The Effects of Marijuana Smoking on Human Subjects: a Literature Review

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THE EFFECTS OF MARIJUANA SMOKING ON HUMAN SUBJECTS: A LITERATURE REVIEW

BY

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B.S., Virginia Polytechnic Institute and State University, 1975

SPECIALTY PAPER

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This paper is a critical review of current research on the effects of marijuana use in human subjects. The first three sections provide basic information on the pharmacology of marijuana, the methodological difficulties in marijuana research, and the subjective effects associated with its use. The main body of the paper deals with psychological and physiological effects separately. The intent of this division is to simplify discussion of the literature, not to suggest an actual dichotomy of effects. Since the physiological actions of marijuana in the nervous system are largely responsible for the observed psychological effects, the two groups of effects are interrelated. However, some physiological effects (e.g. carcinogenic potential, lowered intraocular pressure) appear to have no direct bearing on the behavior of the marijuana user. These effects are briefly summarized in the concluding pages of the physiology section. The topics of primary interest are the psychological effects of marijuana use and the physiological basis of these effects.

The cultivation and utilization of marijuana has a long history. Its use as a medicinal agent was first recorded in 2737 B.C., in a pharmacopeia written for the Chinese Emperor Shen Nung (Lieberman & Lieberman, 1971). Despite this extensive history, there have been relatively few attempts to study its intoxicating effects in a scientific manner. Of
the research conducted in the first half of this century, the most extensive investigations were those of the La-Guardia Commission in New York and the U.S. Army in Panama. The conclusions of these studies were suspect on the grounds of inadequate experimental procedures and the persistent pharmacological difficulty of standardizing the dosage administered to subjects when the psychoactive ingredient of marijuana was unknown and the percentage present in the plant apparently varied widely. In the last fifteen years, knowledge of marijuana's chemical structure has increased and as a result, the pharmacological problems in research methodology have been resolved. At the same time, marijuana's growing popularity as a recreational drug has brought the government under pressure from both proponents and opponents of the drug to assess the potential risks associated with marijuana smoking. Toward this end, the government has eased the legal obstacles to research by contracting to provide authorized researchers with adequate supplies of marijuana of known potency. The most reliable information available on the psychological effects of marijuana smoking on human beings comes from this recent research and forms the basis of this paper.
PHARMACOLOGY AND METABOLISM

This section is comprised of a short discussion of the botanical characteristics, pharmacology, and metabolism of marijuana. Its intent is to provide basic background information for the studies in later sections and to discuss, in a rudimentary fashion, the metabolic basis of marijuana intoxication. More extensive discussion of the physiological aspects of marijuana, such as tolerance, will be addressed later in this paper.

Marijuana is derived from the Indian hemp plant, Cannabis sativa L. There are numerous morphological and chemical differences in the plants grown from seeds of different varieties, making it probable that the species has not yet stabilized. The plant is a herbaceous annual which matures in four to five months and grows in temperate and tropical climates throughout the world. Although some hermaphroditic variants are reported, distinct male and female plants are the general rule for Cannabis sativa subspecies. Contrary to popular belief, there is no significant difference in drug content between mature female and male plants (National Commission on Marijuana and Drug Abuse, 1972, pp. 16-20).

The psychoactive ingredients of marijuana are contained in resins produced by the plant to protect it from the sun,
In tropical climates, plants produce more resin and are consequently more potent (Talbott & Teague, 1969). Drug content of the plant parts is variable, decreasing in the following order: bracts, flowers, leaves. Virtually no active material is present in the stems, seeds, and roots (Commission, 1972). Because of this variability, marijuana preparations produced by crushing portions of the plant have an extremely wide range of potency due to the fluctuations in the resin content of the plant and the proportions of different plant parts present in the mixture. The most potent marijuana preparation is called "hashish" and is produced by collecting the resin from the flowering tops of the plant. It is this substance which has been analyzed to determine the psychologically active chemical constituents of marijuana.

The chemistry of marijuana resin is quite complex and isolation of the psychoactive ingredients did not occur until 1964. These ingredients are members of a family of chemicals known as the cannabinoids. A great variety of these chemicals are present in the resin, including cannabinol, cannabidiol, cannabigerol, and numerous carboxylic acid analogs of these compounds. The compound believed to be the principal active agent is an isomer of tetrahydrocannabinol known as levo-delta-9-trans tetrahydrocannabinol. Due to the use of two different numbering systems in organic chemistry, some studies state the name of this compound with the prefix "delta-1" rather than "delta-9". There is another isomer,
delta-8, which appears to have some psychoactive potential but it appears in very small amounts and does not seem to be as active as delta-9. For convenience, this substance will be referred to in the remainder of this paper as THC (Report of the Secretary of HEW, 1972, pp. 134-141).

The nature of THC has an additional capacity for variable potency because it is a product of reactions among other cannabinoids and is an unstable compound (i.e., changes structure easily). During aging, a process called decarboxylation occurs which converts cannabidiolic acid into cannabidiol; this is in turn altered by intramolecular condensation to produce the active isomers of THC. With more time, THC converts by spontaneous dehydrogenation to cannabinol. Consequently, the potency of marijuana changes with age (Grinspoon, 1977, p. 48). To further complicate the issue, analysis of marijuana has not been completed; additional compounds are being found and there is evidence that they may join synergistically with THC to augment its effects (Commission, 1972).

Isbell, Gorodetzsky, Jasinski, Claussen, von Spulak, and Korte (1967) estimated that THC is about two to three times more potent if it is smoked rather than ingested. When THC is taken orally, a portion of the dose is probably inactivated in its passage through the gastrointestinal tract. An additional loss of potency is apparently due to
the fact that the process of converting cannabidiol to THC is accelerated by heat; such a conversion does not occur during ingestion (Commission, 1972). Smoking provides a more direct route of administration, with the THC entering the bloodstream through the alveoli (air sacs) within the lungs; very little drug is lost in combustion as the THC evidently becomes a gas in advance of the burning portion of the cigarette. However, inefficiency does occur in this mode of administration due to the escape of smoke into the air and its exhalation from respiratory dead space. As a result, dose delivery may range from twenty to eighty percent, with most experienced smokers averaging fifty percent (Hollister, 1971).

Through the use of radioactive labelling techniques, researchers have been able to observe human metabolism of THC within the body. Lemberger, Weiss, Watanabe, Galanter, Wyatt and Cardon (1972) determined that the metabolism of THC proceeds in two phases. The initial rapid phase involves distribution of the substance to the body tissues and its metabolism by the enzymes of the liver. The size and quantity of the blood vessels serving an organ are the principal determinants of the amount of THC it receives. The brain receives a large amount quickly, as do the liver, spleen, lung, and kidney (Secretary of HEW, 1972, pp. 164-176). Within ten minutes after smoking, metabolites of THC appear in the
bloodstream; chief among these substances is 11-hydroxy-THC (Lemberger, et al., 1972). Other studies indicate that this metabolite is equal to or more potent than its parent compound (Snyder, 1971). The structure of this metabolite appears to be responsible for an uneven distribution of material within the brain, with the frontal and visual cortex areas being most affected, and accompanying concentrations appearing in the cerebellum, hippocampal, and amygdaloid areas (Secretary of HEW, 1972). The peak level of intoxication, or "high" is temporally correlated with the peak blood plasma levels of THC metabolites. Conversion of THC into metabolites occurs more rapidly in experienced users than in nonusers (Lemberger et al., 1972). This phenomenon may be related to the increased drug sensitivity that experienced users often exhibit. Given this evidence it seems likely that 11-hydroxy-THC supersedes delta-9-THC as the primary psychoactive agent during metabolism.

As metabolism proceeds, 11-hydroxy-THC is converted in turn to inactive substances and removed from the bloodstream over a span of two to four hours; these metabolites tend to concentrate in the bile and leave the body in the feces. Some of the drug may remain unchanged in the bile and be re-absorbed in the intestine so that it returns to the liver for conversion. Conversion and excretion conclude the first phase (Commission, 1972, pp. 26-28).
The second phase occurs as THC retained in body tissues is gradually released and metabolized. Virtually all THC is converted into metabolites in the process. THC has a plasma half-life of 57 hours for non-users and 28 hours for users (Lemberger, Tamarkin, Axelrod & Kopin, 1970). This is another indication of the development of drug sensitivity with regular use. The majority of THC and its metabolites is excreted in the urine and feces in the three days following intoxication; however, remnants have been detected in blood samples as much as a week or more after a single large dose (Secretary of HEW, 1972).

With the isolation and synthesis of THC, it has become possible to perform toxicity studies with accurately quantifiable dosages. While precise generalization from these studies is difficult due to differences in modes of administration and types of animals used, one statement seems to be firmly supported: the ratio of lethal dose to effective dose is very large. For example, it has been hypothesized that to achieve lethal intoxication, a man weighing 154 pounds would have to smoke almost three pounds of marijuana containing one percent THC on a single occasion. This is roughly 250,000 times more than the average dose of a typical smoker (Commission, 1972). Human overdoses seem to occur most frequently among inexperienced users and those who have orally ingested the drug (Secretary of HEW, 1972). Common physical
symptoms reported include respiratory difficulty, nausea, dizziness, sedation, and tachycardia (rapid heart rate) (Secretary of HEW, 1972; Weil, 1970). Although fatal intoxication is apparently rare, Nahas (1971) has reported that an individual in France experienced a coma lasting four days induced by smoking a large amount of a tobacco-hashish mixture. A reported fatal cannabis intoxication occurred in Belgium. Circumstances surrounding this death are unclear, but autopsy and toxicological evidence support the hypothesis of death by cannabis intoxication.

Summary. Marijuana is a preparation of crushed flowers bracts, and leaves produced by the Indian hemp plant. The plant grows readily in a variety of climates and locations and its resin content determines its potency. This potency is also affected by the mixture of plant parts, the aging of the material, and the method of administration. Delta-9-THC appears to be the principal active ingredient, although it may interact with other chemical constituents of the plant to produce effects. There is evidence that 11-hydroxy-THC, a polar metabolite of Delta-9-THC, is primarily responsible for marijuana's psychoactive properties. Although the major activity of the compound is completed in a matter of hours, THC and related compounds remain in body tissues for several days after intoxication until they are eventually excreted in
feces and urine. The acute lethal dose of marijuana is very large; however, overdoses have been reported, including a recent report of a fatality apparently due to cannabis intoxication.
Methodological Problems in Marijuana Research

Marijuana research with human subjects poses particular problems related to the controversial social phenomenon of marijuana use and the nature of the drug itself. The polarity of opinion on marijuana use tends to promote experimenter bias. Lack of agreement on the operational definitions used in determining the effects of marijuana is another problem. Additionally, random sampling of a population engaged in an illegal practice is a difficult procedure. If the problems of experimenter bias, operational definition, and random sampling are surmounted, the problem of assuring the delivery of an accurate dosage of THC to the subject still remains.

Early in the planning of a study, the researchers involved must formulate an experimental hypothesis which can be used as a predictor of the study's results. Naturally, these researchers will select hypotheses which coincide with their understanding of the problem at hand. In this case, the problem is marijuana use. Marijuana use is a complex, controversial phenomenon. The opponents and proponents of marijuana engage in heated debate over almost every conceivable facet of its use. In such a charged atmosphere, the scientist is usually expected to be the neutral party capable of finding the facts and quieting the confusion. However, the
scientist is still a human being possessing a variety of values and beliefs. When these beliefs guide the scientist's research, the understanding of the problem can be distorted by experimenter bias. If an experimental hypothesis is selected which owes philosophical allegiance to one side of the debate, the design of the experiment and the results derived from it may be manipulated in order to support the hypothesis.

Selectivity can bias some studies, particularly those dealing with subjective data. For instance, a researcher may select statements for a questionnaire which are phrased in positive or negative tones. Tart (1971) formulated his questionnaire on subjective effects using descriptions of effects gathered from interviews with users: the result was a survey containing statements which were largely positive or neutral in tone. One positively-toned survey statement was "I empathize tremendously with others, ... I have a tremendous intuitive understanding of what they're feeling". This statement was endorsed by 83 percent of the respondents. Interpretation of this data would have to take this factor into account. Selectivity can also occur after the experimental data is acquired. By skillfully manipulating data and placing differential emphasis on the results, the researcher may use some findings to support the original hypothesis and minimize the importance of divergent findings from the same experiment (Goode, 1970, pp. 50-66).
Biasing of data may take more subtle forms than selectivity. Labelling is one form of subtle bias. Clearly the same base of information can be combined with labels of varying emotional "charge". Some words have an inherent negative connotation. Using these words in describing experimental results may evoke images for the reader which have little relationship to the actual events being described. For example higher doses of marijuana have a noticeable effect on visual perception; this effect is variously described as: "colors, images" (Tart, 1971); "hallucinations" (Keeler, 1968); "psychotomimetic effects" (Isbell et al., 1967). In clinical studies, Talbott and Teague (1969) used the term "toxic psychosis" to describe the condition of some soldiers in Vietnam; Weil (1970) favored the term "panic reaction". The labelling process is a very effective form of bias. The design and results of the study show no overt tampering, which maintains scientific credibility. Consequently, the study lends an air of empiricism and rationality to the emotional convictions underlying it (Goode, 1970, pp.50-66).

Not all marijuana research suffers from experimenter bias. Many other problems in experimental design are evident in a review of the literature. One persistent problem is lack of adequate operational definitions. Researchers investigating the same field may report seemingly
contradictory results because their studies were based on slightly different experimental models; the existence of two similar models leads to a confusion in terminology so that two researchers use the same term to refer to different elements of the phenomenon under study, or vice versa. Such confusion is apparent in a review of research on THC and memory. One group envisions human memory as divided into a permanent storage element called "long-term storage" (LTS), an intermediate element called "short-term storage" (STS), which transfers some of its contents to LTS, and an encoding element called "immediate memory". Another group divides memory into the two elements of long-term and short-term storage, subsuming immediate memory into the latter element. The differences seem minor, yet they result in diverging claims and considerable confusion. Darley, Tinklenberg, Roth, Hollister and Atkinson (1973) acknowledged STS impairment but locate the deficit in immediate memory. Dornbush, Fink and Friedman (1971) place the impairment in STS; using procedures which seem similar to Dornbush, et al., Gianutsos and Litwack (1976) attribute the difficulty to impaired transfer into long-term storage (LTS). If the terms employed by the researchers were more carefully defined within the context of their experiments, the ensuing confusion produced by conflicting conclusions could have been prevented.

Differences in operational definitions are also a
problem in the evaluation of other research. Cognitive processes, for example, is a general psychological activity comprised of a variety of relatively distinct functions. In conducting research on cognitive processes, marijuana's effect on cognition is defined experimentally as the score on a test of cognitive function; there are many tests of this kind and the degree to which the score on any one measure of a specific function reflects overall cognitive efficiency is open to question. The Digit Symbol Substitution Test (DSST) is considered a test of cognitive function (Weil, Zinberg, & Nelsen, 1968), and so is the Goal-Directed Serial Alternation Task (GDSAT) (Melges, Tinklenberg, Hollister & Gillespie, 1970). However, the results achieved with these tests appear to make contradictory statements about THC and cognitive function because of the differences in the abilities being assessed by each test. Operational definition is a pervasive problem in the areas of memory, cognition, and personality.

Sampling is a difficult problem in marijuana research. It is impossible to draw a random sample of marijuana users, as no list of all users is available (Goode, 1970, p. 313). Unlike heroin use, which tends to separate individuals into addicts and experimenters, marijuana use spreads across a broad continuum from the chronic heavy user to the person who smoked once and quit. Distinguishing categories of use with-
in this range is an arbitrary procedure. Sampling to examine marijuana effects is further complicated by the tendency among the heavier users to use several other drugs, notably LSD and amphetamines (Goode, 1970, pp. 184-185). The questionable reliability of the drug history data supplied by such polydrug users has been noted in several sources.

Lacking a comprehensive list of potential subjects, researchers draw samples from nonrandom populations, commonly from groups of college students and those people who respond to advertisements in the newspaper. These individuals have a variety of reasons for volunteering to participate in marijuana research. These reasons could include receipt of a small fee or credit for a college course. Some potential subjects may have a desire to prove marijuana is harmless or to prove it has no effect. This is a problem, as subjects with these attitudes might affect the results (Zinberg & Weil, 1970). Another obstacle to sample collection is the illegality of marijuana smoking; if the local legal authorities object to the research, potential subjects become scarce. A fine example of this problem is presented in a study by Lord (1971). Local police sought to learn the identities of Lord's subjects, rendering direct contact between experimenters and subjects practically impossible. By using young confederates to find subjects, Lord was able to administer his tests surreptitiously. Unfortunately, all he
learned about his sample besides their test scores were their respective sexes and ages; he knew nothing of their drug histories, college rank, socioeconomic level or other pertinent personal data, and he knew equally little about the setting in which the test was taken, the skills of his examiners, and the subjects' frame of mind at the time of the testing (Lord, 1971, pp. 24-26). Legal interference precipitated a loss of control over sampling, setting and procedure, making the findings of this study practically useless.

Establishing a control group also poses problems. Comparison of frequent marijuana users and nonusers is potentially treacherous because these are two populations which probably differ on more variables than marijuana use alone (Greenfield & Sternbach, 1972, p. 151). Differences in personality have been shown to produce differences in drug response (Wolman, 1965, p. 1308), and there is evidence of personality differences between users and nonusers (Zinberg & Weil, 1970). If the lifestyles of the two populations is markedly different, additional error may be introduced by factors of diets, physical activity, use of prescribed medications and amount of sleep. Many factors can affect drug response and matching all of them except for marijuana use is unlikely (Greenfield & Sternbach, 1972, pp. 789-790).

A pretest-posttest design would seem to provide the necessary control. Each subject would be tested twice, once as
as a control and once as an experimental subject; however, this presents other problems. At the present time, there is no simple, convenient test for marijuana intoxication. THC can be detected in the blood, but this would require the taking of blood samples and extensive analysis. If this procedure is not performed, the only assurance that the experimenter has that the subject is "straight" (not under the influence of THC) when he is in the control condition is the word of the subject. The necessity of two trials separated by time introduces a greater possibility of error due to external variables (diet, sleep, etc.), as well as the possibility of data lost as a result of subjects failing to appear for a second trial. The experimenter must schedule subjects for trials at the same time of day to minimize the effects of the subjects' circadian rhythms and must be aware of possible practice effects on the tests. Some experimenters have tried to control the effects of prior drug use, eating, and time of day by having subjects abstain from drugs for a day before testing and then reporting to the laboratory in the morning before eating. The weaknesses of this approach lie in the inability to test for compliance and in the length of the abstinence period. If THC can be detected in the bloodstream after three days or more (Lemberger et al., 1972), terming a subject "drug-free" after one day is questionable.
A common practice in marijuana research is the use of placebo control for the purely psychological effects of smoking marijuana. The National Institute of Mental Health (NIMH) provides excellent placebo material in the form of marijuana from which the THC has been removed. The material maintains the appearance and characteristic odor of marijuana but contains no significant amount of the active ingredient. Some researchers have used other, less satisfactory placebo. Two examples of substitute placebos are oregano (Dornbush et al., 1971) and coltsfoot (Pihl, Hickcox & Costa, 1977). The efficacy of these placebos is proportional to their similarity to the actual drug and to the gullibility of the subjects in the study. If the placebo is detected its power as a control element is impaired.

After dealing with all the problems related to research with marijuana, the researcher must deal with the idiosyncratic nature of the drug itself. The variable potency of the drug has already been discussed. NIMH puts great effort into standardizing research marijuana, attempting to maintain a constant of 1.5 to 2 percent THC content (Secretary of HEW, 1972, p. 136). They also keep their raw batches and extracts refrigerated until distribution to prevent deterioration. However, if individual researchers do not follow suit, the dosages they administer will be less than calculated (Caldwell, Myers, Domino & Merriam, 1969b).
Method of administration must be decided. Oral ingestion has the advantages of allowing an extended testing period and easy placebo procedures but the THC ingested does not undergo decarboxylation as it would when smoked and may be trapped in the intestinal mucosa. Potency is thus lessened to an unpredictable extent. There is also the predictable disadvantage of a prolonged latency of onset.

Intravenous administration of THC results in rapid onset of drug effects and allows accurate control of dosage, making it ideal for some studies. However, it presents definite difficulties for psychological studies. Subjective effects differ according to the type of solvent used in preparing the solution for injections (HEW, 1972, p. 204). In addition, some people will react negatively to the use of a hypodermic syringe (Greenfield & Sternbach, 1972, p. 790). Chronic users seem particularly anxious about injections and other overtly medical procedures (Zinberg & Weil, 1970).

Inhalation of marijuana smoke is the method most commonly employed in a social setting. The inaccuracy of this procedure for laboratory study has been previously discussed. Any attempt to estimate dosage must take into account the smoker's technique. Attempts to standardize the technique have been made, alternate smoking systems have been devised, but the inherent inaccuracy of this method remains a confounding variable.
An alternative approach to the problem of dosage accuracy utilizes the subjective report of the smoker, rather than the amount smoked, as the criterion of intoxication. Meyer, Pillard, Shapiro and Mirin (1971) allowed subjects to smoke until they reached their "usual" level of intoxication. While this may seem to be a feasible way to examine marijuana's effects at "social" doses, the procedure introduces far too much variability in dosage for serious research. Between-subject variability would be expected, as would within-subject variability due to differences in immediate set (i.e., the subject's expectations, attitudes, and emotional state at the time of testing). The degree of subjective intoxication can be affected by seemingly minor variables. For example, a study by Cappell and Pliner (1974) showed that the size of the cigarettes smoked by subjects can have almost as much influence on subjective intoxication as the actual amount of THC consumed. Since some effects may be dose-dependent, rather than subjective, the possible variability of doses in this type of study would produce significant variability in measurement of these effects.

Perez-Reyes, Timmons and Wall (1974) used as their constant an elevation of heart rate to 25% above baseline; however, this was a physiological study. Inconvenience and differential sensitivity to tachycardic effects across individuals would probably make such a measure unsuitable
for use in a behavioral study. Still, a preliminary pulse rate measurement might be a useful check for intoxication in a pretest-posttest design; subjects would be tested only when their heart rates were at or near baseline levels prior to administration of drug or placebo.

There has been some concern about whether the relatively sterile laboratory setting would limit the applicability of this data when the social setting seems to play such a significant role in the perceived effect of marijuana. The experience of a subjective high seems to depend upon or vary as a function of the social setting. Hollister, Overall and Gerber (1975) examined this question using two settings and two different measures of subjective effects; the Subjective Drug Effects Questionnaire (SDEQ) and the Addiction Research Center Inventory (ARCI). One setting was a laboratory, the other was the living room of a private home outfitted to be comfortable for smokers. They found that the different settings had no significant effect on reported subjective high. Carlin, Post, Bakker and Halpern (1974) attempted to influence levels of subjective high and performance of five tasks by having a confederate model "stoned" behavior for a sample of forty subjects. A verbal learning task was significantly affected by modeling; the remainder of the tasks and the ratings of intoxication were unaffected. Carlin concluded that the effects of experimental settings are not significant in
most cases; that the element of previous experience with marijuana plays a much stronger role in determining reactions to marijuana in the laboratory. Both studies support this contention, but the presence of one significant finding on the verbal learning task in the Carlin study raises the possibility that resistance to laboratory-induced confounding is not uniform across all aspects of the marijuana experience.

Even if the effect of the laboratory is totally innocuous, researchers remain at the mercy of uncontrolled variables in their subjects' environment which may affect their drug responses. One way to minimize these variables is the use of a research ward to house all subjects while the experiments are going on. This is seldom done because of the prohibitive expenses involved. There are other drawbacks as well: Environmental constancy is a boon for some studies, but it can become sheer boredom for subjects and adversely affect other studies. In addition, interpersonal friction may develop during a long-term experiment. Finally, there are problems with maintaining control over drug use. Mendelson, et al. (Commission, 1972, pp. 68-103) conducted a study on a research ward which extended for 31 days: 5-day baseline (no marijuana or other drugs); 21-day experimental period (marijuana available); 5-day post-experimental period (no drugs available). All smoking was done in the presence
of an observer in order to ascertain amount used and to pre-
vent hoarding. In spite of the precautions taken by the
investigators, examination of the ward during the segment of
the study employing heavy users as subjects revealed not
only marijuana but a small quantity of hashish. These were
evidently being saved for the 5-day postsmoking period, but
could have been used at any time. Obviously, the research
ward serves a useful purpose, but it should not be seen as
the perfect setting for marijuana research.

One final methodological consideration concerns the
statistics used to analyze the effect of marijuana on per-
formance. Marijuana has been reported to increase vari-
bility of a subject's performance over a number of trials
his subjects as experiencing "intermittent lapses in atten-
tion". Most statistics used in experiments are measures of
central tendency, rather than degree of variance. If such
variability exists, then the performance of one individual
or even a small group of individuals on a test with a small
number of trials may not be representative of the effects of
marijuana in the general population. If the present stat-
istical methods are to be retained, then researchers would
be well advised to deal with larger samples and, when poss-
ible, larger numbers of test trials to counter the varia-
bility induced by the drug.
Summary. A review of literature on marijuana research with human subjects reveals numerous methodological difficulties. The problems include experimenter bias, confusion stemming from differences in operational definitions, non-random sampling, lack of control over numerous external variables, dubious placebo measures, and persistent difficulty in delivering an accurate dose of the drug in a manner that does not induce spurious effects in itself. There is also some question about the applicability of laboratory findings to the world outside the laboratory; this question of applicability stems from the nature of the statistics used in evaluating performance and the possible influence of the laboratory setting on performance.

Fortunately, not every study suffers from all of these flaws. Dosage and nonrandom sampling are probably the most pervasive problems, followed by operational definitions. The primary means available for administering marijuana to humans are ingestion and inhalation, and these are both inherently inaccurate. An experimenter can deal with this by calculating the administered dose to achieve a desired range of delivered dose. If an experiment is designed to measure effects of different dose levels, then the administered dose must be different enough that the likelihood of significant overlap between adjacent delivered dose ranges is small. Nonrandom sampling is unavoidable in marijuana research at
this time, but some studies will be less affected by this problem than others. Sensory and psychomotor tests are probably less affected by sampling bias than memory and cognition tests. While the possibility of a substantial basic difference in the sensory and psychomotor capabilities between user and nonuser populations, or college and non-college populations, must be admitted, it seems highly unlikely. The presence and severity of other flaws varies from study to study. Careful planning in selection of a sample large enough to minimize the effects of individual variability and uniform execution of experimental procedures seems to produce dependable results. Laboratory setting exerts a negligible effect in most cases and the present statistics are capable of dealing with the data if they are gathered properly.

At the risk of being redundant, many of the studies to be discussed are flawed. Some are more flawed than others. Despite their flaws, these studies provide the best information presently available on the effects of marijuana smoking on human subjects. Hopefully, an examination of both the findings and the flaws in these studies will cause a fairly reliable picture of these effects to emerge.
Subjective Effects

The behavioral changes observed in an individual as a result of marijuana intoxication are rather subtle. Users often report that their intoxication goes unnoticed by others (Grinspoon, 1977; Tart, 1971). The findings of Pihl et al. (1977) lends partial support to this contention. He showed forty observers, selections balanced for sex and previous experience with marijuana, a series of videotapes depicting a group of four individuals interacting after all four had smoked a placebo cigarette, a low dose of marijuana or a high dose of marijuana. The low dose was felt to be roughly equivalent to the amount used by smokers to attain their usual "high". At this dose level none of the observer groups correctly detected intoxication. On the other hand, all groups made correct discriminations of the high dose condition, with experienced observers being more successful than inexperienced observers.

For the first-time user, the dosages commonly used produce psychological changes so subtle that they are barely discernible to the individual, if he notices them at all. Marijuana folklore cites the rarity of the "first-time high" and experienced users usually advise novices that multiple experiences are necessary in order to become high. In a questionnaire study conducted in the Los Angeles area, two
hundred fifty-four people who had smoked marijuana gave information regarding their initial experiences, frequency of use, and reasons for initial use. Only sixteen percent claimed to have experienced the full effects at first usage, while fifty-nine percent claimed no effects at all (Burns & Sharma, 1976).

The reports of subjective effects vary in tone and content due to a number of factors. One factor is the bias of the reporter toward the drug, positive or negative; another factor is the amount of the drug taken and the method of administration, ingestion or inhalation (Isbell et al., 1967). Tart (1971) lists five other variables which can affect the level of intoxication. These are: long-term characteristics of the user; immediate expectations regarding the experience; past experiences with psychoactive drugs; immediate emotional state; and the social and physical setting in which intoxication takes place.

While marijuana can be cooked and ingested, often as an ingredient in brownies or cookies, it is usually smoked in a cigarette or pipe. Effects from smoking appear rapidly and last from two to four hours; effects from ingestion generally take an hour or more to appear and last from five to twelve hours. Aside from differences in latency of onset and duration of intoxication, the effects seem to be roughly similar. There appears to be a short period of post-smoking
anxiety accompanied by some general restlessness lasting ten to thirty minutes followed by the development of a calmer, more euphoric state. Time sense is distorted, with short periods of time seeming much longer. Dryness of the mouth and throat occur, resulting in thirst which is often accompanied by hunger and increased appreciation for the taste of food (Grinspoon, 1969).

Tart (1971) conducted a questionnaire survey of young marijuana users, mostly living in California to acquire information about the nature of subjective responses to the drug. This sample (N=150), which was intended to be drawn from a population of experienced marijuana users, has several sources of potential sampling bias, including sex (the male-to-female ratio being two-to-one), high educational level (only seven percent had no college training), and use of more powerful psychoactive drugs (seventy-two percent had used LSD-25 or a similar agent at least once). Attempts to assure response validity within the sample were made, and the results seem to agree with and elaborate upon the conclusions of previous studies. The Tart study is useful not only in testing the range of subjective effects in this sample of users, but also in providing some notion of their respective frequencies of occurrence.

The effect on sensory perception is best described as one of increased meaningfulness. Visually, objects seem in
sharper focus, perspectives are more pronounced, colors seem brighter, and patterns appear in sets of objects where there had previously been no pattern. Auditory effects are similar; sounds are more distinct, music played over a stereo system appears to have greater spatial separation, subtle changes in music become discernible to the listener. Taste and smell are affected in the same manner. Tactile perception is generally enhanced while perception of the body itself seems to vary; some report increased awareness of the body, others report feelings of disembodiment, while still others report that attending to a specific body part or function brings that body part into sharp focus while the rest of the body fades away (Tart, 1971).

Almost all respondents in the Tart study report an impairment of their memories during intoxication. They report that forgetting what one is saying in mid-sentence is a frequent occurrence; paradoxically they still feel capable of maintaining an intelligent conversation. Confusion as to whether one has made a statement or performed a task rather than merely thinking about such an act is common. In contrast to such short-term difficulties, many report the recall of distant memories during intoxication.

Cognitive processes during intoxication place less emphasis on sequential logic, acts and consequences, and tend instead toward immediacy of experience, free association and
imagistic thinking. Users are less perturbed by contradictions and more inclined to embrace intuitive conclusions to problems (Tart, 1971). Many users find the cognitive aspects of their experiences particularly enjoyable. They titrate their dosage to reach a manageable level of "high" and then "maintain" themselves; that is, they attempt to forego the immediate pleasures of intoxication and concentrate on the pursuit of intellectual, psychological, or spiritual insights (Grinspoon, 1977, p. 186). Others appreciate subtle humor in conversations and see new meaning in commonplace phrases. Virtually all feel capable of "coming down" at will if it becomes necessary to perform some task requiring all of their cognitive ability (Tart, 1971).

While the predominant mood experienced during intoxication is euphoric, users report that other emotions are experienced more intensely than usual. Some users report an amplification of mood; if they feel good, they feel better after smoking; if they feel bad, they then feel worse. The general attitude toward the immediate environment and those who occupy it is one of calm acceptance with little or no desire for control. The amount of interpersonal communication varies among individuals, but understanding of others seems enhanced to all. Many feel a certain camaraderie within the smoking group and speak of their level of
intoxication being increased by the presence of others higher than themselves.

There is less general agreement among users about the effects of marijuana on sexual activity, although the majority report feeling in closer mental contact with their partner during intercourse and that the physical act is more enjoyable. Slightly over half of the Tart sample claim heightened sexual drive with marijuana. However, three-fourths of the sample feel that they become sexually aroused only in situations which would normally arouse them, and it is in these situations that their arousal is heightened.

Relaxation seems to be a pervasive quality of intoxication. The user is disinclined to engage in physical activity. Those who do, however, feel that their movements are fluid and well-coordinated. A substantial number also report restlessness and a desire for activity; this is a minority and it is difficult to determine in the context of the Tart study if this is a different reaction to the drug or a reference to the initial restlessness often noted at the onset of effects. Drowsiness followed by sleep apparently terminates most smoking experiences (Tart, 1971).

The minor alterations in sensory perception associated with social doses apparently become more pronounced at higher doses. Isbell (1967) and his associates demonstrated
this intensification of effects in a study using high and low dosages administered by both ingestion and inhalation. They found that higher dosages distorted perception to the extent that visual and auditory hallucinations occurred, although they did not describe the nature of these hallucinations. Keeler (1968) reported cases of vivid color and design hallucinations to apparently minimal stimuli (i.e., blank walls) with high dosages; individual dosage ranging from four to eight cigarettes. Instances of phantasmagoria - the sensation of objects rushing toward the observer or rushing away - are cited in Grinspoon (1977, p. 146). According to the same publication (p. 146), subjects have reported seeing "flying masses of color" after smoking hashish. Users in the Tart survey reported the development of visual images or colors associated with the sounds they were hearing. Use of other more powerful psychoactive drugs, such as LSD-25, increase the probability of such effects during marijuana intoxication and also increase the probability of "flashbacks" during which a user experiences the spontaneous recurrence of marijuana effects without the use of the drug (Keeler, 1968; Weil, 1970; Bialos, 1970).

Most individuals who smoke marijuana experience a degree of paranoid ideation at some time. Their suspicions may range from trickery on the part of their cohorts to an imminent police raid (Tart, 1971; Keeler & Moore, 1974).
Keeler and Moore considered paranoia to be an accurate description, as fifty-four percent of their subjects reported that they were convinced that they were the targets of trickery or a police raid.

Reactions to these phenomena - hallucinations, flashbacks, paranoia - are dependent on the variables of dosage, set, and setting. While paranoia is by definition unpleasant and apparently has a high incidence in the smoking population, it is evidently short in duration, low in intensity, or low in frequency for the majority of individuals. To whatever extent it occurs, it seems to have little dissuasive affect on smokers. Hallucinations and flashbacks are upsetting to some; others deem them pleasant and actively seek to experience them. The term "adverse marijuana reaction" has been coined to encompass those instances in which the variables of dosage, individual characteristics and expectations (set), and environmental factors before, during, and after consumption (setting) combine to induce an experience unpleasant enough to necessitate clinical intervention. (Bialos, 1970).

The majority of adverse reactions occur in neophyte users. One possibility is the simple depressive reaction: this occurs mainly in obsessive-compulsive individuals who felt ambivalent about trying marijuana or placed great emotional emphasis on their decision to smoke. In
interviewing these patients, Weil (1970) felt that they used marijuana as an excuse for depression rather than experiencing a psychopharmacological precipitation of their condition. Of the twenty cases seen by him, all resembled transient neurotic depressions and all cleared spontaneously. The most common adverse reaction is a panic reaction. In this reaction, the subjects misinterpret the psychological and physiological effects of the drug as evidence that they are dying or losing their minds. Depending on the dosage, set, and setting, the anxiety may become so incapacitating as to simulate acute psychosis. This can be exacerbated by the setting of a hospital emergency room; the subjects' presence in the emergency room, combined with the actions of the doctors and nurses, provide substantiating evidence that their condition is as bad as they suspect (Weil, 1970). The most extreme cases of panic may be seen in reports from the Vietnam war. In this situation, extreme vigilance was emphasized, the possibility of death was very real and could come in many forms and at any moment, and the marijuana accessible to the soldier was roughly twice as potent as any available in the United States. Approximately half the marijuana sold was laced with opiates as well. Talbott and Teague (1969) diagnosed twelve soldiers stationed in Vietnam as experiencing acute
toxic psychoses after initial exposure to Vietnamese mari­
juana; Weil (1970) considered these "acute panic reactions" but agreed with the previous authors that the peculiar set and setting of Vietnam contributed significantly to the symptoms. Panic reactions are generally alleviated by re­assuring the patient that the effects being experienced are transient; occasionally sedation is necessary. It is poss­ible that the symptoms of the soldiers seen by Talbott and Teague were prolonged by their being treated as psychotics (Weil, 1970).

As previously mentioned, sufficiently high doses of marijuana will cause most individuals to experience psycho­tomimetic effects, including hallucinations and paranoia (Isbell, et al., 1967). Use of unusually high doses seems to precipitate the majority of adverse reactions in experi­enced users. Unexpected effects occur, and the users react with varying degrees of anxiety. This anxiety may also be triggered by a flashback, a spontaneous recurrence of effects. For the most part, these people recognize the transient nature of their experiences and can tolerate the effects if they are given reassurance (Bialos, 1970). Flashbacks seem to diminish in intensity and frequency with time and seldom reappear if the individual abstains from marijuana (Weil, 1970).

The evidence regarding the existence of a "cannabis
psychosis" is unclear. Much evidence comes from Eastern countries, such as India, Morocco, and Egypt, and its relevance to usage in North America is questionable for a number of reasons. The preparations used are much more potent and sometimes mixed with opiates, first-rate psychiatric staff and institutions are a comparative rarity, and diagnostic procedures are often questionable. Upon examination of diagnosis in India, for instance, one group of investigators discovered that the diagnosis of "hemp insanity" had usually not been made by a physician, but by a referring policeman or magistrate (Secretary of HEW, 1972, pp. 234-244). Grinspoon (1977, p. 261) points out that Eastern populations are often poorly fed and subject to a high incidence of chronic illnesses due to overcrowding and poor sanitation; these health factors undoubtedly influence their reactions to a wide spectrum of drugs, including marijuana. However, there appears to be a slow accumulation of evidence in the United States and Western Europe supporting the existence of an "acute toxic psychosis" which parallels in some respects the Eastern reports of a cannabis-induced psychosis (Commission, 1972, pp. 47-50). Symptoms include anxiety, confusion, paranoid ideation, depersonalization, tachycardia, dyspnea, delusions and visual and auditory hallucinations. The subject's history appears free of any underlying disorder prior to onset (Talbott & Teague, 1969). Kroll
(1975) found that onset usually occurs early in an individual's usage history, a time span ranging from a few days to a few months; however, his patients were stationed in Thailand and his results must be weighed with the high potency and dubious purity of the marijuana being used kept in mind. Weil believes that overdoses leading to acute toxic psychoses happen most frequently when the material is ingested orally, whereas the excessive smoking of low-to-moderate potency marijuana seems to promote sedation rather than hallucination. It may be that certain toxic constituents are altered or eliminated by smoking and retain their efficacy during ingestion, as Weil suggests. However, this does not account for reports of toxic psychoses related to smoking of high-potency material (Commission, 1972). Therefore, it seems more likely that there is a dose-time relationship operating to produce the psychosis: A large amount must be inhaled or ingested in a short span of time to produce toxic effects. The time-consuming procedure of smoking enough low-potency marijuana to precipitate toxic psychosis probably precludes its being done rapidly enough for a toxic level to be reached. Acute toxic psychoses are self-limited and usually clear in a few days or a few weeks (Secretary of HEW, 1972).

In addition to acute toxic psychosis, there appears to be a small percentage of individuals who suffer psychotic
decompensations some months after the use of marijuana or another hallucinogen despite having no prior psychiatric history. It is unclear in these cases whether the relationship between the drug and the disorder is causative to some degree or simply correlative (Weil, 1970). In subjects with past psychiatric histories, marijuana use apparently aggravates psychotic tendencies and may provoke a functional psychosis (Commission, 1972; Kroll, 1975). Weil found that a high percentage of those who disliked the effects of marijuana had been diagnosed as ambulatory schizophrenics at some time and tended to shun marijuana after an initial experience with it.

One other set of acute effects to be mentioned is an extremely rare one. This stems from the relatively infrequent employment of intravenous injection as a means of marijuana use. The material is boiled in water, then injected into a vein. Compared to the careful laboratory preparation of THC for injection, this procedure is extremely crude and the solution produced is unsafe for intravenous use. The results of injection are apparent within fifteen to thirty minutes and include chills, cramps, vomiting, diarrhea, peripheral anesthesia, blurred and double vision, tachycardia, and low blood pressure. Medical examination reveals gastroenteritis, toxic effects on the liver and kidneys, and changes in blood chemistry. These effects
seem to clear within a few days to a few weeks (Payne & Brand, 1975; Pugsley & Henderson, 1968). Detailed accounts of the psychological effects were not obtained since the physical symptoms required immediate attention and medical aid.

In conclusion, the acute subjective effects of marijuana are heavily dependent on the interaction of the variables of dosage, set, and setting. They are also influenced to a degree by method of administration. At the dosages commonly employed in this country, those experimenting with the drug probably experience little or no effect as a result of their initial use. At the same dosage levels, experienced users undergo mild alterations in perception and cognition, enjoy a sense of relaxation and well-being preceded by a short period of anxiety and restlessness, and must contend with impairments in short-term memory and a tendency toward suspicious thinking. Higher dosages intensify effects to the point of inducing hallucinations and possible paranoia; the extreme endpoint of this range appears as acute toxic psychosis. Depression and panic sometimes occur among novice users; the chronic user may also experience anxiety if unexpected effects appear. Marijuana tends to exacerbate existing psychotic tendencies and may trigger a psychotic episode in a premorbid personality. Injection of a homemade marijuana solution,
an act rarely performed, has resulted in intensely unpleasant physical effects; the psychological effects are unknown.
Objective Psychological Effects

Perception

Altered sensory perception is an effect of marijuana consistently reported by its users. Effects on visual function have been of particular concern to researchers. Many tasks involve a substantial visual component and drug-induced impairment of vision in these instances could lead to serious consequences. The first researchers in recent years to examine the effect of marijuana on visual functions were Clark and Nakashima (1968) and Caldwell, Myers, Domino, and Merriam (1969a). Neither group reported any significant effects upon visual acuity. The validity of the findings is questionable in view of the absence of control over dosage in both studies.

More recently, well-controlled studies have shown a similar lack of significant findings. Dosages ranging from 2 to 8 mg. of THC have been smoked and oral doses up to 23 mg. (varying in proportion to body weight) have been ingested with no measurable effects. For comparison, a cigarette containing 500 mg. of 1% potency marijuana contains 5 mg. of THC and roughly half the material will be lost in the smoking process. At these dosages, marijuana has no significant effect on static visual acuity (the ability to focus on a stationary target) (Brown, Adams. Haegerstrom-Portnoy, Jones & Flom, 1975; Milstein,

Static visual acuity is only one aspect of visual function, and the results on other measures have varied. Adaptation to darkness is unaffected (Moskowitz, et al., in Lewis, 1972) while glare recovery time is lengthened significantly for several hours after smoking (Secretary of HEW, 1972, p. 219). Kasachkoff (1974) found no significant decrement in the capacity to detect distortion in a straight line when subjects were given marijuana. However, the possibility that this capacity may be diminished at higher dosages is not excluded by this study, since no effort was made to provide a precise dose to each subject. In a well-controlled study, Adams, Brown, Haegerstrom-Portnoy, Flom, and Jones (1976) found that smoking 8 mg. of THC had no effect on color vision, whereas 15 mg. significantly reduced color discrimination in the blue region of the spectrum with a second region of impairment in the red to yellow-red hues. This impairment follows a short time-course with normal vision returning within 1½ hours.

One test which has been cited as providing evidence for marijuana induced perceptual sharpening makes use of the critical flicker fusion (CFF) threshold. In CFF, a subject observes a pair of rapidly flashing lights. On an ascending trial, the frequency of the "flicker" is
increased, and flashes are perceived as a steady beam. The descending trials ask the subject to determine when the apparently steady light begins to flicker. The CFF phenomenon was first examined by Clark and Nakashima (1968). Their findings were nonsignificant, but the question of dosage arises with this finding as it did with visual acuity. In a study using a larger sample (N=31), uniform dosage and a timed smoking technique, Schwin, Hill, Goodwin, and Powell (1974) found that subjects who had smoked 15 mg. of THC were able to observe flashes at a significantly higher rate before reaching fusion. A more recent study by Peters, Lewis, Dustman, Straight, and Beck (1976) disputes this, having found no significant difference. Resolving the discrepant findings is very difficult because there are many methodological differences in the two studies which may account for the conflicting results. The samples differ in size, (N=31 vs. N=20), sexual representation, (100% male-Schwin vs. 50% female-Peters), and amount of smoking experience. Peters et al. administered THC orally in doses ranging from 10 to 50 mg. in contrast to the 15 mg. maximum inhaled by the subjects of Schwin et al. There is also some question as to amount of information gathered. Schwin et al. gave ten pairs of ascending and descending trials before and after drug, while Peters et al. failed to state number and types of trials. Further study of this topic will be
required before a definite conclusion can be drawn regarding the effect of marijuana on CFF.

In performing a study of signal processing demands and marijuana, Moskowitz, Sharma, and McGlothlin (1972) noted incidental reports by subjects that the central stationary light in their testing device seemed to move. This led to formulation of a study specifically designed to examine the effect of marijuana on the visual autokinetic phenomenon (Sharma & Moskowitz, 1972). Twelve male subjects were employed; they were reported to have had a minimum of ten prior experiences with the drug and their frequency of use at the time of study was reportedly once a week or less. Marijuana was smoked according to a timed procedure with dosages adjusted for body weight. Dosages ranged from 0 to 200 micrograms per kilogram. Results revealed a dose-dependent increase of apparent movement with the two highest doses (100 and 200 micrograms) producing results significantly different from placebo. Apparent movement followed no consistent pattern, but varied from one subject to another.

The search for an explanation of increased autokinesis due to THC led to an intensive study of basic visual functions (Moskowitz, Sharma & Shapiro, in Lewis, 1972). A sample of twelve male subjects with smoking histories similar to the sample used in the autokinesis experiment was
assembled. Once again the doses were adjusted for body weight. However, oral administration was chosen in this case rather than inhalation; a dose of 310 micrograms per kilogram was calculated to be roughly equivalent to the previous smoked dose of 200 micrograms. Tests of static visual acuity and dark adaptation found no effects, as previously mentioned. Tests of oculomotor function, the capacity to move the eyes, revealed that marijuana had a significant detrimental influence on lateral phoria and abduction. Lateral phoria is a measure of the position the eyes assume relative to each other when presented with two different targets; an impairment would diminish the subject's capacity to focus on a target moving laterally across the field of vision. Abduction is a measure of the capacity of the eyes to maintain single binocular vision on a target as it appears to move away from the subject; impairment would mean that objects moving away from the subject would become blurred at a point closer to the subject.

Corroboration of marijuana's effect on the oculomotor system can be found in several other studies. Brown, Adams, Haegerstrom-Portnoy, Jones, and Flom (1975) found that dynamic visual acuity, the ability to track a moving target, was significantly diminished when subjects smoked 15 mg. of THC. Performance was more variable at the 8 mg. level, with some subjects showing improvement over pretest performance.
Berger (1972) demonstrated impairment of depth perception under both the oral and inhalation methods of administration using a sample of twenty-four male subjects. In clinical practice, Coleman, Tacker, Lemmi, and Britton (1976) examined twenty chronic heavy marijuana users who complained of frequent headaches. In this instance, chronic use was defined as "...ten or more days a month for more than a year..." and heavy use as "...more than six 'joints' per day". All proved to be experiencing paresis of the oblique superior muscle on one side, producing impaired lateral phoria and abduction. Using the previous definition of chronic and heavy marijuana use as a selection criterion, Coleman, Evans, and Britton sought more subjects in other facilities and eventually screened twenty-three additional subjects. 82.6 percent of those screened proved to be experiencing the same oculomotor difficulty. Bloomquist, (1968, p. 99) reported a case of oculomotor paralysis lasting a week after an eighteen-year old male orally ingested cannabis indica, a botanical relative of marijuana. Coleman, et al. speculated that these effects might be due to the action of THC upon the fourth cranial nerve; of all the cranial nerves, the fourth is the longest, the least myelinated, and contains the fewest fibers. Also, its sole function is control of the ocular muscles. Thus it appears as the most likely site for THC to act upon to produce the
observed deficits. Coleman et al. estimated the prevalence of the observed specific paresis of the superior oblique muscle to be about five percent in the general population. No control group was tested to confirm this estimate. Still, the high prevalence of the disorder in the subjects screened subsequent to the initial group examined, combined with the laboratory evidence of similar impairment for short periods at high dosages, lends some credence to the speculation that chronic heavy use of marijuana may have serious adverse affects on the visual system.

Auditory research has not been pursued to the extent of visual research. Caldwell et al. (1969a) reported an apparent decrease in the capacity to discriminate between tones of differing intensities, but interpretation of this finding is difficult due to methodological flaws in the experiment. The reported difference was between an experimental group and a separate group; the pretest-posttest difference for the experimental group on this measure was nonsignificant. The dosage smoked was low and was allowed to vary according to subject preference. The mean amount of marijuana smoked was 483 mg.; potency was estimated between 0.5% and 0.2% making the THC content between 2.4 mg. and less than 1 mg. (Caldwell et al., 1969b). In a well-controlled study, Martz, Sunday, Rodda, Brown, Kiplinger, and Forney (1972) employed double-blind procedures to
administer either placebo cigarettes or cigarettes designed to deliver 50 micrograms per kilogram of THC to eight male subjects. Both ears were tested separately in counterbalanced order across test sessions in a range from 125 to 8000 Hz. No significant differences in auditory thresholds were found at any of the six octave-intervals studied.

Cutaneous sensation and its logical extension, cutaneous pain, have been subjected to study by two teams of investigators. These teams arrived at divergent conclusions. Although there are differences in the samples employed by the respective studies, both studies were carefully performed and the observed differences seem unlikely to account for the divergent findings. One likely explanation is to be found in the different methods of cutaneous stimulation employed. Hill, Schwin, Goodwin, and Powell (1974) performed their measurements with electric stimulation, while Milstein, MacCannell, Karr and Clark (1974) used heat and mechanically induced pressure. Pain researchers commonly find that results may vary depending on the means used to induce pain.

A second factor contributing to the divergence was dosage; both teams employed a smoking device designed to aid in uniform administration, but they burned different amounts of raw material. Hill et al. found that smoking 14 mg. of THC resulted in increased sensitivity to both nonpainful and painful electrical stimulation and diminished pain tolerance.
Milstein et al. utilized four different objective measures - absolute thresholds of pain and sensitivity, two-point tactile acuity, tactual fusion, thermal pain - and found no change in cutaneous sensitivity and pain after subjects smoked 8 mg. of THC. A later study (Milstein et al., 1975a) at the same dosage found increased tolerance to pain induced by pressure on the thumb. This confusion should be alleviated by experiments on cutaneous sensitivity and pain which utilize multiple THC dosage levels and, if possible, both electrical and nonelectrical stimulation.

Research in the area of THC and sensory perception is incomplete in many respects. Visual function has received the most attention. Generally, effects of THC seem to be minimal, although there seems to be potential for damage to the oculomotor system from chronic or heavy marijuana use. Difficulty in tracking a target, depth perception, and glare recovery could pose an indirect danger to those who drive while intoxicated. Auditory research has yielded little evidence of an effect of THC on hearing, but few studies have appeared in the literature. The senses of taste and smell have been unexplored, probably due to the difficulties of measuring these senses. Tests of cutaneous sensitivity and pain have shown significant levels, but the exact relationship of THC to cutaneous experience is uncertain until further studies are performed.
Attention

The construct of attention has elicited considerable interest among those studying marijuana. Much of the evidence gathered about the effects of marijuana on perception, memory, and cognition seems to be explainable in terms of attention. Three theoretical models which attempt to explain the relationship of marijuana and attention have been proposed. This section will examine these theories and the evidence supporting them.

The hypothesis that attention played a role in affecting the results of perceptual experiments with marijuana was developed as an outgrowth of a series of experiments by Moskowitz and his associates. The observation of increased autokinesis in marijuana-intoxicated subjects by Sharma and Moskowitz (1972) noted in the previous section, was experimental confirmation of anecdotal information received in a study of peripheral vision (Moskowitz, Sharma & McGlothlin, 1972). In the peripheral vision study, a subject was seated facing a central light and required to note the appearance of lights which appeared briefly at points throughout the visual field; twelve subjects and four dose levels were used. To distract the subjects, the central light blinked in some sessions. Error rates increased significantly with increases in dosage and processing demands. A test of auditory signal detection under conditions of divided and
undivided attention revealed similar results (Moskowitz & McGlothlin, 1974). After examining the effects of marijuana on visual acuity, Moskowitz, Sharma, and Shapiro (in Lewis, 1972) concluded that the minor impairments they found were insufficient to account for the results found in their previous work on peripheral vision and autokinesis. They suggested that the problem underlying visual and auditory decrements was impaired vigilance due to "...momentary lapses of attention" (Moskowitz, Sharma & McGlothlin, 1972). The hypothesis of central attention deficit also appears in studies of marijuana and memory impairment. Abel (1971c) concluded that the deficits in memory induced by marijuana were due to inadequate rehearsal in short-term memory and cited "...inability to concentrate..." as the reason. Tinklenberg, Meldes, Hollister, and Gillespie (1970) cited "...intermittent lapses in attention..." to account for memory impairment in their subjects. In a direct examination of vigilance under two levels of attention demand, Sharma and Moskowitz (1974) found that marijuana reduced initial vigilance at both levels and vigilance decreased over time.

An attention-related factor bearing on marijuana induced decrements is impaired time sense. Subjective reports of slowed time sense have been confirmed in many studies (Andrew & Bentley, 1976; Butler, Gaines & Lenox, 1976; Hollister & Gillespie, 1970; Mendelson, et al. in Commission
1972, p. 84; Vachon, Sulkowski & Rich, 1974; Weil, Zinberg, & Nelson, 1968). Melges, Tinklenberg, Hollister and Gillespie (1970) found that marijuana intoxication was correlated with a diminished subjective capacity to distinguish past, present, and future time periods.

Melges et al. (1970) stated that impaired attention and time sense were the major factors interfering with goal-directed cognitive behavior; they cited as evidence the marijuana-induced decrement on the Goal-Directed Serial Alternation Task (GDSAT). In this task, a subject was assigned a starting number between 106 and 114 and asked to alternately subtract 7 and add 1, 2, or 3 until reaching an exact goal between 46 and 54; the subject was required to recite operations aloud, and the scoring took errors and time required into account. In order to perform well, a subject had to keep track of the goal number, current total, the operation to be performed next, and the amount to be added or subtracted. Lowering of scores on this test after marijuana use appears consistently and in proportion to dosage level (Butler, Gaines, & Lenox, 1976; Casswell & Marks, 1973; Melges et al., 1970). According to Melges et al., GDSAT scores fell because subjects experienced difficulty in distinguishing between operations already performed and those yet to be done. Combining this evidence
with results obtained from their subjective indexes; these researchers formulated the hypothetical construct "temporal disintegration" to account for a number of marijuana's psychological effects.

In describing temporal disintegration, Melges et al. use the analogy of movie film. Conscious activity is viewed in frames, one succeeding another. Sequential thinking requires the coordination to obtain information from a previous frame, transpose it into the frame being viewed, and direct activities in that frame toward arriving at the next frame. A lapse in attention due to marijuana can leave the user confused about the position in the sequence that has been reached. This accounts for the decrement seen in complex tasks such as GDSAT and Serial Subtraction of Sevens (SSS) (Casswell & Marks, 1973). It would also account for the common finding that simple reaction time shows little impairment under marijuana, but this impairment increases with the increasing complexity of the reaction time paradigm (Braden, Stillman, & Wyatt, 1974; Clark & Nakashima, 1968; Clark, Hughes & Nakashima, 1970; Moskowitz, Shea, & Burns, 1974; Peeke, Jones & Stone, 1976; Peters, Lewis, Dustman, Straight & Beck, 1976; Schaefer, Gunn & Dubowski, 1977).

Using the same film analogy, the subject at peak intoxication becomes fixated on one frame, the present, with
fragments of other frames flashing in and out. These thoughts of past and future are superimposed on the present so that the subject experiences a sense of "timelessness". An outgrowth of this experience is the narrowing of time perspective to concentrate on the events of the immediate present, the "here-and-now" perspective. This change in perspective would account for the subjective reports of vivid perceptions and feelings of euphoria during marijuana use. With greater concentration on immediate experience, sensory perception seems fresher and brighter. Old ideas and expressions gain an air of novelty, and tedious tasks seem more interesting. The concerns of the past and future seem far removed from the present and have no immediate importance. With past and future troubles temporarily put aside and replaced with a world full of interesting thoughts and sensations, euphoria would seem a natural by-product of temporal disintegration.

Temporal disintegration is not always associated with euphoria. Melges found that temporal disintegration correlated highly with feelings of confusion and depersonalization. The use of the Mood-Adjective Check List (MACL) revealed that each subject had unique emotional reactions to the drug state. Some tolerated the potential threat posed by confusion and depersonalization and enjoyed those aspects of the experience they deemed positive. Others experienced
confusion and depersonalization as loss of individuality and self-control and consequently labelled the experience as unpleasant. At higher doses, 50 and 60 mg. ingested orally, three subjects lost awareness of the time-limited nature of their experience and developed panic reactions. These observations support and extend the reports of Tart (1971), Weil (1970), and Becker (1963). Personality characteristics play a major part in the reaction to temporal disintegration and this reaction probably determines whether the novice user continues to experiment with marijuana. It may be, as Becker (1963, pp. 48-58) suggested, that most novices experience a certain amount of fear as they learn to get high, but the experienced users they smoke with direct their attention to the pleasant points of the high and calm the novices' fears as they arise. The panic reactions described seem typical of those encountered by Weil in clinical practice. The feelings of depersonalization and loss of self-control described by some experiencing temporal disintegration closely resemble the reports of borderline psychotics in Weil's clinical work. Weil noted that these individuals displayed a tendency to abstain from marijuana after initial use; unpleasant reactions to temporal disintegration would account for this tendency.

In its limited role as a hypothetical construct, temporal disintegration has its strong points. Its existence
is supported by data from subjective and cognitive testing. It seems to account for impairments in complex cognitive problem solving and complex reaction time studies as well as providing a basis for different emotional reactions to the drug. It has a certain predictive value in that tasks requiring sequential coordination of information would be expected to show greater impairment than those requiring immediate performance. Temporal disintegration also has its weaknesses. Attention is not well defined in these writings yet "lapses of attention" is a key element of the construct. The problem of impaired time estimation directly related to "impaired time sense" as it is used by Melges et al., is never directly addressed. Impaired time sense and lapses in attention are "given" elements in temporal disintegration. For these reasons, a broader, more well-defined theoretical model is needed to explain the cognitive effects of marijuana.

An attempt to provide this model is made by DeLong and Levy (1973). The model used by these authors is a model of attention devised by Sack in 1972. It includes three factors of attention which are relatively independent of each other. These factors are:

(1) Resistance to distraction. Degree to which one has resistance to nonvolitional change in the focus of attention (concentration is at one end of the continuum, while distractibility is at the other.)
(2) **Set-shifting.** The capacity voluntarily to shift the focus of one's attention. **Set-shifting** is the adverse of **perseveration.**

(3) **Selectivity or field articulation.** The degree to which the appropriate information is selected for the solution of the problem.

The authors state that these three factors are affected by marijuana in varying degrees and cite a number of studies to support their contention.

After reviewing the literature, DeLong and Levy select inability to resist distraction as the main factor operating to produce impairment of performance in immediate memory (e.g. Abel, 1971b), simple and complex reaction time (e.g. Clark, Hughes, & Nakashima, 1970), and relatively simple tests of cognition and psychomotor skills such as Digit Symbol Substitution and Pursuit Rotor (e.g. Weil, Zinberg & Nelsen, 1968). There seems to be a general consensus among marijuana researchers on this point.

Set-shifting is cited as the underlying cause of slowed time sense. DeLong and Levy argue that time estimation involves some form of counting (conscious or sub-conscious) and that intoxicated individuals tend to perseverate slightly on each number, thus elongating the total time elapsed. The principal support offered for marijuana-induced impairment in set-shifting is predrug-postdrug performance differences on a subtest of the Halstead-Reitan Battery, Trail-Making A and B. Three studies reviewed by the authors, one by Klonoff
in 1973 and two by Drew and associates (one unpublished), noted significant decrements in set-shifting. An equal number of studies can be found which noted no significant changes in Trail-Making subsequent to marijuana use (Culver & King, 1974; Mendelson et al., in Commission, pp. 85-86; Peters et al., 1976). One of these, Mendelson et al., was performed in a research ward, with measures taken before, during, and after a twenty-one day period of ad lib marijuana smoking. Five-day drug-free periods preceded and succeeded the smoking period, allowing for fairly reliable baseline measurements. The sample included ten casual users (a history of one year's use at 1-4 smoking sessions per month) and ten heavy users (two to five year history of use with a current smoking rate of one a day). Set-shifting may play a part in impaired time sense. Basing such a claim on Trail-Making scores is questionable, however, given the divergent findings on this test. It seems especially questionable when Mendelson et al. failed to find significant differences in spite of relatively ideal conditions and setting and a sample representing both casual and heavy users.

DeLong and Levy found little evidence for drug-induced impairment of field articulation. Hollister and Gillespie (1970), however, noted a trend toward impairment on the Closure Test, but no significant differences. A similar trend was noted by Meyer, Pillard, Shapiro, and Mirin (1971)
on the Hidden Patterns and Stroop Color-Word tests, but again no significant differences appeared. Weckowicz, Collier, and Spreng (1977) were unable to find impairment on the Stroop Color-Word test as well. No impairment has been found on the most frequently used measure of field articulation, the Rod-and-Frame test (Hollister & Gillespie, 1970; Jones & Stone, 1970; Weckowicz et al., 1977). Marijuana evidently has little, if any, effect on this element of attention.

The principal merit of the attention model used by DeLong and Levy lies in its delineation of attentional factors. Other investigators had noted the role of attention in marijuana-induced impairment, but DeLong and Levy were the first to specify limited resistance to distraction as the key element in the impairment. The other two factors of the model are less useful in explaining the effects of the drug. Set-shifting may exert some influence on time sense, but this has not been directly tested. The evidence that marijuana affects set-shifting is weak. The third factor, field articulation, seems to be largely unaffected by marijuana.

The most comprehensive theory for explaining the psychological effects of marijuana was developed by Feeney (1976). This theory is based on a combination of electrophysiological and behavioral data obtained from a variety
of species, including humans. This is the only theory that describes a physiological basis for the observed effects and offers a set of testable predictions.

The focus of this theory is the hippocampus, a large neural structure lying below and between the cerebral hemispheres of the brain. This structure has afferent and efferent connection to other elements of the limbic system (the amygdala, cingulate gyrus, septal region) to the hypothalamus, and to the cerebral cortex (Netter, 1968, pp. 152-153).

While understanding of the hippocampus is incomplete, one hypothesis of hippocampal function which handles the data well is that the hippocampus acts cholinergically to selectively inhibit response to incoming stimuli. This process of active inhibition is termed "gating".

There are two hypothetical types of gating mechanisms, one of which is known as nonspecific gating because it results in the widespread exclusion of irrelevant stimuli during the process of the concentration of attention. ...Nonspecific gating has been postulated to have the function of protecting memory traces from interference during consolidation, and the recent memory loss (associated with hippocampal damage) is theoretically caused by the lack of nonspecific gating and the consequent presence of interference with selective consolidation. ...

The other type of gating is known as specific gating because it acts to inhibit reception of specific stimuli which have been associated with nonreinforcement. The specific gating system is postulated to be involved in habituation (the purest example),
extinction, reversal, active error reduction, passive avoidance, and in other allied types of decremental behavior (Douglas, 1967).

This model of the hippocampal function comes into play because of the uneven concentration of THC in the brain produced by taking marijuana. One of the areas of highest concentration is in the hippocampal region (Secretary of HEW, 1972). While studying hippocampal seizures, Feeney (1976) discovered that THC produced a marked intrasubject variability in the reaction of the structure to stimulation; this finding was replicated by Chesher and Jackson (1974) and Ishikawa and associates (1966). Feeney hypothesized that increased variability in hippocampal function could induce increased response variability in the organism.

While estimates of variance were rather sparse in the literature, Feeney found evidence of behavioral variability induced by THC in rats, chimpanzees, and pigeons. This variability is also noted in human research (e.g., Clark et al., 1970; Peters et al., 1976). Feeney also found that LSD does not share this characteristic with THC. This could be the psychophysiological factor underlying the differing subjective effects of LSD and THC (Waskow, Olsson, Salzman, & Katz, 1970).

If THC has an effect on the hippocampus, then this effect should also appear in studies of habituation. In
1971, Brown noted that THC-injected rats failed to show habituation when retested after a habituating experience; this was apparently not a simple case of state-dependent learning as equal doses of chlorpromazine, dextroamphetamine, and LSD did not produce the same lack of habituation. In 1973, Drew and Miller demonstrated that rats habituated to running wheels increased running speed after receiving THC; this was not a direct locomotor effect as nonhabituated rats decreased their running speed when given the same dose. A similar increase occurred when novel stimuli were introduced. These studies support the Feeney model on the subhuman level.

On the human level, the Feeney model accounts for the lapse in attention commonly noted in perception, memory, and cognition experiments by postulating variable stimulation of the cortex due to impaired efficiency in the hippocampal gating mechanisms. This also provides a rationale for explaining altered time sense; Feeney cites several studies demonstrating periods of time filled with variable stimuli are perceived as longer than those filled with invariant stimulation. The popularity of the drug is explained in much the same manner as Melges et al., except that Feeney uses different terminology. According to Feeney, habituation to old reinforcers like food, sex, and social interaction is diminished and the changes in
processing present the possibility of novel experiences to the users; the emotional reaction to these changes is still dependent on the individual personality.

The effects of marijuana on contingent negative variation (CNV) can be explained with this model. CNV is "a slow cortical potential that develops during anticipation of motor or sensory activity" (Braden, Stillman, & Wyatt, 1974). An increase in the amplitude of the CNV is believed to be indicative of increased attentional arousal. Kopell, Tinklenberg, and Hollister (1972) found increased CNV with an oral dose of THC measured at 20 to 29 mg.; on the other hand, Braden et al. (1974) found increased CNV when subjects smoked 4.8 mg. THC and decreased CNV at 9.1 mg.

Methodological differences aside, it could well be, as Kopell et al. suggest, that 'simple attention' is not being measured. CNV results are probably an interaction of the sympathetic and parasympathetic nervous system. Being a surface potential, CNV is affected by general cortical arousal; according to the Feeney model, selective attention is modulated by the hippocampus which is within the brain. This location makes monitoring of its potentials more difficult; the relationship of these potentials to THC dosage should be more uniform, if they can be measured.

Another aspect of cognitive functioning which can be explained within the proposed framework is the psychological
refractory period. This is the period during which the brain is believed to be organizing and executing a response. If an organism is presented with another stimulus to which it must react during this period, the reaction time is substantially lengthened. The length of this delay can be approximated using an assumption of single-channel processing. Moskowitz, Shea, and Burns (1974) presented 12 subjects with a reaction time experiment that attempted to examine this variable at two THC dose levels. This experiment exposed each subject to two stimuli on each trial: After a warning signal the subject heard and reacted to a tone; this was followed by a neon lamp pulse at a time interval of 0, 50, 150, or 550 msec. The interval was constant for each set of thirty trials. The first reaction time (RT1) was essentially the same at either dose level (100 or 200 mcg. / kg.) while RT2 was twice as slow at high dose as it was at low dose. Analysis of the data showed RT2 to be much slower than predicted by single-channel theory. Failure to find a dose-dependent relationship for RT1 can be explained by noting that the subjects were extensively trained. Peeke, Jones, and Stone (1976) demonstrated that THC-induced impairment of RT can be virtually eliminated by practice. This seems to result from increasing automatization of the response; the role of attention is lessened as frontal motor areas are conditioned
to respond. The fact that the two stimuli used were related to different senses and appeared in such rapid succession may have temporarily "overloaded" an already impaired hippocampus. After selectively attending to an auditory warning signal and an auditory stimulus and attempting to operate on that incoming information, the hippocampus was then forced to rapidly alter its sensory gating to initiate a second response to a different sensory modality before it had recovered from the first response. The result was a hyperextended refractory period.

A persistent finding of several investigators is that marijuana-intoxicated subjects frequently tend to produce "false positive" signal detection (Moskowitz & McGlothlin, 1974), recognition memory (Abel, 1971c), and oddity discrimination (Schaefer et al., 1977). This lends further support to the Feeney model, as the hippocampus would normally act to suppress such responses.

The strong neural relationship of the hippocampus and the hypothalamus provides a possible explanation for the effect of marijuana on appetite. Appetite is often enhanced by marijuana although this varies on an individual basis (Abel, 1971b). The hypothalamus has a strong influence on eating behavior. The hippocampus may then serve a dual role in relation to appetite; the flavor of food may seem enhanced by dishabituation to the taste of each
bite and eating may be disinhibited to a variable extent by the influence of the hippocampus on the hypothalamus.

The Feeney model accounts for many marijuana effects, but direct testing of hypotheses derived from it will be required to ascertain its validity. Feeney suggests several approaches to this problem. These include: statistical analysis of the significance of variance differences across conditions in THC experiments; direct studies of habituation and dishabituation using as a dependent variable a measure like GSR or alpha-blocking in man and startle response in animals; employing an adolescent population for longitudinal correlative analysis of marijuana use and attitudes toward novel experiences as determined by test scores tabulated prior to the initiation of drug use; and examination of nonhuman THC self-administration in conditions maximizing need for novel stimulation and minimizing fear of the unfamiliar, placing a monkey in sensory deprivation and initially combining a nonaddictive tranquilizer with THC doses, for example.

In conclusion, THC has a significant effect on attention and this effect is reflected in many ways. Three attempts to explain the relationship of THC and attention have been discussed: temporal disintegration by Melges et al.; the attention model of Delong and Levy; and the hippocampal model of Feeney. Of the three, the hippocampal model
offers the most satisfactory explanation for a wide variety of experimental results. However, this theory still awaits direct confirmation.
Memory

Memory is important to the human being. Adaptation to both the physical and social environment requires that a human being be capable of learning to discriminate the salient clues in a given setting, respond appropriately to them, and retain that learned response for later use. Aside from its obvious importance for the individual, the study of memory has long been of interest to psychologists for a more pragmatic reason: memory is one of the most easily quantified faculties of the human brain. For both these reasons subjective reports of impaired memory associated with marijuana smoking have stimulated considerable research on marijuana and memory.

The research of Darley, Tinklenberg, Hollister, and Atkinson (1973a, 1973b, 1974) has contributed to the understanding of the memory deficits associated with marijuana use. In the first of their studies, the memory items were common two-syllable words taken from the Toronto Word Pool and arranged in 20-word lists; the words had roughly equal frequencies of occurrence. The subjects were 48 males who reportedly used marijuana no more than once a week. This was the procedure:

Following presentation and immediate free recall testing of ten 20-word lists, 48 Ss were divided into two groups, one of which received an oral dose of marijuana extract calibrated to 20 mg. of delta-1-THC
and one of which received placebo. One hour later all Ss were administered delayed recall, recognition, and order tests on the first set of words. Presentation of another set of 10 lists followed and there were immediate and delayed recall, recognition, and order tests on these words (Darley et al., 1973a).

A recall test requires the recall of list items without the aid of cues provided by the examiner. A recognition test provides the subject with a group of list items and a group of nonlist items. The subject's task is to discern which of the items appeared on the memory list. There were no differences between drug and placebo subjects on the first set of tests; on the second set, however, drug subjects performed more poorly on the immediate recall, delayed recall and delayed recognition tests. The subjects had no difficulty in recalling material learned prior to intoxication or in recognizing the same material when it was incorporated into a three-alternative forced-choice test; memory deficits appeared only on material presented after intoxication. Given these results, Darley et al. concluded that marijuana has no measurable effect on retrieval from memory, but it impairs the storage of information.

The use of list learning enabled Darley et al. to examine indications of impairment in different areas of memory by using serial position curves, curves which graphically represent the probability of recall for an item
relative to its position in the list. Serial position curves tend to assume a "U" shape, with the first and final items of a list more likely to be recalled than items in the middle of the list; the elevations of the endpoints of the probability curve are termed "recency effect" for terminal item recall and "primacy effect" for initial item recall. Recency effect is believed to be the result of recall from short-term memory (STM). The first items in a list become subject to primacy effect because they are the first to be transferred from STM to long-term memory (LTM); if an item is not rehearsed in STM, then it will disappear by spontaneous decay. Upon examination of the serial position curves in this study, Darley et al. found virtually no difference in recency effect between placebo and drug conditions, while the remainder of the curve was depressed in the drug condition. The conclusion was that the critical source of memory impairment in the drug state was transfer of information from short-term storage to long-term storage.

This conclusion is supported by similar findings of other investigators (Abel, 1971a, 1971c; Miller, McFarland, Cornett, & Brightwell, 1977). However, other findings of Miller et al. challenge the idea that the impairment is solely the result of transfer problems due to lessened rehearsal. Miller and his associates employed much the same procedures as Darley except that they repeated a single list
four times during the twenty lists presented and followed the recall testing with a "yes-no" recognition test composed of test words and unused "lures". The multiple presentations allowed them to calculate rates of acquisition for both drug and placebo groups; these rates proved to be the same. In addition, the recognition test proved to be only mildly affected by the drug. It should be noted that this result was obtained after analysis of the test and lure distributions indicated they were not normal; initial analysis, using parametric statistics, had found a tendency for drug subjects to produce "false positives", similar to the result found by Abel (1971a). Abel failed to perform this analysis for his recognition test and neglected to control subjective confounds with a placebo control; Darley et al. apparently neglected analysis of the recognition test as well. Citing two-factor memory theory, Miller suggested that the recognition score indicated that the material was stored, but at a level of intensity, a "trace strength", too low for free recall. Combining this with the finding of equal acquisition rates, Miller hypothesized that the impairment is due to interference with initial encoding of information, resulting in lowered trace strength.

Other studies, including two by Darley and his associates, pose problems for the transfer explanation and indirect support for the alternative proposed by Miller.
Darley et al. (1973b) performed an experiment which allowed closer examination of retrieval from short-term memory. In this paradigm, the subject was presented with a small memory set on each trial and then given the test stimulus. The subject, who had to determine whether the stimulus was or was not a member of the set, was consistently correct. Reaction time was the principal measure of performance. This time can be theoretically separated into the components of encoding, response, and memory search. Mathematically, memory search can be separated from encoding and response by an equation and the test results plotted graphically to determine the time spent searching the memory store. Initial analysis found increased reaction times for drug subjects; subjecting the data to the analysis described demonstrated that the impairment was not in memory search, but in response and encoding. Of course, this is merely suggestive evidence, as it is not possible to determine if the impairment is in encoding, as Miller predicts, or in response. A later study (Darley et al., 1974) is more damaging to the transfer hypothesis. This study returned to the list-learning format and compared a fixed-rehearsal procedure with the commonly-used free-rehearsal procedure. In this procedure, the subjects repeated the list words aloud six times as they were presented. Fixed rehearsal did not eliminate the memory deficits, contrary to the
prediction of the transfer hypothesis. This impairment is also immune to volitional control (Cappell & Pliner, 1973). After performing baseline testing and allowing each of 24 experienced users (mean frequency of use = twice a week) to smoke a cigarette containing 12 mg. of THC, Cappell and Pliner urged half of them to use whatever mental techniques they needed to "come down" and perform well on the tests. Motivational measurements indicated that the instructions had the desired effect on the motivational set of the subjects. However, the memory impairment was identical for both groups.

If impaired transfer from STS to LTS is solely responsible for THC-induced memory impairment, it would seem to be impervious to consciously applied efforts to diminish its effect from within (by any freely chosen technique) and without (by forced rehearsal). The notion of spontaneous decay in STS is not congruent with the observations of Miller et al. on acquisition and recognition. The Miller hypothesis in which encoding problems diminish trace strength and lower the possibility of retrieval, is more credible.

The use of non-list procedures has produced interesting results, but interpretation of these results is difficult. One of the other procedures represented in the literature is digit-span, the reciting of a series of random numbers in the order presented or in reverse order. Tinklenberg,
Melges, Hollister, and Gillespie (1970) found digit-span impaired after administering 20 mg. of THC orally. Waskow et al. (1970) found no effect on digit-span using an equal oral dose, but their subjects were not fasting and this probably altered the amount and rate of THC absorption, accounting for the conflicting results. During their 21-day study, Mendelson, et al. (in Commission, 1972) found a decline in digit-span performance following smoking at the start of the study and steady improvement with practice over the course of the study. Dornbush and her associates found analogous results in two studies of paired-associate learning of trigrams. Both studies (Dornbush, Fink & Friedman, 1971; Dornbush, Clare, Zaks, Crown, Volavka & Fink, in Lewis, 1972) noted initial learning decline, while the latter experiment, a 21-day administration study, noted steady improvement and eventual return to the baseline performance. To explain these results, the transfer hypothesis might assert that the subjects developed effective strategies of rehearsal, while the encoding hypothesis could claim the subjects found means to better encode these types of material. On the other hand, conscious changes may not be involved; subjects may develop some tolerance to the memory impairing action of THC. The possibility that improvement with practice is task-specific must also be considered. More evidence is needed before an accurate interpretation can be made.
State-dependent learning experiments provide some of the evidence needed to account for the findings on digit-span and paired-associate learning. State-dependent learning is a phenomenon which relies upon the stimulus role of drugs for explanation. A learned task can be viewed as a conditioned response; as such, it is emitted in the presence of a given set of stimuli. To demonstrate optimum response strength, the stimulus conditions which occurred during learning should also occur at emission of response. While some stimuli are external to the subject, others are internal, and an important internal stimulus is the prevailing condition of the central nervous system (CNS) at the time of learning. Objective and subjective evidence indicates that marijuana has a marked effect on some portions of the CNS. If state-dependency occurs in marijuana use, then reinstatement of intoxication would be necessary to maximize recall of material learned in the drug state; conversely, return to the non-drug state would be necessary to maximize recall of material learned in the non-drug state (Greenfield & Sternbach, 1972, pp. 792-793). When both of the previous statements hold, then the phenomenon is termed "symmetrical state-dependent learning"; if only one holds, then the phenomenon is "asymmetric" (Eich, Weingartner, Stillman & Gillin, 1975).

State-dependent learning does occur with marijuana use.
However, state-dependency appears only on certain types of tasks. The type of state-dependency shown is also related to the nature of the task. Stillman, Weingartner, Wyatt, Gillin, and Eich (1974) found symmetric state-dependency for two tasks involving pictorial stimuli, Picture Arrangement and Four-Way Picture Choice. Hill, Schwin, Powell, and Goodwin (1973) noted similar results on two tests of sequential recall. In the first test, the memory set was verbal, and, in the second test, the set consisted of seven plastic objects. Rickles, Cohen, Whitaker, and McIntyre (1973) examined paired-associate learning in casual (less than 3 smoking periods a week) users and found symmetric state-dependent learning. Using subjects with a similar usage history, Darley et al. (1974) found asymmetric state-dependent learning. However, this conclusion should be viewed with caution because the task performance for all groups in this experiment was atypically low. Asymmetric state-dependence can be more reliably cited in the learning of categorized lists (Eich et al., 1975).

In analyzing these results, and the results preceding them, a valuable construct is "interitem association". Most of the material used in the cited experiments is familiar material. The words comprising memory lists and acting as responses to trigrams were common words chosen from any of several word pools. The pictures chosen by Stillman et al. came from popular magazines; the photographic subjects
were familiar. The numbers of digit-span were hardly novel. In previously learned material,

the problem of storage is circumvented and remembering depends on the effectiveness of retrieval cues at the time of the test. What is stored consists of ancillary information about the to-be-remembered items which segregates them from the rest of an individual's vocabulary. ...This occurs mainly through the formation of interitem associations which usually result in clusters of items being emitted together (Miller, Cornett, Brightwell, McFarland, Drew & Wikler, 1976).

Hill et al. (1973) noted that tests requiring sequential ordering seemed most prone to state-dependent effects. This recalls the findings of Melges et al. (1970, 1971) that subjects performing serial alternation had difficulties retaining the sequence of operations. Sequential memory is a special case of interitem association which is particularly demanding because it requires the coordination of many elements of the memory set; the items must be not only clustered but the clusters themselves must be in order. It seems reasonable, then, that sequential memory would be most affected by an altered capacity to develop and maintain interitem associations. The extent to which each of the tasks surveyed requires interitem associative capacity is reflected by the degree to which task performance covaries with variables affecting this capacity. Apparently, marijuana is one of these variables.
According to Feeney (1976) marijuana's effect on the hippocampus tends to limit that structure's capacity to suppress responding to stimuli. Given a set of ambiguous stimuli, an intoxicated individual tends to produce a slightly larger quantity of associations and these associations are often tangential or novel in some respect. This tendency has been demonstrated on the Rorschach (Grinspoon, 1977, p. 159) and the Thematic Apperception Test (TAT) (Roth, Rosenbloom, Darley, Tinklenberg & Kopell, 1975; Crockett, Klonoff & Clark, 1976). These two associative tendencies can have a marked effect on the memorization of ambiguous stimuli: Extended tangential association can impair the development of trace strength because it precludes adequate rehearsal of major associations (Miller et al., 1976) and unusual interitem associations may be rehearsed which will be less accessible in the non-drug state (Stillman et al., 1974).

The effects of altered associative capacity appear most frequently in tasks where the elements of the memory set have little intrinsic associative value, as in a list of random words, numbers, or objects. Memory involving numbers and arithmetic operations pose special problems. People have well-practiced habits regarding the order of numbers and the performance of operations with them. These strong associations are likely to be triggered when an intoxicated
subject is confronted with a numerical task. If the task involves unusual numerical manipulation, such as memorization and reordering of numbers or backwards sequential addition and subtraction, then previous habits will proactively inhibit task acquisition.

When contextual retrieval cues are available in a memory set, THC-induced impairment is reduced and, in some cases, eliminated. Hill et al. (1973) composed four five word "word strings" with four different levels of word interrelationship: sentence, anomalous sentence, anagram, and unrelated. Only the recall of the latter string was affected by marijuana and this effect was state-dependent. Using taxonomic norms, Eich et al. (1975) developed four lists, each of which contained "a unique group of 12 categories". Each category had four representative words, two words were highly related to the category (e.g. vehicle-car, truck) and two were more distantly related. After these lists were given to placebo and drug subjects, a free-recall test was performed. The results revealed state-dependent learning. When category labels were placed on the recall protocols, state-dependent effects disappeared. Miller et al. (1976) noted improved recall of lists with cues as well, although the effect was not as robust as that of Eich. Miller's cue was the first letter of each list word; this would not appear to have the same degree
of associative value as categories.

When fixed-rehearsal is instituted, opportunity for covertly developing interitem associations as retrieval cues is limited. In a random list, overt rehearsal of unrelated words provides little associative value; sequential rehearsal actually serves to displace initial list items before the trace strength needed for recall is developed. The result, as Darley et al. (1974) discovered, is an overall decline in recall scores due to loss of primacy effect, a decline which extends across both placebo and drug groups.

In casual marijuana users, the drug acts as a stimulus to produce state-dependent learning. Cohen and Rickles (1974) tested heavy users (four or more smoking periods a week) on a paired-associates learning task which had previously shown state-dependency in casual users (Rickles et al., 1973). They found no difference in performance related to the drug state. Beautrais and Marks (1976) noted analogous results in an examination of state-dependent learning of psychomotor tasks; the amount of drug-induced impairment was inversely related to intensity of previous drug use, although all users demonstrated drug-related impairment. Both groups suggested that some type of tolerance had developed with heavy chronic marijuana use. Development of tolerance would account for the steady improvement of digit-span and paired-associate scores in long-term
studies (Dornbush et al., in Lewis, 1972; Mendelson et al., in Commission 1972). In these cases, tolerance appears as a return to baseline performance. The relationship of this baseline to drug-free baseline performance cannot be ascertained in these instances. The baseline period for Dornbush et al. was one day; the baseline period for Mendelson et al. was five days, but there was evidence that THC in the form of hashish or marijuana may have been smoked by the heavy-user group during this period. Since THC has a minimum plasma half-life of roughly 28 hours (Lemberger, et al., 1972), a true drug-free baseline may not have been attained in either study.

Lack of longitudinal studies leaves the question of residual memory deficits from marijuana smoking unresolved. Examination of extremely heavy, long-term users in other countries has noted little significant memory deterioration but these findings are questionable due to lack of testing prior to drug use and generalizing these findings across cultures would be a dubious practice (Commission, 1972, p. 99). Some studies (Entin & Goldzung, 1973; Gianutsos & Litwack, 1976; Marx, 1974) have attempted to compare users and non-users on memory capacity. They have matched subjects on age, sex, grade-point average, and other variables. Unfortunately, the fact remains that they may be selecting subjects with fundamentally different personality types.
The residual-deficit question will not be satisfactorily answered without longitudinal study.

The results of memory research with marijuana are interesting. Interitem association is an important construct in understanding these results, since difficulty in encoding these associations seem to be the basic obstacle to memorization under marijuana. Marijuana induces state-dependent learning in casual users. Some form of tolerance appears to develop in heavy users which precludes state-dependent effects; heavy users apparently experience less memory impairment than casual users at the same dosage level. The question of whether long-term users experience residual memory deficits in the undrugged state is still open.
Cognition

Cognition is a general term which encompasses the various facets of conscious thought: attention, memory, evaluation, logical and arithmetic operations, creativity, etc. Clear specific definitions of cognitive processes have been persistently elusive. For the purposes of this paper, the general term will be sufficient.

Marijuana produces characteristic changes in cognitive "style"; these changes are demonstrated most vividly in non-objective contexts, on projective tests and in conversation, for example. As noted elsewhere, marijuana has a dose-related effect on attention and memory, two key elements of cognition. The degree of impairment shown on objective cognitive tests appears to be largely a function of the attentional and recall demands of the specific test administered. Extent of prior drug experience also seems to be a factor in the degree of observed impairment.

Melges et al. (1970, 1971) labelled the cognitive changes induced by marijuana "temporal disintegration". Feeney (1976) posited that variable cortical stimulation was the underlying basis for these changes. The critical alterations are the focusing of attention on immediate experience and the emergence of a sense of timelessness, of drifting effortlessly through time with minimal distinction between past, present and future. The capacity
to handle sequential logical operations is diminished under these conditions (e.g. Casswell and Marks, 1973); imagistic and intuitive thinking, processes requiring less temporal organization, take precedence over their more demanding counterparts. Consequently the intoxicated individual is more willing to accept logically contradictory ideas (Tart, 1971).

Studies of informal speech and responses to the TAT illustrate the style of "stoned" thinking. These studies (Crockett et al., 1976; Roth et al., 1975; Weil & Zinberg, 1969) employed a variety of samples, dosages and procedures to elicit verbal protocols. One procedural commonality was the scoring of protocols by judges who were blind to the conditions under which the protocols were produced. Crockett et al. and Roth et al. both evaluated the reliability of their judges. The work of Weil and Zinberg was a preliminary study; they were unable to maintain double-blind procedures with the chronic users in their sample (8 daily users, 9 naive individuals) or ascertain the reliability of their five judges. Despite procedural differences and the inadequacies noted, the studies report similar findings. Weil and Zinberg concluded that "marijuana tended to cause greater and more vivid imagery, shift of time orientation from past or future to present, increased free associative quality and intimacy, and decreased awareness of a listener". Responses to the TAT were characterized by
Roth et al. as being timeless, non-narrative, free-associative, and often containing ideas that were novel and, in some instances, contradictory. Crockett et al. found subjects less capable of integrating and organizing themes after smoking doses of 4.8 mg and 9.1 mg THC. Low-dose subjects tended to produce responses with more abstraction and multiple meanings whereas high-dose subjects did not differ from placebo on these variables; this is probably due to the increased sedating effects at higher doses noted in subjective reports (Weil, 1970).

Creativity, one of the least understood of the cognitive processes, is the subject of a hotly contested debate between the opponents and proponents of marijuana use. Some proponents claim that marijuana promotes greater creativity by enabling the user to transcend rigid outmoded patterns of thought by means of imagery and free association and reach conclusions by synthesis of disparate elements that would be unobtainable by logical induction. Opponents state that free association and imagistic thinking are counterproductive to the logic needed to produce works of coherence and substance (Grinspoon, 1977, pp. 153-157). Obviously, this question cannot be readily resolved in subjective disciplines like music and art. Objective measures, such as the Alternate Uses or Matching Problems Tests, must be limited in scope to be workable as tests and may not adequately assess creativity as a result. In the few
instances that such tests have been given to stoned individuals, divergent results have been found (Berger, 1972; Carlin et al., 1974). Projective test responses have noted novel ideas, but novelty alone does not constitute creativity; creativity occurs when initially divergent elements are combined to produce a coherent new whole, and, as the same tests point out, novel responses under marijuana tend to be part of a disorganized set of ideas. The data suggests that marijuana adversely affects the convergent elements of creativity while exercising a variable effect on divergent thinking. The overall effect is the sum of these two tendencies and probably varies across doses, individuals and tasks. Whatever the case may be, no clear-cut relationship between marijuana and creativity has been demonstrated thus far.

The influence of the physical and social setting on cognitive performance while stoned has been the subject of several studies. Those studies bearing directly on the effect of physical setting and role modeling have been previously discussed. (See Methodology, pp. 21-22). Briefly, Hollister et al. (1975) found no significant effects for setting, and Carlin et al. (1974) found that only one of five objective tasks (a verbal learning task) was significantly affected by role modeling. On the basis of these studies it was concluded that previous experience with the drug plays the predominant role in shaping an individual's
performance while intoxicated. Shaping seems an appropriate word, for most of the basic objective impairments withstand manipulation of expectation and motivation. Marijuana folklore posits the existence of a capacity to perform normally when necessary (Tart, 1971). When Cappell and Pliner (1973) investigated this, they found that impairment of time sense was lessened, but not eliminated; memory impairment remained the same. There are studies indicating that intoxicated people are more susceptible to external influence on their cognitions and perceptions (Crawford, 1974; Kelly, 1975). Yet when a sample was selected on the basis of differential suggestibility and then subjected to different imposed expectations, no differences were found in the extent of cognitive performance deficit on digit span, time estimation, or GDSA (Butler, et al., 1976). Two notes of caution must be appended to these findings, however. The first, applying specifically to the previous study, is that there is some question regarding the degree of correlation between an individual's score on the suggestibility scale used and that individual's actual susceptibility to social influences (Butler et al., 1976). Secondly, the doses used in these studies ranged from 7.5 mg to 19 mg; social and physical setting may play a larger role at lower doses. Casswell (1975) found evidence that motivation improved performance on GDSA following the smoking of 2 and 4 mg of THC, a finding which supports this hypothesis.
A considerable number of objective tests of cognitive functions have been given to marijuana users. Samples, dosages, and procedures have differed from one experiment to another. Combination and comparison of the results permit certain generalizations to be made on the relationship of marijuana to objective cognitive test scores.

Field articulation, the ability to select salient cues from a stimulus field in order to solve a problem, is minimally affected by marijuana. Basic tests of this ability, such as the Rod-and-Frame Test, the Stroop Color-Word Test, and the Size-Weight Illusion Test, have been unaffected by THC doses as high as 32 mg. (median high dose in Hollister and Gillespie, [1970]) (Hollister & Gillespie, 1970; Jones & Stone, 1970; Meyer, et al., 1971; Pearl,Domino & Rennick, 1973; Schaefer et al., 1977). Subjects tend to exhibit slight dose-related impairment with increasing field complexity. Meyer et al. (1971) noted a significant trend toward impairment on Hidden Patterns. On a similar test, Embedded Figures, Pearl et al.,(1973) found increased problem-solving time for subjects who had smoked 9 and 18 mg. of THC; solutions to the problems were unaffected, and only the times in the high dose condition were significantly different from placebo.

Performance deficits are negligible in simple cognitive matching tasks like digit-symbol substitution (Butler et al., 1976; Dornbush et al., in Lewis, 1972; Hollister & Gillespie
Similar tasks which place greater demands on memory, such as automatic DSST (Vachon et al., 1976), generally exhibited undiminished overall accuracy with slowed response times and greater performance variability between trials.

As task complexity increases and more demands are made upon the attention and memory of an intoxicated subject, performance deficits become larger. Tests which require simple discrimination of rhythms or geometric figures, like the Halstead Category Test, Tactual Performance Test, and the Seashore Rhythm Test, show no deficits (Mendelson et al., in Commission, 1972, pp. 85-86; Peters et al., 1976). When a pattern must be abstracted in order to perform a discrimination, performance decreases as difficulty of abstraction increases; subjects find it more difficult to discover the underlying relationship in Word Grouping than to find the underlying pattern in Letter Series and perform more poorly on the former test as a result. Conceptual Clustering requires both abstraction and immediate recall of related words; performance is depressed even further on this test (Pearl et al., 1973). Impairment on the Iowa Silent Reading Test, a test requiring comprehension and recall of material, is greater on the paragraph level than on the sentence level (Clark & Nakashima, 1970). The source of these deficits appears to lie in the ability to systematically recall items and abstractions relating them rather than the ability to
generate abstractions; projective testing shows abstractive capacity does not suffer extensive adverse effects.

Task performance is dose-dependent as well as task-specific. Some problem-solving tasks - Anagrams, Hidden-Words, Water-Jar Problems - are resistant to effects at smoked doses up to 18 mg. THC (Abel, 1971b; Pearl et al., 1973). Cappell and Pliner (1973) found no effect on simple arithmetic problem-solving at smoked doses of 12 mg. THC. At 32 mg. (oral), arithmetic problem-solving was significantly impaired (Hollister & Gillespie, 1970). When basic arithmetic operations are used in a novel manner, as in a serial alternation task, deficits appear at lower doses; Casswell and Marks (1973) found significant impairment on GDSA at a smoked dose of 3.3 mg. THC. Pearl et al. noted a dose-dependent deficit for Closure Speed, the ability to detect and identify a missing element of a figure; Hollister and Gillespie found Flexibility of Closure unaffected, but this test appears to measure field articulation rather than closure. Pearl et al. found similar relationships between dosage and performance for Letter Series, Word Grouping, and Embedded Figures. It appears that if a task is complex enough to be impaired by marijuana, the induced performance deficit will be dose-related.

Daily marijuana smokers exhibit some degree of tolerance on basic cognitive tasks. Comparing naive individuals with chronic smokers, Weil et al., (1968) found that both
groups exhibited equivalent baseline performance on DSST, but the postsmoking performance of the naive group deteriorated in a dose-related manner while the performance of the chronic group actually improved slightly. Meyer et al., (1971) obtained analogous results on the Continuous Performance Test, a simple test of sustained attention; casual users (once a week) declined in performance and daily users improved. Casual users apparently possess some limited capacity to compensate as well. Casual users show less impairment on DSST than naive individuals and are able to diminish time sense deficits by concentration (Butler et al. 1976; Cappell & Pliner, 1973; Dornbush, et al., in Lewis, 1972; Jones & Stone, 1970). The extent to which this behavioral compensation is a learned capacity or an acquired physiological tolerance is presently undetermined.

Findings on the long-term cognitive effects of chronic heavy marijuana use differ. Fried (1977) stated that Indian investigators had concluded that moderate use does not lead to intellectual deterioration while excessive use does; the terms "excessive" and "moderate" were not defined. In the same article, psychiatric and neuropsychological examinations of Greek and Jamaican heavy users were cited as providing little evidence of deterioration. The generalizability of foreign studies is limited. Drug potency and usage patterns differ and the dubious aspects of matching samples become more pronounced. Two illustrations
are provided by the studies of Beaubrun and Knight (1973) in Jamaica and Soueif (1975) in Egypt. The conclusions on intellectual deterioration differ; the principal commonality is an inadequacy of sample control which leaves both conclusions suspect. Beaubrun's nonsmoking controls regularly drank cannabis tea, while Soueif was unable to control the variables of literacy, cultural deprivation and surreptitious drug-taking. North American studies, more easily generalized to a modern industrialized population, have shown no signs of intellectual deterioration with prolonged use (Culver & King, 1974; Weckowicz, Collier & Spreng, 1977). However, only the Weckowicz study focused on heavy users, and heavy use was defined as daily use for a minimum of three years. This may not be an adequate period to develop detectable deficits. Long-term longitudinal study will be needed to resolve this question.

Review of experimental studies on marijuana shows that the drug has a significant influence on cognitive processes. Intoxicated thinking is characterized by a free-associative, imagistic quality and a tendency to employ intuitive reasoning rather than logic. The relationship between marijuana and creativity is unclear. At minimum doses of 7.5 mg THC, factors of set and settings seem to have little effect on objective performance. Task complexity and dosage level are the major factors affecting performance. Individual tolerance is also a factor, although this has only been noted in
relatively simple tasks. The possibility of intellectual deterioration from long-term heavy use requires more study.
Personality

The question of whether marijuana can induce significant personality changes is highly controversial. Early opponents of the drug charged that acute intoxication could drive the user to commit violent crimes; prolonged use was said to induce madness (Abel, 1977; Grinspoon, 1969; Grinspoon, 1977, pp. 309-321). More recently, the claim has been made that marijuana use results in a passive, introspective lifestyle lacking in conventional motivation (Kolansky & Moore, 1971, 1972). A related concern of long standing has been that marijuana use might lead people to use harder drugs like LSD and heroin. This debate has been fueled by an abundance of strong opinions and a lack of hard evidence.

The relationship of marijuana and psychosis has been previously discussed (See Subjective Effects, pp. 34-40). Briefly, the principal adverse reaction to acute intoxication is panic. On rare occasions, acute toxic psychoses have been noted, usually precipitated by oral ingestion of a large dose. Marijuana tends to exacerbate the psychological problems of those predisposed to psychosis and may precipitate psychotic episodes in these individuals. The likelihood of such an episode occurring in a person of average mental health following moderate use of marijuana
appears to be remote (Bialos, 1970; Weil, 1970).

In addressing the issues of chronic and acute personality changes, a useful distinction may be made between casual users and heavy users. Casual users smoke intermittently and usually in the company of other users. Casual users often do not own a private supply of marijuana and must rely on others for the opportunity to smoke. Usage varies from two or three times a month to two or three times a week; they may experience occasional periods of daily smoking, but these intervals are rare and widely interspersed in their drug history. Heavy users smoke on a daily or near-daily basis, sometimes two or three times a day. Working or attending classes while stoned is very commonplace. A heavy user keeps a personal marijuana supply and dwindling supplies usually initiate a determined search for more of the drug. Heavy users frequently engage in multiple drug use, taking LSD, amphetamines and barbiturates in addition to marijuana. While a continuum of usage and users exists, there is evidence that individuals at this extreme of the continuum differ significantly in personality from those occupying the middle ranges (Grinspoon, 1977, pp. 207-209; McGuire & Megargee, 1974; Mirin, Shapiro, Meyer, Pillard & Fisher, 1971; Zinberg & Weil, 1970).

Zinberg and Weil (1970) conducted interviews with 62 males while recruiting subjects for an experiment. The
interviews gathered personal information in addition to drug history. On marijuana use, subjects were categorized as naive, non-naive and chronic. They were also rated on a compulsiveness-hysteria scale. Compulsiveness was characterized as a desire to control one's life in all its physical, social and emotional aspects, often at the expense of isolation from emotional experience and loss of spontaneity. Hysteria was characterized as ready access to one's emotions and a sense of immediacy in interpersonal relations at the expense of organization, continuity in relationships and precision of expression. Most people possess a mixture of these traits. Compared to nonusers, smokers showed more hysterical qualities, with these qualities becoming more pronounced in heavier users. The majority of the subjects were judged to be within normal limits on this scale; five of the nine chronic users were judged to exhibit an abnormal degree of hysteria. This group regarded their drug use as the most significant single factor in determining their pattern of life. Mirin et al., (1971) made similar observations; seven of the twelve heavy users in their study expressed the opinion that marijuana was an integral part of their lives and essential to their performance in the everyday world. Differences on standardized personality tests were apparent in a study of 96 male prisoners performed by McGuire and Megargee (1974). The Minnesota Multiphasic Personality Inventory, California Psychological Inventory,
State-Trait Anxiety Inventory and Beta were administered to this group, whose reported drug history ranged from nonuse to heavy marijuana use in combination with other drugs. Nonusers exhibited more rigid, authoritarian attitudes than users, supporting Zinberg and Weil's finding of relative compulsiveness in nonusers. Weekly marijuana users displayed less hostility and impulsivity than the other comparison groups and appeared to be the best socialized and most mature of the groups studied. Heavy users tended to be egocentric, withdrawn, suspicious, exploitive of others, and highly impulsive and were considered the most maladjusted sample in the study. Mendelson et al. (in Commission, 1972, pp. 89-91) observed that heavy users engaged in less social interaction before, during and after smoking. While some correlative relationship between personality factors and extent of marijuana use seems evident, the question of causation is not answered by these studies.

Brill and Christie (1974) performed an extended three-year study of marijuana use and psychosocial adaptation in a population of UCLA undergraduates. Roughly 90% of the respondents felt that marijuana had little or no effect on their adjustment to school, marriage or work. Objectively, level of academic achievement was unaffected by marijuana usage. A small proportion, about 10%, reported negative effects of marijuana use and had diminished or terminated use. If this study is considered in light of the previous studies, the
evidence seems to indicate that the majority of those who use marijuana do so for enjoyment, ascribe little importance to the activity, partake on a social basis, and experience no discernible personality changes as a result. A small percentage impart more significance to smoking. A portion of these people conclude that marijuana is detrimental to their well-being and terminate use. Others embrace the drug as a way of life (Mirin et al., 1971). For these smokers, marijuana may become "...an essential catalyst to the experience of pleasure; or, perhaps more accurately for others, a respite from psychic pain" (Grinspoon, 1977, p. 235). By conventional standards, these individuals show signs of maladjustment in their social, sexual and working lives (McGuire & Megargee, 1974; Mendelson et al., in Commission, 1972, pp. 71-72; Mirin et al., 1971; Zinberg & Weil, 1970). Relatively little is known about this group, as experimental studies routinely exclude individuals with signs of psychological abnormality, heavy marijuana use, or multiple drug use.

Public fear that marijuana use could induce violent crime was instrumental in the initiation of some of the earliest large-scale research studies on the marijuana problem (Clark & Nakashima, 1968). Experimental evidence argues against this believed connection of marijuana with violence. Projective test responses show no increments in aggressive content (Crockett et al., 1976; Roth et al.,
1975; Wagner & Romanik, 1976). In aggression studies which allowed subjects to deliver shocks to another person, smokers lessened the intensity, frequency and duration of shocks after smoking either marijuana or placebo (Alioto, 1975; Bloom, 1973). Anxiety, a condition which can precipitate violence, is apparently unaffected by smoking (Pillard, McNair & Fisher, 1974). No increase in hostile interactions has been noted in studies of marijuana and small-group communications. Smokers in small groups tend to emit fewer hostile statements and the tone of these statements is generally sarcastic rather than openly critical (Mendelson et al., in Commission, 1972, p. 91). None of the groups studied showed any tendency to deviate from social norms for verbal and physical behavior (Galanter, Stillman, Wyatt, Vaughan & Nurnberg, 1974; Mendelson et al., in Commission, 1972, pp. 90-91; Salzman, Von der Kolk & Shader, 1976; Slatterie, 1976). However, only the Mendelson study employed heavy users, and these users were screened for psychological health. Those who use marijuana heavily often exhibit poor mental health, and the potential for antisocial behavior during intoxication is probably highest in this group. The incidence of violent behavior in this population, and its association with intoxication, is unknown.

In the proper circumstances, marijuana may induce violent behavior in novice users. Some novices experience
panic reactions at their initial use. If this free-floating panic is combined with stressful circumstances, the novice may lash out violently in fear. In at least one instance, this reaction has had fatal results (Talbott & Teague, 1969).

Marijuana may also induce violence in individuals with neurological problems. Paranoia, depersonalization, memory loss, and perceptual changes, all commonly associated with marijuana, are also symptoms which frequently precede epileptic seizures. Seizures have been recorded following marijuana use, although the temporal association of the two events has not always been clear (Abel, 1977; Keeler & Reifler, 1967). Some epileptics are violent during seizures; individuals with epileptoid personality disorders engage in short, seizure-like, periods of intense violence. While the relationship of marijuana to epileptoid activity is not firmly established, it appears that the use of the drug by individuals with epileptoid disorders is potentially hazardous (Abel, 1977).

Most studies linking cannabis and violence have employed dubious methods to do so. Among cannabis users, those most likely to become violent after smoking are probably the novice, the heavy polydrug user and the epileptoid user. The violent epileptoid seizure is the purest example of marijuana-induced violence, if this relationship is confirmed. In the other two cases, the variables of set and
setting apparently play a larger role in violent behavior than the drug itself. If these individuals are eliminated from analysis, the incidence of violence in the cannabis-using population is roughly equal to that of the nonusing population (Abel, 1977).

In recent years, concern about acute behavioral effects has been supplanted by concern about chronic effects on personality. The common description of heavy smokers as withdrawn, apathetic, maladjusted and lacking in motivation has led to the coining of the term "amotivational syndrome" (Commission, 1972, p. 51). Other characteristics of this syndrome are: short attention span, indifference to personal appearance, suspiciousness and difficulty in organizing thoughts. Hand tremors, staggering gait, slurred speech, and disturbed depth perception have also been noted. This syndrome occurs in all age groups and is apparently more frequent and more pronounced in adolescents (Kolansky & Moore, 1971; Kornhaber, 1971; Maugh, 1974b; Shean & Fechtmann, 1971). The affected individuals often have no previous history of psychological problems. Given the lack of historical predisposition, the common factor of heavy daily marijuana use, and the uniform symptomatology displayed by their patients, Kolansky and Moore (1977) concluded that chronic marijuana use has a toxic effect on the CNS, creating an organic brain syndrome.

The conclusions of Kolansky and Moore have been
attacked on several grounds. No effort was made to examine a comparable group of individuals to determine incidence of psychological difficulties. This would have been particularly valuable in their 1971 study of adolescents, since adolescence is a period marked by psychological upheavals. While Kolansky and Moore emphasized commonality of symptoms, the 1971 study sample actually presented a broad range of problems including disruptive behavior, psychoses, suicide attempts and sexual promiscuity (Secretary of HEW, 1972, p. 242). The authors cited neurological toxicity as the basis for amotivational syndrome, although there is no mention of a neurological or biochemical examination being performed on any of their patients (Meyer, in Tinklenberg, 1972, p. 145).

The validity of amotivational syndrome as a clinical entity is further weakened by a variety of studies which have discovered no direct link between marijuana and motivational level. Scher (1970) published a report on daily users who functioned quite normally in all respects despite five years of marijuana use and an admitted dependence on the drug. Casswell (1975) compared the performance of naive subjects and moderate users (3 times/week, 3 year history) on a series of tasks with and without monetary incentive. Monetary incentives produced an equal performance increment in both groups. In the long-term study of Mendelson et al., (Commission, 1972) heavy and casual users
worked for points to exchange for marijuana or money. Both groups had an average drug history of at least six years. All users smoked daily during the study, with individual variation in the amount smoked. "Almost without exception, every subject earned the maximum number of reinforcement points every day" (Commission, 1972, p. 74). In a later study without earning constraints, both heavy and casual users "...worked between 2 and 5 times as many hours as were necessary to earn the number of cigarettes smoked" and maintained this behavior throughout the 21-day study (Mendelson, Kuehnle, Greenberg & Mello, 1976). The dollars saved exceeded drug expenditures in both groups. Marijuana had a deleterious effect on operant behavior the day after heavy intake, but this effect was more apparent in casual users than in heavy users. In Jamaica and Costa Rica, heavy users exhibit productivity equalling or exceeding nonusers (Carr [NORML reprint], 1978; Commission, 1972, pp. 55-57). If amotivational syndrome is a viable clinical entity, then heavy use alone is evidently insufficient to produce it.

While experimental evidence and the methodological shortcomings of Kolansky and Moore weaken the case for amotivational syndrome, its existence cannot be entirely discounted. Significant personality changes (i.e. apathy, withdrawal) did not occur until marijuana was used and these changes apparently subsided subsequent to termination of use. Gross neurological signs (i.e. slurred speech,
ataxia, pronounced hand tremors), normally absent in heavy users, were noted in these patients. Differential drug susceptibility seems the most feasible explanation for amotivational syndrome. There is indirect evidence supporting this. Animal research indicates higher susceptibility to THC in younger animals. Experimental evidence suggests that the "blood-brain barrier" may be less efficient at earlier stages of development, allowing more THC to pass into brain tissue (Fried, 1977). Amotivational syndrome appears to be more pronounced in adolescents than adults, which is consistent with the differential susceptibility hypothesis. As Dornbush noted, the samples of Kolansky and Moore had atypical drug history profiles: immediate enjoyment of the drug, rapid progression to daily usage, and psychiatric referral within three years of initiating use, all suggestive of high susceptibility. Differential drug reactions are commonplace, and this would serve as the most parsimonious explanation for the symptoms observed (Dornbush, in Tinklenberg, 1975, p. 107).

Although physiological factors apparently play a role in amotivational syndrome, personality changes can stem from the psychosocial factors surrounding marijuana use. Smoking is generally performed in a group and the smoker is therefore subject to group norms; in addition, the act of smoking deviates from the prevailing societal norm (as defined by law)
and the smoker is consequently subject to social sanction. The extent to which a smoker uses the drug correlates highly with self-definition as a member of a deviant, marijuana-using subgroup. This subgroup may constitute a "counter-culture" with a normative system substantially different from that of the general culture. Heavy use increases the likelihood that the user will adopt group norms as guidelines for personal behavior and selection of friends and activities. Heavy use also takes time; the heavy user may be so preoccupied with smoking-related activities that there is time for little else. These factors would account for many of the attitudes shared by heavy smokers. Individual differences in age, personality traits, and pattern of usage modulate the extent of group influence (Becker, 1963, pp. 41-78; Goode, 1970, pp. 184-214; Grinspoon, 1977, pp. 206-209).

An issue related to chronic personality change is the question of marijuana's role in leading people to the use of harder drugs. Brill and Christie (1974) found no such relationship for casual users; in fact, 20 percent had quit or curtailed their marijuana use during the two-year follow-up period. The "steppingstone hypothesis", progression from marijuana to LSD and heroin, has been based largely on statements of heroin addicts that they had smoked marijuana prior to taking heroin. Surveys indicate increased prevalence of multiple drug use among heavier marijuana users.
(Goode, 1970, pp. 184-187). Causal relation cannot be assumed because of these correlative relations, however. Goode (1970, pp. 198-200) cites a multiple drug use study which indicates higher correlations between alcohol, tobacco and marijuana than those between marijuana and opiates. Correlations may vary among studies, but the claim that the use of one drug directly causes the use of another cannot be logically maintained (Grinspoon, 1977, p. 242). Psychosocial factors seem to be most effective in explaining multiple drug use. A daily marijuana user is exposed to positive attitudes about other drugs in his peer group. When the heavy user becomes interested in trying other drugs (in order to evaluate the claims of others or to seek their approval), the group provides readier access to these drugs than would be possible in the general population. Group norms dictate the relative values of different drugs and thereby influence extent of use. Among heavy marijuana users, the hallucinogens are highly regarded and heroin is held in low esteem. These attitudes are reflected in the respective rates of usage for these drugs (Goode, 1970, pp. 184-187, pp. 190-196). Hence, extensive marijuana use and peer group norms are the critical determinants of subsequent hallucinogen or opiate use among marijuana smokers.

Drawing firm conclusions regarding marijuana and personality change is a hazardous undertaking. One can never
be sure whether to assign causal status to predisposing personality factors or to the actions of the drug. Heavy users do share certain personality characteristics. Some combination of these characteristics may have existed prior to drug use and predisposed these individuals to adopt heavy marijuana use, and the pattern of behavior surrounding it, as their way of life. Other characteristics (e.g. attitudes toward use of hallucinogens and opiates) were probably acquired by interaction with their drug-using peers. The fact that some heavy smokers appear to be quite conventional in social interaction and work habits (Carr [NORML reprint], 1978; Commission, 1972, pp.55-57; Scher, 1970) suggests that the social and psychological factors surrounding marijuana use outweigh drug effects in shaping personality. Still, the possibility of chronic personality change due to heavy marijuana use cannot be excluded on the basis of present evidence. Acute personality change, psychotic or aggressive behavior, is rare. In those instances when acute changes have occurred, the role of personal, situational, and neurological determinants appears to be substantial. Extensive chronic personality change, in the form of an amotivational syndrome, seems to develop in individuals with an atypically high sensitivity to the drug. The effects appear to be largely reversible following cessation of marijuana use. The majority of casual marijuana users exhibit no measurable personality changes resulting from drug use.
Psychomotor Skills

The increasing mechanization of modern culture places a premium on attention and coordination. Complex machinery occupies both the work area and the family garage. Careless operation of such machinery can have serious consequences. The study of psychomotor skills and marijuana indicates that intoxication could precipitate these consequences.


Longer average reaction times apparently stem from attention deficits (Moskowitz, Sharma & McGlothlin, 1972). Loss of fine-motor coordination seems to arise from a common symptom of marijuana use - fine hand tremors. These are most prevalent in chronic users, but may be experienced by naive subjects during acute intoxication (Mendelson et al., in Commission, 1970, p. 80, p. 98, p. 100). Both attention and tremors probably affect tracking performance.

Behavioral compensation appears to exist for some psychomotor tasks, as it does for some cognitive tasks. Tasks
with a large attentional component, e.g., tracking and reaction time, are subject to this capacity (Beautrais & Marks, 1976; Mendelson, in Commission, pp. 84-85; Meyer et al., 1971; Weil, Zinberg & Nelsen, 1968). Fine hand tremors are evidently resistant to compensation and may actually be more severe in heavy users (Milstein et al., 1975b; Salvendy & McCabe, 1975).

A common, complex and frequently dangerous psychomotor task is driving a car in traffic. An early study of marijuana and driving found only a significant increase in speedometer monitoring errors after inhalation of 8 mg of THC (Crancer, Dille, Delay, Wallace & Haykin, 1969). The study employed a driving simulator on which the subjects were intensively trained prior to testing, which probably accounts for the lack of findings. Using the same dosage, Klonoff (1974) observed that subjects drove more poorly on a set course and in city traffic. Preoccupation, confusion, poor speed control and inappropriate reactions to pedestrians, moving traffic and stationary vehicles were characteristic of postdrug performance. Behavioral compensation was also noted, with a few individuals improving over baseline performance. This occurred most frequently at the lower dose of 4.9 mg. Analogous performance decrements have been obtained on a flight simulator with experienced pilots as subjects (Janowsky, Meacham, Blaine, Schoor & Bozzetti, 1976). The visual search component of these
tasks is apparently unaffected by marijuana; central factors are the basis of performance decrements (Moskowitz, Zeidman & Sharma, 1976). These factors, combined with marijuana-related perceptual deficits, make driving while intoxicated a very dangerous practice.

Psychomotor testing demonstrates a dose-related adverse effect of marijuana on tasks requiring alertness and coordination. Some users demonstrate a task-specific ability to compensate for drug effects. Fine hand tremors, the basis of fine-motor coordination problems, are apparently resistant to behavioral compensation. Complex machinery and automobiles should not be operated by intoxicated individuals.
Physiological Effects

Sexual Activity

The relationship of marijuana and sexual activity has been widely disputed. Some claim the drug is an aphrodisiac and that its use promotes hedonism and promiscuity. Other claim marijuana diminishes sexual interest; this belief is apparently cross-cultural, for Indian priests employ cannabis to curb libido (Grinspoon, 1977, pp. 315-316). Research in this area has been limited and firm conclusions must await further study.

Survey and projective methods provide some data on the subjective experience of marijuana and sex. The majority of those surveyed reported greater sexual enjoyment, citing enhanced sensory perception as the principal reason (Koff, 1974; Tart, 1971). Surveys report near-even division on the question of increased sexual desire, with women more likely to affirm this than men (Grinspoon, 1977, pp. 320-321; Robbins & Tanck, 1973; Tart, 1971). Aphrodisiacal effects are most likely to be reported by those who smoke low doses (i.e. one cigarette) several times a week (3 times/week, minimum) Grinspoon, 1977; Koff, 1974). Three-quarters of Tart's sample indicated that sexual arousal required situational cues in addition to the drug, the drug alone was insufficient to induce arousal. This assertion is supported by projective
results; reactions to ambiguous stimuli showed no significant increase in sexual content (Crockett et al., 1976; Roth et al., 1975).

Physiological research has centered largely on variations in plasma testosterone levels. Kolodny, Masters, Kolodner and Toro (1974) examined smokers after they had consumed an average of 9.4 cigarettes per week for five weeks and reported depressed plasma testosterone levels. Other chronic use studies performed on inpatient research wards have not replicated this finding, nor has a field study of Costa Rican heavy users (Fried, 1977; Mendelson, Kuehnle, Ellingboe & Babor, 1974; Schaefer, Gunn & Dubowski, 1975). Several explanations have been proposed for the Kolodny et al. finding. One explanation is periodic fluctuation in hormonal level, a well-documented phenomenon. Another is that a variety of other factors, including consumption of alcohol or other drugs, could have produced the observed levels since the research team had no control over subject behavior outside the laboratory (Mendelson et al., 1974). Also, the comparison was made to a control group matched solely on age (no control for diet, sleep, physical health, etc.) and the estimated average level was higher than other estimates in the literature (Schaefer et al., 1975). The subjects of Schaefer et al. and Mendelson et al. actually exceeded average testosterone levels, although the results
were considered to be within normal limits of fluctuation.

The importance of hormonal levels in human sexual behavior is unclear. Sexual performance apparently remains stable over a wide range of hormonal levels (NORML reprint, 1978). It seems likely then, that psychological factors hold precedence in this area. The tendency of frequent users to report heightened postdrug sexual interest supports this; those who use marijuana frequently impute greater influence to the drug in all facets of their lives (Zinberg & Weil, 1970). Occasional users are less likely to make this connection, whereas heavy users who smoke more than one cigarette at a sitting are more likely to become sedated than aroused. Marijuana's major assets in the sexual sphere are probably concentration on immediate experience, perceived enhancement of sensory faculties and prolongation of time. By temporarily suspending thought of future consequences, it may also relax inhibitions. This may account for the greater tendency of women to report heightened sexual desire. Women have traditionally been subjected to greater social constraint on sexual expression. Marijuana is widely believed to have sexual properties, and this belief provides women with an effective means of over-riding social prohibitions. Men do not experience the same social pressures and are therefore less likely to incorporate this belief into their ideas on marijuana (Koff, 1974).

A general consideration which is occasionally overlooked
in discussing marijuana and sexual activity is that the vast majority of marijuana smokers are between the ages of fourteen and twenty-five. This population readily engages in sexual activity without external prompting. The contribution of marijuana to inducing sexual behavior is probably small in comparison to that of the psychological and biological imperatives operating within these individuals (Grinspoon, 1977, pp.316-321).

Most of the research techniques employed in this area of study have been indirect. Subjective data is the principal basis for formulating hypotheses. Hormone studies have been made and have reached differing conclusions. In the final analysis, the relevance of hormonal levels to sexual behavior is undetermined. Few direct studies of marijuana and sexuality have been produced. Masters and Johnson have conducted this type of research, but their published report has received only limited circulation and was unavailable when this paper was prepared. Without such direct information, conclusions in this area must be drawn cautiously. For the moment, it appears that the aphrodisiacal properties of marijuana derive more from its basic psychological effects and the expectations of its users than from any direct stimulation of the sexual system.
Nervous System

Observations in Waking State. The physiological effects of marijuana stem primarily from its actions on the central nervous system (CNS). Efforts to examine marijuana's neurological activity have employed many different procedures and have obtained diverse results. Some specifics are disputed, but certain general conclusions seem apparent.

Electroencephalographic (EEG) examinations of cannabis smokers consistently demonstrate small changes in potentials within normal EEG limits (Commission, 1972, p. 35). The most commonly reported changes are a general reduction in cortical voltage, an increase in percent-time alpha activity, and a slight slowing of the dominant alpha frequencies (Domino, Rodin & Porzak, 1970; Dornbush, Clare, Zaks, Crown Volavka & Fink, in Lewis, 1972; Dornbush, Fink, & Friedman, 1971; Fried, 1977; Hollister, 1971; Volavka, Crown, Dornbush, Feldstein, & Fink, 1973). Other effects have not been as extensively replicated, and may be experimental artifacts not directly related to marijuana intoxication. These effects include decreased beta activity (Dornbush, et al., 1971; Volavka et al., 1973), increased beta activity (Cohen, Rickles, & Naliboff, 1975; Fried, 1977; Jones & Stone, 1970), decreased theta (Dornbush et al., 1971) and increased Stage 1 sleep (Dornbush et al., in Lewis, 1972). There are also
two reports of decreased alpha and higher dominant alpha frequencies (Jones & Stone, 1970; Naliboff, Cohen, Rickles, & Naimark, 1976) which run counter to the prevailing results on these measures.

Several problems complicate the evaluation of these results. There are differences in doses and postdrug monitoring periods. With the exception of Volavka et al., (1973), these studies did not use an ongoing alerting task; consequently, drowsiness may have masked some of the effects (Secretary of HEW, 1972, p. 214). All of the studies used subjects with prior marijuana experience. Nonhuman research indicates that EEG indices of lowered arousal (i.e. alpha slowing, increased percent alpha) diminish with chronic administration (Fried, 1977). The possibility therefore exists that EEG records will differ in relation to degree of prior smoking experience. At the moment, the only major EEG measures that seem to be dependably correlated with cannabis use are increased alpha activity, alpha slowing and general voltage reduction.

Increased alpha activity and general lowering of arousal have been observed in certain meditative states. Like smokers, meditators become intent on immediate experience and report a form of euphoria associated with release from external considerations. Like meditators, smokers learn from others how to recognize and cultivate
this state of consciousness. Both seem to experience less need for an external aid, mantra or marijuana, as experience in achieving this state is gained. This learned capacity is apparently the basis for "reverse tolerance", the reason that experienced users require less pot to get high (Volavka et al., 1973).

Decreased levels of EEG response to auditory stimuli have been reported, as has decreased GSR response to learning and stress (Cohen et al., 1975; Naliboff et al., 1976). There has been speculation that this illustrates the reported ability of smokers to "tune out" the world (Secretary of HEW, 1972, pp. 214-215; Tart, 1971). However, marijuana has been found to increase visual evoked potentials and to have a variable effect on contingent negative variation (Braden et al., 1974; Feeney, 1976; Kopell et al., 1972). Lack of uniformity across objective measures of evoked response contradicts the hypothesis that dissociation, "tuning out", is directly related to surface potentials. Surface EEG records only the outer shell and a small portion of the ventral and medial area of the cerebrum, about one-third of the brain's volume. The fact that substantial changes in cognitive performance are associated with only minor measurable changes in surface EEG 'strongly implicates subcortical, medial, or basal brain structures.
as being primarily responsible for the experimental and performance changes induced' (Dornbush, in Tinklenberg, 1975, pp. 110-111). A strong candidate for this responsibility is the hippocampus, with other elements of the limbic system and the hypothalamus contributing to the process (Feeney, 1976). (For further discussion, see Attention pp. 62-68).

Subhuman and "in vitro" studies have found concentrations of THC in the hippocampus, amygdala, and nearby structures. Associated with these concentrations are increases in catecholamines, particularly norepinephrine, and serotonin (Secretary of HEW, 1972, pp. 177-180). These preliminary findings have not been directly confirmed in humans (Commission, 1972, p. 34). Indirect support for generalization to humans comes from behavioral observations made following experimental manipulation of serotonin and catecholamine levels. Increased catecholamine levels are often associated with euphoric mood, while slowed time sense, hallucinations, and depersonalization frequently accompany increases in serotonin levels (Coleman, 1972, p. 286, pp. 331-333); all of these symptoms have been reported following acute THC intoxication (e.g. Isbell et al., 1967). Additionally,
decline in serotonin levels is positively correlated with diminished slow-wave sleep, and chronic THC administration appears to produce both of these deficits (Barratt, Beaver, White, Blakeney, & Adams, in Lewis, 1972).

At the autonomic level, THC is believed to stimulate the sympathetic system and block the parasympathetic system. This may be due to differing actions of THC and its metabolites (Dornbush, in Tinklenberg, 1972, p. 111). The main effect attributable to THC-induced sympathetic stimulation is the tachycardia noted during intoxication; this can be eliminated by administering a sympathetic blocking agent. Parasympathetic blockade has less objective support and is actually contradicted by some findings in cardiovascular research. The symptom most regularly imputed to parasympathetic blockade is dryness of the throat and mouth. Continued research is likely to clarify this point (Clark, 1975).

The autonomic cardiovascular effects of THC have received considerable study. THC seems to suppress the normal sinus arrhythmia produced by respiration as well as inducing tachycardia. Blood pressure is unchanged in the supine position, but may be lower when measured in the upright position. This may indicate impairment of the body's vasomotor reflex system (Clark, 1975; Renault, Schuster, Freedman, Sikic, Nebel de Mello & Halaris, 1974). There is preliminary evidence to suggest that mild
cerebral ischemia (inadequate blood supply) resulting from lowered blood pressure may contribute to postdrug performance deficits (Schueneman, 1974). This suggestion merits further study. THC has already been shown to adversely affect individuals with angina pectoris and could represent a potential hazard to others with subnormal cardiovascular systems (Aronow & Cassidy, 1974).

Aside from cardiovascular effects, the physiological changes induced by THC's influence on the autonomic system are few and unremarkable. A slight increased briskness in knee jerk has been observed with no change in threshold or elicitation of deep tendon reflexes. There have been two reports of pupillary constriction with most investigators finding no effect. Conjunctival injection, reddening of the eyes, is commonly noted and appears to result from blood vessel dilation and drying of the sclera due to reduced tear secretion (Commission, 1972, p. 34; Domino, Rennick & Pearl, 1974; Isbell et al., 1967; Weil et al., 1968). Respiratory rate and body temperature seem unaffected (Secretary of HEW, 1972, p. 212). Fine finger tremors, lateral gaze nystagmus, and ataxia, possibly due to cerebellar concentrations of THC, have been reported (Manno, 1971; Mendelson et al., in Commission, 1972, p. 80; Secretary of HEW, 1972, p. 174).

There is one report in the literature of cerebral atrophy associated with marijuana use. Campbell, Evans,
Thompson, and Williams (1971) performed pneumoencephalography on ten patients with a history of marijuana use and compared their records with a control sample. They noted enlargement of the third ventricle of the brain, implying tissue atrophy, and ascribed the atrophy to marijuana use. Replication of this study has not been attempted, due in part to the hazardous and painful nature of pneumoencephalography. The histories of the ten experimental patients revealed numerous possible confounds: one was retarded, one was a grand mal epileptic, one exhibited petit mal symptoms, three had sustained head injuries, one was a diagnosed schizophrenic, and one had been continuously treated with sedatives from the age of two years. Additionally, 8 of 10 used amphetamines, all had taken LSD (5 had 20 or more "trips"), and there were individual histories of heroin, morphine, alcohol, methaqualone, and barbiturate use. Attribution of brain damage exclusively to marijuana use seems questionable in these cases (Dornbush, in Tinklenberg, 1975, p. 106; NORML reprint, 1978; Secretary of HEW, 1972, p. 228). Recent x-ray studies of heavy marijuana users have revealed no evidence of cerebral atrophy (NORML reprint, 1978). Neuropsychological testing in this country and abroad has not uncovered signs of an organic brain syndrome associated with long-term use (Commission, 1972, p. 34, pp. 53-58; Culver & King,
The influence of THC on directly quantifiable indices of neural activity is relatively small. Surface EEG generally shows decreased cortical voltage, more alpha activity, and a slight slowing of peak frequencies. Direct animal data and indirect human data indicates an increase in biogenic amine levels, particularly norepinephrine and serotonin, in the hippocampal-hypothalamic region during acute intoxication. The observations of fine finger tremors, lateral gaze nystagmus, and ataxia may be related to THC concentrations in the cerebellum. Conjunctival reddening and tachycardia are the principal signs of THC’s effect on the autonomic system. One report of marijuana-induced cerebral atrophy is unsupported by other work and is weakened internally by a substantial number of subject confounds. With the exception of this study, no objective evidence of a link between marijuana use and organic brain damage has been produce. Of course, this does not eliminate the possibility that subtle damage, undetectable by tests of organicity, may occur with prolonged use.

Observations During Sleep. Neurological activity does not cease with the onset of sleep. The brain remains active during sleep, and this activity has been divided into discrete stages for re-
search purposes. The effect of THC does not end at sleep onset, either. THC affects overall sleep behavior and appears to exert specific influence in certain stages of cortical sleep activity.

Initial confirmation of marijuana's effect on sleep was made in the inpatient research ward setting. Smokers slept longer and were generally less active on the day following a day of heavy consumption, although this may have been partially due to smoking late in the evening on heavy-use days (Babor, Mendelson, & Kuehnle, 1976; Mendelson et al., 1976). In a direct test of the drug's hypnotic capacity, Cousens and Di Mascio (1973) gave oral doses of 10, 20, and 30 mg. of THC to nine insomniacs on a sleep research ward. All experienced more rapid sleep onset. Sleep patterns were not significantly altered after onset, although there was a trend toward fewer awakenings in the first four hours of sleep. The main side effect, most pronounced at 30 mg., was a sensation of being slightly stoned the next morning. With one exception, this dissipated in a few hours and reportedly did not interfere with daily activities. Long-term daily efficacy was not determined as administration was performed once a week.

The quality of THC-induced sleep has been questioned following studies of marijuana smoking and REM sleep. In the view of some researchers, REM sleep plays an
important role in maintaining the equilibrium of the waking personality, although this view is disputed by others (Vogel, 1975). Concern arose when sleep studies found decreased REM time following a single administration of THC (Barratt, Beaver, & White, 1974; Barratt, Beaver, White, Blakeney, & Adams, in Lewis, 1972; Freeman, 1974; Pivik, Zarcone, Hollister, & Dement; Zarcone, 1973). However, chronic administration studies indicate that REM suppression is quickly attenuated so that baseline levels are reached or exceeded within a span of three to five days (Barratt et al., 1972, 1974; Zarcone, 1973). Subjects generally show a return to baseline or a moderate REM increase on nondrug nights following REM suppression (Freemon, 1974; Zarcone, 1973). Preliminary studies indicate that daily cannabis users actually show a slight increase in REM activity (Zarcone, 1973). Given the rather transient REM suppression that THC displays, there is little likelihood that marked personality changes would be associated with this drug action.

A seemingly more robust effect does appear with chronic administration. Barratt et al. (1972, 1974) observed that slow-wave sleep (SWS) increased over a period of four days, then steadily decreased for the remaining six drug days of their study and remained below baseline levels during the postdrug week (readings
on day 1, 4, and 7). Animal studies have disclosed a related drop in serotonin levels associated with this deviation in sleep pattern. A suggested correlate of these changes in brain chemistry and sleep behavior is passive, hypoactive behavior. Such behavior is commonly attributed to marijuana use in humans (Barratt et al., in Lewis, 1972). Further investigation seems warranted.

One problem in current sleep studies is that time limitations on drug and post-drug periods may not allow adequate time for long-term drug effects to be assessed. This seems to be a particular problem with marijuana. THC has a long metabolic half-life and tolerance to some effects seems to develop with extended use. This has been illustrated in the case of REM sleep, and it may also hold true for SWS suppression. Barratt et al. (1972, 1974) had a drug period of 10 days and then performed three measurements over the 7-day postdrug period. There are reports that the depressant effects of daily THC administration are attenuated over a period of three to four weeks (Commission, 1972, pp. 23-25; Fried, 1977). If these effects are associated with SWS suppression, sleep studies may require a month-long monitoring period to record tolerance to this effect.

Research on marijuana and sleep is still in its early stages. The most reliable findings are those for acute intoxication. This state is conducive to sleep
induction; initial acute exposure to THC depresses REM and increases SWS. With extended exposure, REM returns to normal while SWS declines markedly. This decline has been reported to persist over a weeklong postdrug period. Tolerance to SWS suppression may occur following a month of smoking, but this has not been verified. The combined difficulties of sleep and marijuana research will probably prevent extensive investigation of this question and others in this area of inquiry. Those few researchers with the resources to examine this relationship should have many years of fruitful research ahead of them.
Respiratory System

The respiratory system performs the gaseous exchange essential to sustaining human life. If the efficiency of this system is substantially impaired, the psychological and physical well-being of the human being will suffer. Long-term marijuana smoking has adverse effects on the respiratory system.

Chronic bronchitis and asthma have long been associated with heavy cannabis smoking. Most reports of this kind come from foreign sources and must be interpreted cautiously. However, bronchitis and asthma have also been treated in American soldiers smoking hashish in West Germany. The cause of bronchial problems is not clear-cut in any of these populations. Many Eastern and European smoking mixtures combine hashish with tobacco, and many hashish smokers are also heavy cigarette smokers (Maugh, 1974a, Secretary of HEW, 1972, pp. 224-225). In Jamaica, subjects with lower cigarette intake show comparatively few bronchial problems despite heavy cannabis use (Commission, 1972, pp. 53-58). While serious cannabis-related bronchial dysfunction is apparently not widespread among American smokers, doctors report treating sore throats and bronchial irritation on numerous
Marijuana use is implicated in more serious respiratory dysfunction. Two prime indicators of pulmonary function are vital capacity (total volume of air exhaled in one normal breath) and one-second forced expiratory volume (the volume of air in the first second of exhalation) (Ayers, Whipp, & Ziment, 1974). Vital capacity is reduced in chronic obstructive lung disease (e.g. emphysema) and forced expiratory volume is commonly affected in bronchospasm and some acute pulmonary disorders. Mendelson et al. (in Commission, 1972, p. 78) discovered that 12 of 20 subjects (6 casual users, 6 heavy) failed to attain computed normal levels on one or both of these measures. How these computed values were obtained is unclear. Four of the seven most impaired were cigarette smokers and one was a nonsmoker with a history of childhood asthma. The remaining individuals had no record of prior pulmonary disorder and were not cigarette smokers, at least at the time of the experiment. Foreign studies have also found indications of reduced pulmonary efficiency (Commission, 1972, pp. 53-58).

As in the case of bronchial dysfunction, the relative contributions of tobacco and marijuana to reduced pulmonary function are hard to calculate. The role of air pollutants must also be considered. Studies of eight marijuana users who abstained from tobacco revealed no
significant changes in a comprehensive respiratory examination. Minor changes were noted in the structure and function of some microscopic structures, but these were not considered indicative of lung damage. The usage pattern in this group might be considered moderate (Commission, 1972, p. 45). No pulmonary function changes were observed by Mendelson et al. following 21 days of heavy, daily smoking (Commission, 1972, p. 81). Long-term heavy use, perhaps years of use, may be necessary to produce damage from marijuana alone (Maugh, 1974a). However, there is the distinct possibility that damage from tobacco and air pollution may be accelerated by marijuana use. Marijuana, whether ingested or inhaled, dilates air passages within the lung, allowing freer movement of gases into the alveoli (Tashkin, Shapiro, & Frank, 1973; Vachon et al., 1974). This property might allow smoke and pollutants to penetrate more deeply into the delicate tissues of the lung than would otherwise be possible. This is only speculation, however. More research is needed before the role of marijuana in pulmonary dysfunction can be clearly defined.

This has been a short section. Research on marijuana and the respiratory system is only beginning. Experimental confirmation of respiratory difficulty due to marijuana has thus far been hampered by the extensive concurrent use of tobacco among chronic marijuana smokers. The pre-
ponderance of clinical evidence shows smoking is related to throat and bronchial irritation and suggests that extended use could induce bronchitis and possibly asthma. Some long-term smokers show signs of chronic obstructive lung disease. This seems ample justification for more pulmonary function studies.
Other Physiological Effects

Aside from the studies of the nervous and respiratory systems, there is little evidence that major physiological effects occur with marijuana use. If these effects do occur, their psychological significance for the marijuana smoker would seem to be minimal. The medical significance of some findings has yet to be established; a few are probably more interesting than important. At present, most studies have been preliminary and their conclusions have been tentative; replication of findings seems the exception rather than the rule. For these reasons, this discussion will be limited to a brief survey of major findings.

The functional and biochemical integrity of the human body seems largely unaffected by THC. Examinations of blood chemistry report no significant changes (Mendelson, et al., in Commission, 1972, p. 81; Secretary of HEW, 1972, pp. 212-213). Liver function is unchanged in most instances; the few report cases of abnormality show equivocal etiology (Commission, 1972, pp. 54-57; Mendelson et al., in Commission, 1972, pp. 80-81; Secretary of HEW, 1972, pp. 225-226). No other changes in organ function have been reported. There are two reports of necrotizing arteritis associated with heavy cannabis use. One of these originates from
Morocco and lacks comparative study of arteritis in the general population. The other study was an examination of American polydrug users; the factor of greatest commonality in this sample was intravenous methedrine use (Secretary of HEW, 1972, p. 227).

Differential sensitivity to marijuana has been demonstrated. There is one report of an anaphylactoid response to the drug in a young woman. Subsequent testing confirmed that the patient was allergic to cannabis. Prevalence of this allergy is unknown, but it is believed to be uncommon (Secretary of HEW, 1972, p. 229).

Increased caloric intake and weight gain have been recorded. Heavy and casual users housed on a research ward experienced increments on both measures over a 21-day period. This was most evident in the first five days, with intake subsequently declining toward baseline in the remaining days. It was unclear whether this decline arose from the development of tolerance or from conscious measures to avert massive weight gain. Heavy users gained an average of 3.7 pounds, casual users gained an average of 2.8 pounds; controls housed on the ward gained an average of 2 pounds. Differential water retention may have affected these results, so the extent of actual body fat gained is uncertain (Greenberg, Kuehnle, Mendelson, & Bernstein, 1976; cf. Renault et al.,
Subcellular effects of THC have been examined in relation to the body's immune response. Depression of cellular activity has been found in some types of thymus-derived lymphocytes (Maugh, 1974a; Peterson, Graham & Lemberger, 1976). This depression has not appeared in other studies; some researchers have observed that this effect is related to the period of postdrug measurement and may be an acute, transitory phenomenon (Fried, 1977). Suppression of immune response has been found in mice at high dosages; this has not been demonstrated in humans (Maugh, 1974a). Since the immune system is complex and not fully understood, extensive basic research will be required before definite conclusions in this area can be drawn (Marijuana and Health [abstract], 1979, p. 2).

Another subcellular effect under examination has been THC's action on chromosomes. Gilmour, Bloom, Lele, Robbins, and Maximilian (1971) found no differences in numbers of chromosomal aberrations between a control sample and light (once/month) marijuana users. More aberrations were found in the heavy user group. However, these subjects were multiple drug users. The increased frequency of aberrations was not uniform across subjects; two of the eleven heavy users accounted for the majority of the observed increase. Using a larger sample (29)
males, 20 females), Stenchever, Kunysz, and Allen (1974) found a significantly greater number of aberrations in both light (once/week) and heavy (72 times/week) users: 3.4% for smokers versus 1.2% for controls. There are few other studies in this area, and these few are divided into separate camps behind Gilmour et al. and Stenchever et al.

There are at least two problems complicating chromosome research and possibly contributing to divergent results. The first problem centers on laboratory technique. The cell-preparation technique of Gilmour et al. was designed to minimize breakage induced by experimental procedure and differed in several ways from that of Stenchever et al. Gilmour's controls had a breakage frequency of .52%, while Stenchever's controls had a frequency of 1.2%. The increased breakage observed by Stenchever may represent greater susceptibility to experimentally induced damage. A second problem concerns assigning responsibility for breakage. "In vitro" studies of THC and cannabis resin have not found aberrations in exposed cells, while studies employing cannabis smoke have (Martin, 1969; Maugh, 1974a; Neu, Powers, King, & Gardner, 1969). Evidently some other fraction of the smoke produces the observed changes. This fraction may vary widely in marijuana, just as the psychoactive fraction does, and the amount absorbed is
undoubtedly subject to fluctuations related to mode of administration. Isolation of this fraction will be necessary before assessment of its damage potential can be made.

A broader consideration in the area of chromosome research is the clinical significance of the observed changes. A direct relationship between marijuana use and aberrations has not been shown; the increased average reported by Stenchever was based on an extended range of aberrations: 0 to 8 for users, 0 to 5 for controls. All subjects displayed good physical health. While it seem intuitively obvious that fewer aberrations are better, there is no established standard for clinically significant levels of damage. Consequently, the importance of these findings is still in question (Marijuana and Health [abstract], 1979, p. 3).

Medical research on the ancillary effects of THC is in its nascent phase. Few effects have been found, and fewer have been confirmed. Presently, the major foci of concern are subcellular effects on the immune response and chromosomal integrity. Vascular and hepatic anomalies have been reported, but they have not stimulated extensive research. Subjective reports of increased eating have received some objective support. Differential sensitivity to the drug has been confirmed. The majority of the present findings will be open to dispute until more work is performed.
Dependence and Tolerance

One of the oldest questions in marijuana research has been: Does chronic smoking create a physiological need for continued and escalating use of the drug? Two facets of physiological need, dependence and tolerance, are the topics of this section. Psychological dependence has been discussed elsewhere (See Personality).

Physical dependence is evident with some drugs, particularly heroin and barbiturates. When the drug of dependence is denied, the affected individual experiences withdrawal symptoms which can include nausea, cramps, diarrhea, hot and cold flashes, hyperthermia, hypertension, vomiting, and hyperventilation. Withdrawal symptoms of this severity have never been observed upon discontinuation of chronic heavy cannabis use (Commission, 1972, p. 43). The main abstinence symptoms reported have been irritability, restlessness, headache, mild gastrointestinal upset, and minor sleep disturbances. The abstinence syndrome appears with greater frequency and intensity following chronic hashish use, but, in any case, the symptoms subside within three days (Fried, 1977). It is likely that the relative mildness of this syndrome arises primarily from two pharmacological
properties of marijuana. First, marijuana has few remarkable physiological actions; its action is largely confined to the cortical, rather than the autonomic, level. This limits the extent of autonomic disruption seen during withdrawal. Secondly, THC has a long metabolic half-life; this means withdrawal proceeds at a slow pace. Slow diminution of the drug is less of a shock to the body.

The second aspect of physiological need is tolerance. Psychological dependence is distinguishable from physiological tolerance; while physiological dependence and tolerance are essentially different terms for the same organic process. The distinction is mainly contextual; dependence is used to discuss withdrawal, and tolerance is used to discuss continued drug use. Tolerance has occurred "when after repeated administration, a given dose of drug produces decreasing effect, or conversely when increasingly larger doses must be administered to obtain the effects observed with the original dose" (Secretary of HEW, 1972, p. 190). Tolerance extends to specific drug actions and should not be construed as a global organismic response. There are two broad classes of tolerance. Dispositional tolerance is the term for changes in absorption, distribution, excretion, and metabolism that reduce the intensity and duration of contact between a drug and its site of action. Functional
tolerance involves lessened sensitivity of the target tissue to the drug through altered properties and functions. Functional tolerance includes learned behavioral tolerance as a subtype of altered function (Commission, 1972, pp. 23-26).

Tolerance to specific drug actions is well illustrated in the case of marijuana. People who smoke on a daily or near-daily basis have exhibited tolerance on certain basic tests of memory, cognition, and psychomotor skills while their performance on other tasks maintained characteristic impairment. Those with more moderate usage patterns show more impairment than daily users on the same tasks. Tolerance to certain psychological effects evidently occurs, and the degree of tolerance displayed in different tests depends on individual level of drug usage and the psychological demands of the task (Beautrais & Marks, 1975; Cohen & Rickles, 1974; Meyer et al., 1971; Weil et al., 1968).

The tachycardial action of THC is attenuated by daily smoking. The duration of the tachycardia is lessened while the initial intensity remains relatively constant. Tolerance only appears with prolonged heavy use. Chronic administration studies with daily doses below 20 mg. of THC and smoking periods of less than 16 days have been unable to demonstrate significant tolerance (Perez-Reyes, Timmons, and Wall, 1974; Renault et al., 1974). 21-day
studies of smokers averaging 40 mg. of THC per day indicate that these people have a measurable decline in heart rate 25 minutes after smoking (Babor, Mendelson, Greenberg, & Kuehnle, 1975; Dornbush et al., in Lewis, 1972; Mendelson et al., in Commission, 1972, pp. 99-100).

Tolerance to subjective effects exists, but its appearance is complicated by the presence of reverse tolerance. With increased smoking experience, users respond more readily to ancillary cues (smoke, smell, taste) with subjective intoxication; given the proper circumstances, they may become stoned on a THC-free marijuana placebo (Galanter, Wyatt, Lemberger, Weingartner, & Roth, 1972; Jones & Stone, 1970). Tolerance has been observed to affect the duration of high, but not the intensity; reverse tolerance may underly the reported stability of intensity (Babor et al., 1976; Cappell & Pliner, 1974). At least a portion of the increased daily dosage employed by heavy users is used to maintain, rather than intensify, their high, since tolerance has reduced the duration of drug effect. This smoking leads, of course, to more tolerance. As a result, some smokers can absorb dosages that would incapacitate the nontolerant individual. Unlike other drug users who must face severe abstinence symptoms or the escalating costs of their habit, heavy marijuana users have the option of a short uneventful abstinence period with a subsequent
return to more moderate smoking levels when they tire of smoking large doses. Apparently many exercise this option during their smoking careers (Commission, 1972, pp. 23-26, pp. 53-58; Domino, Rennick, & Pearl, 1974; Mendelson et al., in Commission, 1972, p. 99).

While the exact nature of cannabis tolerance is undetermined, learning is probably involved in tolerance to cognitive and psychomotor deficits. The role of learning in subjective intoxication is evident (Carlin et al., 1974; Jones & Stone, 1970). A study by Cappell and Pliner (1974) provides a rough index of nonpharmacological influence in the subjective high. The authors examined the capacity of 30 heavy (18 cigarettes/week) users and 30 infrequent (2.3 cigarettes/month) users to titrate their smoking to a desired level of high. Each individual was supplied with marijuana in one of six conditions generated by two variables: potency (.36%, .45%, 1.45%), cigarette size (1g., 5g.). All groups obtained uniform levels of subjective intoxication across conditions; however, levels of THC consumed differed significantly. A capacity to titrate dosage was demonstrated, but this fell far short of compensating for potency changes. The difference between low and high potency was 400%. Subjects decreased intake only 60% between these dosage levels. Cigarette size was almost equal to potency in affecting amount consumed. As might
be expected, the users smoking small cigarettes smoked more cigarettes than those smoking large cigarettes. However, less marijuana was actually consumed in the small-unit group than in the large-unit group. These results illustrate the extensive influence of set and setting in determining subjective rating of intoxication. While objective test performance is more consistently dose-dependent, it is likely that expectations and experience still play a prominent role in affecting performance. Since daily users have more opportunities to learn compensatory behaviors while stoned and more emotional investment in showing that pot is harmless, these factors will augment any physiological factors underlying behavioral tolerance.

Some form of physiological tolerance must occur to account for tachycardial tolerance. Functional tolerance, in the sense of structural changes, has little supporting evidence. If such changes occur, they are apparently quite subtle. Distribution of the drug shows no measurable alteration during prolonged administration (Fried, 1977). The mechanism for tolerance may have a cellular or subcellular basis (McMillan & Dewey, in Lewis, 1972). Subhuman studies have found that tolerant animals have fewer molecules of THC and related compounds in their neuronal synaptic vesicles. There is also evidence that tolerant cells convert THC more rapidly to inactive
compounds (Fried, 1977). Postulating a cellular mechanism for THC tolerance development would account for the variable appearance of tolerance to specific drug actions, since the uneven distribution of THC in the tissues would differentially expose some cells to the drug and promote tolerance in that area. Confirmation of this possibility requires further study.

In psychopharmacology, complete detailed explication of all aspects of drug action from site of action through tolerance development is a goal sometimes likened to the Holy Grail; in both cases, the prize is elusive and the search frustrating. Part of the problem, of course, is that the human body itself is not fully understood. As a result, many drugs are used simply because they work, while the difficult causational questions are left unanswered. This is the case with marijuana. People smoke marijuana and enjoy it with little concern for its precise mode of action. Research indicates that people develop a tolerance to some effects of marijuana, but much of the drug will be consumed before scientists learn how the body adapts to THC exposure.
Overview

The initial topics of this paper were the pharmacology, methodological obstacles, and subjective experiences associated with marijuana. In each of the subsequent sections, evidence from a specific area of research was examined and evaluated. Some research allowed reasonably firm conclusions to be drawn. Methodological inadequacies and lack of corroborative evidence precluded definite conclusions in other areas of inquiry. The purpose of this final overview is to survey the general findings of marijuana research with human subjects and suggest future research directions.

Psychological Effects

While many subjective effects of marijuana smoking have been objectively supported, substantially enhanced sensory perception has not been demonstrated (Martz et al., 1972, Moskowitz et al., in Lewis, 1972). The subjective experience of vivid sensory perception apparently derives from the drug's effect on attention. By focusing attention on immediate experience and inhibiting comparison of present with past, the drug imbues familiar stimuli with an air of novelty and promotes a sense of timelessness. By the same mechanism, marijuana produces impairment of
memory and logical thought (Melges et al., 1971, 1972). A limited ability to compensate for these impairments has been observed in some individuals (e.g. Casswell, 1975). Euphoric mood and limited physical activity are commonly reported elements of the high; the possibility of an individual of average mental health becoming psychotic or violent in this state seems remote. Psychotic decompensation is most likely to occur in individuals with pre-existing psychotic tendencies (Weil, 1970). Violent behavior during intoxication is most commonly associated with the novice user experiencing an acute panic reaction and the heavy polydrug user who is highly impulsive, egocentric, and socially immature (McGuire & Megargee, 1974). The epileptoid individual may also risk precipitation of a violent episode by smoking marijuana (Abel, 1977). A more salient hazard for the average smoker is that posed by driving while intoxicated since reduced alertness and coordination increase the chances of an accident (Klonoff, 1974).

Acute effects are more easily assessed than the chronic effects of prolonged use. There is some clinical evidence that prolonged heavy use may adversely affect the eye muscles, and this warrants further study (Coleman et al., 1976). Chronic effects on memory and cognition have not been substantiated by current research. Psychosocial factors surrounding marijuana use, coupled with predisposing personality traits are better able to account for personality change and
progression to harder drugs than marijuana use alone (Goode, 1970, pp. 184-214). Certain aspects of severe amotivational syndrome (Kolansky & Moore, 1971) suggest that the affected individuals have been subject to THC hypersensitivity; these elements of the syndrome include gross neurological signs, e.g., pronounced ataxia, hand tremors, and slurred speech, and aspects of drug history such as immediate reaction to the drug at initial use, rapid progression to heavy use, and behavioral disturbances leading to psychiatric referral within three years of beginning use. The majority of heavy users do not exhibit such extensive neurological and behavioral changes (Dornbush, in Tinklenberg, 1975, p. 107).

The pattern of effort in perceptual research is one of feast or famine. For example, visual perception has received much attention and auditory perception very little. Of the visual measures attempted thus far, the only one still disputed is critical flicker fusion; a study combining oral doses adjusted for body weight and a series of ten ascending and descending trials would expedite resolution of this dispute. Of the auditory measures, only auditory detection thresholds have had well-controlled study (Martz et al., 1972). An experiment utilizing two dosage levels and several auditory parameters (e.g. frequency discrimination, intensity differentiation, etc.) is needed to determine whether these parameters are affected by THC and to establish a dose-response curve if they are. In cutaneous
sensitivity research, a multiple-dose-level study employing both electrical and non-electrical stimulation should resolve the discrepancies of current findings derived from differing doses and stimuli.

Current research on memory and cognition delineates the basic drug effects fairly well. One possible extension of current memory work would be the use of unfamiliar stimuli (e.g. nonsense syllables), as the majority of present experimentation has utilized familiar stimuli. One interesting finding has been the resistance of daily users to state-dependent learning in a paired-associate task (Cohen & Rickles, 1974): elaboration of this phenomenon might be achieved by exposing daily smokers to list-learning and other memory tasks in a state-dependent paradigm. A final procedure which deserves more emphasis is the use of retrieval cues. Retrieval cues have had a marked effect on the recall performance of intoxicated subjects (Eich, et al., 1975); experimental manipulation of cue type (e.g. synonyms, category labels) which might provide new insights into the nature of THC-induced memory deficits.

Personality research currently suffers from ex post factor analysis of the relationship of marijuana use and personality change. The same problem arises in evaluations of chronic memory and cognition effects. Satisfactory resolution of these issues will require longitudinal study. Memory, cognition, and personality data could be gathered
on a group of adolescent users and controls, held for five years or more, and then compared with retest results. Obviously the practical difficulties of such a study are numerous, overshadowed only by the difficulties of gathering a large random sample prior to onset of drug use and maintaining contact with the sample for the duration of the work. The latter procedure would provide the most reliable data, while the former may be the most feasible.

There is little doubt that marijuana impairs driving skills and general psychomotor performance (Salvendy & McCabe, 1975). Some elements of driver impairment remain to be elucidated. While individual compensatory ability has been noted (Klonoff, 1975), no systematic attempt has been made to compare daily users with casual users on driving performances. Despite evidence of increased glare recovery time and autokinesis, evaluation of performance under simulated night driving conditions is lacking. Both these studies would be valuable in accurately assessing the hazards of intoxicated driving.

This section ends with a few general considerations. As previously mentioned, some areas of psychological research have received much attention, and some have had considerably less. No area has received so much attention that replication of results would not be valuable. Replication would serve to reinforce present findings. A second consideration
regards the mode of administration. Oral administration seems to offer the best results in terms of dosage accuracy and extended period of intoxication, allowing completion of lengthy experimental procedures. For those wishing to use a smoking method, the best available seems to be that of Milstein et al. (1975a); this approach employs an electric crucible for complete burning and a storage vessel to contain the smoke, eliminating some inherent inefficiencies of the cigarette method. Finally, current research has established basic drug effects by means of relatively large doses. Now that this step has been taken, examination of effects at smaller doses might be of value, as such studies could be more easily generalized to the social setting.
Physiological Effects

Human physiological research has mainly focused on the neurological concomitants of intoxication with secondary interests in respiratory, cardiovascular, and hepatic activity. Some researchers have examined the quasiphsiological topic of sexual activity, and a few have studied immune response and chromosome damage.

Neurological experiments reveal slight reversible EEG changes, most notably increased alpha activity, slowing of peak frequencies, and lowering of cortical voltage; there is also indirect evidence of significant neurochemical changes within the brain (Fried, 1977). EEG sleep records indicate REM suppression at initial use followed by renewed REM activity and declining slow-wave sleep with successive doses (Barratt et al., in Lewis, 1972). Drug effects on cerebellar and autonomic activity include ataxia, fine finger tremors, lateral gaze nystagmus, tachycardia, and conjunctival injection (Mendelson et al., in Commission, 1972, p. 80).

As might be expected, respiratory studies disclose throat irritation as a common complaint of pot smokers. More serious are reports of chronic bronchitis and asthma (Maugh, 1974a). Still more serious are preliminary
indication of chronic obstructive lung disease in some individuals (Mendelson et al., in Commission, 1972, p. 78). While these findings are preliminary and somewhat equivocal, they provide ample cause for concern.

There are scattered reports of hepatic dysfunction and necrotizing arteritis in the literature. The relationship of cannabis use to these problems is poorly substantiated at this time (Secretary of HEW, 1972, pp. 225-227).

The physiological basis for the study of marijuana and sexuality has been measurement of plasma testosterone levels. One study (Kolodny et al., 1974) reported depressed testosterone levels in smokers and two (Mendelson et al., 1974; Schaefer et al., 1975) reported no change; the results of the latter two studies appear more reliable on the basis of better experimental controls. This may be a moot point, however, as psychological factors are apparently predominant in sexual activity. Likewise, psychological factors predominate in attribution of aphrodisiacal properties to marijuana (Grinspoon, 1977, pp. 316-321). Accurate evaluation of marijuana's effects on sexual activity will require more direct research methods than those of present studies.

Research on the cellular response to THC is at an early stage of development. "In vitro" studies of human lymphocytes and nonhuman experimentation have shown lowered immune
response after smoking, but this result has not been replicated in the human body (Maugh, 1974a). Some marijuana smokers show more chromosomal aberrations than a control sample (Stenchever et al., 1974). The exact breaking agent is uncertain, as is the clinical significance of the observed breakage (Maugh, 1974a).

Tolerance apparently develops to the behavioral effects of THC. This appears during repeated examinations of diminishing response to a given dose of the drug, or, conversely, as the need to use more of the drug to obtain the same level of response. Cardiovascular and subjective effects are also subject to tolerance. The exact mechanism of tolerance is unknown, but some combination of learned compensation and altered cellular metabolism seems likely (Fried, 1977).

Most studies of neurology and tolerance are currently performed on animals. While this is a prudent approach, evidence indicates that chronic administration studies with humans, on the order of thirty to forty days, can be safely performed and these studies would offer the most reliable answers to some questions. For instance, EEG tolerance has been shown in animals (Fried, 1977); if this tolerance appears in humans, its nature could be carefully detailed in such a study. The extended time period would also allow thorough analysis of chronic effects on sleeping EEG activity.
Of course, acute administration studies are simpler and more economical undertakings. On this level, human experimentation could use "labelled" THC and computerized x-ray scanning techniques to gain a more definite picture of drug concentrations within the brain. In chronic studies, this technique might also detect dispositional changes associated with tolerance.

To summarize, the acute psychological effects of marijuana smoking are largely transitory; the same holds true for the majority of the observed physiological effects. However, physiological research on THC is still in its early stages. While most studies report no major effects, some report respiratory damage, hepatic and circulatory dysfunction, reduced immune response, and chromosomal aberrations. Although these findings are in many instances preliminary and equivocal, they suggest that serious and sometimes irreversible consequences may accompany chronic marijuana smoking. For this reason, more studies of chronic smokers are needed. Longitudinal study would be an extremely valuable tool for assessment of long-term health risks, if a suitable sample could be recruited and maintained. In the short term, compilation of clinical statistics on the health problems of marijuana smokers could be useful for comparison with the general population, even though this method of data collection might be difficult and subject to many possible
confounds. Until carefully planned studies can be carried out, the degree of health risk incurred by a marijuana smoker will be an open question.

As a final note, the increasing popularity of marijuana as a recreational drug has spawned a debate characterized by strong opinions on the drug's psychological and physiological effects, opinions often based on little supporting evidence. Present evidence indicates that marijuana is neither the totally innocuous substance that its proponents claim, nor is it necessarily the first step on a path to madness, physical illness, and narcotic addiction that its more fanatical opponents believe. The state of present knowledge is not far enough advanced to exclude the many possibilities lying between these extremes. Controlled marijuana research with human subjects is only twelve years old, hardly enough time to ascertain all the possible effects of marijuana. Without the support of scientific evidence, opinions on the effects of marijuana are speculative at best. At present, the task of learning the effects of marijuana smoking on the human being would be better served by engaging in more meticulous research and less strident debate.
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