannabis combined with its induction of tachycardia makes it particularly deleterious for those suffering from arteriosclerosis of the coronary arteries or congestive heart failure. Nahas (1984) summarises what he believes to be the cardiovascular threat of cannabis ingestion based on the above findings:

> The smoking of marihuana increases the work of the heart by increasing heart rate, and in some cases by increasing blood pressure. This increase in work load poses a threat to patients with hypertension, cerebro-vascular disease, and coronary atherosclerosis.
> Marihuana can also cause postural hypotension. The drop in blood pressure could be hazardous in those individuals with compromised blood flow to heart or brain, especially if they are volume-depleted or if other drugs have impaired reflex control of their blood vessels. In older patients treated by delta-9-THC or who had smoked marihuana for glaucoma, orthostatic hypotension has been disabling and a risk factor of cardiovascular complications.
> Marihuana appears to intensify the effects of the sympathetic nervous system on the heart, an undesirable consequence in patients with coronary artery disease and in those susceptible to arrythmias (p. 127).

Jones (1980) admits that distinguishing chronic from acute effects of cannabis on the cardiovascular system is problematic. Chronic, long term oral administration of THC can result in mildly depressed heart rate and slight lowering of blood pressure (Benowitz and Jones, 1975). Although these changes appear to be of little biological significance, Jones feels that long term use might be associated with lasting health consequences, drawing his argument from the accumulated data now existent on tobacco use and heart disease. It was, he argues, years before the connection was made between smoking and coronary artery disease. Jones claims that THC has "far more profound effects on the cardiovascular system than does nicotine," but fails to tell us how. In fact, the findings of Benowitz and Jones he presents on long term oral administration of THC (above) shows an effect which could be construed as potentially useful in combating the negative cardiovascular effects of long term stress. As is often the case in THC research, interpretation is in the eye of the beholder.

Jones' prediction concerning the effect of long term cannabis use as having potentially more serious effects than nicotine ingestion is somewhat peremptory. Until the effects of the "tars," particulates, carbon monoxide and differing smoking styles involved in marijuana smoking are disconfounded from the effects of the cannabinols (THC in particular),

prognostications about the future effects of cannabis on the cardiovascular system are somewhat precipitous. His statement comparing nicotine with THC is particularly ill founded. Most studies have not looked at comparisons between THC and nicotine, per se, but have made comparisons between smoked cannabis and tobacco cigarettes. The actions of both compounds are no doubt altered by the method of delivery (smoking) as well as by the combination of responses caused by other constituents of the smoke such as carbon monoxide, for example. Nicotine itself is known to be a strong activator of sympathetic pathways of the autonomic nervous system thereby having a direct, stimulating effect on the heart (Kalat, 1988). No such direct action has been demonstrated for THC or its other psychoactive derivatives.

Again, as in the case of possible pulmonary action of THC, conjecture seems to far outweigh empirical evidence. What evidence there is appears to be flawed by studies which are either uncontrolled, anecdotal, or based on small, idiosyncratic cases. Even more importantly, the research cited above does not control for the effect of psychological factors on cardiovascular activity. As will be described later in this paper, cannabis intoxication is well known for producing mild to severe panic reactions in naive users (Cohen, 1986; Hollister, 1988; Jones, 1980; Nahas, 1984; Weil, 1970). The level of stress produced by such states, and by altered consciousness experiences in general, often may be responsible for the clinical signs of stress syndrome such as shortness of breath, tachycardia, etc. There is little doubt that any individual with incipient cardiopathology may show symptoms of cardiac distress when so psychologically taxed.

Teratogenicity

Central to the issue of teratogenicity and THC is the possibility that there is a direct action of the cannabinoids on chromosomes. In studies by Stenchever, Kunysz, and Allen (1974) and Herha and Obe (1974) a significant increase in chromosomal abnormalities was observed in marijuana users as opposed to non-users. These changes consisted largely of breaks or translocations of chromosomes and more of the latter were found in chronic users than non-users. However, when breaks were included in the count, the effect was drowned and the differences were lost. A later study, however, found that after 72 days of chronic marijuana smoking, no increase in chromosomal breakage rate could be found when compared to the base level existing before the study (Hollister, 1988; Matsuyama, Jarvik, Fu, and Yen, 1976). The pre-test, post-test design of this last study can be considered superior to the previous two clinical investigations because of the built-in controls of a within-subject statistical design. Studies not using this particular design usually cannot approximate the dose rate received by their subjects nor are they able to rule out other causes of chromosome anomalies, which may be related to differences in life-style between users and non-users and/or the effects of other drugs rather than being due to the action of THC alone.

In addition, one must take any chromosome studies in the proper context. Many commonly used licit drugs are capable of causing chromosome abnormalities as well. For example, in a recent *in vitro* study it was demonstrated that Paracetamol is capable of producing concentration-dependent chromosomal aberrations in primary rat hepatocytes (Muller, Kasper, and Madle, 1991). Although these clastogenic effects in vitro were observed only at very high concentrations, pharmacokinetic data and other published mutagenicity data suggest that there might be a risk for human use. According to the authors, *in vivo* studies suggest Paracetamol is also weakly clastogenic in human lymphocytes when used at the maximum human therapeutic dose range. However, there appears to be no public alarm regarding this and earlier studies which made similar observations about the effects of aspirin. For both THC and Paracetamol the long-term effects of induced chromosomal abnormalities remains unknown and thus we must be cautious in extrapolating to any possible teratogenic consequences without considerably more controlled research.

One of the more contentious areas of cannabis research concerns the effect on foetal development of the mother's use of THC containing preparations during pregnancy. As Cohen (1986) suggests, these effects can be highly confounded by other factors such as nutrition, alcohol, tobacco, other drug use and socioeconomic status. He further suggests that fairly large numbers of matched-pair subject would be required for the maintenance of external validity in such studies. Hingston *et al* (1982) studied 1,690 mother/child pairs in which 234 mothers used marijuana in varying amounts during the course of their pregnancies. The outcome of this study revealed that cannabis use was associated with lower infant birth weight and length for the babies of users. This results revealed a proportional effect for the level of consumption of THC, with higher use rates delivering greater birth weight deficits. Zuckerman *et al* (1989) obtained similar results in which they found a statistically significant average 79 gram decrement in foetal weight and a 0.5 cm reduction in body length for maternal THC users as opposed to non-users. In this study they further raise the issue of the importance of biological markers in differentiating users from non-users. When analysing the results of their subjects on verbal reports alone, the significant differences disappeared in contrast to a differentiation made by urinanalysis for THC metabolites.

Cohen (1986) states in his interpretation of the results of Hingston *et al* (1982) that maternal marijuana use was the strongest independent predictor of the occurrence of features compatible with foetal alcohol syndrome (FAS) and was better than alcohol as a predictor of FAS. In a later study Hingston *et al* (1984) clarified their earlier study and concluded that some adverse effects attributed to maternal drinking and smoking may be the result of an interaction with marijuana. In other words, there may be an additive effect of drug combinations on the foetus.

In a related study Gibson, Bayhurst, and Colley (1983) found that, of the 7,301 births sampled for abnormal infant characteristics, mothers using marijuana were significantly more likely to deliver premature babies of low birth weight. However, the largest study reported in

Cohen's (1986) review of the literature is that of Linn, Schoenbaum, Monson, Stubblefield, and Ryan (1983). In this study 10 independent variables were analysed for 12,718 women who gave birth at the Boston Hospital. Marijuana was the most highly predictive of congenital malformation above alcohol and tobacco. Further, Qazi *et al* (1985) studied the infants of five regular marijuana only users and found that each infant had low birth weight, small head circumference, tremors at birth, abnormal epicanthic folds, posteriorly rotated ears, a long philtrum, a high arched palate and abnormal palm creases which are all considered signs of FAS. Cohen suggests the cause of these morphological anomalies can be found in the results of research conducted by Morishima (1984) in which he found that 5% of ova are damaged by exposure to THC.

Cohen (1986) admits that gross malformations in human infants have not yet been conclusively linked to THC exposure. Fried (1985), on the other hand, observed that any possible neonatal nervous system effects occurring from the result of regular marijuana use by mothers during pregnancy do not manifest in poorer performance on cognitive and motor tests at one and one half and two years of age. In addition, a later study by Fried (1989) found that, by age three, a dose response relationship between lower language scores, lowered cognitive scores and prenatal cigarette (tobacco) exposure is observable. At this age, some cognitive and language deficits are also observable with prenatal marijuana exposure. In summary, although Fried observed that at one, two and three years of age, there are persistent effects of prenatal exposure to cigarettes, the effects of prenatal marijuana exposure, if present, are not as readily ascertained.

If, as noted in the introductory section of this paper, neonatal weight, length and head circumference are critical variables predictive of later psycho-motor development, there is good reason for concern based on the results of most of the studies cited above. However, Fried's (1985, 1989) work appears to contradict the conventional wisdom in the case of the THC users he studied vis-à-vis reduction in foetal body size and its relation to later learning and behavioural deficits. These contradictory findings would tend to indicate either that the research into birth effects is somewhat confounded, or there is not a simple relationship between foetal body size and behavioural development. Again, as in other areas of research into the effects of THC on humans, the disentangling of these issues awaits more exacting and controlled studies in the future (Nahas and Latour, 1992).

Neurological Effects

In many ways the existence or not of permanent, harmful changes to the nervous system caused by the use of cannabis is central to the debate on the drug's long-term effects. Obviously, any substance which has definite psychoactivity must, ipso facto, be neurologically active. That cannabis alters brain function there is no doubt. The questions addressed by

most research is how and to what degree. Jones (1980) summarises the nature of cannabis intoxication and its relation to neurological clinical signs.

> Acute cannabis intoxication includes not only the pleasant state of relaxation, euphoria, and sought-after sensory alterations, but also impairs judgments of distance and time, memory for recent events, ability to learn new information, and physical coordination. At slightly higher doses the acute intoxication includes tremor, transient muscular rigidity, or myoclonic muscle activity. The subjective feelings of muscular "weakness" or stiffness can be measured objectively. Low doses produce no changes in tendon reflexes, but high doses cause hyperexcitability of knee jerks with clonus. At even higher doses a full blown acute brain syndrome is possible (p. 67).

Jones (1980) goes on to add that some researchers would argue that such altered and impaired brain function represents a prima facie case of temporary neurological damage during the period of acute intoxication. The health issue which arises from this is whether these neurological alterations last only a few hours or whether they persist with deleterious cumulative effects. As will be seen below, the data is by no means consistent and conclusions are difficult to draw.

In the early 1970's press reports appeared which claimed that scientists had found that cannabis use caused 'shrinking of the brain'. These claims were based on the work of Campbell (1971), who used pneumoencephalography to examine a small sample (10) of cannabis users by examining the size of their neural ventricles. These measurements appeared to reveal that the ventricles were enlarged, a finding consistent with cerebral atrophy. The problem with this early research is that it was conducted on a population of patients who were suffering from various neurological disorders. This fact, together with the inaccuracy of the earlier air-volume measurement technique, is deemed by Jones (1980) to render the work invalid. Later, similar, small-scale studies conducted by Co *et al* (1977) and Kuehnle *et al* (1977) using computerised transaxial tomography (CAT scans) found no evidence of anatomic changes. In the latter research the subjects were preselected for being healthy, normal cannabis users. However, these last two studies beg the research question by, in effect, choosing subjects who have not yet developed any pathology for an examination of possible permanent neurological effects of cannabis use.

Electroencephalographic (EEG) changes in humans using cannabis usually entail an increase in mean-square alpha energy levels and a slight slowing of alpha frequency. In general, only very minor changes tend to appear in the surface EEG's of cannabis users and those that do, such as increases in alpha wave activity, tend to be synonymous with drowsiness and relaxation (Jones, 1980; Cohen, 1986; Klonoff, Low, and Marcus, 1973). Although scalp EEG changes are minimal, Heath (1973) and Heath *et al* (1979) report significant alterations in electrical activity recorded in mid-brain structures of primates, most notably in the septal and amygdala areas. Although the focal EEG changes reported in this research have been seen only in the brains of monkeys which were exposed to marijuana smoke or given THC intravenously, the research of these authors has been quoted widely in both scientific review articles as well as in various anti-cannabis tracts. Therefore, a closer examination of some of this work is in order.

Heath *et al* (1979) found that continuous, daily exposure to the equivalent of the smoke from about 3 marijuana cigarettes per day produced abnormal electrical alterations after 2 to 3 months. Additional exposure of up to 3 to 6 months produced electrical abnormalities which persisted for up to 8 months. Heath also conducted histological examinations on brain tissue from the monkeys and found anatomic changes were apparent in the electronmicrographs, suggesting long-lasting changes related to the THC exposure. These changes included widening of the synaptic cleft, clumping of synaptic vesicles and other unspecified changes in morphology of neurones which occurred in monkeys after 6 months of forced cannabis intake and were still evident 6 months after cessation of cannabis use. However, it is unclear from his report whether a methodical evaluation of the supposed histopathology was made which included an independent panel of judges or whether these were his own personal judgements.

The deep sites from which abnormal EEG recordings were recorded are generally believed to be involved in emotional expression and hence affect disorders.[2] Heath's earlier work remains somewhat problematic when his experimental setup is examined in more detail. Although his monkeys included controls who were exposed to both very low THC containing marijuana and tobacco smoke alone,[3] this research remains highly confounded. The monkeys were strapped into chairs with transparent, sealed plastic boxes surrounding their heads. The smoke, together with oxygen, was pumped into the box for a pre-determined period while EEG recordings were made through permanently implanted deep electrodes. Given that in humans THC can induce panic anxiety attacks and given that monkeys do not like to be restrained, it is impossible to tell whether the abnormal electrical activity recorded in limbic areas was directly induced in the brain by the action of THC or whether this activity was what one would observe when panic is induced in restrained monkeys intoxicated by THC.

Heath describes the monkeys' behaviour.

> All displayed dilated pupils and sharp reduction in level of awareness. The monkeys would stare blankly into space, sometimes displaying spontaneous nystagmus, and would become much less attentive or completely unresponsive to environmental stimuli. When their hands or feet were grasped, the clasping response, which was consistently elicited on baseline examinations, was absent. Responses to pain (pinprick) and to sound (hand claps) were minimal to absent. Although the monkeys were not particularly drowsy, spontaneous motor movements were notably slowed, and passive tests of muscle tone suggested a degree of catatonia, although true waxy flexibility never developed (Heath, 1973, p. 4).

This certainly is not the way that the vast majority of human beings react to cannabis intoxication. The behaviour Heath describes appears to be more in line with an animal frozen in panic or manifesting what used to be called 'animal hypnosis'. Hunt (1984), a cognitive

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[2]The earlier, 1973, study of Heath, in addition to the septal area, included recording sites in the cerebellum, postero ventral lateral thalamus, hippocampus, and orbital and temporal cortices. The thalamic and hippocampal sites are major components of the limbic system and hence intrinsically involved with emotional expression and would most likely show unusual and significantly different activity in a situation of induced stress.

[3]The experimental group received exposure to marijuana smoke containing 2.29% Δ-9-tetrahydrocannabinol and the controls were exposed to either marijuana smoke containing 0.1% Δ-9-tetrahydrocannabinol or tobacco smoke.

psychologist, has called this the "negative capability" and it appears to be part of a neurophysiological mechanism for behavioural and cognitive shutdown when an animal is overwhelmed by, for example, a predator.

Another major problem with Heath's 1973 study was the control of O_2 partial pressure (PP) in the head chamber. From tables in his paper one can see that the PP of O_2 inside the monkey's "breathing chamber" was 75% greater than room PP in the marijuana run but only 9% above for the control tobacco sequence. The measured serum PP of O_2 was 143% above pre-exposure levels as seen in his data for the marijuana sequence as opposed to a rise of only 22.4% in the case of the tobacco run. There is little doubt that high partial pressures of serum O_2 will affect brain function and hence the EEG recordings (p. 9). Thus, any comparisons between THC exposure and tobacco exposure in this study are at best spurious. Finally, Heath states that, as the choice of subjects for cannabis studies moves up the phylogenetic scale, it is observed that THC produces a more localised effect in the brain involving fewer areas. In other words, humans show the least generalised reactions to THC. In summary, apart from the confounding factors of behavioural variables and O_2 partial pressures in this research, any attempt to generalise from monkeys to humans is fraught with the possibility of committing a logical category error.

As mentioned above, the research of Heath and his colleagues has been widely reported and appears to have been accepted somewhat uncritically by a number of serious researchers as seen in two of the review articles being reported on here (Cohen, 1986; Jones, 1980). This seems to be a recurring theme in much of the cannabis research today. In most research into psychopharmacological effects on EEG reliable conclusions are rarely drawn from so small a number of studies. The interaction of pharmacological agents with brain and behaviour is complex and even the simplest relationships require many experiments in order to delineate the causal connections with any degree of reliability. It appears as though any findings in cannabis research are immediately set upon by the those opposed to it use for the purpose of adding power to already pre-drawn conclusions.

Sleep EEG recordings sometimes can be more sensitive indicators of drug effects than waking EEG (Jonew, 1980). Reduction in rapid eye movement (REM) sleep accompanied by increases in total sleep time have been reported in humans together with considerable changes in surface EEG recordings as effects of cannabis use (Feinberg , 1976). The cessation of cannabis intake after prolonged use will then lead to a rebound effect in which REM sleep stages and eye movements rise above baseline levels. This rebound is not unlike those seen after the cessation of other sedative hypnotic drugs. In addition to these EEG changes, cortically evoked potentials consistent with altered central nervous system (CNS) function have been recorded from scalp electrodes of waking subjects (Herning, Jones, and Peltzman, 1979). However, as is often the case in cannabis research, "the pattern of change varies with dose and measurement technique, and between laboratories. The biological or functional significance of these alterations remains obscure" (Jones, 1980, p. 69).

Jones (1980) summarises the difficulties and uncertainty which must be accepted as part of cannabis research into its neurological effects.

> Many survey and laboratory studies comparing user and nonuser populations have reported no differences in cognitive, intellectual, or perceptual function between these two groups....Many of the studies reporting no neurological differences between users and nonusers have compared very selected people using 1, 2, or 3 marijuana cigarettes per week to those using none. It may well be that lasting impairment will be evident only at a greater dosage level or that the marijuana use interacts with some other unrecognised factor to produce lasting effects. The impairment will thus be missed in such limited studies. On the other hand, when deleterious, possibly marijuana-related, effects on function have been noted in groups of cannabis users, it is very difficult to determine whether the cannabis use caused the impairment, or was simply associated with it, or followed it.
>
> If one considers neurochemical data from test tubes, animal data, clinical case reports, survey data, controlled laboratory data, and semicontrolled field studies, the weight of the evidence so far is that lasting neuropsychological impairments are possibly but not inevitably associated with some undetermined level of heavy, prolonged cannabis use. However, the many factors that would determine the appearance of clinically evident cannabis-induced neuropsychological changes in any given user are so complex as to make any simple pronouncement of risk almost meaningless (pp. 70-71).

The research paradoxes revealed in the above section on physiological effects of cannabis can only be adequately resolved through the application of controlled experimental research techniques on large groups of humans. It is obvious that this is neither ethical nor practical. Of course, the tautological trap created by subject choice, as described in most of the above clinical research into cannabis, applies to all epidemiological studies, not just cannabis research. As we have seen with both tobacco and alcohol research in the past, reliable conclusions can only be pieced together slowly through large-scale and methodical data collection. So, it must be recognised that decisions probably cannot wait for the final datum to be collected because it is unlikely that all the data will ever be 'in'.

As with many decisions in other aspects of life, we must examine the apparent 'facts', while attempting to understand their context and accuracy, and then make the best possible choice based on the pragmatics of the circumstances rather than on absolutist principles posing as facts. One might well argue that if there is any doubt, whatsoever, that cannabis is safe to use, then it should be permanently banned. However, there may be useful social purposes served by allowing controlled use of cannabis which outweigh any possible deleterious effects it may have on the human organism. This is obviously the kind of thinking behind the current freedom we have to use analgesics, such as aspirin and Paracetamol, in spite of their well documented negative side-effects.

PSYCHOLOGICAL

In any review of the psychological effects of cannabis, a clear distinction should be drawn between cannabis use, abuse and dependency. Because of the problems involved in determining potency, as delineated in the opening section of this paper, it is often difficult to distinguish casual users from those who are abusers or dependent on the drug. The standard

reference for differential diagnosis of psychiatric disorders, the Diagnostic and Statistical Manual of the American Psychiatric Association (1987), defines cannabis dependence.

> Cannabis Dependence is usually characterised by daily, or almost daily, use of the substance. In Cannabis Abuse, the person uses the substance episodically, but shows evidence of maladaptive behaviour, such as driving while impaired by Cannabis Intoxication (p. 176).

The DSM-IIIR asserts that the impairment of occupational and social functioning and the resultant physical pathologies associated with cannabis dependence tend to be less than those seen in other psychoactive intoxicants, such as heroin, cocaine and alcohol. As a result, people showing signs of cannabis abuse or dependency are less often seen by medical doctors and psychiatrists. This fact further clouds any attempts at delineating an accurate definition or symptomatology of cannabis abuse and/or dependency.

The Manual does list a set of general symptoms characteristic of dependency, however. These include lethargy, anhedonia, and attentional and memory problems. This dependency syndrome usually develops with repeated use over a considerable period of time with rapid development following initial use being rare. Although there has been considerable debate over the issue of the development of tolerance in cannabis users, the DSM-IIIR asserts that "tolerance may develop to some of the substance's psychoactive effects and thus promote increased levels of consumption" (p. 177). This increase is not very great, according to the Manual, and if levels of consumption become very high, there may be a decrease in pleasurable effects with a concomitant increase in the number of dysphoric effects experienced by users. Jones (1980) summarises.

> Tolerance, that is, a diminished response to a repeated cannabis dose, is clearly associated with repeated use...It appears now, both in animals and in humans, that tolerance develops quite rapidly to many of the effects of THC. The more frequent the administration and the higher the dose the more rapidly it develops, but even subjects smoking as little as one marijuana cigarette per day in a laboratory experiment demonstrate tolerance on some behavioural and physiologic dimensions when they are carefully measured....Most of the tolerance seems to be lost rapidly, but this rate may vary with the sensitivity of the measures used (p. 74).

Other researchers, on the other hand, argue from both clinical and personal experience that one must learn to get 'high' and, therefore, it takes less cannabis for experienced users to obtain the desired effect than for neophytes (Tart, 1971; Weil, 1975). However, Weller, Halikas, and Moorse (1984) found, in a five-year follow-up study of regular marijuana users, that continuous use was associated with decreasing pleasurable effects. Cohen (1986) summarises their results.

> Users who had earlier reported positive feelings of relaxation, peacefulness, enhanced sensitivity, floating sensations, self-confidence, subjective impressions of heightened mental power, and other sought-after effects now said that these effects had significantly diminished. The undesirable aspects of the experience, however, persisted essentially unchanged (p. 158).

Psychopathology

Nahas (1984), a major contributor to the cannabis literature, takes a strongly proscriptive stand towards cannabis use and underscores the potential psychological dangers inherent in cannabis intoxication when he argues that exposure during the key developmental periods of foetal growth and adolescence may produce long-term, permanent psychopathological changes in individuals thus exposed. In order to further emphasise the allegedly unseen threat of cannabis use, Brill and Nahas (1984) address the issue of the paradox of the apparent minimal physiological effects recorded in most cannabis users warning us that

> The discrepancy between the marked psychological alterations and the slight physical symptoms associated with *Cannabis* intoxication represents another aspect of its deceptive nature. Many people today believe that since no apparent gross physical damage results from the absorption of *Cannabis* derivatives, there is little or no danger associated with their use. They are mistaken: *Cannabis* and all other hallucinogens have a common characteristic, their psychotoxicity and their ability to disintegrate mental function, which is not accompanied by any major alterations of the vital physiological functions. Mental illness, especially in the young, is also characterised by a similar discrepancy between the functions of the mind, which are markedly impaired, and those of the body, which are well preserved (p. 263).

This strongly held position, only loosely based on empirical data, often characterises the quality of discussion seen in the research literature concerning the psychological effects of cannabis. In the work of Brill and Nahas (1984) the unclear relationship between the physiological cause and psychological effect of cannabis intoxication is used to insinuate an almost 'devious' and/or 'sneaky' action for Δ-9-tetrahydrocannabinol. On the other hand, the actual argument given in the last section of the above quote, aimed at establishing a potent relationship between the minimal physiological causes arising from cannabis ingestion and its apparent strong psychological effects, is, again, typical of the cannabis debate and, in this case, spurious on at least two counts.

The first is the obvious logical category error of arguing from the class of mental illness to the psychological effects of cannabis intoxication without any evidence that these two phenomena are in any way the same category of event, physiologically or psychologically. The second, the argument as to the universality of deleterious psychological consequences of cannabis use, is based on a small minority of cases who have demonstrated some psychopathological effects directly attributable to cannabis use and thus have come to the attention of medical authorities. However, it should be remembered that the vast majority of users, whether occasionally experiencing some negative states or not, manage the use of cannabis and are able to integrate it into productive life-styles without developing any apparent psychopathology (Weil, 1975). The size of this majority is in the many millions whereas the minority from which most of the pathological data is drawn is a non-representative (statistically) few hundred.

In contrast to the view of cannabis as psychologically dangerous in itself, Weil (1975) has argued that it should be understood to be what he calls an "active placebo." Weil describes an "active placebo" as "a substance whose apparent effects on the mind are actually placebo effects

in response to minimal physiological action" rather than being a direct cause of the psychological changes seen in users (p. 95). This effect is attested to, empirically, by the wide variety of responses individuals make to similar batches of cannabis in similar situations. Weil's conclusions, based on hundreds of clinical observations, led him to argue that it was highly unlikely that cannabis alone could be responsible for the very varied psychological responses and effects which he observed.

From the recent work of Herkenham *et al* (1990), cited earlier in this paper, there is no doubt that the cannabinols have affinities for specific brain structures. However, it is as yet unclear as to whether cannabis has any predictable specific behavioural, cognitive, and/or affective effects resulting from the particular receptor site bindings mapped in their study. To date it is not possible to describe a unique and repeatable constellation of psychological responses to the action of the cannabinols as is possible for the opiate derivatives or the neuroleptic compounds used in the treatment of schizophrenia. This observation alone must cast some considerable doubt on most psychopharmacological ascriptions made for the actions of the cannabinols in humans.

There have been numerous attributions made about the psychological effects of cannabis. In the sections below a number of areas which have had considerable attention in the research literature will be reviewed. However, before embarking on issues, such as "panic reaction" and "toxic psychosis" amongst cannabis users, at least one popular misconception concerning cannabis intoxication requires clarification.

As a result of press and electronic media coverage there is a widely held belief by the community-at-large that those intoxicated by cannabis are more prone to show aggressive and violent behaviour. This idea also has found its way into scientific discourse (Brill and Nahas, 1984; Imade and Ebie, 1991). In their exploration of this issue, Brill and Nahas attempt to distil a phenomenology of cannabis intoxication based, to a large extent, on the idiosyncratic reportage of Jacques-Joseph Moreau who recorded observations about himself and other hashish users in the mid-Nineteenth Century. Moreau describes the quality of affect experienced during the mood swings he encountered while intoxicated on hashish.

> With hashish, the emotions display the same degree of overexcitement as the intellectual faculties. They have the mobility and also the despotism of the ideas. The more one feels incapable of directing his thoughts, the more one loses the power to resist the emotions they create. The violence of these emotions is boundless when the disorder of the intellect has reached the point of incoherence (Brill and Nahas, 1984, p. 270).

Not only is this description contexualised in Nineteenth Century cultural values and convictions, and thus not applicable as a direct comparison with late Twentieth Century experience, but the language itself is not easily interpretable from current contexts. The culturally embedded beliefs regarding the nature of emotions and mind have changed radically since Moreau's time as have the way individuals understand their relationship with their subjective lives. Therefore, using such a source in order to understand cannabis

intoxication in the present is dubious at best. Claims concerning violence thus appear to be somewhat confounded and in summarising this issue Jones (1980) reports that

> Most commissions and review groups that have specifically studied the relationship between cannabis and violence have concluded that the use of marijuana is not a major cause of aggression. There is little new that would change that conclusion (p. 73).

In fact, it is most often the case that chronic cannabis users have a depressed demeanour, a lack of drive and rarely show signs of violent behaviour (Tennant and Groesbeck, 1972). In contrast to the myth of 'hashishim' running amok, is the often witnessed syndrome referred to as "panic reaction", which has likely been confused with aggression and violence in many cases.

Panic Reaction

One of the most common dysphoric responses to cannabis intoxication is what has been called the "panic reaction." "Panic reaction" most often appears as part of an anxiety reaction in relatively inexperienced users, or in those ingesting a higher than expected dose, and is characterised by the appearance of an acute fear reaction sometimes associated with panic connected to the experient's possible, imminent death (Tennant and Groesbeck, 1972). This "panic reaction" typically follows or is followed by an acute paranoid state characterised by mistrust of others and a belief that others have malintent towards the intoxicant. These reactions are generally acute and disappear with the loss of intoxication within hours (Cohen, 1986; Hollister, 1988).

Of this acute panic syndrome, Jones (1980) delineates the possible psychological progression.

> This reaction, which usually starts off with an exaggeration of normal cannabis effects, can range from mild anxiety and restlessness to panic with paranoid delusions, to a full-blown acute toxic psychosis with loss of contact with reality, delusions, hallucinations, and agitated and inappropriate behaviour. The reaction is more likely to occur in inexperienced users or in the user who unknowingly consumes more potent cannabis material than is anticipated. Preexisting psychological difficulties may also contribute. The symptoms usually diminish over a few hours and are somewhat alleviated by reassurance, a quiet environment, and generally supportive atmosphere (p. 71).

Kolansky and Moore (1971) studied a group of 38 subjects who had smoked marihuana twice per week or more, consuming two or more marijuana cigarettes per session. They found that their subjects consistently demonstrated poor "social judgement", poor "attention span", poor concentration associated with confusion, anxiety, depression, apathy, passivity and indifference. These changes appeared to be part of an alteration of consciousness characterised by: 1) a bifurcation of the ego into observing and experiencing selves; 2) an apparent inability of the subjects to bring their thoughts together; 3) a paranoid suspiciousness of others; and 4) a seeming regression to a more infantile state (p. 487). They summarise using a mixture of psychoanalytic and physiological metaphors, which appear to owe more to speculation than to good scientific inference.

> It was our impression in these cases that the use of cannabis derivatives caused such severe decompensation of the ego that it became necessary for the ego to develop a delusional system in an attempt to restore a new form of reality. It would appear that this type of paranoid reaction is a direct result of the toxic effects of cannabis upon the ego organisation of those patients described in this study (p. 489).

However, in this paper Kolansky and Moore (1971) appear to indulge in generalisations concerning the effects of THC which are based on a tiny, psychiatrically referred sample. Any conclusions thus drawn concerning the action of cannabis on the general population commit the logical error of inferring a universal from an existential instantiation. In addition, value judgements are made about their patients throughout which reflect a strong cultural bias in favour of American middle-class professional standards.

> There was marked interference with personal cleanliness, grooming, dressing, and study habits or work or both. These latter characteristics were at times present in some patients prior to smoking marihuana, but were always markedly accentuated following the onset of smoking (pp. 487-488).

There seems to be little introspective awareness on the part of the authors regarding their strong prejudices and value judgements. If science is supposed to be a value-free activity, then this current report does not begin to represent science in either spirit or praxis. These two psychiatrists appear to be blissfully unaware of the cultural changes taking place around them at the time (1968 - 1971) and thus much of their criticism is confounded by their cultural blinkeredness. Further, the appearance of opposite and contradictory symptomologies (some became apathetic while other became hyperactive) in their study group suggests that THC is not a strictly a causal agent of the observed psychopathology, as argued by Weil (1975), but, rather, a facilitator of predisposed conditions.

Negrete *et al* (1986) offers a conceptual description of what might be the underlying psychological mechanisms of the panic, ego decompensation and paranoid ideation sometimes seen in cannabis users. He states that it has been

> ...observed that tetrahydrocannabinol (THC) impairs the rate, sequence and goal directness of thinking; that under the influence of cannabis the individual experiences an intermittent loss of information; that the feed-back and feed-forward perceptive mechanisms - which are essential in the process of reality testing - are upset. In addition, there is a distortion in the sense of time which leads to a telescoping of past, present and future. Unrelated events become peculiarly connected in the user's own 'psychological time'. All these phenomena foster projection and stimulate paranoid ideation (pp. 515-516).

Therefore, the evidence that new or inexperienced cannabis users are prone to panic, paranoid, or anxiety attacks must be seen from the perspective of this effect being largely a function of particular personality types (psychological 'set') and the quality of the 'setting' in which these personalities find themselves when intoxicated. Any substance or situation which is capable of facilitating (directly or as an "active placebo") a fairly radical change in cognitive sequencing and affective states and, hence, an individual's relationship to and understanding of social reality, has the potential of generating panic, anxiety and paranoid states as a response to loss of control and attendant feelings of uncertainty. No doubt this is a danger in the use of

cannabis as well as being a danger when one leaves home for the first time, marries, gives birth for the first time, or starts a new job.

When this type of psychological response does occur, there is, of course, a real possibility of it escalating into a fully fledged psychotic reaction. The literature on cannabis is, in fact, replete with cases and discussions of the relationship of cannabis use and abuse to the formation of toxic psychoses, a subject to which we will now turn.

Cannabis Toxic Psychosis

In 1944 the New York La Guardia study concluded that given a suitably oriented personality, marijuana use could lead, in the right time and environment, to a true psychotic state.[4] Even earlier, however, a physician from British Guyana in 1893 described the symptoms of what he believed to be a cannabis psychosis.

> The cannabis psychosis gives the impression of acute mania or melancholia. Most often the patient is in a state of mania, suffering from delusions and visual and auditory hallucinations. He moves incessantly, waving his arms, throwing himself from one side to another, running up and down in the room, crying and singing. The psychosis might be associated with violent behaviour. Sometimes the patient refuses to eat, sometimes he gets an intense hunger. The state may change rapidly and very soon the patient will recover and seem quite normal again. - But after two or three recurrences, every time triggered by relapses into cannabis abuse, the patient runs the risk of becoming apathetic and blunt. The cases of melancholia triggered by cannabis abuse are more rare. I have, however, observed such cases where the patients have become deeply depressed - to the limit of committing suicide (Tunving, 1985, p. 209).

Imade and Ebie (1991), working in Nigeria, assert that cannabis psychosis "has gained recognition as a nosological entity" (p. 134). According to these authors cannabis psychosis is categorised by the ICD-9 and DSM-III as either a form of drug dependence or an induced organic mental disorder. The diagnostic criteria given include intoxication marked by delusional disorder. The delusional behaviour appears to be caused solely by the ingestion of cannabis and persists for about 2 - 3 hours. Both social and occupational functioning are claimed to show impairment and these reactions, argue Imade and Ebie, "vary according to the socioeconomic class, personality and attitude of the users" (p. 134).

These authors claim that members of lower socioeconomic classes derive feelings of power and self-engrandisement from cannabis use whereas members of the higher status classes perceive cannabis as a relaxant and thus take it to achieve greater calm. In contrast to Imade's and Ebie's position, Brill and Nahas (1984) maintain that "at the present time there seems to be insufficient evidence to state that a purely cannabis-induced psychosis exists as a separate clinical entity" (p. 294). However, the latter two authors do argue strongly that cannabis is psycho-toxic and may precipitate a psychotic reaction.

Whether or not the dysphoric, psychotic-like response of some cannabis users is a "nosological entity", the work of the Nigerian researchers may be over-generalising from the special conditions of their cultural and economic circumstances since there do not appear to be

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[4]Mayor's Committee on Marihuana, 1944, cited in Nahas, 1984, p. 285.

similar sociodemographic differences in response to cannabis reported by researchers in economically more developed countries. In fact, Brill and Nahas (1984) point out that most reports of 'cannabis psychosis' have their origins in the Third World which may reflect a special vulnerability of those people to any toxic substance due to malnutrition with its attendant low body fat and plasma protein concentration in affected individuals.

In addition to the cultural, social and economic mismatches of many reports concerning cannabis induced psychosis, the problem with most of the data reported in these studies is that they are highly confounded and hence not scientifically sound. There is rarely any clear, clinical data on the psychiatric condition of these individuals pre-dating their cannabis 'psychosis' and, hence, no way of assigning cause or any other relationship between use and psychopathology. In addition, the age range in most of these studies is that of young adults which is a common time for the onset of psychotic disorders for non-drug takers as well.

Thornicroft (1990) summarises the possible relationships which may exist between psychosis and cannabis use.

> Previous reviews of the possible association between cannabis and psychosis have proposed six types of association. Cannabis may cause psychoses *de novo*. It may reveal a previously latent psychosis. Cannabis may precipitate a relapse of a pre-existing psychosis. Established psychotic mental disorder may lead to an increased intake of cannabis. There may be a spurious relationship. Finally, there may be no relationship between psychosis and cannabis.
> These views have, however, failed to make three vital distinctions. Firstly, they have not adequately separated organic from functional psychotic reactions to cannabis. Secondly, they have insufficiently discriminated between psychotic symptoms and the syndromes of psychosis. Thirdly, they have not balanced the weight of evidence for and against the category of 'cannabis psychosis' (p. 25).

Further, the symptomatology of the hypothesised 'cannabis psychosis' is very varied and often contradictory, indicating a lack of a true and coherent constellation of symptoms one would expect with an actual definable disorder. The only consistent set of responses appears to be those associated with any toxic brain syndrome whether caused by cannabis or any other neurologically active substance (DSM-IIIR; Weil, 1975). This lack of specificity is underscored by the following sample of symptom constellations given by various modern cannabis researchers including: a) shyness, irritability, hypersensitivity and arrogance with chronic cannabis users being more often alienated from the environment and indulging in day dreams (Stringaris, a Greek psychiatrist described in Tunving [1985]); b) loss of contact with reality, delusions, and hallucinations as well as agitated and inappropriate behaviour (Jones, 1980); c) depression and agitation (Cohen, 1986); d) the occurrence of extravagant ideas such as being 'ageless' (Brill and Nahas, 1984);[5] e) the delirium similar to that of high fever (in its acute toxic phase) which includes confusion, prostration, disorientation, derealisation, and, at times, auditory and visual hallucinations (Brill and Nahas); and f) paranoia and depersonalisation occurring in a manner indistinguishable from acute brain syndrome and a

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[5]This idea, of course, is also the claim of many famous, historical mystics and religious leaders. Cf. Happold (1963).

belief on the part of the subject that s/he is going mad in spite of remaining oriented with unimpaired consciousness (Kaplan, 1971). The above group of symptoms taken with the descriptions given earlier could, in fact, constitute a wide range of conditions ranging from severe anxiety neurosis to true psychotic bipolar affect disorder.

Thacore and Shukla (1976) indicate that patients with 'cannabis psychosis' show panicky and violent behaviour with greater frequency, but they do "not consider this behaviour psychotic, because reality contact is maintained" (p. 385). Further, from my own clinical and personal observations it often appears that many users who are having extreme dysphoric reactions are suffering from the fear of 'going crazy' rather than actually becoming truly psychotic. Thus, it is possible to interpret many of the so-called psychotic responses to cannabis use as extreme panic reactions which have escalated out of control. The force of this argument derives from the fact that a) the vast majority of these cases recover fully when the acute phase of intoxication is past and b) interpersonal support during this process is most often positively and constructively received by the victim in a non-psychotic manner, viz., consciousness is unimpaired thus allowing self-reflection and understanding in rational and non-delusional ways.

Individuals suffering from clinically diagnosed organic or psychodynamically identifiable psychoses do not respond in this manner. The acute phase of psychosis, for the majority of cases, moves into a chronic phase with life-long consequences. With these psychotics the clinician finds it almost impossible to penetrate the patient's delusional, referential thought process and, similarly, positive support appears not to be capable of penetrating the psychotic's world when in this acute phase. This is not to say that such a psychotic episode never happens in association with cannabis. However, it has not been possible, to date, to disconfound the role of cannabis as a conceivable facilitator of psychosis from its other possible roles as self-medication used to treat an impending psychosis or its coincidental use as part of a syndrome of disturbed behaviour in an already troubled individual.

Jones (1980) suggests that the toxic psychotic-like reaction sometimes associated with cannabis intoxication is often caused by unexpectedly high doses in experienced users, the reaction to intoxication by neophyte users, and/or the response of individuals with a pre-existing psychopathology. It has been observed that this "toxic" response is not consistent with cannabis type or potency suggesting no direct, predictable pharmacological link. He summarises the overall state of research into 'cannabis psychosis'.

> As is often the case with clinical reports, studies describing cannabis psychosis rarely present data in a way that would withstand rigorous scientific scrutiny. A number of reports finding no evidence of links between cannabis use and psychoses unfortunately have the same methodologic problems as studies claiming drug-related associations, making it very difficult to draw unequivocal conclusions (p. 72).

Moreau, in his mid-Nineteenth Century writings, seems to recognise that there is a difference between delusional psychosis and "hashish fantasy" which suggests that researchers,

today, may have to delineate, with some precision, this difference before any definable and consistent 'nosology' of extreme cannabis dysphoria can be found. One possible suggestion is that there is no such clinical entity as a 'cannabis psychosis' but, rather, a series of fear and panic reactions which sometimes achieve the intensity of a psychotic-like state. This extreme but temporary response should be understood more as a result of the user's inability to cope with the cognitive and affective reorganisation caused by THC rather than as a direct and permanent "poisoning" of the CNS leading to a permanent psychosis.

Schizophrenia

There have been a number of studies which make a connection between cannabis and schizophrenia. As in the case of reports on toxic psychosis and cannabis, the relationship between cannabis use and onset of pathology is unclear. Again, cause and effect are difficult to establish because of the fact that most cases studied are the result of psychiatric referrals from which only post hoc attributions can be made.

In one of the very few longitudinal studies of cannabis and psychopathology designed to disconfound the aetiology of schizophrenia in relation to cannabis use Andreasson *et al* (1987) studied Swedish military conscripts. Commencing in 1969-70 this investigation used a pre/post research design, which, in its first stage, included obtaining a history of drug use, social background, psychiatric history, a current psychological assessment and, where necessary, a psychiatric interview. In their current paper, reviewing follow-up assessment made fifteen years later, Andreasson *et al* state that, in addition to cannabis consumption, increased occurrence of schizophrenia in the conscripts was strongly correlated with diagnosis of psychiatric disease other than schizophrenia at the time of conscription; indicators of a disturbed childhood; abuse of solvents; and poor adjustment at school. However, in this study no relationship was observed between the increase in schizophrenic occurrences and alcohol consumption, smoking, or socioeconomics.

Although the authors suggest that the association of cannabis usage with schizophrenic onset may possibly be a result of an "emerging schizophrenia", they argue for the interpretation that cannabis is a likely a precipitating factor in schizophrenic onset for "vulnerable" individuals. This conclusion was drawn as a result of the observation of an increasing risk for development of schizophrenia being associated with increasing cannabis consumption in individuals with previous psychiatric symptoms. For the authors, this conclusion is underscored with the additional finding that conscripts with no psychiatric symptoms initially also demonstrate an increased risk of schizophrenia with increasing cannabis consumption. In conclusion, Andreasson *et al* (1987) state

> ...an individual might be vulnerable to schizophrenia but not get the disease unless it is triggered by some life-event stressor. The findings in this study suggest that cannabis may be such a stressor. The effect of cannabis on the central nervous system support this hypothesis (p. 1485).

The effect of THC on the nervous system, they argue, is localised in the hippocampus and is accompanied by a lowered turnover of acetylcholine. However, the more recent and comprehensive study of Herkenham *et al* (1990) reported earlier in this paper appears to contradict this hypothesis of Andreasson *et al* (1987). The distribution of THC in the human CNS is much more diffuse than these authors suggest and, to date, there is no definite evidence that acetylcholine systems in the hippocampus are associated with schizophrenogenesis. In fact, it is more strongly argued that dopamine pathways in the ventral medial brain are more directly involved in some of the 'schizophrenias' (Helmchen and Henn, 1987).

Another problem with the Andreasson *et al* (1987) study is that the causal relationship of cannabis to the onset of schizophrenia still remains equivocal. Although the data appears to be suggestive of a possible link between cannabis and the precipitation of a schizophrenia in vulnerable individuals, the authors go beyond their data by strongly suggesting that cannabis is, nonetheless, another clue to the ***cause*** of schizophrenia. However, even a cursory examination of the literature on schizophrenia (which is beyond the scope of this paper) reveals that the stresses of late adolescence and early adulthood appear to be one of the major precipitating factors in the development of schizophrenia in vulnerable individuals - with or without the use of cannabis. Since this study examined young men of this age group, the relationship of increasing cannabis use with increasing incidence of schizophrenia may be an artefact related to the overall range of deviant behaviours adopted by young men suffering from the stresses of life change for which they are unprepared.

And finally, of the 55,000 conscripts entering the initial phase of the Andreasson *et al* (1987) study, only 274 schizophrenics emerged of which 21 were in the high cannabis consuming group with a total of 49 having ever consumed THC at all. Thus, taken together with the fact that the causal connection between cannabis use and the onset of schizophrenia was still left unclarified, these results should be considered insufficient for drawing any scientifically sound conclusions concerning a meaningful link between cannabis and schizophrenia.

In another large-scale military study of cannabis use carried out on American soldiers Tennant and Groesbeck (1972) found that for the 720 hashish users culled from the 36,000 subjects of the research sample direct medical and psychiatric observation revealed

> that the casual smoking of less than 10 to 12 gm of hashish monthly resulted in no ostensible adverse effects other than minor respiratory ailments. Panic reactions, toxic psychosis, and schizophrenic reactions were infrequent occurrences except when hashish was simultaneously consumed with alcohol or other psychoactive drugs (p. 133).

The authors found 115 cases of acute psychosis analogous to schizophrenia amongst hashish smokers but only 3 were of hashish users only. The remainder were multiple drug users which included amphetamines, hallucinogens and alcohol taken together with hashish. In these cases treatment with chlorpromazine did not entirely resolve the symptoms in these cases and most appeared to move into a stage which resembled chronic schizophrenia. However,

Tennant and Groesbeck (1972) argue that because of the nature of such a soldier sample, they had good access to premorbid records for the entire group. "In each case there was considerable evidence that latent schizophrenia probably preexisted" (p. 134). However, no indication is given in this paper as to how the pre-trial screening was carried out nor is there any evidence of how the criteria for determining pre-morbid latent psychosis was established.

Jones (1980) argues for a partial causal relationship between the onset of schizophrenia and cannabis use. He believes that patients with schizophrenia, or with a genotype for schizophrenia "may be more prone to develop schizophrenic-like psychoses after consuming only modest amounts of cannabis" (p. 72). However, his use of the term "schizophrenic-like" may indicate, as in the case of toxic psychoses, that some of these more extreme but transient negative responses to cannabis have characteristics in common with schizophrenic disorders but are not fully constitutive of the pathology itself. Imade and Ebie (1991), on the other hand, in an empirical statistical study comparing schizophrenic and cannabis psychosis symptomologies, conclude that there is no significant difference between the two groups leading them to speculate that cannabis may be a possible additional risk factor in the development of schizophrenia. Surprisingly, this conclusion of no statistically significant difference in symptoms is contradicted by Table 2 (p. 135) in their published results which shows a statistically significant difference in 9 of the 13 symptom categories presented. One can only speculate as to why the authors draw conclusions in direct contradiction to their empirical findings.[6]

Other researchers appearing to agree with Imade's and Ebie's conclusions concerning the similarity of cannabis psychosis and schizophrenia are Thacore and Shukla (1976). Their study of chronic cannabis abusers in India found a constellation of symptoms some of which are similar to schizophrenia while other are not. Their work indicates that the special characteristics of schizophrenic thought disorder (loosening of association, thought blockage, disturbance in conceptual thinking, alienation of thought) occur statistically significantly more frequently in schizophrenic patients than in cannabis intoxicants suffering psychotic-like reactions. Hallucinations were experienced equally in both conditions but "all (cannabis) patients had predominant persecutory delusions in a setting of clear sensorium" (p. 384) in contrast to schizophrenics who do not show any capacity for rational self-reflection while in an acute phase. Although these findings suggest some fundamental differences between the two conditions, caution must be applied in accepting these results because of the small sample involved and the culturally idiosyncratic method of scoring and interpreting patients' symptoms.

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[6]A possible reason for this apparent contradiction may lie in the sources of funding for cannabis research. Most money comes from government coffers and most governments are in opposition to cannabis use. Therefore, one may conclude that researchers will attempt to minimize findings which do not satisfy the views of their funders in order to insure future support. This may seem harsh, if one accepts the myth of scientific objectivity, but scientists are as competitive as any other group in their attempts to stay in the "game" and to win.

In conjunction with Jones (1980) Hollister (1988) asserts, based on research conducted by Knudsen and Vilmar (1984) as well as by Tunving (1985), that cannabis use may aggravate an already existing schizophrenia, and this would be true whether the pathology was as yet unmanifest, but he is not convinced that THC can cause schizophrenia or depressive disorders on its own. Moreover, referring to Rottanburg *et al* (1982), he declares that cannabis use may lead to "a self-limiting hypomanic-schizophrenic-like psychosis" (Hollister, 1988, p. 112). Again, this statement suggests that the relationship between drug use and pathology may be linked through an as yet unidentified third factor involving the preference by schizophrenics for particular classes of drugs in their attempts at self-medication and thus control of frightening delusional states. Consequently, there appears to be an association between cannabis use by diagnosed schizophrenics which confounds the interpretations of a causal link between cannabis and schizophrenia. Needless to say, the connection is problematic and unresolved and certainly needs considerably more and better controlled research before any firm conclusions can be drawn.

Behaviour and Social Adjustment

Weller (1985) summarises a number of findings across a variety of studies aimed at establishing a profile of cannabis users.

> One study found that marijuana users were more impulsive and nonconforming than nonusers. Another study discovered more "psychiatric impairment" in users based on personality tests. A self-administered drug survey conducted at two colleges found that users were less likely to be at the top of their class, had looser religious ties, and were more dissatisfied with school. They were also more likely to be bored, anxious, cynical, disgusted, moody, impulsive, rebellious, or restless. In still another study, marijuana users were more opposed than nonusers to external control and likely to use the drug to relieve tension (p.101).[7]

He criticises much of this characterisation by arguing that little effort was made to determine the personality types and differences before subjects became involved in a cannabis 'lifestyle'. Thus, it is arguable that any ascription of personality type for cannabis users must be seen as not scientifically grounded and hence somewhat spurious. This logical error of explanations given *post hoc propter hoc* appears to be a commonly repeated one throughout the cannabis literature. However, Weil's (1975) argument that cannabis is an "active placebo" (p. 95) which facilitates already existent covert behaviours and pathologies offers an equally credible explanation for most observations made concerning pathological syndromes and cannabis use with the added benefit of accounting, in part, for the great variation seen from individual to individual. One such constellation of behaviours which has been repeatedly claimed as unique to chronic cannabis users is the so-called "amotivational syndrome" to which we now turn.

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[7]For his summary he draws extensively on Halikas, Shapiro, and Weller (1978).

Amotivational Syndrome

McGlothlin and West (1968) first reported that regular cannabis use can lead to the development of passive, inward-turning, amotivational personality characteristics. At about the same time, Smith (1968) made a similar observation, based on several young marijuana users, that regular cannabis ingestion leads to a loss of desire to compete and work which, like McGlothlin and West, he labelled the "amotivational syndrome". Weller (1985) describes the characteristics associated with this hypothesised syndrome.

> This contention was based on clinical observation of middle-class, heavy marijuana users referred to them for treatment. Conforming, achievement-oriented behaviour had changed to relaxed and careless drifting. Inability to concentrate for long periods, endure frustration, follow routines, and carry out complex, long-term plans, as well as apathy and loss of effectiveness, were noted. Such individuals became totally involved with the present at the expense of future goals. They had less objective productivity and seemed to withdraw subtly from the challenge of life (pp. 95, 98).

He reminds us, however, that no specific studies or case reports were cited to support McGlothlin's and West's (1968) observations. Other descriptors which supposedly characterise this syndrome include: shift or decline in ambition; unproductive, aimless life; poor class attendance; lack of goals; poor school performance; apathy; disorientation; and depression (Weller, 1985). Nevertheless, in most cases symptoms disappeared if marijuana was discontinued suggesting not so much as a syndrome but behaviour of chronically intoxicated individuals using their intoxicated state as a way of focusing their resentment of social and parental pressure.

In addition, Weller (1985) cites a number of studies which report lowered levels of sperm and testosterone. The latter change was observed in a closed ward situation with subjects at first showing no alteration in testosterone levels for about four weeks, followed by a subsequent and gradual drop in testosterone level which continued until cannabis intake stopped. This situation reversed itself on cessation of cannabis intake with levels beginning to rise after one week's abstinence. Weller concludes that "if testosterone affects aggression and drive, low testosterone might affect motivation. However, this relationship must be considered hypothetical without additional research (p. 102)."

Cohen (1986) reminds us that the syndrome is so variable in presentation and influenced by the magnitude and type of premorbid pathology, the very existence of such a syndrome remains quite controversial. On the other hand, lethargy and loss of ambition and goal orientation persist during intervals of withdrawal from cannabis. In many cases this anergic condition is apparently reversed after months of abstinence, but Cohen indicates that some clinicians report what they believe to be the occurrence of permanent brain dysfunction in some subjects. Again, as in reports of other psychopathologies being connected to cannabis usage, the constellation of symptoms tends not to constitute a definite syndrome with great variation being observed in each case.

The symptoms of what is being called "amotivational syndrome" could be understood as a facilitated endogenous depressive disorder which is brought to the fore by chronic

cannabis use in a minority of individuals. Halikas *et al* (1978) reported a high incidence of depressive disorder in regular cannabis users who had smoked at least fifty times in the past six months before the commencement of the study. Weller (1985) indicates that an examination of the subjects of that study reveals that most were young (mean age = 22 years), middle-class and had been smoking cannabis for an average of 2 years. "Systematic evaluation revealed that most of their psychiatric problems predated marijuana use. About 18% had a history of definite or probable depression before significant marijuana use (p. 102)."

It should be borne in mind, once again, that the subjects of many of these studies are referred for treatment and hence do not represent the population of cannabis users. In fact, from the numbers given in many sources, those presenting with psychopathologies of any kind represent a very small minority indeed. For example, the 1991 NCADA survey of drug use in Australia reveals that 30+% of all Australians have tried cannabis at least once. 13.1% have used it within the past year and 5.4% within the last week. Thus, there are hundreds of thousands of cannabis users who apparently function well enough so that they do not come to the attention of medical or legal authorities. If "amotivational syndrome" was a fact of cannabis use, Australian society would unmistakably feel its impact. One can only conclude that this supposed 'syndrome' is, in actuality, the mis-labelling of a latent affect disorder which, in a small minority of unfortunate individuals, becomes manifest when facilitated by chronic cannabis use.

Task Performance

It is not surprising to find repeated assertions in the literature of reduced performance on learning and memory tasks in a population of cannabis users who are available for evaluation largely through psychiatric referral. The pathological symptoms leading to referral most often include agitation (panic disorders) and/or lethargy (amotivation). These symptoms are often primary manifestations of on-going affect disorders and, in the case of depression, are frequently accompanied by feelings of alienation, depersonalisation, flattened affect, memory and other cognitive impairments. A large-scale study by Mullins *et al* (1974) conducted for the United States Air Force on recent conscripts who were, for the most part, young, healthy and not psychiatrically morbid, reveals a different picture regarding performance among cannabis users.

The authors compared 2,842 US Air Force trainees who had used only cannabis with 1,843 who had used cannabis and/or other drugs and with a control sample of 9,368 on whom no drug-using information was available. Comparisons were made on five separate aptitude measures, on educational level attained prior to enlistment, and on three measures of performance of Air Force duties. These aptitude measures are the Armed Forces Qualification Test (AFQT) and four aptitude indexes of the Airman Qualifying Examination (AQE); Mechanical (M), Administrative (A), General (G), and Electronic (E). Comparisons of scores

were made between those who used only cannabis; those who used cannabis in conjunction with some other drug; those who used other drugs singly, but not cannabis; those who used other drugs in combination, but not cannabis; and the control group. It was found that every mean score for the drug using groups was significantly different from the control group at $p = 0.01$ or better. The most interesting finding, however, is that for level of performance "all means are significantly lower than the control mean except the means for the cannabis-only group, which are significantly higher than the control means" (Mullins *et al*, 1974, p. 4)

Mullins *et al* (1974) argue that the differences between the cannabis-only group and the other drug groups in relation to the controls may be the result of the degree of drug use. In other words, multiple drug users are seen by the authors as likely heavy users as opposed to cannabis-only user group. Thus, the lower means for the multiple drug groups are interpreted as resulting from the total overall consumption of drugs rather than the mixing of mind-altering substances. In addition, when controlling for total ingestion of cannabis, the authors conclude that the cannabis-only group is more talented on average (according to the operational definition of talent embedded in the Air Force aptitude tests) than any of the other groups tested. Although the authors argue that the lower scores of the multiple group are likely due to the degree of overall consumption of drugs, they conclude that one of the more notable dangers of cannabis is in coupling it with other drugs.[8]

The authors attempt to explain the results by first observing that the use of other drugs, with or without cannabis, is correlated with lower overall educational attainment in the study's subject group. They continue by noting that there are significantly more cannabis-only users who have graduated from high school (76.4%) than there are in the control group (70.7%), which is offered in partial explanation of the higher aptitude scores achieved by the cannabis-only group. In light of our earlier discussion concerning motivation, both achievement scores and educational level tend to be good indicators of higher motivation in the cannabis-only users than in the other experimental groups and the controls. On the other hand, of those controls and cannabis-only users who entered university, Mullins *et al* found a significantly higher percentage of control subjects (37.5%) than of cannabis-only subjects (24.9%) completed their studies.

Strangely, in summarising their study the authors conclude that this last difference indicates the possible existence of an "amotivational syndrome" in cannabis-only users and, in their final remarks, strongly suggest that cannabis has definite serious, negative effects on behaviour. However, in summarising their findings they state

> ...in general, the use of cannabis-only appears to be associated with a much less serious performance deficiency than the use of other drugs, singly or in combination" (Mullins *et al*, 1974, p. 11)

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[8]However, the authors qualify this statement later on by indicating that it is the heavy use of cannabis in conjunction with other drugs which is most likely the cause of the reduced scores. They fail to make the observation that heavy drug users of any kind, particularly heavy multiple drug users, are very likely to be suffering from some other psychiatric disorder which may affect motivation and/or performance.

This statement can only be seen as a distortion of the empirical findings of these researchers. Except for the issue of university completion rates for the various groups, cannabis-only users in their study appear to be superior in performance on every measure used by the United States Air Force. The authors' conclusion, on the other hand, stresses that the performance of the cannabis-only group is merely less worse than the multiple drug groups rather than better than all other groups. Again, this is an good example of the problems which occur with value-driven research in the investigation of cannabis. No doubt this method of interpretation of the empirical findings arises because it is very unlikely that positive conclusions concerning cannabis use in young airmen would lead to career advancement for members of the military who conduct social science research on their own organisation.

Of course, there have been a number of other studies which have obtained very different results when measuring performance. It should be noted, however, that most of these have been conducted on a more select population than the Mullins *et al* investigation, with considerably smaller sample sizes and often on individuals who have been psychiatrically referred. Cohen's (1986) general review of these issues in relation to cannabis leads him to conclude that

> A wide range of intellectual performance impairment due to marijuana intoxication is known. Cognitive tasks, such as digit symbol substitution, complex reaction time, recent memory and serial subtractions, are all performed with an increased error rate as compared to the sober state. These abilities are all generally recognised to be necessary to perform skilled tasks. Marijuana interferes with the transfer of information from immediate to short-term storage. Less demanding tasks such as simple reaction time are performed as well during the non-drug condition. A major unresolved question is whether long-term use produces irreversible effects (p. 157).

Two confounding issues are generally not critically addressed in the literature on cannabis and performance summarised by Cohen (1986) above. The first is proper control for the role of motivational levels in the outcome of performance tests conducted on cannabis intoxicated individuals. THC may have differential effects on motivation depending on the type of task to be completed. Cohen acknowledges that the apparent attenuation of the ability to learn while intoxicated with cannabis may be due to possible perceptual and motivational changes experienced by intoxicants. He speculates that the concomitant impairment of immediate recall associated with these changes is linked to a lack of motivation to learn and to the related attenuation of logical thinking abilities which makes the acquisition of new information more difficult.

Simply stated from a more phenomenological perspective, while intoxicated, "right brain" activities appear to be preferred by those using cannabis. Logico-deductive cognitions tend to be usurped by metaphoric imaging arising as a result of an intensified 'absorptive state'. "Absorption", a personality characteristic often studied in relation to hypnosis and other altered state of consciousness experiences, appears to deploy attention in ways antithetical to the more usual linguistically ordered information processing of daily life activities (Tellegen and Atkinson, 1974; Tellegen, 1982). Since the majority of memory and

performance tasks used in many of the studies on cannabis and performance are dependent on language processing ("left brain") for recall, it is not surprising that most cannabis users do less well on these tests when intoxicated.

The second issue is, naturally, the notion of 'long' and 'short' term memory employed by Cohen (1986) and others. If we recognise that different styles of cognition and learning are associated with different states of consciousness (Tart, 1972), then the model of memory storage and transfer deployed by Cohen is likely to be inapplicable to the study of individuals in an "Absorptive" state of consciousness. In addition, the statement about information "transfer" as used by Cohen is, at this stage of learning and memory research, more metaphor than fact since the actual neuropsychological substrates and mechanisms of this hypothetical construct have yet to be located and their mechanisms delineated.

Creason *et al* (1981), on the other hand, do attempt to control for motivation in relation to cannabis consumption levels in their study of 55 high school adolescents. From this group four sub-groups were identified consisting of nonusers ("Never"), casual users ("less than once a week" or "once or twice a week"), heavy users ("three or more times a week" or "daily"), and heavy users who are now ex-users (p. 449). Motivation was operationally defined as

> ...the difference between the subject's performance on a task when working for a reward and when the subject is not externally motivated. A subject who performed better working for a reward than when not was considered more motivated than a subject who performed at the same level regardless of whether there was a reward at stake (p. 448).

"The dependent variable was the difference in the number of solved single-solution anagrams between the first and second trials," the assumption being the first trial measured actual ability and the second measured performance level when motivated, with the difference showing the effect of motivation (p. 449). From this research design the authors found that heavy users and heavy ex-users were significantly (statistically) lower in motivation than non-users or casual users, the latter two groups showing no significant difference. The authors thus conclude that the effect of heavy use on motivation is not dependent on the presence of the drug in the user's system. To account for this they hypothesise the existence of an intervening variable, such as a personality factor, which distinguishes those who are high users from low or non-users. In conclusion they argue that there is good evidence in the research literature to suggest that "heavy marijuana use is limited to those who are already inclined to low motivation and depression" (p. 452) Unfortunately, Creason *et al* were not able to assess for any possible pre-existing psychiatric morbidity or personality differences which may have indicated any prior conditions in heavy users before the commencement of their cannabis habit. Thus, there is no empirical evidence arising from this study which is able to support their explanatory hypothesis.

Although there have been suggestions regarding brain damage in cannabis users, as cited earlier in this paper, Varma *et al* (1988) find no evidence of a real difference between users and controls on measures of intelligence and memory. These findings are consistent with two United States Government studies (National Institute of Mental Health, 1972, cited in Rubin

and Comitas, 1975; National Institute on Drug Abuse,1980) in which the authors suggest that any differences found between cannabis users and non-users in cognitive functioning pertain more to perceptuo-motor tasks. However, Varma *et al* (1988) observed that in Indian cannabis users who are not part of a deviant sub-culture, the users still appear to be significantly more disabled in "personal, social and vocational functioning" (p. 151). However, the higher rating of disability in this group of cannabis users did not, in the opinion of the authors, amount to a noticeable difference.

In assessing the work of Varma *et al* (1988) it is necessary to understand that the group studied is the equivalent, in the West, of heavy, chronic drinkers of alcohol. This is underscored by the authors' recruitment of subjects amongst a known group of heavy users whose life-style revolves around congregating together specifically for the purpose of consuming cannabis. In addition, findings of higher 'neuroticism' and 'psychoticism' test scores for these individuals also indicates that they are not average members of the society being studied (Eysenck, 1960).

In effect, this research is confused by the usual problems of personality disorder and psychopathology almost certainly existing in the study group prior to cannabis addiction as indicated by membership in and adherence to a cannabis-based sub-group in the context of a country (India) in which this substance is widely accepted and probably broadly used in other social circles as well. If pathology was not present prior, then such extreme use could be regarded as a cause of the psychological problems (as in the case of severe alcohol abuse). Nevertheless, this cannabis sub-culture is an inappropriate group to estimate the long-term effects of social cannabis ingestion, just as it would be inappropriate to estimate the social, physiological and psychological effects of alcohol by studying chronic, intractable drunks.

In contrast to Varma *et al* (1988), a study by Schwartz *et al* (1989) claims to demonstrate definite adverse effects of cannabis on memory. The latter researchers evaluated the auditory/verbal and visual/spatial memory for groups matched on age, IQ, and absence of previous learning disabilities. The study used 10 cannabis-dependent adolescents and compared them with the performance two control groups consisting of 8 adolescent drug abusers, who had not been long-term users of cannabis, and 9 adolescents who had never used any drug. Significant differences between the cannabis-dependent group and the two control groups were demonstrated on the Benton Visual Retention Test and the Wechsler Memory Scale Prose Passages. The authors also found that, after 6 weeks of supervised abstention from intoxicants, those in the cannabis-dependent group demonstrated some improvement on the Wechsler Memory Prose Passages score and on the Benton Visual Retention Test. This improvement, however, failed to achieve statistical significance leading the authors to conclude that cannabis-dependent adolescents develop selective short-term memory deficits which appear to continue for at least 6 weeks after the complete cessation of cannabis intake.

This last study employs very small numbers of subjects in its experimental and control groups, which makes the results somewhat weak in a statistical sense. Further, in this research

the experimental subjects consumed approximately 900mg/week of THC (18 grams of high-potency marijuana @ 5% THC) which is about equivalent to 130 mg/day for a 4 month period - considerably higher than most heavy users. This level of cannabis was consumed to within a couple of days of end of the trial.

Heavy users, according to a recent survey conducted by the Criminal Justice Commission of Queensland, Australia use about 10 grams of cannabis containing about 2-3% THC, or 300mg of THC/week.[9] The ward study by Schwartz *et al* (1989) referred to here provided subjects with about 900mg THC/week, or three times the amount of *in vivo* heavy users. If the physiological half-life is taken as one week (Cf. Nahas, 1984), then at the end of a 6 week abstinence period following 12 weeks of cannabis ingestion at the rate of 900mg THC/week, the lipid burden of THC will be approximately 28mg THC.[10] Further, if, as revealed in the work of Chesher *et al* (1985), 1-2 mg of ingested cannabis causes a similar level of behavioural deficit as a 0.05 blood alcohol level, then the retest situation in the Schwartz *et al* study is on subjects who are still in a highly THC affected state.

Unlike alcohol, THC is highly soluble in body lipids and it is this property which causes it to remain systemically present much longer than water soluble alcohol. Thus, the resultant levels of THC accumulated by participants in the Schwartz *et al* (1989) study would be extremely high at the end of the first part of the study. With a half-life of 5-7 days it would be many weeks before the serum THC would be at an equivalent zero level for these extremely high-dose subjects. It is quite conceivable, therefore, that the subjects were, at re-test time, still at or above the intoxication equivalent of 0.05 blood alcohol.[11] This, of course, does not include an approximation for the effect of any additional THC remaining in brain lipids which, conceivably, could still be quite high. Therefore, low or zero measures of serum THC do not guarantee that participants in the post-test section of the Schwartz *et al* study are cannabis-free and, hence, the test subjects may still be affected by a low-level, background intoxication.

Returning to the issue of perceptuo-motor and cognitive performance, Chesher *et al* (1985), using nine different tests, attempted to ascertain the effects of cannabis consumption on performance in a controlled study employing individuals in a dose level by time pre- post-drug experimental design. Employing the centroids of the combined test scores for each condition, the authors compared the performance effects of smoked cannabis, orally ingested cannabis, and alcohol with the resulting evidence suggesting that "the duration of impairment produced by all three drugs at the doses used was very similar" (p. 624). However, the earlier findings of Weil *et al* (1968), that some dose-related impairment is observable on simple

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[9]This was a preliminary report released in March, 1993 at a public forum held in Brisbane. It will soon be published by the commission and copies are obtainable through the Criminal Justice Commission, Coronation Drive, Toowong, QLD.

[10]This was calculated using a discrete approximation of a half-life decay.

[11]It should be remembered that 1-2 mg of THC to be consumed is the equivelant of an alcohol blood level of 0.05 (Chesher *et al*, 1985).

intellectual and psychomotor tests for naive subjects but not for regular users, indicates a need for finer elucidation of the observed effects, if the results of Chesher *et al* are to be taken at face value.

Chesher *et al's* (1985) results also suggest that orally administered THC is 4000 times more potent than ethanol in its pharmacological action. Although exact comparisons could not be made between smoked cannabis and imbibed alcohol, it was estimated that 1-2 mg of THC in the marijuana-to-be-smoked produces a decrement in performance equivalent to 0.05 blood alcohol level (p. 627). This finding suggests that, since the average marijuana cigarette contains approximately 1-3 mg of THC, similar restrictions would have to be placed on cannabis consumption and driving as now exist for alcohol.

Hollister (1988) reports a summary of four separate studies in which the occurrence of positive serum tests for drugs in dead drivers involving 2610 fatalities was estimated. Alcohol was found in 1680 cases and THC in 351 with 294 of the latter involving alcohol as well. Of those found with THC, 278 had serum concentrations less than 5mg/ml, suggesting that "THC plays a relatively minor role in fatal traffic accidents as compared with alcohol" (Hollister, 1988, p. 113; McBay, 1986). In other words, only 2.2% of cannabis-only users were involved in these fatal accidents. Of course, the long half-life of cannabinols in the body and the presence of them in blood long after acute intoxication has ceased, as seen from the studies cited above, does not indicate whether or not those individuals who tested positive in the quoted road fatalities were intoxicated.

Cohen (1986) asserts, in his summary of the drug and driving research literature, that 70% of all fatal auto crashes involve alcohol. However, he reports that 37% of the fatal crashes studied tested positive for the presence of serum cannabinols, but these were found mainly in combination with alcohol and other psycho-active drugs with cannabis-only users representing 12% of all those cases involving cannabis. Alcohol was mixed with cannabis in 81% of the cannabis cases and, again, it is impossible to tell, unlike with alcohol, whether those testing positive for cannabinols were in the acute phase of intoxication rather than several days away from last cannabis usage. From his summary of the statistics Cohen therefore argues that

> Although alcohol is the prime cause of automotive accidents, marijuana and cocaine are currently being found frequently enough to constitute potentially significant problems. It is established that marijuana and alcohol have additive effects upon driving skills. Since marijuana metabolites were found in more than a third of the drivers, impairment due to marijuana is contributing to the problem (p. 158).

The above research likewise is confounded by the presence of alcohol in the majority of cannabis cases. In order to support Cohen's contention, data would be required to show that accidents are increasing, in any given demographic area, in direct proportion to the increase in use of drugs such as marijuana and cocaine while simultaneously controlling for alcohol use. Without such clear-cut quantitative relationships one must still conclude that alcohol is the primary cause of fatal crashes even where other drugs are present. Again, the findings of THC metabolites in 37% of the drivers involved in fatal crashes do not indicate that these

individuals were intoxicated with THC at the time. However, the data may be suggesting that there is an increased danger when driving on alcohol for cannabis users even post acute intoxication. Whether the hypothesised additive effect of THC and alcohol is a fact and/or whether this effect happens post acute cannabis intoxication remains to be elucidated through carefully controlled research which has not yet been done.

Weil (1975), although writing in the early 1970s, still provides a useful and insightful summary of research on cannabis and performance.

> Because marihuana is such an unimpressive pharmacological agent, it is not a very interesting drug to study in a laboratory. Pharmacologists cannot get a handle on it with their methods, and because they cannot see the reality of the nonmaterial state of consciousness that users experience, they are forced to design experimental situations very far removed from the real world in order to get measurable effects. There are three conditions under which marihuana can be shown to impair general psychological performance in laboratory subjects. They are: (1) by giving it to people who have never had it before; (2) by giving people very high doses that they are not used to (or giving it orally to people used to smoking it); and (3) by giving people very hard things to do, especially things that they have never had a chance to practise while under the influence of the drug. Under any of these three conditions, pharmacologists can demonstrate that marihuana impairs performance (p. 86).

Most altered states of consciousness, such as those produced in hypnosis, meditation and ecstatic experiences, involve deployment of attention strongly in the present. This 'unreflected', unself-conscious attentional state, which is focused primarily in the 'now', will, whether induced by drugs or not, possibly interfere with the normal memory processes associated with the 'reflected' conscious state required for discursive thought and logico-temporal activities usually associated with memory and learning. Thus, any discussion of memory and THC use must consider the possibility that THC facilitates a free-floating 'absorptive' state which favours engagement in spatial-metaphoric cognitive styles of the 'unreflected' state (Fabian and Fishkin, 1981). It is thus possible that the apparent memory deficits seen in individuals intoxicated with THC, who are being required to perform and attend to verbal, temporal, logico-deductive activities, is the result of 'time-sharing' between the two states. The effect is to interrupt the usual cognitive and memory consolidation processes.

This 'time-sharing' process can be conceptualised as a temporary and rapid movement out of the induced 'unreflected' state of consciousness into 'reflected' consciousness when enough 'demand' is made to attend to a temporal, discursive information stream. As soon as demand falls below some critical threshold required for attention, the 'unreflected' state resumes thus disrupting any on-going learning process. The laying down of short-term memory and the ability to attend accurately to objective (clock) time may require a certain level of continuous background 'self-observation' - a primarily 'reflected' state activity. Therefore, assigning the cause of memory deficits measured in THC intoxicated individuals to the pharmacological action of cannabis may be an attribution error with cannabis being primarily a catalyst for these altered states which are the actual cause for a failure to process discursive information in the usual way.

Conclusions

Although this review has ranged over a rather broad area encompassing a number of different research disciplines, there appears to be a common concern linking most of the research reviewed - is cannabis a significant public health risk? It is the opinion of this author that this question is still, after almost thirty years of research effort, unclarified.

In the physiological domain there certainly appears to be reasonably strong evidence of the potential threat to the human respiratory system associated with chronic, heavy cannabis smoking. However, whether use amongst moderate, social cannabis smokers poses the same risk is a question as yet unanswered. This risk is, of course, from the combustion by-products of the cannabis leaves, stems, and flowers and is not directly associated with the active ingredient for which cannabis is sought and used, Δ-9-tetrahydrocannabinol. One method for obviating such a health risk would be to make pharmacologically pure forms of orally ingestible THC available to those who want it in a similar manner to the way in which governments now regulate the production and distribution of alcohol.

In general, the results of much of the research concerning the effects of THC on the CNS appears to be either negative or inconclusive. The work of Heath and colleagues is an exception, of course, but as was shown above, this research is highly confounded and cannot be considered to be reliable in spite of the fact that it is widely quoted in scientific and other literature on cannabis.

Turning to the psychological dimension, the "amotivational syndrome" appears to be a not very useful hypothetical construct which is poorly grounded in empirical psychological data. The populations studied in this type of research are often psychiatric referrals and it has been revealed in other, more methodologically thorough research, that supposed sufferers of cannabis-induced "amotivational syndrome" often had signs of clinical depression prior to their use of cannabis. As argued earlier in this paper, "amotivational syndrome" appears to be a category seeking content, especially when the profile of individuals studied is better understood through the more conventional psychiatric diagnostic category of depressive disorder. Nevertheless, there is little doubt that cannabis has some effect on behaviour and performance. Driving a motor vehicle while intoxicated with cannabis will certainly increase the risk of an accident. However, the apparent 'permanent' changes to memory and performance as demonstrated in some 'ward' studies are not entirely convincing considering the exaggerated dose levels used and the long half-life of THC in humans.

Studies in performance and aptitude such as that by Mullins *et al* (1974) highlight the value-driven quality of much of the research reviewed here. When the effects of alcohol and other drugs are controlled, cannabis-only users apparently show significantly greater overall aptitude than any other group amongst U.S. Air Force recruits. Nevertheless, this did not stop

the authors from sounding alarms concerning the potential harmful effects of cannabis on performance in young men. In fact, it appears as if most of the research reviewed by this author commenced from an *a priori* position that cannabis is dangerous to human health, physiological and psychological, it only remains to discover just how dangerous. In pursuing these objectives authors such as Brill and Nahas (1984) breached all current good scientific practice by using the writings of a Nineteenth Century physician to make a supposed empirical case in the late Twentieth Century without any apparent recognition on their part of the potential for misinterpretation or misapplication.

It appears as though two possible hypotheses are available regarding cannabis and public health. The first is that cannabis is a potential public health problem, it merely remains to be discovered to what degree. The second states that cannabis represents no significant or unreasonable threat to the general public well-being. According to the physicist, James Jeans (1958), expanding on William of Occam's 'Razor'

> When two hypotheses are possible, we provisionally choose that which our minds adjudge to be the simpler, on the supposition that this is the more likely to lead in the direction of the truth. It includes as a special case the principle of Occam's razor - 'entia non multiplicanda praeter necessitatem' (p.183).

From the position of this widely held scientific principle it is arguable that only the second hypothesis is reasonable regarding the current debate on cannabis. From the use levels observed in Australia (31.9% have ever tried cannabis and 7.1% (1.3 million Australians) use it once a month or more [Department of Health, Housing and Community Services, 1991]), when taken in conjunction with the very small number of cases who actually come to the attention of medical authorities as a direct result of cannabis use, one can only conclude that the simpler hypothesis which covers the facts is that cannabis use does not pose a significantly increased risk to public health over and above many other activities which are considered necessary and/or socially acceptable.

As suggested by Weil (1975) altered state experiences appear to be a natural human capacity which can be facilitated by the ingestion of psychoactive substances such as THC. The negative reporting, vis-à-vis cannabis and performance, may be understood as a value judgement regarding what type of mental state and hence style of performance is deemed useful by society. In other contexts, the present-centred altered state of consciousness, which can be induced by cannabis, is highly prized in the contemplative religious traditions of Christianity, Buddhism and Islam. The ability of this altered state to open broader perspectives and, hence, new life meanings appears to be part of a growth process which has the power to bring about personal renewal and relieve psychological suffering. Although these religious traditions have developed methods for achieving these altered states without the use of pharmacological facilitators, the need for such experiences is probably innate to human personality. In the age of high-tech medicine the use of chemical substances to achieve these ends should not be surprising.

The psychiatrist Arthur Deikman (1982) suggests that the bifurcation of consciousness into "observing" (objective) and "experiencing" (receptive) selves is the basis of mystical experience with the latter, 'unreflected' state, too often missing in our lives. He further reminds us that without the cultivation of the "experiencing self" we may fail to enter into mystical awareness and therefore be unable to heal the psychopathology innate to our human condition. He thus argues for a return to mysticism as both outlook and technique in the process of human growth.

> The mystical tradition has been concerned with the very problems that modern psychotherapy has been unable to resolve. It makes sense, therefore, to investigate mysticism with a view to dealing more effectively with those problems and gaining wisdom as human beings (p. 4).

Finally, it has been suggested by numerous renown philosophers and psychologists that without the ability to enter wholly into these "experiencing" altered states, we may fail to fully actualise our human creative and cultural potentials (James, 1936; Jung, 1960; Maslow, 1968; Wilber, 1977). Thus, we may understand the use of cannabis in society not only as a public health issue, but as a sign of a fundamental but unfulfilled human need, which cannabis users attempt to fill by use of the drug, albeit inadequately.

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