EFFECTS OF NALOXONE ON STRESS AND PERFORMANCE

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ABSTRACT

Title of Dissertation: Effects of Naloxone on Stress and Performance

Laura M. Davidson, Doctor of Philosophy, 1987

Dissertation directed by: Andrew Baum, Ph.D., Department of Medical Psychology

Studies suggest that exposure to unpredictable stressors results in performance deficits following stressor termination. Stressor exposure may also be accompanied by activation of the endogenous opioid system which may play a role in affective responding to stressors. It is possible that opioid effects are related to these aftereffects of stress because opioids cause effects that are similar to aftereffects. The major hypothesis of this study was that naloxone, an opioid antagonist, would ameliorate aftereffects due to exposure to uncontrollable noise. It was also hypothesized that naloxone would increase the reported aversiveness of the stressor, but would have no effect on simple performance during stressor exposure.

A total of 40 male subjects participated in this study. Naloxone or saline was administered prior to exposure to 23 minutes of random intermittent bursts of 100 to 108 dBA noise or silence. Mood was assessed three times throughout the experimental session; before the injection, four minutes following the injection, and following the twenty-three minutes of noise or silence. During the period of twenty-three minutes of noise or silence, subjects worked on an addition task, a

number comparison task, and a letter finding task. Following the stressor manipulation, and after rating the aversiveness of the twenty-three minute period, subjects worked on three aftereffects performance measures. They worked on a five minute proofreading task, a five minute encoding task, and a line tracing puzzle task.

Results replicated previous work on the effects of noise on performance. Subjects exposed to noise rated the session as more aversive and performed more poorly on the proofreading and the encoding tasks. Contrary to predictions, naloxone did not ameliorate the performance deficits associated with the noise exposure. Naloxone, however, was associated with some changes in mood and performance. Subjects given naloxone were less hostile following the injection. And, subjects given naloxone and exposed to noise performed more poorly on the addition problems than subjects given saline. Subjects given naloxone did not rate the noise as more aversive than saline subjects. In short, naloxone failed to improve performance following the stressor. Some possible explanations for this failure are examined.

EFFECTS OF NALOXONE ON STRESS AND PERFORMANCE

by

Laura Marie Davidson

Dissertation submitted to the Faculty of the Department of Medical Psychology Graduate Program of the Uniformed Services University of the Health Sciences in partial fulfillment of the requirements for the degree of
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Introduction

Stress is the process by which events threaten an organism and the way in which the organism responds to that threat (Baum, Singer, & Baum, 1981). It is an interactive process between the person and the environment which involves perceiving, coping, and adapting to a stressor. Stress may also be viewed as a "whole body" response because it has been associated with a variety of physiological and psychological changes including hormonal changes, cardiovascular changes, (heart rate and blood pressure) and increases in anxiety and depression (Baum, Singer, & Baum, 1981).

This research explored the role of physiological changes during stress in the development of psychological aftereffects of stress. It was hypothesized that the release of endogenous opioid peptides during stress was responsible for the behavioral and performance decrements which have been documented to occur following stressor exposure. Before considering the present study, the nature of physiological changes that occur during stress will be reviewed. Emphasis in this review will be on the so called "classical stress" hormones and opioid peptides which may also serve as hormone-like substances. In addition, psychological aspects of stress will be discussed. Mediators of stress aftereffects will be given particular attention. Finally, hypotheses relating opioid peptides and aftereffects will be derived.

The Stress Process

Although most people are familiar with the concept of stress, there continues to be a debate over its exact

definition. Stress has been used to refer to an environmental condition, the appraisal of that condition, response to environmental conditions, appraisal of threat, and to the interaction between the person and the environmental condition (Kasl, 1984). This lack of agreement over the definition has led to considerable confusion in the literature. Results and interpretations of studies differ, depending on the definition used and some argue that "stress" has little value because of this lack of conceptual clarity. Others, however, indicate the usefulness of stress as an heuristic that suggests mechanisms by which bodily responses and psychological states may derive from environmental events.

Theories that have been derived from one or another of these definitions have focused on different mechanisms or sequences of events. For example, Seyle's (1976) model is mainly physiological, focusing on adrenal cortical activity, while Lazarus's (1966) model focuses on psychological factors and appraisal. The development of independent literatures on physiological and psychological stress has contributed to confusion about stress.

Physiology of Stress

Cannon (1914) was the first modern scientist to describe the response of an organism to a severe environmental stressor. When confronted by danger, the organism readies itself to respond; Cannon referred to features of this readying response as the emergency responses or the "fight or flight" reaction. Focusing on adrenal medullary activity, Cannon associated response to danger with sympathetic arousal

involving discharge of epinephrine from the adrenal glands.

Hans Selye is considered by many to be the father of modern stress research. Although his role in popularizing the concept of stress is undeniable, his model has been criticized, revised, and expanded by other researchers. In the early part of the twentieth century, Selye (1936) found that a variety of different stimuli, ranging from physical stressors such as injection of foreign substances in the body, exposure to temperature variation, and exercise, to psychological stressors, could produce the same triad of responses in an organism. The triad included enlargement of the adrenal glands, involution of the thymus, and gastrointestinal ulcerations. Because all stressors resulted in the same triad, the process by which these effects were generated was said to be nonspecifically induced.

Selye further described the process of stress as driven by the pituitary-adrenal cortical axis and called it the general adaptation syndrome (GAS: Selye, 1956). The syndrome consisted of three stages. The first phase was alarm, during which the organism encountered the stressor and readied itself to respond. When adaptive reserves were ready and had been released in the form of corticosteriod discharge, the stage of resistence was reached. If the stressors lasted long enough or adaptive reserves were not great enough, exhaustion could occur. During exhaustion, diseases of adaptation were likely to be seen and death could result.

Subsequent to these contributions, a number of models of stress have emphasized psychological aspects of stress

rather than physiological mechanisms and some have focused on the interaction of psychological and physiological changes during stress. Mason (1975), for example, argued that stress was neither nonspecific nor unitary as Selye had argued and that patterning of endocrinological responses occurred for different stressors depending on psychological meaning. Mason argued that Selye found a nonspecific response because all of his stressors were accompanied by emotional responding. When Mason controlled for psychological distress, different hormonal patterns emerged for different stressors. Mason further emphasized the role of psychological factors in stress responding; he felt that psychological awareness was necessary for stress to occur and if stressors were not perceived as such, stress responding was unlikely (Mason, 1968). Frankenhaeuser (1972) further highlighted the importance of psychological factors in eliciting a physiological response to stress by showing that adrenal medullary responses to situations varied with psychological variables such as perceived control. Psychological components of stress will be addressed in greater depth later in this chapter.

Stress Hormones

Originating from Cannon and Selye's work, much of the early stress research focused on the responses of the adrenal glands during stress. Cannon (1935) focused his attention on the sympathomedullary system, recognizing the role of epinephrine released during periods of stress. Selye (1956) later focused his attention on the adrenal cortex, and the release of ACTH and cortisol during stress. Other hormones

have been found to fluctuate during stress as well and they appear to play an adaptive role in the organisms response to a stressor.

Adrenal hormones. More than thirty steroids have been isolated from the adrenal cortex. In humans, two are primary; the major hormones secreted by this portion of the gland are aldosterone and cortisol. Aldosterone is the primary mineralocorticoid, responsible, among other things, for regulating the electrolyte balance of sodium and potassium in the body. Investigators have found that aldosterone levels are elevated during times of anxiety or stress such as examination periods and surgery (e.g., Venning, Dyrenfurth, & Beck, 1957: Genest, 1957). Cortisol is the primary glucocorticoid released by the adrenal cortex in humans. Glucocorticoids operate to increase blood glucose concentration, play an important role in protein and fat mobilization, and have a potent anti-inflammatory effect.

Selye's work on stress focused primarily on the relationship between stress and the pituitary adrenal cortical axis. According to Selye (1976), the alarm phase of the GAS is characterized by secretion of adrenocorticotropic hormone (ACTH) from the pituitary. ACTH in turn stimulates the production of cortisol by the adrenal cortex. In fact, research has shown that a wide variety of stressors are associated with immediate increases in ACTH followed by rising levels of cortisol (Rose, 1980). The exact adaptive nature of this response is not well understood, but it probably serves to mobilize energy stores in times of need.

Cortisol elevations have been found in chronically ill patients, during pregnancy, in some psychiatric conditions, as well as during emotional distress associated with oral examinations, exercise, and surgery (e.g., Moncrief, Weichselbaum, & Elman, 1954; Bayliss, 1955; Bridges & Jones, 1967). Findings in animals and humans suggest that adrenocortical activity adapts rather rapidly to periods of chronic stress (Rose, 1980). Further, re-exposure to the same stressor fails to reinitiate the original response (Rose, 1980).

Sympathomedullary response during stress, centering on the adrenal medulla, has long been recognized as playing a primary role in the stress response (Cannon, 1914). The adrenal medulla is functionally analogous to a postganglionic neuron of the sympathetic nervous system. It contains chromaffin cells that secrete the hormones epinephrine and norepinephrine directly into central circulation. Concurrent sympathetic nervous system arousal, also involving release of norepinephrine by sympathetic nerve endings, is intensified and extended by this medullary activity. The actions of medullary hormones are about the same as the actions which result from direct sympathetic stimulation, but their effects last about ten times longer because it takes longer to clear these hormones from circulation than when released at a synapse (Guyton, 1976).

Norepinephrine and epinephrine have similar actions. They both increase basal metabolic rate, as well as rate and force of contraction of the heart, they cause dilation of the

pupil and the bronchi and constrict blood vessels. Epinephrine has a greater effect on basal metabolic rate and on cardiac activity. Vasoconstriction is influenced by levels of epinephrine and norepinephrine, but the former has less overall effect on blood vessels (Guyton, 1976; see table 1).

The adrenal medulla is ordinarily stimulated whenever any other part of the sympathetic nervous system is responding. Hence, hormones secreted by the medulla often provide indirect stimulation to organs directly innervated by sympathetic nerves. Research indicates that catecholamine discharge is a consequence of exposure to such stressors as emotional distress, noise, pain, hemorrhage, trauma, and anesthesia (Levi, 1965; Ortiz, Arguelles, Crespin, Sposari, & Villafane, 1974; Frankenhaeuser, 1972). But, epinephrine and norepinephrine are not necessarily released simulataneously. Frankenhaeuser (1975) reported that stressors which are characterized by novelty, anticipation, or unpredictability are associated with rising levels of epinephrine. Situations which require effort, attention, or vigilance more often lead to norepinephrine secretion. Mason (1975) also suggested that epinephrine and norepinephrine levels vary with the nature of a stressor. For example, situations characterized by threat or unpleasantness may be associated with increases in norepinephrine. When uncertainty is introduced epinephrine and norepinephrine levels increase. Unlike the pituitary adrenal cortical system which adapts readily to stress, catecholamines are more resistent to such an effect (Rose, 1980). Rose (1980) suggests that this resistence may be

because catecholamines are more easily replenished following discharge than cortisol (Rose, 1980).

Other metabolic hormones. Stress responding also influences the release of other hormones which are related to energy mobilization including growth hormone, insulin, and glucagon. Growth hormone responds to stress in much the same way as cortisol and catecholamines; however, stimulus intensity must be greater for concomitant discharge of growth hormone (Rose, 1980). Nevertheless, growth hormone increases in response to a variety of situations including surgery, physical exercise, stressful movies, examinations, and venipuncture (Newsome & Rose, 1971; Rose & Hurst, 1975; Salter, Fluck, & Stimmler, 1972; Syvalahti, Lammintauta, & Pekkarinen, 1976). Researchers have found contradictory results while measuring insulin levels during stress. Some have found increases, other no change, and still others have found decreases (Selye, 1976). On the other hand, glucagon produces a clearer pattern of response. Plasma glucagon levels are increased by stressors such as noise, injury, fasting, and exercise (Selye, 1976).

Hormones involved in ovulation can be affected by stress. Acute stress has been found to increase luteinizing hormone (LH) and follicle-stimulating hormone (FSH) in rats as rapidly as two minutes following a stressor (Ajika, Kalra, Fawcett, Krulich, & McCann, 1972). FSH and LH are anterior pituitary hormones which cycle in the female to cause ovarian change necessary for fertility. Other studies have found changes in FSH secretion in rats following stress but not in

LH secretion (Kawakami, Terasawa, & Arita, 1974). Carstensen, Amir, Wide, & Amer (1973) found no change in FSH production following surgery among human subjects, but did find changes in LH secretion. In general, much of the evidence on ovarian functioning indicates that acute stress leads to ovulation whereas chronic stress is associated with amenorrhea (Selye, 1976). Also, prolactin (LTH), the hormone responsible for lactation or milk production, changes during stress. This hormone has been implicated in other functions including osmoregulation and androgen metabolism. A variety of stressors including blood loss, laparotomy, cold exposure, and restraint increase LTH levels or induce lactation in laboratory animals (Kant, Meyerhoff, Bunnell, & Lenox, 1982; Nicoll, Talwalker & Meites, 1960; Grosvenor, 1965). In humans, prolactin rises during surgery, other medical procedures including pelvic examination, and parachute jumping (Eversmann, Gottsmann, Uhlich, 1978; Koninckx, 1978; Noel, Suh, & Stone, 1972).

Stress and Opioid Peptides

Although it has been known for years that stress interacts with a number of endogenous regulating systems, interest in the interaction between stress and the endogenous opioid peptide (EOP) system is more recent. Research now suggests that the EOP system is intimately involved in the stress process. In addition to interacting with and perhaps even regulating the release of many of the "stress hormones," the wide distribution of opioids in the CNS suggests that they may play an important role in affective responding during

stress.

For more than thirty years the actions of exogenous peptides such as morphine have been hypothesized to act through interactions with a receptor system (Beckett & Casy, 1954). However, it was not until 1973 that opioid receptors were found in mammalian tissue (Pert & Snyder, 1973; Simon, Hiller, & Edelman, 1973; Terenius, 1973). The discovery of specific opioid receptors was responsible for a tremendous amount of subsequent progress in the field.

The receptor molecules are specific recognition sites for opioids and hence are the cellular mediators for their action. Today, three major groups of endogenous peptides are recognized. The first two naturally occurring peptides that were found were pentapeptides differing only at the carboxyl terminal amino acid (Hughes, Smith, Kosterlitz, Fothergill, Morgan, & Morris, 1975). They were called methionine-enkephalin and leucine-enkephalin (from enkephalos; in the head). By 1976 part of beta-lipotropin (beta-LPH) was found to have opioid activity and this portion was named beta-endorphin (beta-EP; beta being derived from beta-LPH, endo meaning endogenous, and orphin from morphine) (Li & Chung, 1976). Other fragments of beta-LPH with opioid activity include alpha-endorphin and gamma-endorphin (Bradbury, Smyth, Snell, Birdsall, & Halme, 1976; Ling, Burgus, & Guillemin, 1976). The final set of endogenous opioids that were discovered include the dynorphin family (from Greek dynamis because of their potency) (Goldstein, Tachibana, Lowney, Hunkapiller, & Hood, 1979) which also

include alpha-neo-endorphin (Kangawa & Matsuo, 1979) and beta-neo-endorphin (Menamino, Kangawa, Chino, Sakakibara, & Matsuo, 1981).

Actions. The actions of the endogenous opioids are similar to those of morphine and its relatives. Morphine and related opioids produce their main effects on the central nervous system and bowel. In terms of their action on the CNS they produce analgesia, drowsiness, changes in mood including euphoria, and mental clouding (Reynolds & Randall, 1957). Opiates have been used for centuries for their analgesic action, but seem not to alter the perception of pain so much as the affective response to pain. Snyder (1977), for example, reported that although patients could still feel pain following morphine injection, it was no longer bothersome to them. These affective properties may be adaptive during times of stress. They may, for example, permit the organism to function more effectively by allowing escape rather than paralysis. Opioids may also facilitate narrowing of attention to allow an organism to ignore irrelevant stimuli.

Opioids also cause pupillary constriction, respiratory depression, and stimulation of the chemoreceptor trigger zone which causes nausea and vomiting. Although they have no major effect on blood pressure or on cardiac rate or rhythm, their effects on the GI system are diverse (Guyton, 1976). They decrease the tone and motility in the antral portion of the stomach and propulsive actions are diminished in the small intestines and colon. Other actions of opioids which have received attention include their effects on aging, core

temperature, locomotion, shock, respiration, eating and drinking, learning and memory, mental illness, gastric and renal activity, neurological disorders, and hormones.

Distribution of EOPs. The three general types of opioid peptides are found in separate neuronal networks. The beta-endorphin system, whose common precursor along with ACTH is pre-proopiomelanocortin, (Nakanshi, Inoue, Kita, Nakamura, Chang, Cohen, & Numa, 1979) consists of cells which originate in the hypothalamus and project long axons along the third ventricle and into the brain stem (Barchas, Akil, & Elliott, 1981). Regions in the brain with the highest concentration of beta-endorphin include the arcuate region of the hypothalamus and the periaqueductal gray of the brain stem (Kreiger, 1982). Outside of the brain in rodents, beta-endorphin concentrations are highest in the intermediate lobe of the pituitary, with lesser amounts found in the other lobes (Imura & Nakai, 1981). Since humans do not have an intermediate lobe, concentrations of beta-endorphin in the pituitary are much lower. Beta-endorphin has also been found in the gut, placenta, male reproductive tract, thyroid gland, lung, and pancreas in mammals (Kalin & Loevinger, 1983).

The common precursor for the enkephalin family is called pre-proenkephalin (Cox, 1982). Enkephalins are more widely distributed in the brain than are endorphins. This system consists of numerous cell bodies which have much shorter projections than those of the endorphins (Miller & Pickel, 1980). Highest concentrations of enkephalins are in the basal ganglia, globus pallidus, caudate, and putamen

(Miller & Pickel, 1980). Other areas of distribution include the hypothalamus, periaqueductal gray, and limbic structures, such as the amygdala and hippocampus (Miller & Pickel, 1980). Brain stem structures with high concentration of enkephalins include the substantia nigra, raphe nuclei, locus ceruleus, and reticular formation. Enkephalins are also found in the spinal cord (Stengard-Pederson & Larsson, 1981). Peripheral structures with enkephalin activity include the intermediate lobe of the pituitary in rodents and the posterior lobe of the pituitary in rodents and humans, the adrenal medulla, gut, sympathetic ganglia, vagus, retinal, and carotid body (Kalin & Loevinger, 1983).

There is a close similarity between the distribution of the enkephalin family and the dynorphin family. The dynorphin system is found in the hypothalamus, basal ganglia, hippocampus, amygdala, periaqueductal gray, substantia nigra, locus ceruleus, and the dorsal horn of the spinal cord (Botticelli, Cox, & Goldstein, 1981; Weber, Roth, & Barchas, 1982). In the pituitary, dynorphin is found mainly in the posterior lobe, and other areas of distribution include the gut and the adrenal medulla (Tachibana, Araki, Ohya, & Yoshida, 1982; Watson & Akil, 1981).

The areas of greatest opioid distribution suggest that they may play a major role in the affective response to painful stimuli and other types of behavioral regulation. They are concentrated in both the substantia gelatinosa of the spinal cord and the limbic system structures including the hypothalamus, thalamus, and amygdala. The substantia

gelatinosa may be influential in the primary processing of painful stimuli. According to Melzack and Wall's (1965) gate-control theory of pain a critical amount of information must first be processed in the substantia gelatinosa before a signal is sent to higher brain centers which ultimately mediate painful experiences. Although the exact role of the substantia gelatinosa in pain processing has since been questioned, the role of the spinal cord in pain processing is undeniable (Wall, 1978). The thalamus, which also contains large numbers of opioid peptides, regulates hot, cold, touch, and pain sensations (Bakal, 1979). The amygdala plays a role in aggressive behavior (Bakal, 1979). Finally, the hypothalamus is involved in emotional responses (Bakal, 1979). These areas of distribution support the notion that opioids play a role in affective response to stress and may influence the outcome of stressor exposure by mediating the appraisal of stressful events.

Receptors. There is general agreement that there are at least three receptor subtypes for the opioids and perhaps even more. When an opioid interacts with a receptor binding site a structural change ensues which leads to an observed response such as pain blockade. Other drugs may also interact with a particular binding site, but they do not lead to the configurational change which is necessary for opioid action. The three main receptor types are the mu, delta, and kappa receptors. The mu receptor has the greatest affinity for morphine. This receptor is thought to be involved in analgesia. The Kappa receptor binds ketocyclazacine and may

be related to sedative and ataxic effects. The delta receptor binds preferentially with enkephalin-like opioids and may produce psychotic-like effects. The endogenous peptides each have preferential affinity for different opioid receptors. Whereas endorphins have equal affinity for the mu and delta receptors, met-enkephalin and leu-enkephalin bind at the delta receptor, and the fragments of pre-prodynorphin bind to the kappa receptor. To sum up the receptor effects, the mu receptor is primarily involved in analgesia, the kappa receptor is involved in sedation and ataxia, and the delta receptor is responsible psychotic-like effects

Relationship Between EOP System and Stress Hormones

Endogenous opioid peptides interact with many of the stress-related hormones discussed previously including cortisol, catecholamines, follicle stimulating hormone, luteinizing hormome, prolactin, and growth hormone. The relationship between EOPs and stress hormones suggests that the EOP system plays and important role in stress adaptation.

Whereas met-enkephalin decreases the production of both glucocorticoids and mineralocorticoids from the adrenal cortex, beta-endorphin increases the formation of glucocorticoids alone (Millan & Herz, 1985). Opioids also influence the adrenal cortex indirectly by their effects on ACTH; in humans, exogenous opiates stimulate the production of ACTH (Von Graffenreid, del Pozo, Rubieck, Krebs, Poldinger, Burmeirster, & Kerp, 1978). Evidence suggests that the same environmental stimuli simultaneously trigger the pituitary-adrenal axis and the EOP system probably because CRH

simultaneously causes the release of endorphins and ACTH from the anterior pituitary (Baizman, Cox, Osman, & Goldstein, 1979; Vale, Speiss, Rivier, 1981). Stressors like limb fracture, foot shock, heat stress, insulin-induced hypoglycemia, ingestion of hypertonic saline and immobilization have been shown to cause activation of both systems (Guillemin, Vargo, Rossier, Minick, Ling, Rivier, Vale, & Bloom, 1977).

EOPs also play a role in adrenal medullary response to stress. Since morphine influences epinephrine synthesis, storage, and release and the adrenal medulla contains large numbers of opioid receptors, EOPs are probably capable of producing catecholamine release from the adrenal medulla (Anderson & Slotkin, 1976; Chavkin, James, & Goldstein, 1979). The administration of opioids does in fact enhance sympathetic tone by the release of catecholamines into central circulation (van Loon & Appel, 1983). Because this phenomenon is abolished by adrenal denervation and demedullation, it undoubtedly results from the association between opioids and catecholamines in the chromaffin cells within the medulla (Millan & Herz, 1985).

Opioids also influence luteinizing hormone and follicle stimulating hormone. Exogenous opiates inhibit their release. Since the opioid antagonist naloxone increases both hormones, EOPs probably exert a tonic inhibitory influence on these two hormones (Meites, Bruni, Vugt, & Smith, 1980). These results suggest that EOPs may help to regulate gonadotropin levels during stress.

Finally, both endogenous and exogenous opioids stimulate growth hormone release. Naloxone is capable of antagonizing this effect (Bruni, Vugt, Marshall, & Meites, 1977). However, since naloxone does not influence basal levels of GH, it is unlikely that EOPs play a major role in the regulation of this system (Martin, Tolis, Wood, & Guyda, 1979).

Measurement of Opioid Activity

Three strategies have been used to study the activity of the endogenous opioid system; they are administration of opioid antagonists, administration of agonists, and direct measurement of opioids in body fluids. Although all three methods are discussed here because of the pharmacodynamic information they provide, measuring opioids in body fluids also can be a useful way of establishing the pharmacokinetics of opioids.

One of the most widely used methods to study endogenous opioid activity is by administration of naloxone. Naloxone is an almost pure opioid antagonist with no intrinsic action of its own and hence has proven to be a useful tool to researchers. Changes which occur following administration of naloxone suggest prior activation of the endogenous opioid system. It acts as a competitive antagonist for opioid receptors, therefore blocking the effects of most opioids. Although naloxone has its highest affinity for the mu receptor, at higher concentrations it will antagonize the action of agonists at the delta and kappa receptors. Following intravenous (i.v.) injection of naloxone, the onset

of action is one to two minutes. The drug can also be given subcutaneously or intermuscularly, but under these circumstances the onset of action is delayed. After intravenous injection the effects last from 45 to 70 minutes, but the duration is prolonged following intermuscular or subcutaneous injection.

The side effects of naloxone are minimal. Lasagna (1977) noted a strange biphasic reaction with this drug; doses less than 2 milligrams in humans cause analgesia whereas higher doses cause hyperalgesia. No adverse reactions have been seen in doses up to 24 milligrams i.v. (Drug Theraputics Bulletin, 1981). Doses ranging form 1.2 mg to 20 mg cause no change in heart rate, respiration, or blood pressure (Willer, Boureau, Dauther, & Bonora, 1979; Voluvk, Bauman, Pevnick, Reker, James, & Cho, 1980). However, in doses in the 2 mg/kg range Cohen, Cohen, Pickar, Murphy, & Bunney (1981) found a dose dependent increase in systolic blood pressure and heart rate. It is unknown whether these results indicate a tonic activation of the EOP system which was not apparent with low doses of naloxone, or whether naloxone had actions of its own at high doses. Although some researchers have reported that subjects are unable to differentiate between naloxone injection and placebo in doses ranging from 1 to 10 mg (McCubbin, Surwit, & Williams, 1985; Grevert & Goldstein, 1978) and found no changes in mood along the dimensions of friendliness, tension-anxiety, confusion-bewilderment, vigor-activity, depression-dejection, anger-hostility, and fatigue-inertia, other have found no changes in mood following

doses of .8 mg and 1.6 mg of naloxone (File & Silverstone, 1981). In regard to performance, Wokowitz & Tinklenberg (1985) found that 1.2 mgs of naloxone had no effect of tests of memory, visual psychomotor skills, and reaction time tasks. However, at higher doses (2 mg/kg) Cohen, Cohen, Weingartner, Pickar, & Murphy (1983) found decrements in recognition of twice presented words, free recall of such words, and estimation of frequency of presentation of words. This effect was not found for all subjects tested and hence may represent an idiosyncratic response to the drug at high doses.

Another research strategy has been the administration of both exogenous opiates and opioids and measuring the behavioral effects of such drugs. There are problems with using opiate drugs, however, because their affinities for the various receptors are different than those of endogenous substances. In addition, administration of agonists is generally parenteral and their access to the central nervous system is questionable (Rapoport, Klee, & Pettigrew, 1980).

Unlike these two methods, which are indirect, peptide concentrations can be measured directly using radioreceptor assays (RRA) and radioimmunoassays (RIA). While the radioreceptor assay meaures functional activity, it cannot be used to distinguish between the different peptides. The radioimmunoassay, on the other hand, can provide information about individual peptides (Pickar, Cohen, Naber, & Cohen, 1982). However, RIAs do not provide information about the interaction between the peptides and the receptors. Studies using these methods have found a diurnal variation in

beta-endorphin immunoreactivity (Dent, Guilleminault, & Albert, 1981) which peaks at 6:00 am and has its nadir at 11:00 PM. Using RIAs, measurement of peptides differ considerably among laboratories. While one group using radioimmunoassay found normal human plasma beta-endorphin concentrations to be 50 to 300 pg per ml (Wilkes, Stewart, & Bruni, 1980), concentrations less than 21 pg per ml have been reported by other researchers (Wardlaw & Frantz, 1979).

Activation of EOPs in response to stress.

Researchers have measured opioid activity in response to a variety of stressors. In rats, beta-endorphin levels increased following shock, immobilization, handling, novelty, swimming, and surgery (see Olsen, Olsen, & Kastin, 1985 for a comprehensive review).

In humans the physical stress of surgery, labor, physical exercise, and the more psychological stress of examinations all cause increased opioid activity. For example, in a study of beta-endorphin levels during surgery, plasma levels of beta-endorphin were measured prior to intubation and anesthetic induction, 10 minutes after skin incision, and at 30 minute intervals throughout the surgery (Cohen et al., 1982). All patients were undergoing laparotomies and were medication free prior to the surgery. Surgery was associated with rising levels of plasma beta-endorphin and plasma cortisol levels suggesting a stress response. Examination of post-surgery morphine administration indicated that patients with high presurgery levels of opioids required lower morphine doses and that patients with low

presurgery levels required higher doses. These results were consistent with studies of emotional preparation and surgical outcome which suggested that moderate levels of anxiety were associated with the best postoperative outcome (Janis, 1958).

Other stressors have also been associated with activation of the EOP system. In a study of childbirth, researchers reported that plasma levels of beta-endorphin increased during labor and were eliminated by morphine or epidural anesthesia (Hoffman, Abboud, Haase, Hung, & Goebelsmann, 1984). These results suggested that opioids increased in response to the pain associated with labor. Other researchers have measured opioid activity in trained runners following a run, documenting elevations in opioid activity which varied in relation to effort (Colt, Wardlow, & Frantz, 1981). Finally, Tescchemacher, Briedenback, Konig, Luckhardt, & Davies-Osterkamp (1980) found that beta-endorphin immunoreactivity was greater prior to an examination period than at basal levels. Thus, in humans EOPs have been found to vary in response to a variety of stressful experiences. In addition to these naturalistic human studies, researchers have examined opioid activity in the laboratory. In the lab, opioid activity generally has not been measured directly, but has been inferred through changes which result following the administration of opioid antagonists. These laboratory studies will be discussed in the context of psychological mediators of stress.

Psychological Aspects of Stress

Up to this point, stress has been viewed mainly in

terms of its physiological costs and concomitants. However, it is clear that there are important psychological dimensions to the stress construct. In addition to causing hormonal changes, stress may also change how people feel (their mood, or symptom reporting) as well as their performance on tasks.

Lazarus (1975) emphasized the role of cognitive mechanisms in the stress response. According to Lazarus, a stress response occurs only if stimulation is perceived as a threat. In support of the importance of cognitive processing, Symington, Currie, Curran, and Davidson (1955) found that conscious dying patients had elevated adrenal activity in response to a terminal illness. Those who were in a coma did not exhibit this evidence of a stress response. These data suggested that the stress of dying itself was not sufficient to cause stress-related physiological changes, and suggested that cognitive awareness was the critical factor in determining the occurrence of the adrenal changes described by Selye. In further support of the importance of cognitive processing, Lazarus, Opton, Nomikos, and Rankin, (1965) showed that heart rate and skin conductance changes to a film could be modified by simply altering the narration accompanying the film. Subjects watched a film depicting woodshop accidents. One group was given no explanation for the film, and two other groups were told either that the events were staged or that the film would be used to improve safety. Results indicated that the two narrations reduced stress-related arousal to the film. These results highlight the importance of individual interpretations in stress responding.

In general, a variety of factors will mediate a stress response. The factors include situational variables as well as personal variables like attitudes toward the stress, risk perception, social support, dispositional variables, predictability, and control (Baum, Singer, & Baum, 1981). Partly as a result of autonomic activation which accompanies a stress response, a number of feeling states may be reported following exposure to a stressor including anxiety, depression, and fear.

Aftereffects

In a series of studies designed to study the psychological costs of adaptation, Glass and Singer (1972) evaluated cognitive processes associated with adaptation to noise. Accordingly, adaptation was viewed as "a cognitive process involving re-evaluation of the noise stressor as benign or the use of more direct action strategies for coping with noise such as "filtering noise out of awareness by becoming engrossed in some task." (p. 457, 1972).

Consistent findings suggested that high-intensity noise alone had no adverse effect on human task performance (Broadbent, 1957) unless the task was a long-term vigilance task, was complex, or the noise was intermittent. Glass and Singer (1972) were unable to replicate the intermittent noise effect on task performance unless the task was complex. Simple tasks were unaffected by the noise regardless of the intensity or the pattern of the noise. In general, few effects were found during noise exposure (Glass & Singer, 1972). Skin conductance showed an initial increase when the

noise was loud, but this response quickly adapted as did finger vasoconstriction, and muscle action potentials which were noted at the onset of the noise. However, Glass and Singer found consistent changes in behavior or performance following the termination of the stressor.

In their studies, noise was delivered at either random or fixed intervals. In the fixed condition, noise was delivered at the end of every minute for about 9 seconds and in the random condition both the length between and the length of each burst varied. The total time of noise exposure varied from 3 1/2 to 5 minutes depending in part on whether the noise presentation occurred over a 23-, 24-, or 25-minute period. In some of the experiments each type of noise was presented at both soft and loud intensities.

In order to measure aftereffects, several tasks were presented following the stressor. The first, the Feather task (1961) consisted of four line diagrams. The subject's task was to trace over the lines without lifting the pencil or tracing over any line twice. Two of these tasks were solvable and two were insolvable. The second task was a proofreading task. Subjects were given 15 minutes to read and circle errors in a 7-page passage. The Stroop color discrimination task was also used to test for aftereffects in some of the studies (Houston & Jones, 1967). For this subjects were asked to identify the color of ink that different color names were printed in.

Glass and Singer's results indicated that random noise bursts lowered tolerance for frustration as measured by lack

of persistence on the Feather task and lowered the percentage of errors found in the proofreading passage. The unpredictability of the noise rather than its intensity was more important in determining the deleterious outcome of the stressor.

Glass and Singer further tested the hypothesis that control over the stressor should reduce the effects created by the unpredictability. To give control, they told subjects that they had a switch which would terminate the presentation of the noise. They were asked not to use the switch, but were told that it would terminate the noise if they used it. Compared with subjects not told about the switch, those with perceived control showed amelioration of performance decrements. This was true even though control was never actually exerted, as subjects did not use the switch. The authors hypothesized that uncontrollable noise produced feelings of helplessness and that subjects in conditions with no contol had to cope with the anxiety associated with helplessness along with the stress of the noise. On the other hand, perceived control groups did not experience the same anxiety associated with feelings of helplessness. An interesting note about these conditions was that the subjects did not reliably rate the uncontrollable or unpredictable situations as more aversive even though they performed more poorly on the post-task measures.

Researches have found similar post-stressor deficits following unpredictable and uncontrollable electrical shock, cold stress, bureaucratic frustration, arbitrary

discrimination, and crowding (e. g. Glass & Singer, 1972; Sherrod, 1974).

Psychological Variables and EOPs

Just as psychological variables are important to a general stress response, they are important in activation of the EOP system. Conditions which are known to produce aftereffects also cause activation of the opioid system. Research in rodents suggests that noise stressors can cause activation of the opioid system. For example, Katz and Gelbart (1978) found that exposure to noise-light stress caused stress-related grooming in rodents that could be blocked by administration of naloxone. Similarly, Roth and Katz (1979) found increases in grooming and changes in exploratory behavior following noise exposure. Arnsten, Berridge, & Segal (1985) found similar changes in exploratory behavior following noise exposure. These stress-related effects could be blocked with either administration of naltrexone or naloxone, two opioid antagonists.

Stressor controllability has been implicated in stress-induced analgesia (SIA) in much the same way as in the aftereffects literature. When an experimental animal is exposed to a novel or severe stressor, its sensitivity to painful stimuli will be reduced for a period of time afterwards. This post-stressor analgesia or stress induced analgesia (SIA) may be reversed by administration of naloxone. This reversibility with naloxone suggests the importance of the endogenous opioid system in SIA. Jackson, Coon, & Maier (1979) found that SIA could be reinitiated 24 hours following

exposure to an inescapable shock, but not after escapable shocks. This long term SIA seemed to be opioid in nature because it could be blocked with opioid antagonists and was cross tolerant with morphine (Maier, Davies, Grau, Jackson, Morrison, Moye, Madden, & Barchas, 1980; Drugan, Grau, Maier, Madden, & Barchas, 1981). In addition, the long-term analgesic effect could be blocked by prior experience with escapable shock (Moye, Grau, Coon, & Maier, 1981). Evidence also suggests that SIA is associated with learned helplessness. In fact, it has been suggested that in order for SIA to occur following inescapable shocks, enough shocks must be given so that learned helplessness develops. Grau, Hyson, Maier, Madden, & Barchas (1981) found that while twenty minutes of intermittent foot shock produced naloxone-reversible analgesia, three minutes of continuous foot shock did not cause the same effect.

Other researchers have found an association between performance decrements and SIA in rodents. McCubbin, Kizer, and Lipton (1984) found that animals exposed to inescapable footshock exhibited SIA and deficits in one-way shuttle acquisition. Both of these effects were reversed by pretreatment with naltrexone, an opioid antagonist.

Thus, experiments on rodents suggest that situations that are unpredictable or uncontrollable result in activation of the EOP system. They also produce behavioral changes in animals which are naloxone reversible. Therefore, animal studies suggest that EOPs may play a role in stressor aftereffects.

In humans, changes in the opioid system in response to a stressor are more difficult to document. For example, Grevert and Goldstein (1978) exposed subjects to either 5 minutes of cold water or ten minutes of ischemic pain. They found no changes in pain ratings that could be influenced by naloxone. Similarly, El-Sobky, Dostrovsky, and Wall (1976) failed to find naloxone reversible changes in pain ratings following increasingly painful shocks administered at 1.2 second intervals. However, in each of these studies the stressor may have been too short to result in activation of the EOP system. Animal studies suggest that the timing of a stressor is crucial in the activation of the EOP system. Naber, Bullinger, Zahn, Johnson, Huhtanium, Pickar, Cohen, & Bunney (1981) also failed to find changes in plasma opioid levels or opioid activity following 10 minutes of either a nonverbal intelligence test, a competitive discrimination task, or a bicycle ride. However, they did find a relationship between opioid levels and self-reported stress.

Although Bouloux, Grossman, Al-Pamluji, Bailey, & Besser (1985) did not measure opioid levels directly, they did find that exposure to a cold pressor increased levels of norepinephrine, epinephrine, heart rate, and systolic blood pressure and that naloxone enhanced this response. These results suggest that EOPs moderate the release of catecholamines or that they are linked through mutual feedback systems. Bullinger, Naber, Pickar, Cohen, Kalin, Pert, & Bunney (1984) measured opioids following a cold pressor task and found that opioid activity was negatively correlated with

reported pain intensity. In a paradigm similar to those used by animal researchers, Jungkuz, Engel, King, & Kuss (1983) found that following a cold pressor, that pain tolerance to electrical stimulation increased. This effect could be reversed by treatment with naloxone.

Other researchers have demonstrated changes in the opioid system in humans by introducing anticipation, anxiety, or by correlating opioid activity with other individual difference variables. Willer & Albe-Fessard (1980) studied the influence of shock and the anticipation of that shock on monosynaptic reflex thresholds. The reflex threshold was used as a measure of opioid activation; the longer the latency to reflex threshold, the greater the opioid activation. Their results demonstrated that shock and anticipation increased the reflex threshold over time and that this effect could be reversed with naloxone. Similarly, Schull, Kaplan, & O'Brien (1981) attempted to increase the anxiety associated with cold pressor and tourniquet pain. They found that naloxone increased the aversiveness of the ischemic pain but not the cold pain. Miralles, Olaso, Fuentesa, Lopez, Loardin, & Puig (1983) studied the relationship between opioids and the anticipation of surgery. These researchers reported that endorphin levels increased as a function of the anticipation of surgery. In a study of women in labor, researchers found that Lamaze prepared women had lower plasma beta-endorphin immunoreactivity than a nonprepared group (Delke, Minkoff, & Grunebaum, 1985). The authors suggested that the lower opioid immunoreactivity was related to fear reduction and less

emotional distress in the Lamaze group. Although these data may seem to suggest that the Lamaze prepared women would experience greater pain because of lower opioid levels, this is probably not the case because there are psychological as well as physiological components to pain and the Lamaze prepared group would be better prepared emotionally for the experiences of labor and delivery. Pickar, Cohen, & Naber (1982) measured CSF opioid levels prior to lumbar puncture and found them to be inversely related to self-ratings of anxiety at the time of the puncture.

Thus, data from studies of animals and humans suggest that opioids play a role in response to a stressor and that cognitive factors such as control moderate opioid activity in much the same way that they affect other aspects of the stress response. In addition, research on rodents has shown that opioids play a role in post-stressor behavioral and performance changes. These changes in behavior and performance may be blocked with the opioid antagonist naloxone. These data provide reason to believe that EOP activity is associated with behavioral, perceptual, and physiological aspects of stress and that they may be involved in the generation of aftereffects such as those observed by Glass and Singer (1972).

Theories Explaining Aftereffects

The exact cause of aftereffects in humans remains unclear. Cohen (1980) reviewed eight theories which have been used to explain aftereffects and a ninth one relating to opioids will be proposed here. According to the "original"

adaptive-cost hypothesis (Glass & Singer, 1972) work is required when and organism searches for the best way to cope with a stressor. The more adaptive energy that is used in coping with a stressor, the less is available for subsequent demands. It takes more work to cope with stressors that are unpredictable. Hence, following exposure to unpredictable or uncontrollable noise, fewer resources are available for post-stimulation tasks. Cohen (1978) added that increasing attentional demands lead to cognitive fatigue. Under these circumstances less attention would be available for subsequent demands. Only tasks requiring considerable attention would suffer.

The learned helplessness explanation was also proposed by Glass and Singer (1972. Situations characterized by noncontingencies between response and reward lead to motivational deficits that become apparent on post-stimulation tasks. Thus, in the noise studies, subjects exposed to uncontrollable noise would be expected to experience learned helplessness and be less motivated to perform on post-stress measures.

Arousal theories (Evans, 1978; Glass & Singer, 1972) suggest that performance on tasks is dependent on optimal levels of arousal. Performance on complex tasks is optimal at lower levels of arousal than is performance on simple tasks. This theory suggests that most aftereffects measures are complex tasks and that arousal levels are too high following uncontrollable and unpredictable stressors for optimal performance on these tasks. According to the frustration-mood

hypothesis, exposure to uncontrollable and unpredictable stress causes irritation and frustration. Therefore, subjects exposed to unpredictable or uncontrollable noise are less motivated to perform on subsequent tasks. In another theory, Rodin and Baum (1978) suggested that coping may be overlearned during a stressor and may persist beyond stressor termination. For example, it may be beneficial to limit attention to essential aspects of a situation during a stressor, but this approach may prove detrimental on complex tasks. Glass and Singer also suggested a dissonance hypothesis for aftereffects which they later rejected. Since subjects provided with perceived control choose to be exposed to the stressor, they find it less stressful and hence do not show performance deficits. The final explanation that has been offerred for aftereffects is that the subjects exposed to the more aversive situation develop a negative attitude about the experimental situation and therefore do not work as hard on subsequent measures. Although these eight theories have been proposed, research does not provide unequivocal support for any of them.

The proposed research attempted to explore another explanation for the aftereffects phenomenon; one that hypothesizes that aftereffects are a result of the release of endogenous opioid peptides during exposure to an uncontrollable and/or unpredictable stressor. Although this opioid release may be protective during the actual stressor, the deleterious consequences of opioids may become apparent when the stressor is terminated. Consistent with previous findings, opioids may lessen the aversiveness of the actual

stressor by influencing the affective response to that stimulus (Reynolds & Randall, 1957). Opioid release may cause mental clouding in the same way that morphine would. Jaffe and Martin (1980) report that morphine causes drowsiness, inability to concentrate, difficulty in mentation, and reduced visual acuity. These changes may not influence performance on simple well-learned task, but may effect performance on complex tasks. This would explain why simple tasks during the noise are uneffected and yet complex tasks suffer. Research on rodents indicates that opioid activation may last for more than 120 minutes following stressor exposure (Drugan, Ader, & Maier, 1985). Hence, opioid activation may remain following stressor termination in humans as well. These potential opioid changes may influence performance on tasks which are administered as aftereffects measures.

Consider this opioid hypothesis in light of the paradigm employed by Glass and Singer in their studies of noise. Typically, a no noise control group, an uncontrollable or unpredictable noise group, and a controllable or predictable noise group, were included in the study design. During the no noise condition, the EOP system may not be activated and may not influence aftereffect measures. Similarly, little or no opioid release may occur during the controllable stress condition. On the other hand, the EOP system may be activated during the uncontrollable and unpredictable noise conditions. Research on laboratory animals suggests that the unpredictability of a stressor may be a major component of opioid activation (e.g. Jackson, Coon,

& Maier, 1979). The release of opioid peptides during uncontrollable or unpredictable noise may lessen the aversiveness of the stressor. Therefore, the noise condition may seem no more aversive than the control condition and hence may explain why Glass and Singer's subjects did not rate the noise condition as more aversive than the unpredictable condition. However, following exposure to unpredictable noise, the opioid system may remain activated. Thus, opioids may influence post-stressor performance following exposure to unpredictable or uncontrollable noise and may in fact be responsible for the performance deficits which have been previously documented.

Consider the same conditions under the influence of naloxone. Only the uncontrollable or unpredictable noise group should be affected by naloxone administration since this is the only group with opioid activation. During noise exposure, EOPs will no longer protect the subjects in the uncontrollable or unpredictable group. This group should report more distress following the stressor when pretreated with naloxone. On the other hand EOPs will no longer influence post-stressor performance and the deficits will be ameliorated. Since the opioid system should not be activated in the predictable or controllable noise group or the control group, naloxone should not effect aversiveness ratings following the stressor or performance measures during or following the noise or silence.

Hypotheses

In review, Glass and Singer (1972) found that unpredictable noise was accompanied by changes which occurred only after stressor termination. These changes included cognitive deficits reflected in decreased proofreading ability, and decreased tolerance for frustration as measured by the Feather task (1961). Measurements of task performance during exposure to the stressor were remarkably similar between groups, and while the unpredictable group showed post-stressor effects the group did not rate the experience as more aversive, nor did their performance on simple tasks during the noise suffer.

The present research is designed to test the degree to which the opioid system is involved in this aftereffects phenomenon. It is suggested that unpredictable noise stressors cause the release of endogenous opioids and that the effects of this opioid activity persist beyond the actual stressor to cause performance deficits. Research has shown that noise-light stress is responsible for naloxone reversible changes in grooming and exploratory behavior in laboratory animals (e.g. Katz & Gelbert, 1978). In addition, the release of opioids has been associated with performance deficits in animals (McCubbin, Kizer, & Lipton, 1984). In humans, opioid release during noise exposure may make the stressor seem less aversive (opioids have been shown to modify the affective response to stress, Amir & Amit, 1978). Thus, when given saline, control and noise groups should rate their conditions similarly. Performance on simple, well-learned tasks during

the noise stress should remain unaffected by the opioid release. However, cognitive effects of the opioid release may be seen on the measures of motivation and persistence which are given following the stressor. Therefore, the hypotheses of the research were the following:

1. Blocking opioid release with naloxone will increase the reported aversiveness of the unpredictable noise stress. Subjects given naloxone or saline will not rate the ambient noise differently in the no noise control groups.
2. The administration of naloxone will not change performance on simple tasks during either unpredictable noise or no noise conditions.
3. Naloxone will ameliorate performance deficits on aftereffect measures including tolerance for frustration and proofreading ability in an unpredictable noise group. Again, naloxone will have no effect on these measures in the no noise control group.

Method

Subjects

A total of 40 subjects were recruited for participation in this 2 X 2 study of opioid mediation of stressor aftereffects. Subjects were recruited in several ways. Units of enlisted medics at the army post at Fort Meade were approached and asked to volunteer their time, medical students at the Uniformed Services University were also asked to volunteer as part of a class assignment, and the remainder of the subjects were recruited through posted notices at USUHS. Non-military subjects were paid fifty dollars for their participation. Only male subjects were asked to participate to avoid giving the drug unknowingly to women in their first trimester of pregnancy.

Subjects were randomly assigned to one of four conditions. The four groups included a naloxone unpredictable noise group (NU), a placebo unpredictable noise group (PU), a no noise naloxone (NC), and a placebo no noise group (PC). All subjects and experimenters were blind to the drug condition. Subjects ranged in age from 20-40 (X=27). Multivariate analyses of variance revealed no main effects or interactions for demographic variables (i.e., military status, age, body mass, marital status, education, income, total symptoms, and alcohol use). However, univariate statistics revealed a main effect of drug condition on total symptoms, $F(1,35)=4.26$, $p<.05$ and a main effect of noise exposure on total symptoms, $F(1,35)=6.52$, $p<.02$. These analyses revealed that there were some background differences between subjects

assigned to the four experimental conditions.

Prior to being admitted to the study all subjects were screened for drug use. Past or present use of morphine-like compounds was used as an exclusion criteria. In addition, potential subjects with a medical history of chronic pain, cardiovascular, liver, kidney, or respiratory disorders were excluded from participation in the study.

Informed consent was obtained and subjects were told that they could withdraw from the study at any time.

Procedures

Procedures adhered as closely to Glass and Singer's (1972) as possible. The purpose of the study was explained, all procedures were described, and informed consent was obtained. Each subject then completed the Symptom Checklist-90 and a background questionnaire. Following this all the tasks were described in detail in order to minimize questions following the injection. The subjects then completed a one page mood profile (MAACL; Zuckerman & Lubin, 1965). After the subject fully understood all of the procedures and had completed the MAACL, a physician was asked to come into the experimental room. He injected intermuscularly 10mg/cc of naloxone or 1 cc of saline into the subjects nondominant arm. Following the injection there was a 4 minute break to allow time for the drug to act. At the end of the rest period the mood questionnaire was administered again. At this point subjects worked on an addition task, a finding the A's task and a number comparison task for a total of twenty-three minutes. During this time, half of the

subjects were exposed to 23 minutes of random intermittent noise and the rest worked in silence.

The noise tape was made from the one used by Glass & Singer (1972). It consisted of the following sounds superimposed on each other: (1) two people speaking Spanish (2) a person talking Armenian (3) a mimeograph machine (4) a desk calculator (5) a typewriter. The noise was played at random intermittent bursts. Randomization was achieved as described by Glass and Singer (1972); each minute was divided into quarter parts and bursts of noise ranging from 3 to 15 seconds were randomly assigned to different parts in each one-minute segment. The total amount of noise on the tape was 207 seconds. The noise tape was played between 100dBA and 108dbA. Unlike Glass and Singer (1972) who presented the noise over speakers, this noise was presented over headsets.

After the 23 minute period, post-noise measures were administered. They included a brief questionnaire assessing task aversiveness, the mood questionnaire, a proofreading task, an encoding task, and the Feather task. Finally, subjects were asked if they knew what drug they had been given.

Measures

Stress. The Symptom Checklist-90R (Derogatis, 1977) was used to assess background levels of stress. The inventory contained a list of ninety symptoms and subjects were asked to rate how much they had been bothered by each of the symptoms during the two weeks prior to the session. Although the checklist contained a variety of subscales, only the total

score was used for purposes of analysis since there is a high correlation among subscale scores.

Mood. The Multiple Affect Adjective Checklist (Zuckerman & Lubin, 1964) provided estimates of changes of mood over time. The scale consisted of 132 adjectives which described different types of feelings. Subjects were asked to indicate which ones described the way they were feeling at the time that the scale was administered. The scale consisted of a measure of anxiety, depression, and hostility.

Cognitive performance measures. The number comparison, addition, and finding the A's task were each presented in two parts (French, Ekstrom, & Price, 1963). Each subject worked on the first part of the number comparison task, the addition task, and the finding the A's task for 11 1/2 minutes, they then worked on the second part of each task in the same order. Dividing the task into two halves allowed for comparisons of performance throughout the session. For the number comparison task, the subjects were asked to compare 48 pairs of numbers and to indicate whether numbers in each pair were alike or different. The addition task consisted of two sets of 60 addition problems. Subjects were asked to add three one- or two-digit numbers. Finally, columns of forty-one words were presented and subjects were asked to cross out each word containing the letter A. A total of twenty-five columns of words were presented in each half of the twenty-three minute period.

Post-task questions. After termination of the noise or the cognitive task in the no noise condition, subjects were

asked to rate the aversiveness of the task and noise on nine point scales. They were asked the following: (1) "The noise I heard while working on the verbal and numeral tasks was:" 1=extremely irritating and 9=extremely relaxing (2) "The noise I heard while working on the verbal and numeral tasks was:" 1=extremely pleasant and 9=extremely unpleasant (3) "To what extent was the noise that you heard distracting:" 1=the noise made it extremely easy to concentrate and 9=the noise made it extremely difficult to concentrate (4) "How difficult were the verbal and numeral tasks:" 1=extremely difficult and 9=extremely easy.

Proofreading. Subjects were asked to read a seven-page double spaced passage from Jane Jacob's *The Death and Life of Great American Cities* (1961). They were asked to read and circle errors that they found in the passage. Errors included typographical errors, misspellings, grammatical errors, etc. Subjects were given five minutes to read as much as possible and when they were asked to stop working, they drew a line under the last sentence that they read. The measures of performance were the total number of errors found and a percent score. In a series of studies conducted by Baum and his colleagues at Three Mile Island (TMI) and Frederick, Maryland, the average number of proofreading errors found in a similar passage was 9 for the TMI group and 18 for the Frederick group and the mean percent score was 53 for TMI residents and 71 for subjects living in Frederick (Davidson, 1987).

Encoding task. Subjects were asked to work on a

digit-alphabet encrypting task. This task was obtained from a military manual. Subjects were asked to transform a set of letters and numbers to another set of letters. They worked on this task for a total of five minutes. Subjects were first given a two letter code to establish a working line for each problem. Once the working line was established, they were asked to replace italic numbers and letters with letters from the working line. The number of letters encoded and the percent score were the performance measures used on this task. No normative data were available for this task.

Frustration measure. Tolerance for frustration was measured using the Feather task (1961). Subjects were asked to trace over the lines of the diagrams without retracing any lines or picking up their pencils. Each time they made a new attempt on a puzzle they were instructed to work from a clean sheet of paper. Subjects were given two puzzles to work on. They worked on one puzzle at a time and were allowed to work on each puzzle for as long or as short as they wished. Although the subjects were presented with four one inch piles of puzzles, they only worked on the first two stacks. Each puzzle was presented face down. The first puzzle presented was solvable and the second was insolvable. The number of puzzles worked on and the total number of seconds spent on each puzzle were the measures recorded. Glass and Singer (1972) reported the the average number of puzzles used by their subjects was 14.5. They did not report the number of seconds that subjects spent on the puzzles.

Results

Mood

Analyses were first directed toward establishing changes in mood over time. The Mood Affect Adjective Checklist (Zuckerman and Lubin, 1964) was given three times throughout the experimental session; immediately before the injection, four minutes following the injection, and after the twenty-three minute block of unpredictable noise or silence. It was hypothesized that naloxone would increase the aversiveness of the stressor in the noise group, but would have no effect in the no noise naloxone group. Repeated measures analyses of variance were performed separately on each of the three subscales of the MAACL (i.e., anxiety, depression, & hostility). Results showed that all subjects became more anxious over time, $F(2,72)=6.23$, $p<.004$. Results were similar for the depression subscale. All groups became more depressed with time $F(2,72)=10.62$, $p<.001$. Finally, all groups become more hostile over the experimental session, $F(2,72)=13.2$, $p<.001$ (figures 1, 2 & 3).

In order to more closely examine the relationship between experimental condition and changes in mood over time a series of multiple regression analyses were performed. The first measures of anxiety, depression, and hostiliy were used as the predictors for each second measure. Then 2 X 2 analyses of variance, crossing drug condition (saline and naloxone) with noise condition (noise and no noise), were performed on the residuals generated by each regression equation. These analyses were done to examine changes in mood

at time two that resulted from the experimental manipulation and were irrespective of mood a time one. As expected, anxiety, depression, and hostility at time 1 were significant predictors of anxiety, depression, and hostility at time two in all cases, $F(1,36)=70.1$, $p<.001$; $F(1,36)=96.3$, $p<.001$; $F(1,36)=113.8$, $P<.001$, respectively. Analyses of variance revealed no significant differences between the groups when anxiety and depression residuals were used as dependent measures. However, while subjects given naloxone became less hostile following the injection, subjects given an injection of saline reported more hostility, $F(1,36)=13.1$, $p<.04$.

Next, three separate multiple regression analyses for each subscale were performed using anxiety, depression, and hostility at both times one and two as the predictor variables for anxiety, depression, and hostility at time three. Again, the residuals generated by these three separate regression equations were analyzed using 2 X 2 analyses of variance. This was done in order to explore changes in mood produced by the experimental manipulations. Although time one and time two were significant predictors of time three mood for each subscale, analyses of the residuals revealed no significant differences. Results failed to confirm the hypothesis that naloxone would increase the reported aversiveness of the stressor.

Stressor Ratings

Following the twenty-three minute block of noise or silence, subjects were asked to rate the noise and the task on four nine point Likert-type scales. Subjects were asked to

rate how pleasant and relaxing the session had been, how difficult it had been to concentrate, and how difficult the verbal and numeral tasks had been. It was hypothesized that naloxone would increase the aversiveness of the stressor, but would have no effect in the absence of noise. This hypothesis was not supported. Naloxone had no effect on any of the rating scales. However, there was a main effect for noise on three of the four scales. All subjects exposed to noise reported more difficulty concentrating, $F(1,36)=21.2$, $p<.001$, they rated the session as less pleasant, $F(1,36)=20.5$, $p<.001$, and they reported that the session had been less relaxing, $F(1,36)=39.9$, $p<.001$ (figures 4, 5, & 6). However, although the session was rated as more aversive by subjects exposed to noise, there were no difference between the groups on the way they rated the actual difficulty of the task. Again, results failed to confirm the first hypothesis.

Performance During the Stressor

Following the injection, all subjects worked on twenty-three minutes of numeral and verbal tasks. Three different tasks were given and each was divided into two parts so that changes in performance could be assessed over time. Repeated measures analyses of variance were computed on a raw score of each task as well as a percent score. In order to further assess changes from the first part of the task to the second, separate multiple regression equations were computed for the different measures using the scores at time one as the predictors for the scores at time two. The residuals created by the six regression equations were then analyzed using 2 x 2

analyses of variance.

Repeated measures analyses revealed that the raw number of the math problems solved increased from the first to second half of the session, $F(1,36)=17.4$, $p<.001$ (figure 7). There was also a marginal noise effect, $F(1,36)=3.66$, $p<.06$. Subjects exposed to noise solved fewer math problems. Finally, there was a significant time X noise X drug interaction, $F(1,36)=6.17$, $p<.017$. Subjects in the no noise saline and the noise naloxone conditions improved less over time than the other two groups. Repeated measures analyses revealed no other differences in the raw scores for the math, number comparison task, or the finding the A task. Repeated measures analyses of variance were further performed on the percent scores for each of the three task and no signficant effects were found.

Similary, multiple regression and residual analyses produced a comparable pattern of results. Residual analyses of raw math scores produced a significant interaction between drug and noise conditions, $F(1,36)=6.2$, $p<.02$. Subjects in the naloxone noise and the saline no noise groups improved less over time. No other differences were found using residual analyses on the the finding the A task or the number comparison task. These results failed to confirm the second hypothesis that naloxone would have no effect on simple performance during the actual stressor. Naloxone interacted with the stressor to impair performance.

Aftereffects measures

All subjects worked on three tasks following the

twenty-three minute block of noise or silence; the tasks included a proofreading task, an encoding task, and a puzzle task. These tasks were used as aftereffects measures. It was hypothesized that naloxone would ameliorate performance deficits created by exposure to noise, but would have no effect in the absence of noise.

Analyses of variance were performed crossing drug condition with noise condition and performances on each of the three tasks were used as dependent measures.

Proofreading. Two measures of proofreading ability were computed for each subject, a raw score and a percent score. The raw score was a count of the number of proofreading errors correctly identified, and the percent score was computed by dividing the number of proofreading errors found by the number of errors possible in the amount read. Analyses of variance revealed that subjects exposed to noise performed more poorly on the proofreading task, $F(1,36)=3.78$, $p<.06$ (figure 8). There were no significant differences between the groups when the percent score was used as the dependent variable.

Encoding. Two scores were also computed for the encoding task; a raw score and a percent score. The raw score was a count of the number of letters encoded. The percent score was computed by dividing the number of letters correctly encoded by the number of letters attempted. Two separate analyses of variance were then performed using each of the measures as the dependent variables. Analyses revealed that subjects exposed to noise performed more poorly on the

encoding task, $F(1,36)=5.76$, $p<.025$ (figure 9). Although subjects exposed to noise worked on as many letters as those exposed to silence, they were less likely to encode the letters correctly.

Puzzle task. Each subject worked on one insolvable puzzle. The length of time spent on this puzzle and the number of pages used were both evaluated as dependent measure. It was predicted that the saline noise group would persist the least on this task and use fewer pages and that all other groups would be equal on this measure. Analyses of variance revealed no difference between groups on either the number of pages used or the number of seconds spent on the insolvable puzzle.

Results from these three tasks failed to confirm the hypothesis that naloxone would ameliorate performance decrements caused by exposure to an unpredictable stressor.

Background variables and performance. Because the experimental groups differed on some background characteristics, post-stressor performance was reanalyzed using a series of multiple regression analyses (Cohen & Cohen, 1983). In this manner, the proportion of variance accounted for by the experimental manipulations could be separated from the variance accounted for by original demographic difference between the groups. Eight background variables (military status, age, body mass, marital status, education, income, alcohol consumption, and total symptoms) were simultaneously used as predictor variables for each of the six dependent measures in separate multiple regression equations. When

background characteristics accounted for a significant proportion of the variance, a new regression equation was computed. The background variables were then entered into the regression equation along with the two experimental manipulations and their interaction term. The proportion of variance accounted for by the background variables alone was then compared to the variance accounted for by the experimental manipulations and their interaction combined with the background variables.

Background characteristics were a significant predictor of the percent of letters correctly encoded, $F(8,31)=2.4$, $p<.05$. For this reason a second regression equation was computed including the background variables, the two experimental manipulation, and the interaction. Analyses revealed that the experimental manipulations accounted for a significant proportion of the variance, $F(3,28)=3.9$, $p<.025$, and that the noise manipulation was responsible for this effect, $t=-3.14$, $p<.004$ (see table 2). Further analyses revealed that the regression equations had equal slopes in the four experimental groups

Background variables did not account for a significant proportion of the variance for the remaining five dependent measures, nor did the experimental manipulations account for a significant proportion of the variance (see table 2).

Discussion

This study was designed to examine the role of the endogenous opioid system in performance deficits which occur following stressor exposure. Subjects were given an injection of saline or naloxone and were then exposed to either 23 minutes of unpredictable noise or silence. Following the twenty-three minute period, three aftereffects measures were administered. It was hypothesized that subjects given saline would exhibit a typical pattern of aftereffects. That is, subjects exposed to unpredictable noise would exhibit greater post-stressor performance deficits than subjects working in silence. However, that pattern was expected to differ for subjects given naloxone. It was hypothesized that naloxone would ameliorate performance deficits associated with exposure to an unpredictable noise stressor. Naloxone was also predicted to increase the aversiveness of the noise. It was expected to have no effect in the absence of noise.

Results of this study partially replicated Glass and Singer's (1972) original findings. Subjects exposed to noise rated the session as more aversive and unpleasant than did subjects who were not exposed to noise. In addition, exposure to unpredictable noise was associated with performance decrements on the proofreading and encoding aftereffects measures. Performance on math problems was also impaired during stressor exposure. Noise, however, failed to alter persistence on the insolvable puzzle.

There are several possible explanations for the lack of

persistence differences among groups. When Glass and Singer (1972) allowed their subjects to believe they could terminate stressor exposure, post-stressor performance improved. Gardiner (1978) has suggested that informed consent procedures may be similar to providing subjects with control over stressful experiences. Because this study involved an injection of a pharmacological substance, informed consent was emphasized from recruitment to the conclusion of the study. It could be argued that once having agreed to participate in this study, subjects had the perception of increased perceived control. However, since performance deteriorated on the proofreading and encoding task, this explanation for the lack of persistence differences on the puzzle task is likely only if persistence aftereffects are more susceptible to perceived control than are concentration effects.

Another explanation for the lack of persistence differences revolves around the timing of aftereffects. No one knows the duration of aftereffects and it is possible that by the time the third task was given that the phenomenon could have dissipated.

Perhaps the most likely explanation for equivalent persistence among groups is that all groups experienced a moderate stress response. It is possible that the injection created moderate levels of stress across conditions. Cohen (1980) has argued that the Feather task is a more sensitive aftereffect measure than proofreading, and because there were no differences in persistence, it is possible that all subjects were experiencing stress. There is some support for

this hypothesis. All subjects did become more hostile, anxious, and depressed during the course of the experimental session. In addition, the number of puzzles being used by the no noise control groups in this study was less than the number reportedly used by subjects in control conditions in other studies. The mean number of puzzles used by the groups in this study ranged from 6.7 in the saline no noise group to 9.8 in the naloxone noise group. Glass and Singer (1972) reported that control groups used an average of 16-26 puzzles, whereas groups exposed to unpredictable noise used an average of 4-12 puzzles. Similarly, Percival & Loeb (1980) reported that control subjects used an average of 19 puzzles and subjects exposed to a stressor used an average of 10 puzzles. It appears that all the groups in this study used an average number of puzzles which was comparable to the number of puzzles used by stressed groups in other studies. If persistence is in fact a more sensitive measure of stress, it would follow that moderate levels of stress would impair performance on this task before performance would be impaired on either the proofreading or the encoding tasks.

Although it was predicted that naloxone would ameliorate performance deficits associated with noise stressor exposure, this hypothesis was not confirmed. Naloxone did not effect performance on the tasks chosen following the stressor. These results suggests that the opioid system may not be involved in these performance deficits produced by stressor exposure. The choice of other tasks or stressors might have produced a different set of results.

On the other hand, it is possible that opioids are involved, but that naloxone does not block the appropriate receptor subtypes. Although naloxone has a preferential affinity for the mu receptor, it interacts with other receptors at higher dosage levels. It was assumed that a 10 mg dose would be sufficient to block all receptor subtypes. But, there is no way to determine what was actually blocked by the naloxone in this study. Direct measurement of opioid levels and correlation of these levels with performance would be an additional way of determining whether opioids are involved in performance changes in a follow-up study. However, when measuring levels of opioids directly, there are problems involved because it is unknown what peripheral versus central levels mean. And, direct measurement of opioid levels gives no information about drug receptor interactions.

Another explanation for the lack of findings, may revolve around the pharmacokinetics of the opioids and the opioid blocker, naloxone. Since naloxone is a relatively short-acting drug with a mean half-life of 60 minutes (ranging from 30 to 90 minutes), it is possible that the drug was losing its potency in some of the subjects by the time that the aftereffects measures were administered. Since naltrexone is a longer acting opioid antagonist, it might have been given to address the problem of duration of action of the drug. In addition, opioid activation may not have persisted long enough following stressor termination to influence performance. However, animal research has suggested that stress-induced analgesia persists in rodents for as longer as 90 minutes

following stressor termination (Drugan, Adar, and Maier, 1985).

Also, if the injection of naloxone had been given after the stressor rather than before, the results may have differed. By giving naloxone after the stressor the effect of the stressor on performance could have been viewed in the absence of any interaction between naloxone and stressor exposure. It is possible that performance deficits are caused by a combination of factors, some mediated by the opioid system and others not. Our results indicate that performance deficits occur following noise, regardless of the drug condition. But, by giving naloxone prior to the stressor we may have ameliorated deficits caused by the opioid system but increased performance deficits due to other factors. If the opioid system serves to protect an organism during stressor exposure, the stressfulness of the noise may have been increased by administering naloxone prior to stressor exposure. Thus, the benefits of naloxone may have been negated by greater intensity of stress. If naloxone had been given following the stressor, performance may have improved. Performance on the math problems did provide some evidence that naloxone interacted with stressor exposure. Subjects in the no noise saline and the noise naloxone groups showed less improvement in ability to solve math problems over time. At least two possible explanations exist for these results. Since subjects in the no noise saline condition solved more problems than subjects in any other condition both at times one and two, the results may represent a ceiling effect for

this group. On the other hand, post-hoc comparisons at time one and time two revealed that subjects exposed to noise and given naloxone solved significantly fewer math problems than subjects in the no noise saline condition. Thus, although there was room for improvement in the naloxone noise group, it did not occur. Although Cohen et al.(1982) failed to find changes in performance with injections of naloxone in the .2 mg/kg range, we found impairments in performance in this dosage range when subjects were simultaneously exposed to a stressor. This finding supports the hypothesis that naloxone increases the aversiveness of the stress and suggests that it may be worthwhile to replicate the study giving the injection of naloxone after the stressor.

Another expanation for the noise by drug interaction on task performance may be related to optimal levels of arousal. Subjects in the saline noise group may not have been aroused enough to exhibit maximal performance and subjects in the noise naloxone group may have been too aroused to perform maximally. However, this explanation is not likely since the saline no noise group performed the best at both times one and two.

It is also possible that the stress created in this study was not sufficient to produce opioid activation. In the absence of opioid activation, naloxone would have no effect. Again, by measuring opioid levels in a follow-up study this question could be answered. Nonetheless, data from this study suggest that performance deficits occur in the absence of opioid action. Although opioid activity may still be

responsible for performance changes in some circumstances, it would appear that other factors are responsible for performance changes as well.

Finally, it was hypothesized that naloxone would increase the reported aversiveness of the stressor. This hypothesis was not supported. Subjects given naloxone did not rate the stressor as any more aversive than those given saline. And, there were no interactions between drug condition and changes in mood before or after the stressor. Prior to stressor exposure however, there were changes in mood which related to naloxone administration. Although the injection of naloxone had no effect on anxiety or depression, subjects given the naloxone became less hostile following the injection. This finding may be contrasted to other studies which reported no changes in mood or negative mood changes associated with injections of naloxone (Grevert & Goldstein, 1978; File & Silverstone, 1981).

Even though mood improved following injections of naloxone and performance did suffered during the task, subjects were unable to accurately assess which drug they had received. Twenty-eight subjects reported that they were unable to distinguish which drug condition they had been in, and of the twelve subjects who did guess what drug they had been given, only three were correct.

Unlike the original studies conducted by Glass and Singer (1972), this study did not contain predictable noise groups. If they had been included, it would have been hypothesized that subjects given naloxone or saline and

exposed to predictable noise would not have performed differently than subjects given the drug or saline in the absence noise. Since aftereffects measures were not affected by the drug condition, the addition of the predictable noise group would have added little information about the effects of the opioid system on aftereffects measures. However, since naloxone interacted with the stressor to impair performance during the noise, it would have been interesting to know whether these changes could have been ameliorated by providing the subjects with perceived control.

In short, the present study failed to confirm an association between the endogenous opioid system and performance deficits following stressors. However, follow-up studies giving the injection during different phases of the experimental session may be necessary to thoroughly confirm or refute the association. It may also be necessary to measure opioid activity directly. However, the results of this study suggest that the opioid system is not the sole mechanism responsible for aftereffects.

TABLE 1

THE EFFECTS OF EPINEPHRINE AND NOREPINEPHRINE IN HUMANS

	EPINEPHRINE	NOREPINEPHRINE
CARDIOVASCULAR		
Heart rate	*	–
Cardiac Output	***	0,–
Stroke Volume	**	**
Systolic Arterial	***	***
Diastolic Arterial	*,0,–	**
PERIPHERAL CIRCULATION		
Total Peripheral Resistence	–	**
Cerebral Blood Flow	*	0,–
Muscle Blood Flow	***	0,–
Cutaneous Blood Flow	– –	– –
METABOLIC		
Oxygen Consumption	**	0,*
Respiration	*	*
Blood Glucose	***	0,*

*=INCREASE; 0=NO CHANGE; -=DECREASE

ADAPTED FROM GILMAN, GOODMAN, AND GILMAN (1980)

TABLE 2

MULTIPLE REGRESSION ANALYSES WITH BACKGROUND VARIABLES AND EXPERIMENTAL VARIABLES AS PREDICTORS

Dependent Variable	R_1^2 Background Variables	Sig.	R_2^2 Background & Experimental	$(R_2^2-R_1^2)$	Sig.
% Letters Encoded	.393	.04	.573	.180	.025
# Letters Encoded	.373	.06	.453	.080	>.1
% Proofreading Errors	.306	.15	.325	.019	>.1
# Proofreading Errors	.319	.12	.370	.051	>.1
# Pages on Puzzle	.222	.43	.248	.026	>.1
# Seconds on Puzzle	.337	.11	.429	.092	>.1

Figure 1: Maacl Anxiety

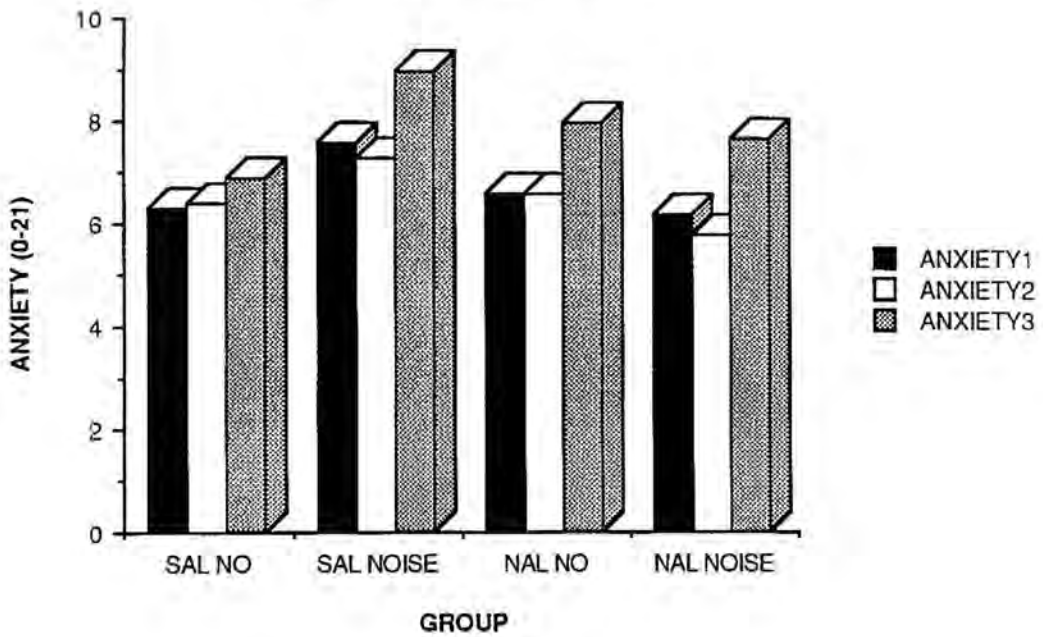


Figure 2: Maacl Depression

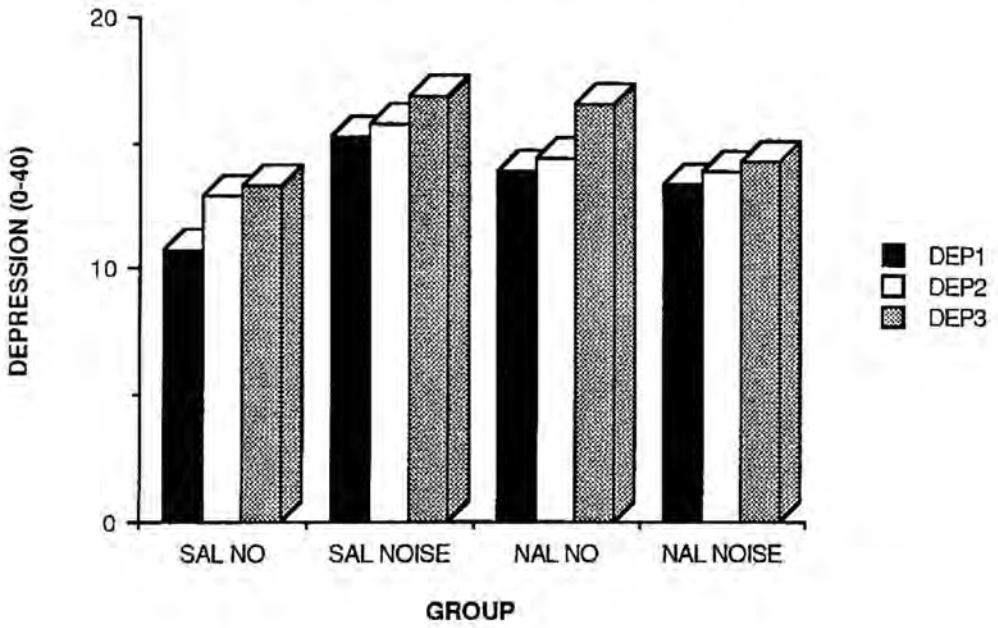


Figure 3: Maacl Hostility

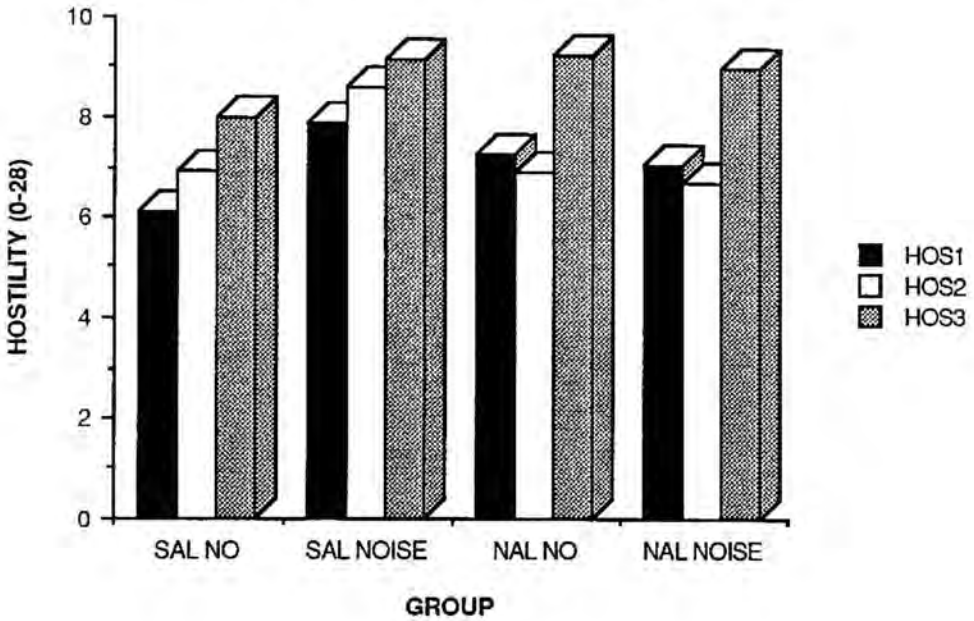


Figure 4: Noise and Concentration

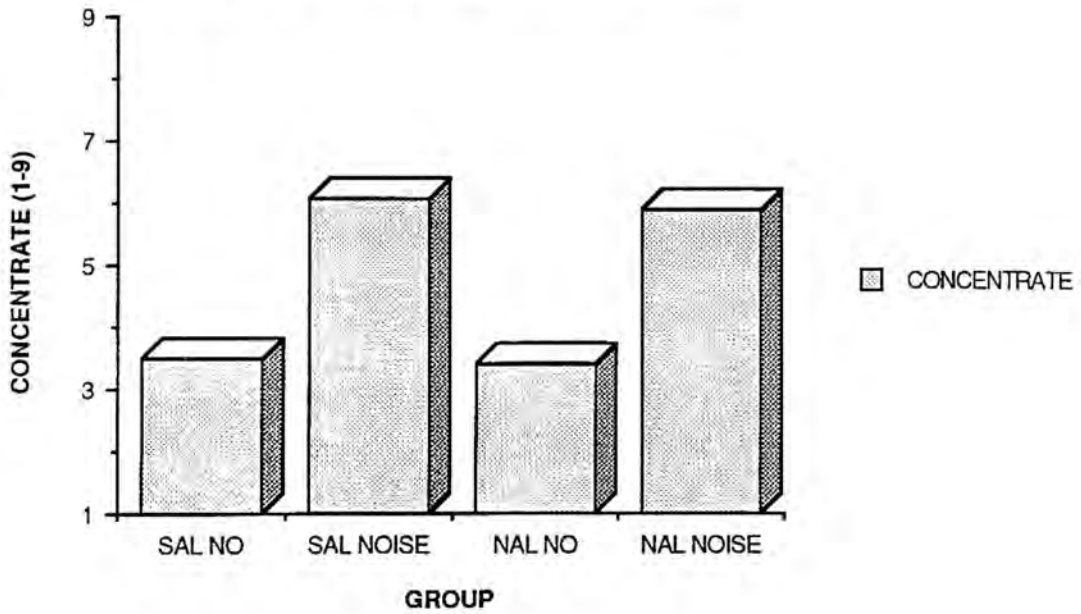


Figure 5: Pleasantness of Noise

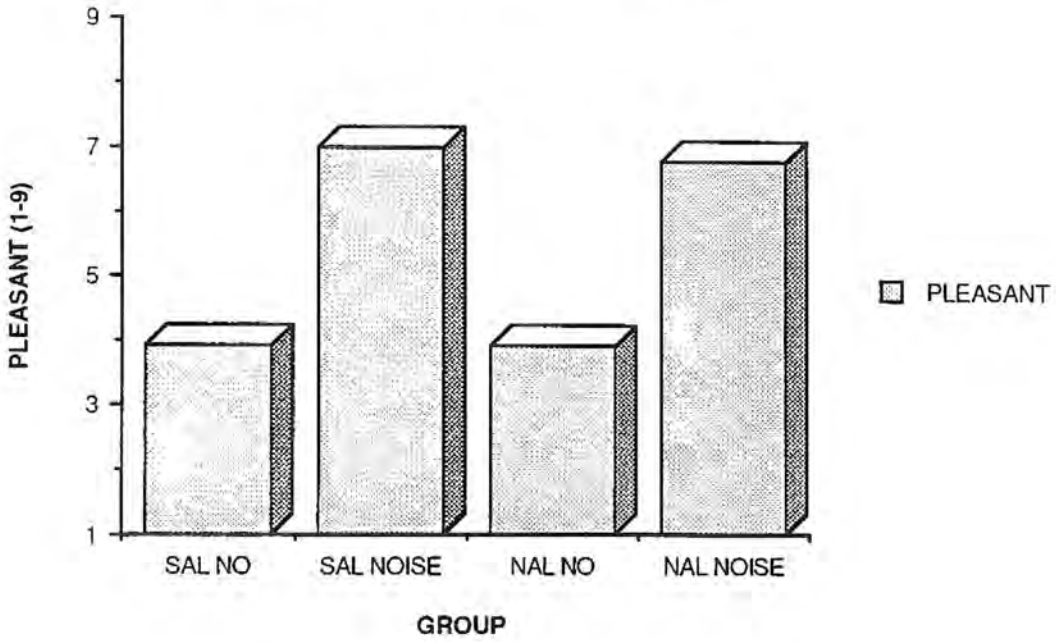


Figure 6: Noise Relaxing

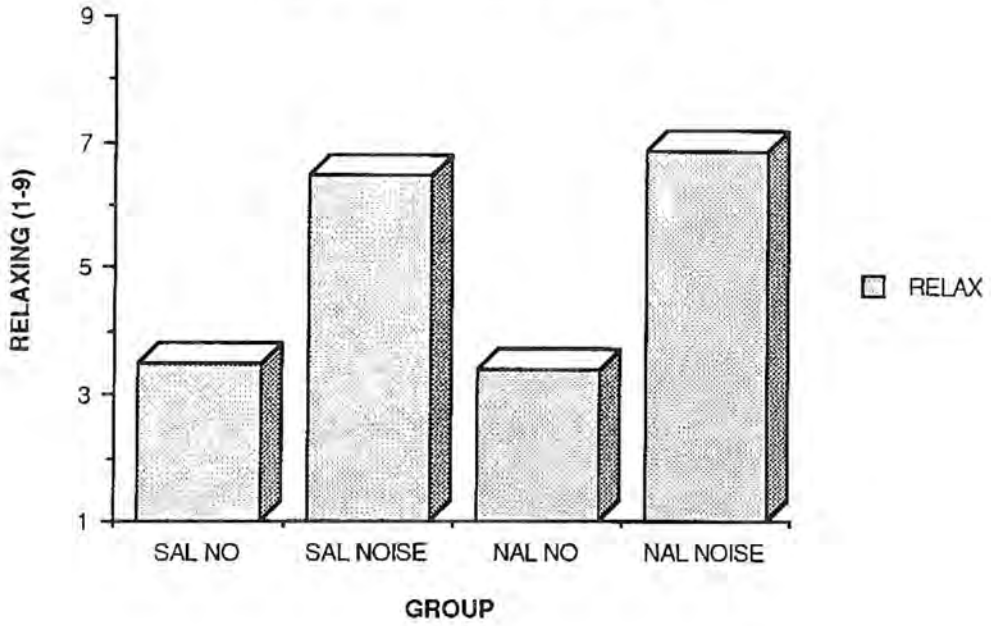


Figure 7: Math Problems Solved

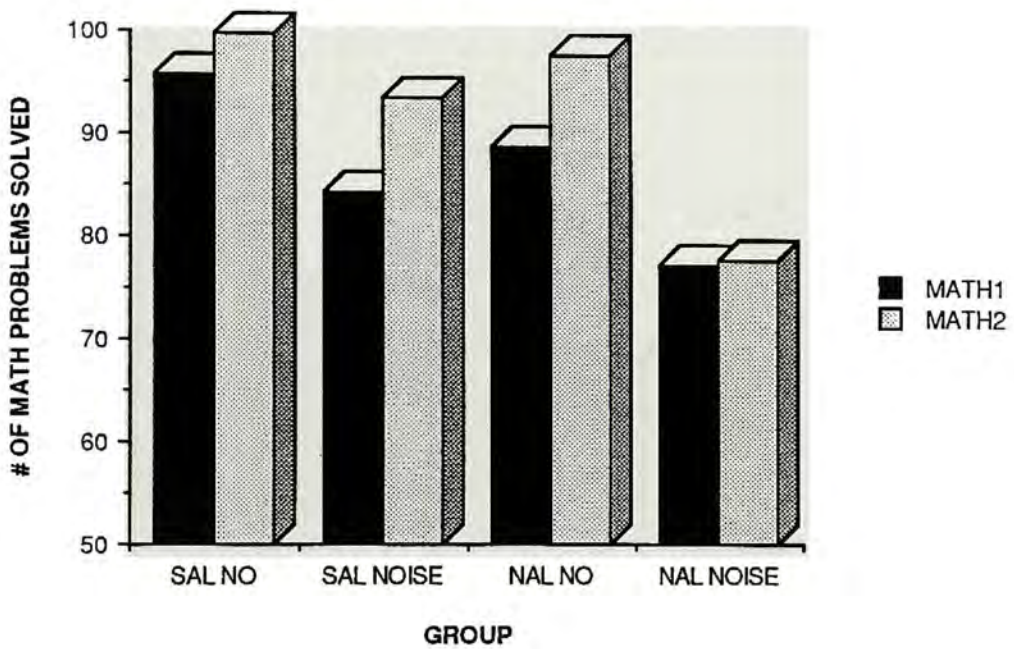


Figure 8: Proofreading

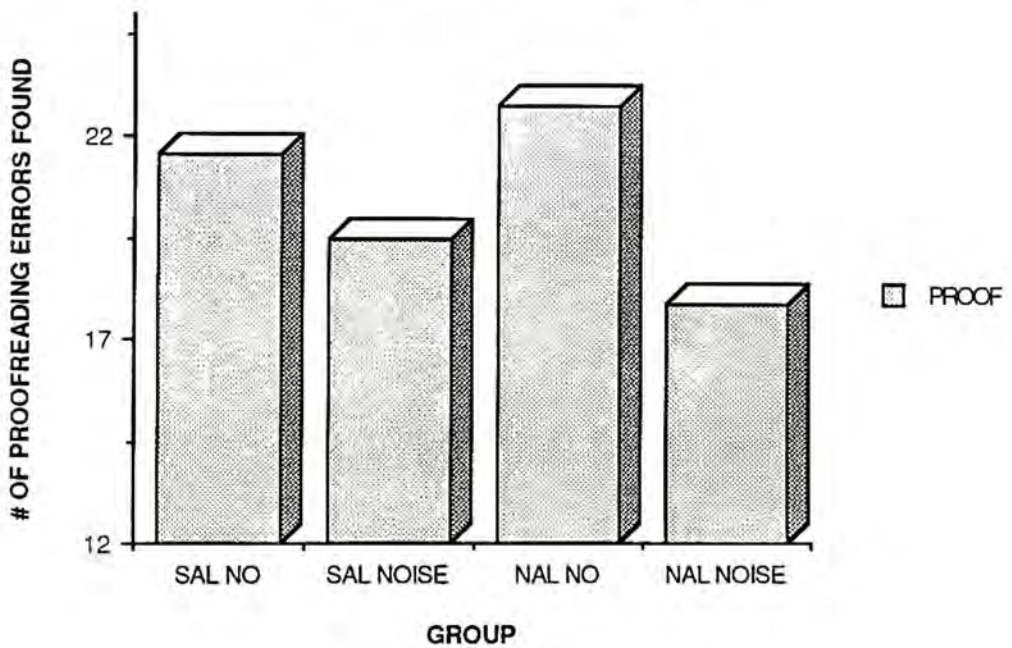
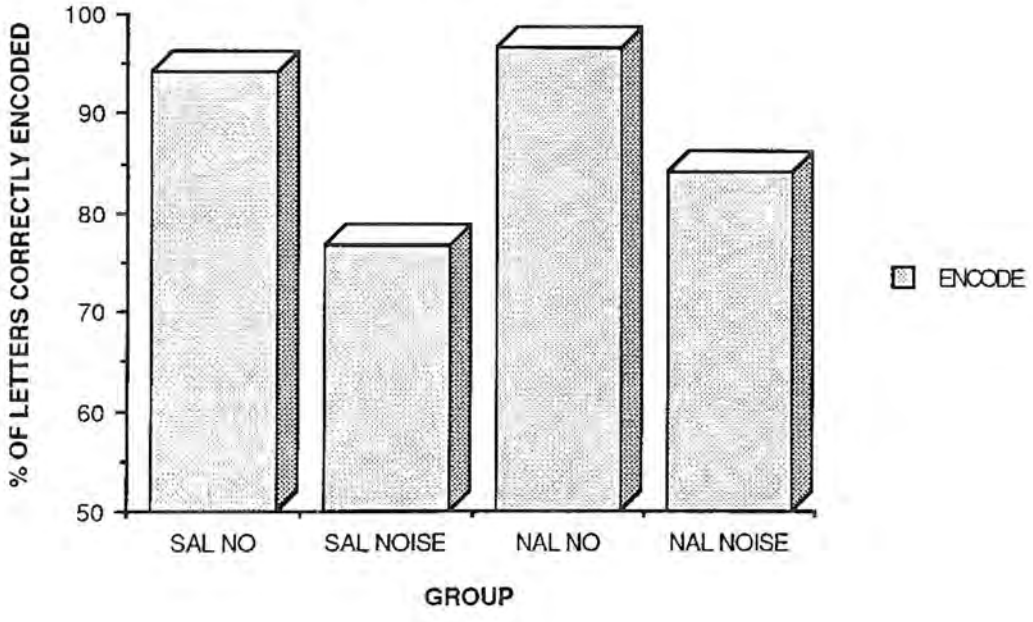


Figure 9: Encoding Problems



Appendix A

Study Script

HELLO, MY NAME IS_____, I WORK HERE AT THE UNIVERSITY IN THE DEPARTMENT OF MEDICAL PSYCHOLOGY. AS YOU KNOW WE ARE A FEDERAL MEDICAL SCHOOL AND GRADUATE SCHOOL AND THIS RESEARCH IS BEING SPONSORED BY THE UNIVERSITY. I AM WORKING WITH DR. HAGMANN WHO WILL MEET WITH YOU TODAY AS WELL AS DR. BAUM AND DR. HOLLOWAY. WE ARE STUDYING THE INTERACTION BETWEEN STRESS AND THE ENDOGENOUS OPIOID SYSTEM ON TASK PERFORMANCE. THE EOP SYSTEM IS THE BODIES NATURAL PAIN CONTROL SYSTEM. IN ORDER TO EXAMINE THE RELATIONSHIP BETWEEN THE NATURAL OPIOID SYSTEM AND PERFORMANCE WE WILL BE ADMINISTERING THE DRUG, NALOXONE, TO SOME OF OUR SUBJECTS. NALOXONE IS A SYNTHETIC SUBSTANCE WHICH BLOCKS THE ACTION OF THE NATURAL OPIOIDS. NALOXONE HAS NO INTRINSIC ACTION OF ITS OWN IN THE ABSENCE OF OPIOIDS. IF HOWEVER, YOU ARE CURRENTLY TAKING OPIOIDS SUCH AS MORPHINE OR CODEINE, THE DRUG CAN PRODUCE A SERIOUS WITHDRAWAL REACTION. THEREFORE, IT IS IMPORTANT THAT YOU HAVE NOT TAKEN ANY OPIOID DRUG RECENTLY AND THAT YOU TAKE NO SUCH DRUGS FOLLOWING THE SESSION. HALF OF THE SUBJECTS WILL RECEIVE NALOXONE AND HALF WILL RECEIVE SALINE. ONLY DR. HAGMANN WILL KNOW WHICH DRUG CONDITION YOU ARE IN.

ALL OF THE INFORMATION THAT YOU PROVIDE US WITH TODAY WILL REMAIN STRICTLY CONFIDENTIAL. YOUR DATA WILL BE IDENTIFIED ONLY BY A CODE NUMBER AND ALL DATA WILL BE KEPT IN A LOCKED FILE CABINET. NONE OF THE DATA WILL BE PUBLISHED WITH NAMES ASSOCIATED WITH. IF AT THE END OF THE SESSION YOU ARE INTERESTED IN RECEIVING ANY INFORMATION ABOUT THE RESULTS, WE WOULD BE MORE THAN HAPPY TO PROVIDE IT, HOWEVER, ALL DATA WILL BE GROUP DATA. WE CAN GIVE YOU NO INFORMATION ABOUT YOUR

INDIVIDUAL RESULTS.

DURING THE SESSION YOU WILL BE ASKED TO COMPLETE QUESTIONNAIRES ASSESSING DEMOGRAPHICS, MOODS, AND BODILY REACTION. YOU WILL BE ASKED TO COMPARE NUMBERS, ADD NUMBER, AND IDENTIFY WORDS CONTAINING THE LETTER A. FINALLY, YOU WILL BE ASKED TO PROOFREAD A PASSAGE, ENCODE LETTERS, AND WORK ON PUZZLES. YOU MAY BE ASKED TO WORK ON SOME OF THESE TASKS WHILE LISTENING TO A TAPE RECORDING. MANY OF THE TASKS ARE TIMED AND I WILL BE HERE WITH YOU TO TELL YOU WHEN TO MOVE ON TO THE NEXT TASK. DO YOU HAVE QUESTIONS?

THE FIRST THING THAT I WOULD LIKE YOU TO DO IS TO READ AND SIGN THIS CONSENT FORM. I WILL KEEP THE COPY THAT YOU SIGN, BUT I WILL GIVE YOU THE ADDITIONAL COPY FOR YOUR RECORDS (***GIVE THEM THE ADDITIONAL COPY).

NOW, I WOULD LIKE YOU TO FILL OUT TWO QUESTIONNAIRES. AFTER THIS I WILL EXPLAIN THE PROCEDURES FOR THE REMAINDER OF THE SESSION. DR. HAGMANN WILL THEN COME IN AND GIVE YOU YOUR INJECTION. FOLLOWING THIS THERE WILL BE A BRIEF REST PERIOD AFTER WHICH YOU WILL BEGIN WORKING ON THE TASKS.

THE FIRST QUESTIONNAIRE ASKS BACKGROUND QUESTIONS. WE ARE INTERESTED IN SUCH THINGS AS YOUR LEVEL OF EDUCATION AND MARITAL STATUS AS WELL AS YOUR MILITARY HISTORY (GIVE BACKGROUND).

THE FOLLOWING IS A LIST OF FEELINGS WHICH YOU MAY HAVE

EXPERIENCED DURING THE PAST TWO WEEKS. PLEASE INDICATE THE FREQUENCY WITH WHICH YOU HAVE EXPERIENCED EACH OF THE FEELINGS DURING THE PAST TWO WEEKS (GIVE SCL-90).

(*WHILE THEY ARE COMPLETING THE SCL-90 PLEASE LABEL ALL QUESTIONNAIRES WITH THEIR SUBJECT NUMBER)**

DURING THE NEXT HOUR YOU WILL BE WORKING ON A NUMBER OF TASKS. IT IS IMPORTANT THAT WE MAINTAIN A STRICT SCHEDULE SO I WILL BRIEFLY EXPLAIN EACH TASK IN ADVANCE SO YOU WILL KNOW WHAT TO EXPECT.

YOU WILL FILL OUT A ONE PAGE MOOD QUESTIONNAIRE THREE TIMES THROUGHOUT THE EXPERIMENTAL SESSION. EACH TIME YOU ARE GIVEN THE QUESTIONNAIRE, YOU ARE TO CHECK THE ADJECTIVES WHICH DESCRIBE THE WAY THAT YOU ARE FEELING AT THAT MOMENT.

YOU WILL WORK ON THREE DIFFERENT TASKS OVER A TWENTY THREE MINUTE PERIOD. (***DEPENDING ON THEIR CONDITION TELL THEM THAT THEY WILL BE WEARING HEADSETS TO BLOCK OUT NOISE DURING THIS TIME **OR** THAT THEY WILL BE LISTENING TO BURSTS OF NOISE DURING THIS TIME) (GET OUT INSTRUCTIONS FOR ADDITION TASK, FINDING THE A TASK, AND NUMBER COMPARISON).

YOU WILL BE ASKED TO ADD COLUMNS OF NUMBERS LIKE THESE. EACH SHEET CONTAINS 60 PROBLEMS AND YOU WILL BE GIVEN 2 MINUTES TO WORK ON EACH PAGE. PLEASE COMPLETE THE FIRST THREE EXAMPLES NOW.

YOU WILL BE ASKED TO IDENTIFY WORDS CONTAINING THE LETTER A. IN EACH COLUMN OF WORDS, FIVE WORDS WILL CONTAIN THE LETTER "A". PLEASE CROSS OUT EACH WORD THAT CONTAINS THE LETTER A. EACH PART OF THIS TASK CONTAINS 4 PAGES. YOU WILL BE GIVEN 2 MINUTES TO COMPLETE ALL FOUR PAGES. PLEASE FIND THE WORDS IN COLUMNS 3, 4, AND 5 WHICH CONTAIN THE LETTER "A".

FINALLY, YOU WILL BE ASKED TO QUICKLY COMPARE TWO NUMBERS AND INDICATE WITH AN 'X' PAIRS THAT DIFFER. YOU WILL BE GIVEN 1 1/2 MINUTES TO COMPLETE EACH SHEET. PLEASE COMPARE THE NUMBERS IN THE LEFT HAND COLUMN AND MARK THE ONE WHICH ARE DIFFERENT.

FOLLOWING THESE TASKS THERE WILL BE THREE MORE TASKS FOR YOUR TO WORK ON (PULL OUT THE PROOFREADING TASK). YOU WILL BE ASKED TO READ THIS 7 PAGE PASSAGE AND CIRCLE ANY MISTAKES THAT YOU FIND. ERRORS INCLUDE MISPELLINGS, TYPOGRAPHICAL ERRORS, PUNCTUATION ERRORS, CAPITALIZATION ERRORS, ETC. DO YOU HAVE ANY QUESTION?

THE NEXT TASK WILL BE AN ENCODING TASK (***PULL OUT INSTRUCTIONS FOR THIS). LET'S GO OVER THE INSTRUCTIONS FOR THIS. IN ORDER TO ENCODE A PASSAGE YOU WILL FIRST HAVE TO ESTABLISH A SET LINE OR THE LINE THAT YOU WILL BE WORKING FROM. IF YOU ARE ASKED TO ESTABLISH "MH" AS THE SET LINE, YOU WOULD FIRST READ DOWN THE COLUMN OF LETTERS ON THE LEFT HAND SIDE OF THE PAGE UNTIL YOU FIND THE "M". THEN READ ACROSS THAT LINE UNTIL YOU FIND THE FIRST "H." THE LETTER TO THE

RIGHT OF THE "H" IS THE SET LINE--IN THIS EXAMPLE THE SET LINE WOULD THEN BE **S**. THIS MEANS THAT THE LETTER WILL BE ENCODED FROM ROW **S**. NOW TO ENCODE THE LETTERS "CF", YOU FIND "C" IN ITALIC TEXT AND THE LETTER DIRECTLY BELOW "C" IN ROW **S** IS SUBSTITUTED FOR THAT LETTER. IN THIS CASE "Y" REPLACES "C". "F" IS REPLACED BY "J". IF YOU ARE ASKED TO ENCODE NUMBERS, YOU WILL SEE THAT ONE NUMBERS IS OVER OF SET OF 2-4 LETTERS. IN ORDER TO ENCODE NUMBERS USE THE LETTER FROM LEFT TO RIGHT IN THE GROUP FROM THE APPROPRIATE SET LINE. IN OUR EXAMPLE OF SET LINE **S**, IF YOU ARE ASKED TO ENCODE '00', YOU WOULD REPLACE THE FIRST ZERO WITH THE LETTER 'A' AND THE SECOND ZERO WITH THE LETTER "K". DO YOU HAVE ANY QUESTIONS?

PLEASE LOOK AT THE EXAMPLES AT THE BOTTOM OF THE PAGE. CAN YOU FOLLOW HOW THE FIRST EXAMPLE HAS BEEN COMPLETED. PLEASE WORK ON THE SECOND EXAMPLE NOW.

THE FINAL TASK THAT YOU WILL WORK ON IS A PUZZLE TASK. YOU WILL BE GIVEN FOUR LINE PUZZLES. YOUR TASK WILL BE TO TRACE OVER ALL THE LINES IN THE PUZZLE WITHOUT LIFTING YOUR PENCIL AND WITHOUT TRACING OVER ANY LINE MORE THAN ONCE. YOU WILL BE GIVEN A RED GREASE PENCIL SO THAT YOU WILL BE ABLE TO EASILY SEE WHICH LINES YOU HAVE ALREADY TRACED OVER. EACH TIME YOU MAKE A NEW ATTEMPT ON THE PUZZLE, I WOULD LIKE YOU TO DISCARD THE USED CARD AND USE A FRESH CARD. WHEN YOU FINISH ONE PUZZLE, MOVE ON TO THE NEXT STACK. YOU MAY WORK ON EACH PUZZLE FOR AS LONG OR AS SHORT AS YOU WISH. YOU DO NOT HAVE TO SUCCESSFULLY COMPLETE ONE PUZZLE BEFORE MOVING ON TO THE NEXT ONE. BUT, IF YOU MOVE ON TO THE NEXT PUZZLE, YOU MAY NOT GO BACK TO THE UNCOMPLETED PUZZLES.

BEFORE I GET DR. HAGMANN, I WOULD LIKE YOU TO COMPLETE THE FOLLOWING QUESTIONNAIRE. THE SHEET CONTAINS A LIST OF WORDS WHICH DESCRIBE DIFFERENT KINDS OF MOODS OR FEELINGS. PLEASE MARK AN 'X' IN EACH BOX WHICH DESCRIBES THE WAY THAT YOU ARE FEELING RIGHT NOW. CHECK ALL WORDS WHICH DESCRIBE THE WAY THAT YOU ARE FEELING. PLEASE WORK RAPIDLY (MAACL # 1).

I AM NOW GOING TO GET DR. HAGMANN AND HE WILL ADMINISTER YOUR INJECTION.

✿✿✿✿**(FOUR MINUTES AFTER THE INJECTION---)**

NOW I WOULD LIKE YOU TO QUICKLY CHECK EACH ADJECTIVE WHICH DESCRIBES THE WAY THAT YOU ARE FEELING RIGHT NOW. REMEMBER TO WORK RAPIDLY (MAACL #2).

PLEASE PUT ON THESE HEADSETS (***DEPENDING ON THE CONDITION****OVER WHICH YOU WILL BE HEARING BURSTS OF NOISE WHILE YOU ARE WORKING ON YOU FIRST SET OF TASKS **OR** WHICH YOU WILL BE WEARING TO BLOCK OUT ANY INTERFERING SOUNDS). NOW YOU WILL BE WORKING ON THE ARITHMATIC TASK, THE FINDING THE "A" TASK, AND THE NUMBER COMPARISON TASK. WHEN YOUR TIME IS UP ON EACH PAGE, I WILL TURN THE PAGE FOR YOU. IF YOU FINISH A PAGE BEFORE THE TIME IS UP EITHER STOP IF "STOP" IS WRITTEN AT THE BOTTOM OF THE PAGE OR GO ON TO THE NEXT PAGE IF THAT IS WHAT IS INDICATED AT THE BOTTOM OF THAT PAGE.

PLEASE PUT ON THE HEADSETS NOW (IF THEY ARE IN THE NOISE CONDITION START THE TAPE PLAYER).

BEGIN WORKING NOW---(START TIMING).

✡✡✡✡ NOTE TO EXPERIMENTER

EACH SUBJECT SHOULD HAVE **18 PAGES** IN THE RIGHT HAND POCKET OF THE FOLDER. THE **ORDER** SHOULD BE:

1. PAGES ONE TO FOUR OF ARITHMATIC PROBLEMS
2. PAGES 2 TO 5 OF FINDING THE A'S
3. PAGE 2 OF NUMBER COMPARISON
4. PAGES 5-8 OF ARITHMATIC PROBLEMS
5. PAGES 6-9 OF FINDING THE A'S TASK
6. PAGE 3 OF NUMBER COMPARISON TASK

✡✡✡✡✡TIMING FOR THIS TASK

1. PAGE 1 (ADDITION) **2 MIN**
2. PAGE 2 (ADDITION) **2 MINUTES**
3. PAGE 3 (ADDITION) **2 MINUTES**
4. PAGE 4 (ADDITION) **2 MINUTES**
5. PAGE 2-5 (A'S) A TOTAL OF 2 MINUTES FOR ALL FOUR SHEETS JUST MAKE CERTAIN THAT THEY ARE GOING ON TO THE NEXT PAGE
6. PAGE 2 (NUMBER COMPARISON) **1 1/2 MINUTES**
7. PAGE 5 (ADDITION) **2 MIN**
8. PAGE 6 (ADDITION) **2 MINUTES**
9. PAGE 7 (ADDITION) **2 MINUTES**
10. PAGE 8 (ADDITION) **2 MINUTES**
11. PAGE 6-9 (A'S) A TOTAL OF **2 MINUTE**S FOR ALL FOUR SHEETS JUST MAKE CERTAIN THAT THEY ARE GOING ON TO THE NEXT PAGE
12. PAGE 3 (NUMBER COMPARISON) **1 1/2 MINUTES**

****WHEN **23 MINUTES** ARE UP

PLEASE REMOVE THE HEADSETS, THIS TASK IS OVER.

NOW I WOULD LIKE YOU TO ANSWER SEVERAL QUESTION ABOUT THE TASK THAT YOU JUST COMPLETED. EACH QUESTION IS ON A 9 POINT SCALE. PLEASE CIRCLE THE NUMBER WHICH BEST DESCRIBES THE NOISE THAT YOU HEARD AND THE TASKS THAT YOU WERE WORKING ON.

I WOULD LIKE YOU TO AGAIN COMPLETE THE ADJECTIVE CHECKLIST. QUICKLY READ EACH ADJECTIVE AND MARK THE ONES WHICH DESCRIBE THE WAY THAT YOU ARE FEELING RIGHT NOW. WORK RAPIDLY (MAACL #3).

NOW, I WOULD LIKE YOU TO COMPLETE THE PROOFREADING TASK. REMEMBER TO READ THE PASSAGE AND CIRCLE ANY ERRORS THAT YOU FIND (HAVE THEM BEGIN READING AFTER THE LINE ON THE THIRD PAGE). THIS IS A TIMED TASK SO WORK AS QUICKLY AS POSSIBLE.

(***AFTER **5 MINUTES**)

PLEASE DRAW A LINE UNDER THE LAST SENTENCE WHICH YOU READ.

THE NEXT TASK IS THE ENCODING TASK, REMEMBER TO ESTABLISH A SET LINE --READ DOWN , THEN RIGHT , AND THEN RIGHT AGAIN. THIS WILL ESTABLISH THE LINE THAT YOU WILL BE ENCODING FROM--PLEASE GLANCE AT THE INSTUCTION SHEET AGAIN. DO YOU HAVE ANY QUESTIONS? REMEMBER TO WORK AS QUICKLY AS POSSIBLE

(***GIVE THEM **5 MINUTES** --START TIMING AND WATCH THEM AND **RECORD** THE TIME AT WHICH THEY MOVE FROM ONE PROBLEM TO THE NEXT).

OKAY, YOUR TIME IS UP.

(***LAY OUT THE FOUR DIFFENT PUZZLE IN A ROW IN FRONT OF THE SUBJECT FACE DOWN -- THERE SOULD BE 40 CARDS IN EACH STACK) FINALLY, THE LAST TASK IS THE TRACING TASK. REMEMBER YOU ARE TO TRACE EVERY LINE IN THE GEOMETRIC FIGURE WITHOUT LIFTING YOUR PENCIL OR CROSSING OVER ANY LINE TWICE. THERE ARE 4 PUZZLES TO WORK ON. YOUR MAY WORK ON EACH PUZZLE AS LONG AS YOU LIKE. IF YOU DECIDE TO GO ON TO THE NEXT PUZZLE BEFORE FINISHING THE LAST ONE, YOU CAN NOT GO BACK. REMEMBER TO USE A NEW CARD FOR EACH NEW ATTEMPT.

(*****DO NOT TELL THEM THAT THERE IS A TIME LIMIT, BUT WHEN THEY HAVE FINISHED THE SECOND PUZZLE TELL THEM THAT THEIR TIME IS UP*** **RECORD THE NUMBER OF CARDS THAT THEY USE ON EACH PUZZLE AND THE EXACT LENGTH OF TIME THAT THEY SPEND WORKING ON EACH PUZZLE)**

THAT COMPLETES YOUR SESSION FOR TODAY. THANK YOU VERY MUCH FOR YOUR PARTICIPATION. DO YOU HAVE ANY QUESTIONS OR COMMENTS ABOUT YOUR SESSION? IF YOU WOULD LIKE A COPY OF THE RESULTS WHEN THEY ARE COMPLETED WE WOULD BE HAPPY TO PROVIDE IT TO YOU.

(***IF THEY WANT THE RESULTS HAVE THEM WRITE THEIR NAMES AND ADDRESSES ON A SHEET OF PAPER).

BEFORE YOU LEAVE, I JUST WANTED TO ASK YOU IF YOU KNEW WHAT DRUG CONDITION YOU WERE IN? (*** IF THEY SAY THAT THEY COULD TELL).

DID YOU THINK THAT YOU RECIEVED NALOXONE OR SALINE?

THANKS AGAIN.

(MAKE CERTAIN YOU FIND OUT WHAT DRUG CONDITION THEY ARE IN AND INDICATE IT ON THE FORM PROVIDED).

Appendix B

Consent Form

Consent for Voluntary Participation in a Research Study

1. I, _____, have been asked to voluntarily participate in a research study.

2. This project is entitled, "Drugs and Noise Tolerance."

3. The purpose of this research study has been explained to me. I understand that the general purpose of this project is to study some of the effects of naloxone on noise tolerance. The purposes of this study are 1) to determine how patients feel when they take naloxone; 2) how blood pressure and pulse rate respond to the naloxone.

4. I will be maintained in this study for a period of one day (90 min.), and will receive $50.00 for my participation.

5. This study involves an intramuscular injection of either a placebo which is an inactive substance or naloxone (5-10 mg) which is a drug which has essentially no intrinsic action in the absence of morphine-like substances. Following the injection the session may consist of the following:

   a. Five minutes of either silence or noise.

   b. Comparing numbers, adding numbers, and finding words with the letter A.

   c. Solving puzzles.

   d. Finding proofreading errors.

   e. A cuff will be attached to measure heart-rate and blood pressure.

   f. Completion of paper-and-pencil measures asking about demographics, moods, and bodily reactions.

6. Specifically, I am aware that the experimental part of this procedure involves a) being given a drug or a placebo and not knowing the particular drug I am taking until the conclusion of the study; b) being given the behavioral tests and completing questionnaires; c) measurement of heart rate and blood pressure by automated equipment.

7. The investigator has informed me that a total of 40 subjects will be enrolled in this study.

8. The risks which are possible are as follows:

   Naloxone has essentially no effects in the absence of a narcotic. It can, however, produce severe withdrawal symptoms in the presence of such a drug. It may also exacerbate heart problems if I currently have any. I understand that I cannot participate in this study if I am currently taking any prescription or nonprescription drugs or if I have any medical condition such as hypertension or heart disease. I also understand that I have been screened by one member of the medical staff and do not have any medical conditions that would make any complications likely to occur.

I UNDERSTAND AND ACCEPT THESE RISKS. I also understand that to further minimize these risks there will be a physician (Dr. Hagmann or Dr. Holloway) physically present during all phases of testing and I will be instructed fully about the procedures in advance.

9. I understand that the study director (Dr. Baum) cannot say whether or not this study will be of direct benefit to me; it may provide knowledge about acute stressors.

10. If I have any questions concerning this research study, my rights as a subject, or if I believe that I have suffered any injury or illness as a result of this research, I may contact the office of Dr. Andrew Baum at 202/295-3270 or the Grants Management Office at 202-295-3303.

11. I understand that participation is voluntary.

12. The investigator may terminate my participation in this study if any medical contraindication or unforeseen side-effect of the medications develop, or if the experimental procedures produce distress.

13. If I should decide to withdraw from the research study, I will notify Dr. Baum at 202/295-3270 to ensure an orderly termination process. I further understand that I may withdraw at any time without prejudice. I further understand that the study directors encourage me to ask questions if I have them.

14. In all publications and presentations resulting from this research study, my anonymity is guaranteed; all individual data will be kept confidential and seen only by the study staff.

15. This study does not entail risks beyond those described above. However, I understand that the Department of Defense will provide medical care for DOD eligibles (active duty, dependents, and retired military) for physical injury or illness resulting from participation in this DOD approved research. Such care may not be available to other research participants. Compensation may be available through judicial avenues to non-active duty research participants if

they are injured through negligence (fault of the government). If you believe that you have suffered any injury or illness as a result of participating in this research, please contact the Office of Grants Management, 295-3303, at the University. This office can review the matter with you and may be able to identify resources available to you. Information about judicial avenues of compensation is available from the University's Legal Counsel, 295-3028.

16. I CERTIFY THAT I HAVE RECEIVED A COPY OF THIS CONSENT FORM.

_____ _____

date volunteer's initials

The implications of my voluntary participation, the nature and duration and purpose of the study, the methods and means by which the study is to be conducted, and the known inconveniences and hazards have been thoroughly explained to me by the principal investigator or by one of the co-investigators in this study, and such inconveniences and hazards are set forth in detail in this Agreement, along with my initials or signature. I have been given an opportunity to ask questions concerning this investigational study and my participation in the study, and any such questions have been answered to my full and complete satisfaction.

I agree to participate in "Drugs and Noise Tolerance."

_____	_____
date signed	patient signature
	_____
	printed name, status
_____	_____
witness signature	investigator signature
_____	_____
printed name, rank, SS#	printed name, rank, SS#

Appendix C

Background Questionnaire

Background

1. What is your age?_____Date of Birth_____

2. What is your height?_____

3. What is your current weight?_____

2. What is your marital status?

____Single
____Married How long?____
____Separated How long?____
____Divorced How long?____
____Widowed How long?____

3. If you were previously married, how long were you married?_____

4. Your highest educational level:

____Grammer School
____High School
____Some College
____College Degree
____Graduate Work
____Other (specify)_____

5. Your rank_____

6. Your occupation_____

7. How long have you been in the military?_____

8. Approximate annual income:

____Under $10,000/year
____$10,000 - $15,000/year
____$15,001 - $20,000/year
____$20,001 - $30,000/year
____$30,001 - $40,000/year
____$40,001 - $50,000/year
____over $50,000

9. Race or ethnicity:

____American Indian
____Asian or Pacific Island American
____Mexican-American
____Black
____White

10. In general, how would you describe your health right now?
    ____Very poor
    ____Poor
    ____Fair
    ____Good
    ____Excellent

11. Has your health changed in the last 6 months? Did it improve, remain the same, or become worse?
    ____Improve
    ____Remain the same
    ____Become worse

12. Have you visited the doctor in the last 12 months? Yes___ No___
    If yes, for what reason(s) and how many times?_____
    _____

13. Do you smoke? Yes____ No____
    If yes, how many cigarettes do you smoke each day?
    ____under 10 (1/2 pack)
    ____10-20 (1/2-1 pack)
    ____20-40 (1-2 packs)
    ____over 40 (2 packs)
    How often do you smoke cigars or pipe tobacco?
    ____never
    ____occasionally
    ____once per day
    ____several times per day
    ____many times per day

14. How many hours of sleep did you get last night?
    ____under 6 ____8 1/2 -10
    ____6-7 1/2 ____over 10
    ____about 8

15. Please indicate the number of 8 ounce servings of each of the following beverages you consume daily:
    coffee_____
    tea_____
    soft drinks(with caffeine)_____
    soft drinks(without caffeine)_____
    milk_____
    water_____
    other_____

16. Are you on a diet? Yes____No____ If yes, what kind?
    ____fasting
    ____calorie counting
    ____carbohydrate counting
    ____other

17. Do you take any prescription drugs? Yes____No____If yes, specify_____

18. Do you take any non-prescription drugs?___If yes, how much and how often?
    ____aspirin_____
    ____vitamins_____
    ____minerals_____
    ____allergy medications_____
    ____cold preparations_____
    ____sleeping pills_____
    ____other_____

19. Do you drink beer or wine? Yes___ No____
    If yes, how many glasses of beer or wine do you drink each week?
    ____1-5
    ____6-10
    ____11-15
    ____over 15

20. Do you drink alcoholic drinks other than beer or wine? Yes___ No____
    If yes, how many drinks do you have each week?
    ____1-5
    ____6-10
    ____11-15
    ____over 15

21. How often do you exercise?
    ____every day
    ____5-6 times per week
    ____3-4 times per week
    ____1-2 times per week
    ____never

22. What kind of exercise do you do?_____

23. When was the last time you exercised?_____

24. When was the last time you were ill (cold, flu, ear infection, cuts, breaks, strains, etc.)?_____

Appendix D

SCL-90

INSTRUCTIONS

Below is a list of problems and complaints that people sometimes have. Please read each one carefully. After you have done so please fill in one of the spaces to the right with a check that best describes HOW MUCH THAT PROBLEM HAS BOTHERED OR DISTRESSED YOU DURING THE PAST 2 weeks INCLUDING TODAY. Make only one check mark for each item.

HOW MUCH WERE YOU BOTHERED BY:

	Not at all	A little bit	Moderately	Quite a bit	Extremely
1. Headaches	1				
2. Nervousness or shakiness inside	2				
3. Repeated unpleasant thoughts that won't leave your mind	3				
4. Faintness or dizziness	4				
5. Loss of sexual interest or pleasure	5				
6. Feeling critical of others	6				
7. The idea that someone else can control your thoughts	7				
8. Feeling others are to blame for most of your troubles	8				
9. Trouble remembering things	9				
10. Worried about sloppiness or carelessness	10				
11. Feeling easily annoyed or irritated	11				
12. Pains in heart or chest	12				
13. Feeling afraid in open spaces or on the streets	13				
14. Feeling low in energy or slowed down	14				
15. Thoughts of ending your life	15				
16. Hearing voices that other people do not hear	16				

	Not at all	A little bit	Moderately	Quite a bit	Extremely
17. Trembling	17				
18. Feeling that most people cannot be trusted	18				
19. Poor appetite	19				
20. Crying easily	20				
21. Feeling shy or uneasy with the opposite sex	21				
22. Feelings of being trapped or caught	22				
23. Suddenly scared for no reason	23				
24. Temper outburst that you could not control	24				
25. Feeling afraid to go out of your house alone	25				
26. Blaming yourself for things	26				
27. Pains in lower back	27				
28. Feeling blocked in getting things done	28				
29. Feeling lonely	29				
30. Feeling blue	30				
31. Worrying too much about things	31				
32. Feeling no interest in things	32				
33. Feeling fearful	33				
34. Your feelings being easily hurt	34				
35. Other people being aware of your private thoughts	35				

	Not at all	A little bit	Moderately	Quite a bit	Extremely
36. Feeling others do not understand you or are unsympathetic					
37. Feeling that people are unfriendly, or dislike you					
38. Having to do things very slowly to insure correctness					
39. Heart pounding or racing					
40. Nausea or upset stomach					
41. Feeling inferior to others					
42. Soreness of your muscles					
43. Feeling that you are watched or talked about by others					
44. Trouble falling asleep					
45. Having to check and double-check what you do					
46. Difficulty making decisions					
47. Feeling afraid to travel on buses, subways or trains					
48. Trouble getting your breath					
49. Hot or cold spells					
50. Having to avoid certain things, places, or activities because they frighten you					
51. Your mind going blank					
52. Numbness or tingling in parts of your body					
53. A lump in your throat					

	Not at all	A little bit	Moderately	Quite a bit	Extremely
54. Feeling hopeless about the future	54				
55. Trouble concentrating	55				
56. Feeling weak in parts of your body	56				
57. Feeling tense or keyed up	57				
58. Heavy feelings in your arms or legs	58				
59. Thoughts of death or dying	59				
60. Overeating	60				
61. Feeling uneasy when people are watching or talking about you	61				
62. Having thoughts that are not your own	62				
63. Having urges to beat, injure, or harm someone	63				
64. Awakening in the early morning	64				
65. Having to repeat the same actions such as touching, counting, washing	65				
66. Sleep that is restless or disturbed	66				
67. Having urges to break or smash things	67				
68. Having ideas or beliefs that others do not share	68				

	None at all	A little bit	Moderately	Quite a bit	Extremely
69. Feeling very self-conscious with others	69				
70. Feeling uneasy in crowds, such as shopping or at a movie	70				
71. Feeling everything is an effort	71				
72. Spells of terror or panic	72				
73. Feeling uncomfortable about eating or drinking in public	73				
74. Getting into frequent arguments	74				
75. Feeling nervous when you are left alone	75				
76. Others not giving you proper credit for your achievements	76				
77. Feeling lonely even when you are with people	77				
78. Feeling so restless you couldn't sit still	78				
79. Feelings of worthlessness	79				
80. The feeling that something bad is going to happen to you	80				
81. Shouting or throwing things	81				
82. Feeling afraid you will faint in public	82				
83. Feeling that people will take advantage of you if you let them	83				
84. Having thoughts about sex that bother you a lot	84				

	None at all	A little bit	Moderately	Quite a bit	Extremely
85. The idea that you should be punished for your sins					
86. Thoughts and images of a frightening nature					
87. The idea that something serious is wrong with your body					
88. Never feeling close to another person					
89. Feelings of guilt					
90. The idea that something is wrong with your mind					
91. Feelings of helplessness					
92. Having to avoid people					
93. Feelings of it not mattering when given choices					
94. Feeling like you really don't care whether you do one thing or another					
95. Sudden noises making you jump or shake badly					

Appendix E

MAACL

1 ☐ active
2 ☐ adventurous
3 ☐ affectionate
4 ☐ afraid
5 ☐ agitated
6 ☐ agreeable
7 ☐ aggressive
8 ☐ alive
9 ☐ alone
10 ☐ amiable
11 ☐ amused
12 ☐ angry
13 ☐ annoyed
14 ☐ awful
15 ☐ bashful
16 ☐ bitter
17 ☐ blue
18 ☐ bored
19 ☐ calm
20 ☐ cautious
21 ☐ cheerful
22 ☐ clean
23 ☐ complaining
24 ☐ contented
25 ☐ contrary
26 ☐ cool
27 ☐ cooperative
28 ☐ critical
29 ☐ cross
30 ☐ cruel
31 ☐ daring
32 ☐ desperate
33 ☐ destroyed
34 ☐ devoted
35 ☐ disagreeable
36 ☐ discontented
37 ☐ discouraged
38 ☐ disgusted
39 ☐ displeased
40 ☐ energetic
41 ☐ enraged
42 ☐ enthusiastic
43 ☐ fearful
44 ☐ fine
45 ☐ fit
46 ☐ forlorn
47 ☐ frank
48 ☐ free
49 ☐ friendly
50 ☐ frightened
51 ☐ furious
52 ☐ gay
53 ☐ gentle
54 ☐ glad
55 ☐ gloomy
56 ☐ good
57 ☐ good-natured
58 ☐ grim
59 ☐ happy
60 ☐ healthy
61 ☐ hopeless
62 ☐ hostile
63 ☐ impatient
64 ☐ incensed
65 ☐ indignant
66 ☐ inspired
67 ☐ interested
68 ☐ irritated
69 ☐ jealous
70 ☐ joyful
71 ☐ kindly
72 ☐ lonely
73 ☐ lost
74 ☐ loving
75 ☐ low
76 ☐ lucky
77 ☐ mad
78 ☐ mean
79 ☐ meek
80 ☐ merry
81 ☐ mild
82 ☐ miserable
83 ☐ nervous
84 ☐ obliging
85 ☐ offended
86 ☐ outraged
87 ☐ panicky
88 ☐ patient
89 ☐ peaceful
90 ☐ pleased
91 ☐ pleasant
92 ☐ polite
93 ☐ powerful
94 ☐ quiet
95 ☐ reckless
96 ☐ rejected
97 ☐ rough
98 ☐ sad
99 ☐ safe
100 ☐ satisfied
101 ☐ secure
102 ☐ shaky
103 ☐ shy
104 ☐ soothed
105 ☐ steady
106 ☐ stubborn
107 ☐ stormy
108 ☐ strong
109 ☐ suffering
110 ☐ sullen
111 ☐ sunk
112 ☐ sympathetic
113 ☐ tame
114 ☐ tender
115 ☐ tense
116 ☐ terrible
117 ☐ terrified
118 ☐ thoughtful
119 ☐ timid
120 ☐ tormented
121 ☐ understanding
122 ☐ unhappy
123 ☐ unsociable
124 ☐ upset
125 ☐ vexed
126 ☐ warm
127 ☐ whole
128 ☐ wild
129 ☐ willful
130 ☐ wilted
131 ☐ worrying
132 ☐ young

Appendix F

Verbal and Numeral Problems

25	11	76	85	33	42	13	31	62	54
47	23	41	47	59	23	87	8	38	34
17	48	53	85	16	18	58	53	49	78

14	74	65	38	58	63	47	84	62	22
41	86	58	25	86	29	74	34	15	83
38	93	34	77	55	22	31	19	26	19

6	91	17	33	73	66	78	19	63	47
37	13	38	51	78	89	34	56	23	2
98	87	67	65	45	32	65	45	43	39

8	2	12	43	67	23	83	63	19	48
3	51	42	71	95	74	14	99	57	17
7	8	53	11	52	8	19	5	83	39

19	69	6	30	50	75	39	52	17	81
8	40	67	98	42	17	90	45	55	83
27	44	38	59	13	19	82	91	58	42

4	75	36	18	40	5	16	49	44	99
98	34	20	63	3	26	18	27	7	88
31	22	54	92	59	89	39	36	80	77

DO NOT TURN THE PAGE UNTIL ASKED TO DO SO

STOP *I*

73	9	49	23	36	58	17	43	17	41
52	27	61	7	32	60	49	15	97	57
61	83	14	69	88	17	51	38	82	78

13	88	67	96	90	77	62	59	97	84
26	45	47	78	50	34	73	19	57	79
58	9	62	14	26	61	23	56	31	8

82	80	55	96	6	91	9	77	86	77
12	39	10	68	85	21	88	24	11	84
65	4	41	29	37	49	43	38	48	59

76	69	34	48	77	53	18	94	38	42
38	93	33	45	24	49	61	5	58	34
71	85	51	99	44	77	22	37	88	76

6	46	57	55	46	85	28	92	14	48
23	53	53	31	37	34	73	34	65	29
44	37	35	13	99	8	44	63	83	77

83	50	67	72	48	62	31	11	98	37
9	34	78	98	1	81	38	74	87	32
13	42	45	62	98	23	48	68	39	62

DO NOT TURN THE PAGE UNTIL ASKED TO DO SO

STOP 2

13	45	67	23	73	85	13	9	76	81
21	47	47	68	83	25	31	21	65	97
41	65	89	74	41	4	56	78	13	69

14	63	56	89	35	89	14	8	78	54
13	56	86	68	42	56	78	68	34	67
31	54	67	89	32	56	68	91	62	31

12	45	23	87	31	76	46	76	56	12
12	42	64	78	59	74	56	95	64	84
47	63	53	45	87	63	55	42	65	89

12	34	89	90	64	3	78	55	77	22
3	56	38	97	56	33	22	76	49	50
23	56	74	81	33	22	42	17	39	80

12	34	65	85	64	54	33	90	76	30
33	67	2	98	45	21	56	66	78	12
27	39	80	69	87	21	44	56	89	66

12	45	25	64	66	68	34	29	38	82
12	14	6	78	5	16	75	93	37	52
56	84	30	45	32	13	76	68	63	78

DO NOT TURN THE PAGE UNTIL ASKED TO DO SO

STOP 3

32	56	32	67	12	56	89	78	12	32
21	56	88	31	66	44	99	34	23	12
31	54	67	89	99	16	19	4	6	22

21	4	77	86	95	21	78	48	44	22
43	67	89	13	41	97	45	23	21	77
21	56	66	23	1	66	77	90	76	32

21	22	44	77	97	56	33	82	33	67
12	33	66	88	90	12	56	45	12	34
12	45	21	11	22	78	3	8	21	21

1	33	44	12	31	44	11	11	23	12
1	21	6	8	12	71	90	76	12	22
32	33	41	55	31	78	32	54	67	98

21	34	21	54	62	31	78	90	12	1
21	54	13	41	78	95	55	78	54	78
11	14	78	90	65	43	67	16	62	82

32	65	88	55	88	43	28	91	31	89
12	56	88	54	23	6	88	79	34	76
32	55	43	22	52	78	43	18	52	23

DO NOT TURN THE PAGE UNTIL ASKED TO DO SO

STOP 4

Page 2

Part 1 (2 minutes)

1	2	3	4	5
mention	running	morning	neighbor	dropping
ladder	numerous	setting	strong	sixteen
bench	promise	puzzle	door	instead
theory	funny	witty	moon	moment
further	skip	dryly	soothe	worker
shutter	bloom	switch	quarrel	swift
publish	perfume	fellow	spelling	joyful
spread	monkey	blotter	wheel	comfort
deliver	eleven	melted	steam	fertile
remind	dismal	expense	sober	divide
improve	sponge	ringing	night	throng
forbid	history	durable	couch	velvet
pudding	biscuit	mixture	swell	readily
sunrise	nobody	touch	correct	descent
reward	temple	picnic	hear	chunk
progress	consist	whistle	window	sense
intense	indeed	lemon	bitter	eight
bridle	distant	within	lively	grease
prize	scenery	shriek	engine	moist
goose	jesting	riddle	compel	rocks
indoor	howl	politics	twinkle	click
winding	jump	leave	serene	empty
temper	figure	wintry	modern	freedom
message	depend	relish	revive	bottle
virtue	race	yonder	fifth	report
endure	sprout	bread	study	demure
sixth	honey	sweep	boast	bushel
chalk	clock	prince	juicy	unfold
motor	duke	confide	scorn	found
route	cliff	socket	mood	locket
syrup	four	fatigue	seize	merit
gold	shawl	monster	ivory	general
spicy	lunch	explode	renew	impulse
lion	crowd	million	colony	notch
wool	extent	empire	loudly	pump
pine	guard	regular	horse	cruise
sour	jolly	church	giant	drift
cork	upper	bulge	visit	tiger
pint	noon	timid	ounce	hilly
sheep	dough	plum	stone	happy
dusty	expect	moss	being	occur

GO ON TO THE NEXT PAGE.

Part 1 (continued)

6	7	8	9	10
ostrich	collect	except	splinter	woods
period	truth	welcome	ribbon	sorting
event	precise	struggle	string	bunch
middle	design	word	linen	saw
right	cotton	blue	express	floor
frozen	resent	orange	picture	settle
dodge	stride	employ	fiery	lowly
white	fierce	sports	envy	trench
tough	uproar	court	board	clutch
ocean	notion	humor	time	plunge
crush	light	great	problem	frigid
grind	rural	index	trumpet	hearing
cloud	color	skilled	powder	ground
drawn	settle	discover	meadow	hunting
bulky	fuel	enormous	opening	whine
supply	proper	secret	crush	polish
double	outburst	clothing	forbid	grieve
equip	puzzle	routine	intense	sensible
bottom	furnish	shock	extent	division
green	grab	numb	trinket	teacher
murmur	sprout	signal	several	degree
thrive	connect	counter	sleepy	order
become	grumble	quick	group	strong
collect	position	error	oasis	length
feeling	forward	evening	creep	portion
suspend	horrible	differ	howl	coating
machine	dense	ruler	enough	expect
yielding	ideal	dislike	yellow	smooth
slight	foggy	worship	blunt	rubbish
increase	gloss	cluster	develop	power
continue	mutter	severe	combine	slender
desire	crutch	touch	blush	common
youth	fiction	smoky	provide	refuse
fresh	house	birth	olive	bubble
wash	energy	botany	seize	board
dress	sooner	orderly	insert	trifle
storm	restless	content	noble	level
excel	sincere	breadth	worth	broken
delight	exclude	record	instant	uniform
figure	impress	choice	flower	flyer
twist	contest	splendid	speech	observe

GO ON TO THE NEXT PAGE.

Part 1 (continued)

11	12	13	14	15
stunned	ditch	recognize	notion	chubby
vicinity	blown	christen	sewing	outpour
luckily	unfit	mercury	drowsy	scoured
shudder	ought	disguise	bugle	offend
nowhere	sirup	wearing	loiter	explore
subsist	knelt	counsel	spool	recline
countess	ridge	bouquet	belle	sledge
sponsor	coral	inscribe	scent	eagerly
profile	tomb	throttle	cease	heroine
faint	doze	zoning	blithe	isthmus
bonfire	stroll	pewter	onset	though
refund	gushing	tyrant	lofty	cistern
offense	preface	debris	epoch	sylvan
custard	sputter	modest	whose	mostly
recover	nicely	refine	knoll	prosper
pitiful	reptile	fleecy	plural	tedious
homely	labor	enroll	siphon	explode
ruddy	boldly	leaves	mount	relieve
citron	single	deluge	bungle	sirloin
ignite	deport	hurled	wrung	wander
squeak	surrey	obscure	superb	hyphen
goblet	college	debtor	mildly	condense
propose	hoarse	quarter	double	veiled
observe	browse	enforce	buried	certify
seldom	inherit	pompous	steeple	vinegar
intrust	repose	burrow	ebbed	industry
resume	behold	humbug	import	heiress
earnest	crouch	apple	woman	fatten
croquet	deride	exploit	furrow	founder
empress	recoil	urgent	sturdy	whoever
corrupt	caught	tumult	embers	surgeon
emotion	slight	jewels	tempt	glisten
neither	invest	unfurl	impose	scepter
endless	gross	grunt	idea	return
instead	inner	beech	secede	shout
exempt	punch	sight	owner	bulky
species	dizzy	horde	ravine	outer
corps	heed	throb	horror	droll
peril	chess	petty	crust	enter
some	oven	numb	buzz	snuff
crew	spurt	whom	seek	item

GO ON TO THE NEXT PAGE.

Part 1 (continued)

16	17	18	19	20
finish	shipping	bliss	pour	sudden
ginger	through	keen	drugs	tissue
slightly	chestnut	road	film	blade
routine	lack	chew	mesh	lonely
wither	mission	glue	cheese	wrist
strife	without	lilies	peace	nursery
eyelet	guessed	poster	thing	urging
jungle	eastern	fumble	police	turnip
willow	deepest	recent	onion	reveal
prison	stuffed	untrue	strict	decided
outline	twenty	disgust	twelve	chimney
pleasing	cottage	reader	furnace	entirely
midnight	opinion	glorious	multiply	jaunty
robbery	sisters	forlorn	chuckle	rejoice
bestow	mitten	nobody	pepper	session
widely	obedient	evident	blend	elbow
curb	blurred	seventh	kettle	result
root	election	earnest	dislike	widow
usual	destiny	pronoun	cause	string
lower	outing	rebuke	trench	hooked
lofty	tunnel	comedy	noted	dentist
cycle	pitch	tribute	consent	pieces
globe	cloves	unjust	morose	legion
negro	knife	leaf	pupil	crisp
slice	plenty	queen	cripple	much
wrong	loyal	method	brook	fully
cordial	fifty	dollar	pickle	scold
better	chorus	bodily	hostile	bounce
dotted	excess	might	chosen	resent
roving	giggle	glove	flutter	smudge
dollar	injury	tenor	sword	senate
wireless	fourth	thorn	eighty	freckle
decrease	beacon	crisis	reliance	stout
outside	frown	pinch	downtown	digest
undue	oblige	vexed	inclose	hobby
roller	unlike	twine	pillow	brush
voter	option	brick	logical	fissure
block	celery	focus	melon	leather
creep	blithe	census	rustic	victory
bite	thirty	buyer	bonus	dozen
cent	none	shrub	invite	prong

DO NOT GO ON TO THE NEXT PAGE UNTIL YOU ARE ASKED TO DO SO.

STOP.

Part 1 (1 1/2 minutes)

Make an X on the line between the numbers that are not the same.

639	____	639	414982	____	415982
4714306	____	4715306	60571	____	60971
65382	____	65372	16253948	____	16253948
710	____	710	42018591760	____	43018591760
43210573	____	43210573	647107569	____	647107569
6182653905221	____	6182653905221	721532992531	____	721582992531
43270105338	____	43276105338	341798301	____	341798701
27109816843	____	27109816853	80537051248	____	80537051248
519605	____	519605	591130581492	____	591130681491
923452170687	____	923452170687	63614081	____	83614081
370543141	____	310543141	47471301	____	47471307
2570665292	____	2570675292	6082649875	____	6082647875
32018591670	____	32018691670	5930582136	____	5730582136
5471075693	____	5471075683	236031294137	____	236031294137
621532992531	____	621582992531	805731195	____	805131195
24179830	____	24179830	48210435612	____	48210435612
70537051248	____	70537057248	405176841309	____	405176841309
7361408	____	7361708	80145549786	____	80145349796
39471307	____	39471507	53210573	____	53210573
508264987503	____	508264987503	718265390521	____	718265390521
4930582136	____	4930582136	5327010558	____	5327010538
136031794137	____	136031794137	37109816843	____	37189816843
705731195	____	705736195	619605	____	619505
38210435512	____	38210535512	123452170687	____	123452190687

DO NOT GO ON TO THE NEXT PAGE UNTIL ASKED TO DO SO.

STOP.

8	2	12	43	67	23	83	63	19	48
3	51	42	71	95	74	14	99	57	17
7	8	53	11	52	8	19	5	83	39

19	69	6	30	50	75	39	52	17	81
8	40	67	98	42	17	90	45	55	83
27	44	38	59	13	19	82	91	58	42

4	75	36	18	40	5	16	49	44	99
98	34	20	63	3	26	18	27	7	88
31	22	54	92	59	89	39	36	80	77

25	11	76	85	33	42	13	31	62	54
47	23	41	47	59	23	87	8	38	34
17	48	53	85	16	18	58	53	49	78

14	74	65	38	58	63	47	84	62	22
41	86	58	25	86	29	74	34	15	83
38	93	34	77	55	22	31	19	26	19

6	91	17	33	73	66	78	19	63	47
37	13	38	51	78	89	34	56	23	2
98	87	67	65	45	32	65	45	43	39

DO NOT TURN THE PAGE UNTIL ASKED TO DO SO

STOP 5

76	69	34	48	77	53	18	94	38	42
38	93	33	45	24	49	61	5	58	34
71	85	51	99	44	77	22	37	88	76
6	46	57	55	46	85	28	92	14	48
23	53	53	31	37	34	73	34	65	29
44	37	35	13	99	8	44	63	83	77
83	50	67	72	48	62	31	11	98	37
9	34	78	98	1	81	38	74	87	32
13	42	45	62	98	23	48	68	39	62
73	9	49	23	36	58	17	43	17	41
52	27	61	7	32	60	49	15	97	57
61	83	14	69	88	17	51	38	82	78
13	88	67	96	90	77	62	59	97	84
26	45	47	78	50	34	73	19	57	79
58	9	62	14	26	61	23	56	31	8
82	80	55	96	6	91	9	77	86	77
12	39	10	68	85	21	88	24	11	84
65	4	41	29	37	49	43	38	48	59

DO NOT TURN THE PAGE UNTIL ASKED TO DO SO

STOP 6

12	34	89	90	64	3	78	55	77	22
3	56	38	97	56	33	22	76	49	50
23	56	74	81	33	22	42	17	39	80

12	34	65	85	64	54	33	90	76	30
33	67	2	98	45	21	56	66	78	12
27	39	80	69	87	21	44	56	89	66

12	45	25	64	66	68	34	29	38	82
12	14	6	78	5	16	75	93	37	52
56	84	30	45	32	13	76	68	63	78

13	45	67	23	73	85	13	9	76	81
21	47	47	68	83	25	31	21	65	97
41	65	89	74	41	4	56	78	13	69

14	63	56	89	35	89	14	8	78	54
13	56	86	68	42	56	78	68	34	67
31	54	67	89	32	56	68	91	62	31

12	45	23	87	31	76	46	76	56	12
12	42	64	78	59	74	56	95	64	84
47	63	53	45	87	63	55	42	65	89

DO NOT TURN THE PAGE UNTIL ASKED TO DO SO

STOP 7

1	33	44	12	31	44	11	11	23	12
1	21	6	8	12	71	90	76	12	22
32	33	41	55	31	78	32	54	67	98

21	34	21	54	62	31	78	90	12	1
21	54	13	41	78	95	55	78	54	78
11	14	78	90	65	43	67	16	62	82

32	65	88	55	88	43	28	91	31	89
12	56	88	54	23	6	88	79	34	76
32	55	43	22	52	78	43	18	52	23

32	56	32	67	12	56	89	78	12	32
21	56	88	31	66	44	99	34	23	12
31	54	67	89	99	16	19	4	6	22

21	4	77	86	95	21	78	48	44	22
43	67	89	13	41	97	45	23	21	77
21	56	66	23	1	66	77	90	76	32

21	22	44	77	97	56	33	82	33	67
12	33	66	88	90	12	56	45	12	34
12	45	21	11	22	78	3	8	21	21

DO NOT TURN THE PAGE UNTIL ASKED TO DO SO

STOP 8

Part 2 (2 minutes)

21	22	23	24	25
fringe	difficult	quick	cutting	provoke
sister	condition	success	summon	gently
meet	river	winner	exercise	judge
thrifty	flush	govern	because	resist
flowing	justice	term	marry	strict
engineer	sought	lawn	soldier	dirty
errand	balmy	chum	perform	pause
profit	fence	limit	subject	tender
vigor	belief	snow	permit	comb
forceful	cunning	organ	observe	equal
tinge	country	brief	feeble	model
weak	blossom	income	return	united
drove	disease	crown	instruct	point
truth	summon	health	control	trust
filmy	sweet	shutter	knight	begin
crawl	fever	costume	friend	keep
loss	unity	silence	subject	post
useless	storm	money	number	quart
border	forgive	editor	printing	grown
product	quality	gossip	effort	blister
liquid	violent	writing	perform	screen
construct	sphere	course	constant	blend
hinder	enroll	request	shiver	thrive
before	blouse	nobler	dinner	bounty
foreign	blind	wound	prosper	knock
divide	style	stock	vessel	sound
thrill	head	boiling	breeze	bloom
last	eyes	punish	bang	critic
conduct	rule	knead	shirt	local
dress	join	defense	complex	gifted
gloom	honest	complete	music	member
volume	commerce	section	wring	burst
consist	bridge	walnut	earth	shortly
muddy	height	bruise	bold	pierce
gleam	tremble	column	rough	brown
depth	spark	uniform	friend	car
fruit	invent	enter	secure	liberty
recent	tissue	offset	dreary	direct
bright	shrink	blend	cover	effect
first	guide	wind	beside	touch
thicken	vivid	meek	noisy	driver

GO ON TO THE NEXT PAGE.

Part 2 (continued)

26	27	28	29	30
discount	button	civil	swimming	grind
buckle	street	trough	struggle	stretch
possible	tooth	wonder	poultry	outcome
building	lusty	pump	journey	kindly
trouble	corner	corn	opposite	thread
exert	turn	bluff	wretch	frolic
believe	throw	short	taught	bonds
source	protect	beach	slight	recite
devote	defeat	keeper	curved	pulse
labor	nerve	cement	pretty	swamp
reserve	trim	muddy	origin	crust
hopeful	pulley	bulletin	behind	shelter
penny	fortune	stumble	certain	choose
learn	thistle	improper	shrink	part
screen	collar	poverty	promise	using
purse	esteem	courage	impulse	folded
sketch	shell	bouquet	current	ceiling
quietly	broken	stencil	dismiss	theme
mischief	feather	purpose	broader	surprise
revolt	clever	heartily	neglect	butcher
flying	floor	question	conceit	plowing
precious	summit	receive	blunder	shingle
similar	benefit	lessen	winter	trunk
sullen	listless	towel	swallow	scheme
grocery	inquire	past	bending	lumber
pottery	definite	rugged	conquer	between
tumble	chicken	weight	praise	describe
throb	ticket	truck	design	distinct
spoil	posture	prompt	tinsel	merchant
ideal	thrust	region	union	offering
pledge	formal	society	pride	steeple
trust	hence	mental	follow	think
circle	become	crest	tower	known
other	coffee	field	sponge	relief
ease	heroism	press	uphill	purple
solid	pleasant	shower	vessel	mildly
bound	courtesy	geese	policy	ready
flood	pushing	likely	needle	flour
bruise	story	custom	persist	erect
scene	gulf	title	verse	spend
office	plume	public	honor	whole

GO ON TO THE NEXT PAGE.

Page 8

Part 2 (Continued)

31	32	33	34	35
extend	sonnet	sherbet	ermine	jockey
derrick	verify	cunning	finest	concur
seeded	ellipse	nominee	lucky	distort
divert	vespers	revelry	trophy	console
toast	referee	dubious	borne	pensive
whine	shrimp	crochet	dump	duchess
jostle	coerce	venison	vigil	impetus
resound	tonic	hygiene	elude	duplex
diverse	vital	zenith	poem	gristle
shrewd	cough	creamy	eagle	race
bristle	suburb	exertion	leech	molest
whence	eclipse	terrace	quick	remedy
pauper	bunting	council	expire	serene
instill	fervent	utilize	muskrat	billow
compile	shortly	coroner	decide	lilacs
expend	tenant	scoffer	triple	medley
redeem	iodine	district	pecan	decline
subside	comely	within	score	fluent
inspire	supple	insult	fresco	unison
convict	orchid	steady	steed	reverie
nearer	deliver	convert	grove	costume
perplex	exploit	siding	strive	dutiful
strain	former	minor	mutiny	servant
widen	chagrin	retort	jester	converse
concise	hustle	thesis	beaver	horizon
trustee	treble	climate	desist	consider
company	using	govern	rigid	deposit
enliven	tendon	brevity	donor	highly
indorse	moose	futile	mumps	unique
keener	closed	docile	profess	marine
tutor	gopher	ethics	chemist	entice
instep	lyrical	cured	flourish	scope
mildew	porter	sleigh	initial	clique
unify	finite	eaves	deprive	broth
rouse	pollen	orbit	pupil	older
signs	search	expose	chore	libel
gorge	piston	longer	flute	crawl
punch	rebel	siren	ivory	tools
sheer	ether	hover	gypsy	soul
pursue	peony	usurp	brook	creep
hotel	throne	myth	knew	odor

GO ON TO THE NEXT PAGE.

Part 2 (Continued)

36	37	38	39	40
sunlight	dwelling	nonsense	silver	mention
rhythm	trumpet	think	mellow	simple
thunder	discover	beauty	generous	seven
outcry	mixture	tenth	second	chalk
morsel	brother	crumb	insect	jumble
frontier	villain	freedom	guilt	worth
frequent	memory	resemble	spring	merely
whisper	indirect	slight	coarse	selfish
industry	vigorous	burning	pocket	ignore
sparkle	ringlet	glisten	turning	carpenter
summer	calmly	moving	flicker	element
shelter	minute	blight	search	blend
enlarge	extreme	comment	spirit	sultry
interest	dignity	neglect	tired	teach
written	living	orchard	resign	review
lower	sturdy	distress	humble	limb
torrid	property	cheer	idleness	melody
lodge	lesson	last	direction	possess
squash	yield	gloss	tempest	shining
proverb	poverty	continue	student	hollow
swollen	motion	suggest	medium	burden
present	thought	mouth	decent	buffalo
rumor	saw	sincere	shortly	complete
science	loose	resort	joint	remind
toward	perfect	mourn	sunny	worm
worry	world	early	forlorn	couple
shout	speech	wreck	discord	earth
endure	robust	confuse	private	cruel
spelling	greedy	pencil	holding	soften
people	orphan	energy	report	poetry
hollow	crude	check	concert	third
lifting	reduce	polite	reason	smiling
crystal	whole	cipher	concern	biology
exhibit	stove	speed	letter	copied
produce	center	repeat	singing	device
nimble	orator	noisy	utmost	future
little	shrill	digest	enjoy	hour
voice	jolly	service	education	robin
words	crow	finger	reflect	view
rent	dimly	nestle	muffle	glory
doubt	notice	listen	junior	home

DO NOT GO BACK TO PART 1 AND

DO NOT GO ON TO ANY OTHER TEST UNTIL YOU ARE ASKED TO DO SO.

STOP.

Part 2 (1 1/2 minutes)

Make an X on the line between the numbers that are not the same.

7573 ____ 7573	289414 ____ 289414
347820 ____ 349820	17906 ____ 17906
4951 ____ 4951	16719581024 ____ 16719581024
4573043 ____ 4571043	16719581024 ____ 16719581024
37501243 ____ 37501243	3965701746 ____ 3665701746
125093562816 ____ 125093562816	135299235127 ____ 135299235127
8350107234 ____ 8350107234	13897143 ____ 13897145
34861890172 ____ 3486170172	84215073508 ____ 84216073508
506915 ____ 596915	941856031195 ____ 941856431195
786071254329 ____ 786071255329	8041638 ____ 8041438
41345073 ____ 41345073	70317494 ____ 70317494
925660752 ____ 925660752	35789462806 ____ 35789562806
16719581023 ____ 167175[illegible]1023	6312850395 ____ 6312850795
3965701745 ____ 3965701745	731497130632 ____ 731497130632
135299235126 ____ 135299235136	591137508 ____ 591167508
13897142 ____ 13897142	21553401284 ____ 21553401284
84215073506 ____ 84215073507	1251373807 ____ 1251373307
941856031194 ____ 941846031194	903148671504 ____ 903148671504
8041637 ____ 8071637	68794353108 ____ 68754354108
70317493 ____ 70317493	37501235 ____ 37501235
35789462805 ____ 35789462805	125093562817 ____ 125093562817
6312850394 ____ 6312850394	8350107235 ____ 8350107235
731497130631 ____ 731497130681	34861890173 ____ 34861840173
591137507 ____ 591127507	506916 ____ 506616

DO NOT GO BACK TO PART 1 AND DO NOT GO ON TO ANY OTHER TEST UNTIL ASKED TO DO SO.

STOP.

Appendix G

Proofreading

PROOFREADING TASK

Your task will be to proofread a passage and to circle any mistakes that you find. Below you will find examples of some common types of errors.

	Mistake	Correct
Misspellings	decreace	decrease
Typographical errors	ata	at a
Punctuation errors	Moreover; it is	Moreover, it is
Capitalization errors	eugene, oregon	Eugene, Oregon
Incorrect word	the dear ran	the deer ran
Verb error	the students takes	the students take

Your task will be to find the errors and circle them. Read the passage from left to right and do not skip any lines.

* *Here is an example of what your task is like:

When sufficient people begin to stay in a slum by choice, several other importantthings also begin to happens.

Please do not begin work until the experimenter gives you the signal.

THE USES OF NEIGHBORHOOD PARKS

Conventionally, neighborhood parks or parklike open spaces are considered boons conferred on the deprived populations of cities. Let us turn this thought around, and consider city parks derpived placces that ned the boon of life and appreciation conferred on them. This is more nearly in accord with reality, for people do confer use on parks and make them successes--or else withhold use and doom parks to rejection and failure.

Parks are vola tile places. They tend to run to extremes of popularity and unpopularity. Their behavior is far from simple. They can be delightful features of city districts, and economic assets to their surroundings as well, but pitifully few are. They can grow more beloved and valuable with the years, but pitifully few show this staying power. For every Rittenhouse Square in Philadelphia, or Rockefeller Plaza or Washington Square in New York, or Boston Common, or their loved equivalents in otehe cities, there are dozens of dispirited city vacuums called parks, eaten around with decay, little used, unloved. As a woman in Indiana said when asked if she liked the town square, "Nobody there but dirty old men who spiit tobacco juice and try to look up your skirt."

In orthodox city planning, neighborhood open spaces are venerated in an amazingly uncritical fashion, much as savages venerate magical fetihses. Ask a houser how his planned neighborhood improves on the old city ad he will cite, as a self-evident virtue, More Open Space. Ask a zoner about the improvements in progressive codes and he will cite, again as a self-evident virtue, their incentives toward leaving

Mre Open Space. Walk with a planner through a dispirited neighborhood and though it be already scabby with deserted parks and tired landscaping festooned with old Klee nex, he will envision a future of More Open Space.

More Open Space for what? For muggings? For bleak vacuums between buildings? Or for ordinary people to use and enjoy? But people do not use city open space just because it is there and because city planners or designers wish they would.

In certain specifics of itts behavior, every city park is a case unto itself and defies generalizations. Moreover, large parks such as Fairmount Park in Philadelphia, Central Park and Bronx Park and Propsect Park in New York, Forest Park in St. Louis, Golden Gate Park in San Francisco, Grant Park in Chicago--and even smaller Boston Common--differ much within themselves from Part to part, and they also receive differing influences from the different parts of their cities which they touch. some of the factors in the behavior of large metropolitan parks are too complex to deal with in the first part of this book; they will, be discussed later, in Chapter Fourteen, The Curse of Border Vacuums.

Nevertheless, even though it is misleading to consider any two city parks actual or potential duplicates of one another, or to believe that generalizations can thoroughly explain all the peculiarities of any single park, it is possible to generalize about a Few basic principles that deeply affect Virtually all neighborhood parks. Moreover, understanding these principles helps somewhat in understanding influences working on city, parks of all kinds--from little outdoor lobbies which serve as enlargements of the street, to large parks with major metropolitan attractions like zooos, lakes, woods, museums.

The reason neighborhood parks reveal certain general principles about park behavior more clearly than specialized parks do is precisely that neighborhood parks are the most generalized form of city park that we possess. They are typically intended for general bread-and-butter use as local public yards--whether the locality is predominately a workingplace, predmoinately A residential place, or a thoroughgoing mixture. Most city squares falls into this category of generalized public-yard use; so does most project land: and so does much city parkland that takes advantage of natura features like river banks or hilltops.

The first necessity in understanding' how cities ad their parks influence each other is to jettison confusion between real uses and mythical uses--for example, the science-fiction nonsense that pakrs are "the lungs of the city." It takes about three acres of woods to absorb as much carbon dioxide as four peopleexude in breathing, cooking and heating. The oceans of air circulating about us, not not parks, keep cities phrom suffocating.

Nor is more air let into the city by a given acreage of greenery than by an equivalent acreage of streets. Subtracting streets and adding their square footage" to parks or project malls is irrelevant to the quantities of fresh air a city receives. Air knows nothing of grass fetishes and fails to pick and choose for itself in accordance with them

It is necessary too, in understanding park behavior, to juk the false reassurance that parks are real estate stabilizers or community anchors. Parks are not automatically anything, and least of all are these volatile elements stabilizersof values or, of their neighborhoods and districts.

Philadelphia affords almost a controlled-experiment on this point. When Penn laid out the city, he placed at its center the square now occupied by City Hall, and at equal distances from this center he placed four residential squares, What has become of these four, all the same age, the same size, the same orignal use, as nearly the same in presumed advantages of location as they could be made?

Their fates are wildly different.

The best known of Penn's four squares is Rittenhouse Square, a beloved, successful, much-used park, one of Philadelphia's greatest assets today, the center of a fashionable neighborhood--indeed, the only old neighborhood in Philadelphia which is spontaneously rehabitating its edges and extending its real estate values.

The second of Penn's litle parks is Franklin Square, the city's Skid Row park where the homeless, the unemployed and the people of indigent leesure gather amid the adjacent flophouses, cheap hotels, missions, second-hand Clothing stores, reading and righting lobbies, pawnshops, employment agencies, tattoo parlors, burlesque houses and eateries. This pa rk and its users are both seedy, but it is not a dangerous or crime park. Nevertheless, it has hardly worked as an anchor To real estate values or to social stability. Its neighborhood is scheduled for large-scale" clearance.

The third is Washington Square, the center of an area that was at one time the heart of downtown, but is now specialized as a massive office center--insurance companies, publishing, advertising. Several decades ago Washington Square became Philadelphia's pervert park, too the point where it was shunned by ofice lunchers, and was an unmanageable vice and crime problem to park workers and police. In the

mid-1950's it was torn up, closed for more than a year, and redesigned. In the process its users, were dispersed, which was the intent. Today it gets brief and desultory use, lying mostly empty exept at lunchtime on fine days. Washington Square's district, like Franklin Square's, has failed at spontaneously maintaining its values, let alone raising them. Beyond the rim of off ices, it is today designated for large-scale urban renewal.

The fourth of Penn's squares has been whittled to a small traffic island, Logan Circle, in Benjamin Franklin Boulevard, an example of City Beautiful planing. The circle is adorned with a great soaring fountain and beautifully maintained planting. Although it is discouraging to reach on foot, and is mainly an elegant amenity for those speeding by, it gets a trickle of population on fine days. The district Immediately adjoining the monumental cultural center of which it is a part decayed terribly and has already been slum-cleared and converted to Radiant City.

The varying fates of these squares--especially the three that remain squares--illustrate the volatile behavior that are characteristic of city parks. These squares also happen too illustrate much about basic principles of park be havior, and I shall return to them and their lessons soon.

The fickle behavior of parks and, their neighborhoods can be extreme. One of the most charming and individual small parks to be found in, any American city, the Plaza in Los Angeles, ringed with immense magnolia trees, a lovely Place of shade and history is today incongruously encircled on three sides with abanadoned ghost buildings and with squa lor so miserable the stink of it rolls over the sidewalks. (Off

the fourth side is a Mexican counter bazaar, doing fine.) Madison Park in Boston, the residential grassy square of a row-house neighborhood, a park precisely of the kind that is popping into many of today's sophisticated redevelopment plans, is the center of a neighborhood that appers to have been bombed. The houses around it—inherently no different from those in high demand at outer reaches of Philadelphia's Rittenhouse Square neighborhood—are crumbling from lack of value, with consequent neglect. As one house in a row cracks, it is demolished and the family in the next house is moved for safety; a few months later that one goes and the house beyond is emptied. No plan is involved in this, merely purposeless, gaping holes, rubble, and abandonment, with the little ghost park, theoretically a good residential anchorage, at the center of the havoc. Federal Hill in Baltimore is a most beautiful and serene park and affords the finest view in Baltimore of the city and the bay. Its neighborhood, although decent, is moribund like the park itself. For generations it has failed to attract newcomers by choice. One of the bitterest disappointments in housing project history is the failure of teh parks and open grounds in these establishments to, increase adjacent values or to stabilize, let alone improve, their neighborhoods. Notice the rim of any city park, civic plaza or project parkland: how rare is the city Oper space with a rim that consistently reflects the supposed magnetism or stabilizing influence residing in Parks.

And consider also the parks that go to waste most of the time, just as Baltimore's beautiful Federal Hill does. In Cincinnati's two finest parks, overlooking the river, I was able to find on a splendid, hot September afternoon a grand total of five souls (three teen-age girls and one young couple); meanwhile, street after street in Cincinnati was

swarming with people at leisure who lacked the slightest amenity for enjoying the city or the least kindness of shade. On a simlar afternoon, witth the temperature above ninety degrees, I was able to find in Corlears Hook park, a landscaped breezy river-front oasis in Manhattan's heavily populated Lower East Side, just eighteen people, most of them lone, apparently indigent, man. The children were not there; no mother in her right mind would send a child) in there alone, and the mothers of the Lower East Side are not out of their minds. A boat trip around Manhattan conveys the erroneous impression that here is a city composed largely of parkland--and almost devoid of inhabitants. Why are there so often no people where the parks are and no parks where the people are?

Appendix H

Encoding Task

	ABC	*DEF*	*GHJ*	*KL*	*MN*	*PQR*	*ST*	*UV*	*WX*	*YZ*
	0	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*
A	VTGK	PSM	CLN	IO	DQ	FHE	WB	RY	XJ	UA
B	BTMS	JHA	EQY	PG	WF	ONL	VX	UI	CD	RK
C	QJLU	WYP	SAN	MD	FT	OHX	VR	EC	GB	IK
D	LIQA	MFB	JGH	UN	CT	XPY	ED	OR	SK	VW
E	HGJX	DTR	YSN	IC	VM	BFK	CQ	PA	UW	EL
F	EXGI	WTF	OYL	BA	MJ	PKH	VQ	DR	NU	CS
	ABC	*DEF*	*GHJ*	*KL*	*MN*	*PQR*	*ST*	*UV*	*WX*	*YZ*
	0	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*
G	HXYJ	OFN	URA	WK	DE	LPB	TM	VS	QI	CG
H	YDTV	PKO	ISH	NJ	FQ	BGX	CL	EM	RA	UW
I	UENJ	ARV	FIP	WD	SY	COM	XG	TH	BQ	KL
J	JTCG	AXM	UVE	SR	DP	QOB	WN	KY	FH	LI
K	VFDT	XIW	UBQ	RC	JY	EPG	HM	LO	KS	NA
L	OXRB	TCQ	INS	PH	KL	WGY	FA	DJ	UV	ME
	ABC	*DEF*	*GHJ*	*KL*	*MN*	*PQR*	*ST*	*UV*	*WX*	*YZ*
	0	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*
M	RVHS	TXQ	AJL	YK	GU	MPW	DO	IE	CN	FB
N	DUGI	WYK	EHL	SJ	TF	XRC	VP	NM	QA	OB
O	CBHR	VYJ	PLG	OX	NT	IFE	MA	DQ	WK	SU
P	VWXS	RIO	LPT	GY	NM	QKU	HF	EC	AD	JB
Q	SUVT	RPL	NID	MO	YW	XBC	FE	QH	AJ	KG
R	RDFO	GYV	PJA	QS	KL	MBE	TI	CH	UX	WN
	ABC	*DEF*	*GHJ*	*KL*	*MN*	*PQR*	*ST*	*UV*	*WX*	*YZ*
	0	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*	*9*
S	AKLY	INJ	ERH	FG	BT	MCO	SV	UQ	PW	DX
T	VYQT	CKN	JEO	MF	GB	PLD	RW	HS	UA	XI
U	JVYM	FOG	PHL	ES	DC	WIR	AB	KU	XO	NT
V	UTNC	WLQ	RKE	BS	JX	ODV	AF	GY	MH	IP
W	RUQC	HBX	TOS	FV	LP	JEA	WG	MN	IK	DY
X	VQMO	JLN	TSI	CF	AP	HKW	BY	UR	XG	DE
Y	LUOP	QMK	CVI	ER	HF	NGS	XT	JD	WA	BY

SET LINE: READ DOWN-RIGHT-RIGHT

1. ESTABLISH **LD** AS SET LINE

   QA86342183=_____

2. ESTABLISH **SC** AS SET LINE

   FD21683121=_____

3. ESTABLISH **AS** AS SET LINE

   CM90384416=_____

4. ESTABLISH **AB** AS SET LINE

   CB976786532=_____

5. ESTABLISH **OO** AS SET LINE

   RM96359824=_____

6. ESTABLISH **MM** AS SET LINE

   PJ95487623=_____

7. ESTABLISH **CM** AS SET LINE

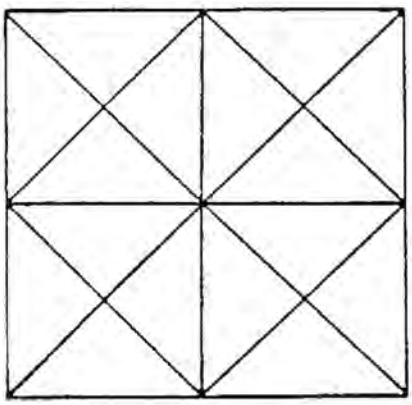
   AL38241432=_____

8. ESTABLISH **NE** AS SET LINE

   BG02445976=_____

Appendix I

Insolvable Puzzle



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