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Historically, theories on aggression only considered the impact of environmental, biological, and sociological factors. However, recent evidence suggests physiological sources of aggression deserve greater attention. One chemical imbalance in the body related to aggression and heightened reactivity involves the neurotransmitter serotonin, 5-HT. In humans, lower than normal amounts of 5-HT are related to violent behaviors, suicide, and depression. Nonhuman animals with low 5-HT levels show inhibited growth, heightened reactivity to stimuli, and increased attacking behavior towards other animals.

The integral component in the relationship between low 5-HT and increased aggression and reactivity is the amino acid tryptophan which organisms normally receive through their diet. Because 5-HT is synthesized from tryptophan, the amount of brain serotonin is exclusively dependent upon the amount of available tryptophan. To test the low 5-HT-increased aggression and reactivity relationship, the present investigations evaluated levels of aggression and reactivity following exposure to two methods designed to reduce tryptophan transfer and 5-HT synthesis in rats. Reductions in 5-HT synthesis were accomplished in two ways. First, dietary intake of tryptophan was significantly limited by feeding rats a diet consisting only of corn grits, a food containing minute amounts of tryptophan. In a second condition, the amount of tryptophan allowed to enter the brain was reduced. Animals received an aspartame-water mixture in addition to a

the brain was reduced. Animals received an aspartame-water mixture in addition to a standard diet. Aspartame, more commonly known as Nutrasweet, blocks the transfer of tryptophan into the brain thereby reducing brain tryptophan levels and serotonin synthesis. Results supported the hypothesis that tryptophan-challenged rats would make longer and more numerous aggressive responses, and show stronger aversions to a novel flavor, than rats with no tryptophan deficiencies. Possible sources of this relationship and applicable conclusions are presented.

INFLUENCE OF REDUCED SEROTONIN ON AGGRESSION AND EMOTIONALITY

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CHAPTER 1

INTRODUCTION

Aggression is a fundamental element in numerous problematic social interactions such as abuse, homicide, and war. Consequently, the topic of aggression receives a great deal of attention in the popular media, the political arena, and the scientific fields of biology, sociology, and psychology. Researchers approach the issue from many angles to study the factors behind aggression and the process by which it develops and is maintained. As a result, many explanations exist as to why aggression occurs. Although several approaches consider the impact of environmental (Dollard, Doob, Miller, Mowrer, & Sears, 1939), biological (Wilson, 1975), and sociological factors (Walster, Walster, & Berscheid, 1978) in the development of aggression, empirical evidence suggests greater attention be given to physiological sources of aggression (Moyer, 1976c). Additionally, because aggressive behavior typically involves a heightened emotional response or reactivity to an external event, any explanation of the physiological causal factors of aggression should incorporate this factor.

The Serotonin-Aggression and Reactivity Relationship

Several chemical imbalances in the body are related to aggression and heightened reactivity. In addition to alcohol and testosterone, the neurotransmitter serotonin (5-HT) is linked to aggressive behavior. Low levels of 5-HT in the brains of human and nonhuman animals produce a variety of adverse effects. In humans, lower than normal amounts of 5-HT are related to behaviors involving elements of violence, increased emotionality, and aggression. Nonhuman animals with low 5-HT levels show inhibited

growth, heightened reactivity to stimuli, and increased attacking behavior towards other animals.

The integral component in the relationship between low 5-HT and increased aggression and reactivity is the amino acid tryptophan, which organisms normally receive through their diet. Because 5-HT is synthesized from tryptophan, levels of brain serotonin are exclusively dependent upon the amount of available tryptophan. In other words, reducing dietary tryptophan or the transfer of tryptophan into the brain suppresses 5-HT levels.

Purpose of Present Research

To test this low 5-HT-increased aggression and emotional reactivity relationship, the present investigations evaluated levels of aggression and reactivity following exposure to conditions of reduced tryptophan transfer and 5-HT synthesis in rats. Reductions in 5-HT synthesis were accomplished in two ways. First, dietary intake of tryptophan was significantly limited by implementing a diet consisting only of corn grits, a food containing minute amounts of tryptophan. In a second condition, the amount of tryptophan allowed to enter the brain was reduced. Animals received an aspartame-water mixture in addition to a standard diet. Aspartame, more commonly known as NutraSweet®, blocks the transfer of tryptophan into the brain thereby reducing brain tryptophan levels and 5-HT synthesis. Animals in these two experimental conditions were subsequently compared with control animals that received a normal dietary regimen of laboratory chow and water.

In Experiment 1, all three groups were evaluated on their levels of aggression with measures obtained from a shock-elicited aggression task. In contrast to control animals, Group Grits and Group Aspartame were expected to exhibit heightened aggression. In Experiment 2, the conditioned taste-aversion paradigm was employed to evaluate emotional reactivity based on differential responses to novel-tasting stimuli. Specifically, it was hypothesized tryptophan-challenged rats would show stronger aversions to a novel flavor than rats with no tryptophan deficiencies.

Literature Review

Research related to this issue is organized into four main categories: a) predominant views on aggression, b) the effects of low 5-HT in humans and nonhuman animals, c) issues surrounding aspartame, and d) the rationale behind the shock-elicited aggression and taste-aversion conditioning techniques.

Predominant views on aggression. Researchers in the fields of biology, sociology, and psychology have developed numerous theories to explain the factors involved in aggressive behavior. Biological views assert some types of aggression are inherited. For example, sociobiologist Edward O. Wilson (1975) views aggression as a response to situations threatening to one's survival. His theory posits aggressive behaviors arise when the ability to satisfy basic needs, such as food and shelter, is blocked by others. Innate aggressionists argue human's evolution was dependent upon the development of aggressiveness (Montagu, 1974). In On Aggression, Konrad Lorenz (1963) wrote:

> When man, by virtue of his weapons and other tools, of his clothing and fire, had more or less mastered the inimical forces of his extra-specific environment, a

> state of affairs must have prevailed in which the counter-pressures of the hostile neighboring hordes had become the chief selecting factor determining the next steps of human evolution. Small wonder indeed if it produced a dangerous excess of what had been termed the 'warrior virtues' of man. (p. 343)

Other views suggest the environment is largely responsible for the display of aggression. For instance, the frustration-aggression hypothesis proposes individuals act aggressively when frustrated or prohibited from achieving some goal (Dollard et al., 1939). Bandura (1965) demonstrated aggressive behavior is facilitated by observing the aggressive actions of others. In his study, children showed increased levels of aggression after watching an adult model hit and kick a large doll. How we are treated by others can also have a major impact on our level of aggression. For example, researchers contend situations of inequity, when we feel we are being treated unfairly, lead to aggression (Walster, Walster, & Berscheid, 1978). Furthermore, it is well documented that social isolation induces aggressive behavior in humans and animals (Carrere, Evans, & Stokols, 1991; Crawley, Schleidt, & Contrera, 1975; Weltman, Sackler, Schwartz, & Stroman, 1970).

Although environmental influences figure prominently, the importance of physiological sources of aggression cannot be ignored. Prior to the mid-1970s, most research implicated learning as the dominant factor in the formation of aggressive behavior. In 1976, of more than 90 books on aggression and violence, only four were devoted solely to physiological factors (Moyer, 1976c). However, in the past 25 years, the empirical focus has shifted to consider nature's role in aggression and emotional

reactivity. Moyer (1976a) argued there are distinct kinds of aggression and that each has a different physiological basis. He operationally defined the following seven different classes of aggression based on the stimuli that elicits each: predatory, inter-male, fear-induced, irritable, territorial defense, maternal, and instrumental. In his hypothesis, particular brain areas and chemical changes are related to each class. For example, stimulation of areas of the hypothalamus heighten irritable aggression (attacking behavior). If a calm cat is electrically stimulated on the lateral hypothalamus, it will ignore the experimenter and attack an available rat. However, if stimulated in the medial hypothalamus, the rat is ignored and the experimenter attacked (Moyer, 1976b). Humans also exhibit specific aggressive responses to differential brain stimulation. Verbally and physically assaultive behavior in one female patient could be turned off and on like a switch with electrical stimulation to the amygdala (Moyer, 1976b). Further evidence of a biological correlate stems from research suggesting a genetic component to the expression of aggression and reactivity. For example, Lagerspetz (1976) selectively bred mice for high and low levels of aggressiveness.

Evidence suggests chemical imbalances in the body are also related to aggressive behavior, lending further support for a physiological focus. For instance, laboratory studies demonstrated a strong relationship between alcohol consumption and aggression. Chermack and Taylor (1995) discovered violence is more likely to occur at higher blood-alcohol levels. Other studies indicate 54% of all murderers were drinking right before committing their crime (Davis & Palladino, 1997). Similarly, higher levels of the hormone testosterone are linked to heightened aggression. Dabbs and Morris (1990)

compared testosterone levels of nearly 4,500 military veterans with occurrences of aggressive behavior. Men with the highest levels were more likely to abuse alcohol and drugs and assault other individuals. Kreuz and Rose (1972) found higher plasma testosterone amounts in male prisoners with histories of violent or aggressive offenses during adolescence (e.g., murder, assault) than prisoners who committed less violent crimes (e.g., burglary, car theft.).

Low serotonin effects in human and nonhuman animals. In addition to imbalances in alcohol and testosterone, a number of recent studies suggest a third possible physiological source of aggression. Low levels of the neurotransmitter 5-HT in the brains of humans produce a variety of adverse effects. Lower than normal amounts of 5-HT appear related to the severity of obsessive-compulsive disorders (Hollander et al., 1992), violent and aggressive behavior (Edman, Åsberg, Levander, & Schalling, 1986; Mann, Arango, & Underwood, 1990), violent suicide attempts (Nielsen et al., 1994; Spoont, 1992), early-onset of alcoholism in men (Virkkunen et al., 1994), and depression (Woolley, 1962). For example, Spoont reported low 5-HT levels result in biases in information processing that may predispose individuals to conditions such as aggression and violent suicide attempts. She further commented that "in terms of human personality, the effects of low 5-HT (serotonin) activity on affective-limbic systems not only may result in a dissociation between behavioral inhibition and affective states but also may result in an increased propensity for affective instability (i.e., greater stress reactivity)" (p. 342). A majority of these studies evaluated blood and cerebrospinal fluid (CSF) levels of 5-Hydroxyindoleacetic acid (5-HIAA), the primary 5-HT metabolite, to measure the

amount of 5-HT turnover in the brain. For example, Virkkunen, Nuutila, Goodwin, and Linnoila (1987) found low CSF levels of 5-HIAA correlated positively with poor impulse control in criminal offenders, particularly male arsonists.

The critical component in an animal's 5-HT level is availability of tryptophan. This amino acid, which is hydroxylated in the body to yield 5-hydroxytryptophan, is the sole substrate for the synthesis of serotonin. Because animals cannot synthesize tryptophan, all necessary amounts of the amino acid must be derived from dietary protein (Lytle, Messing, Fisher, & Phebus, 1975). Consequently, other lines of research have focused specifically on the amount of tryptophan humans gather from their diet. If foods low in tryptophan are ingested in large quantities, thereby decreasing 5-HT levels, it follows that behavioral changes will result. For instance, Mawson and Jacobs (1978) discovered murder rates were highest in countries where corn is consumed in great quantities. Corn contains virtually no tryptophan. High corn diets also induce pellagra, a disease that irritates the skin and disrupts functioning in the digestive and nervous systems (Woolley, 1962).

Nonhuman animals also exhibit negative reactions to low amounts of serotonin. Valzelli and Bernasconi (1979) reported low serotonin in the brains of male mice, resulting from a period of social isolation, was related to increased aggression and attacking behavior towards other male mice. Similarly, rats fed a diet of corn grits, showed inhibited growth when compared to controls exposed to a normal diet (Becker, Davis, Grover, & Erickson, 1989), and increased neophilia or the preference for a novel food or flavor (Davis, Bailey, & Thompson, 1993).

Issues surrounding aspartame. The use of L-aspartyl-L-phenylalanine methyl ester (i.e., aspartame) as an artificial sweetener increased significantly following the Food and Drug Administration's (FDA) approval of the substance in 1981 as a dry substitute for sugar (Farber, 1990). Farber indicated more than 100 million Americans were consuming beverages and food products sweetened with NutraSweet®: aspartame's commercial name. Today, aspartame is the most popular artificial sweetener available. Although advertisements tout the substance as a harmless and efficient alternative to sugar (aspartame is nearly 200 times sweeter than natural sugar), there is little sound empirical evidence indicating the substance is safe. Farber reports that "studies conducted by G. D. Searle, the creator of Nutrasweet, and submitted to the FDA show that aspartame may induce brain tumors in rats. Later medical studies and reports to the Centers for Disease Control suggest aspartame may cause a host of side effects in humans ranging from headaches and seizures" (p. 46). Walton, Hudak, and Green-Waite (1993) studied whether individuals with mood disorders were more vulnerable to the adverse effects of aspartame. In their study, eight adult patients with depression and five nonpatient controls received aspartame (30mg/kg/day) or a placebo for 7 days. Despite the small sample size, there was a significant difference between the aspartame and placebo participants in number of symptoms for those with a history of depression. The authors concluded individuals with mood disorders appear more sensitive to aspartame and cautioned against its use in this population.

More relevant to the present study is aspartame's chemical influence on the brain and the brain's neurotransmitters. The primary components of aspartame, the amino

acids aspartic acid and phenylalanine (PHE), are among the building blocks of all protein. For example, when protein from a hamburger is metabolized, these two amino acids are just two among the 23 different amino acids involved. However, when aspartame alone is metabolized, unnaturally high concentration of aspartic acid and PHE are carried throughout the body to the brain. Transport molecules allow nutrients, including PHE and other amino acids, to pass through the blood-brain barrier. The difficulty is that aspartame consists of only two amino acids, not 23, which causes their levels in the blood to increase and the amounts of other amino acids to either drop or remain the same (Farber, 1990). Subsequently, PHE is transported in higher concentrations into the brain (aspartic acid does not enter the brain via transport molecules). Because at least two amino acids that are precursors to major neurotransmitters, including tryptophan, share the same transport molecules as PHE, heightened PHE levels may decrease synthesis of these neurotransmitters. As mentioned, tryptophan is the primary precursor to 5-HT synthesis. If increases in PHE concentrations act to block tryptophan transfer into the brain, subsequent 5-HT levels will decrease.

Rationale for the shock-elicited aggression and taste-aversion conditioning techniques. The shock-elicited aggression technique was utilized to measure aggression levels in all three conditions. In previous animal studies (Davis, Arb, & Huss, 1995; Davis, Cronin, Meriwether, Neideffer, & Travis-Neideffer, 1978; Davis et al., 1984; Tramill, Turner, Sisemore, & Davis, 1980), the procedure has successfully demonstrated differences in aggressive behavior. In this procedure, the test animal is placed in a

restraint tube and the number and duration of aggressive responses elicited by the application of a mild tail-shock recorded.

The conditioned taste-aversion paradigm was employed to evaluate differential responses to novel-tasting stimuli with the belief that formation of stronger aversions is indicative of higher degrees of emotional reactivity to stimuli. Earlier studies utilizing this method have demonstrated the pairing of a novel taste (e.g., saline) with a toxin (e.g., lithium chloride [LiCl]) results in the development of a strong and lasting aversion to the novel taste (Davis, Bailey, Mayleben, Freeman, & Page, 1990; Davis & Freeman, 1993; Kalat, 1974).

Summary

There is general agreement across studies of both human and nonhuman animals that low levels of serotonin are related to aggression and heightened emotionality or reactivity to stimuli. Tryptophan deficiencies, stemming either from tryptophan-poor diets or the blocking of tryptophan transfer into the brain, are directly related to serotonin synthesis. The present study sought to further elucidate this relationship. Two methods to reduce 5-HT turnover in the brains of rats were evaluated using the shock-elicited aggression and taste-aversion conditioning paradigms. A diet of corn grits was used to reduce animals' intake of tryptophan in one condition, and exposure to aspartame, which blocks brain transfer of tryptophan, was used in a second condition. It was anticipated that rats in these reduced tryptophan conditions would be more aggressive and show stronger taste aversions over rats exposed to adequate tryptophan amounts.

CHAPTER 2

METHOD

Experiment 1

The purpose of Experiment 1 was to evaluate shock-elicited aggression in animals with reduced levels of 5-HT stemming from either a tryptophan-deficient, corn grits diet, or a blocking of available tryptophan via aspartame ingestion. The shock-elicited aggression technique has proven successful in prior research (Davis et al., 1995; Davis et al., 1978; Tramill et al., 1980) in identifying an animal's level of aggression. In this procedure, the test animal is placed in a restraint tube and the number of and duration of aggressive responses elicited by the application of mild tail-shock are recorded.

Method

Test animals. Twenty-five naive, male rats purchased from the Holtzman company served as the test animals. The animals were 60 days old at the beginning of the experiment and 117 days old at the time of aggression testing. All animals were individually caged and maintained on a 12/12 light/dark lighting cycle for the duration of the experiment. Prior to experimentation, Purina Laboratory Chow and tap water were continuously available.

Apparatus. Testing took place in a shock-elicited aggression apparatus consisting of an opaque restraint tube (21.5 cm in length, 7.5 cm in diameter) with one open and one closed end, a shock source (Campden Instruments Ltd., Model 521C), a target rod (Lafayette Instruments, Model 80111, omnidirectional lever), an impulse counter (Lafayette Instruments, Model 5822), and a digital electronic timer (Lafayette

Instruments, Model 54030). An attack upon the target rod, which extended across the midportion of the open end of the restraint tube, activated the impulse counter and the timer, thus yielding an automated record of the number of responses and duration of aggression (in seconds) for each animal.

The animal's tail was extended through a 1.50-cm hole in the closed end of the restraint tube. When an animal was in place in the restraint tube, a wooden dowel rod was secured to the tail by means of adhesive tape, thus prohibiting escape during shock testing. Two copper wires, 7 cm apart and permanently attached to the dowel rod, served as electrodes for the administration of tail shock.

Procedure. Thirty days prior to aggression testing, three groups (Grits, Aspartame, and Control) of animals were randomly formed. Group Grits (n = 8) received free access to water and oven-dried cakes of Quaker Instant Grits.[1] The grits cakes were prepared by mixing 50 ml. of tap water with 226.8 g. of Quaker Instant Grits. This mixture was formed into small, circular shapes, 4-6 cm in diameter, placed on a cookie sheet, and baked at 325° F for approximately 2.5 hr, or until dry.

Concurrently, Group Aspartame (n = 8) received a fluid mixture consisting of .15% aspartame (Nutrasweet®) and water while continuing a diet of Purina Laboratory Chow. Group Control (n = 9) continued the normal regimen of water and Purina Laboratory Chow. Additionally, all animals were weighed every 3 days during the course of the experiment.

Aggression testing occurred on the same day for all animals and was administered in the following manner. Following a 5-min habituation period in the apparatus, each

animal received a 2-min period of tailshock administration during which 1.5 mA shocks 300 ms in duration were administered at 3-s intervals. Therefore, each animal received a total of 40 shocks. The number of aggressive responses and the duration of aggressive responding (in seconds) were recorded for each animal. The order for running animals was determined randomly.

Experiment 2

The conditioned taste-aversion paradigm was employed to evaluate differential responses to novel-tasting stimuli in Experiment 2. Previous studies utilizing this method have demonstrated the pairing of a novel taste (e.g., saline) with a toxin (e.g., LiCl) results in the development of a strong and lasting aversion to the novel taste (Davis et al., 1990; Davis & Freeman, 1993; Kalat, 1974).

Test Animals

The animals used in Experiment 1 served as the test animals in Experiment 2. The animals were 131 days old at the time of conditioning. All testing took place in the animal's home cage; a standard, suspended, wire-mesh cage (17.78 cm x 17.78 cm x 24.13 cm) housed in the animal vivarium. A 12/12 light/dark lighting cycle was in effect for the duration of the conditioning and testing phases. Specific diets for each group were identical to Experiment 1.

Procedure

The dietary regimens begun in Experiment 1 were continued and remained in force during Experiment 2. As in Experiment 1, all animals were weighed every 3 days during the course of the experiment. Eight days prior to conditioning, all groups were

placed on a fluid-deprivation regimen limiting access to 15-min daily. This regimen served the dual purpose of habituating the animals to the water-deprivation schedule and establishing a fluid-consumption baseline for each animal. Conditioning took place 24 hr following the end of the deprivation phase. Graduated, 50-ml centrifuge tubes fitted with spill-resistant stoppers were used to dispense fluids during conditioning and preference testing. Fluid consumption was recorded to the nearest .50-ml.

The conditioning process was conducted as follows. First, each animal was allowed to consume a saline solution (.15% w/v) for 15 min. Immediately following this consumption period, each animal received a .12% body weight intraperitoneal (ip) injection of .15M LiCl to induce toxicosis. The order for conditioning animals was determined randomly. The fluid-deprivation regimen (i.e., access to plain tap water for 15-min daily) remained in effect for the 6 days following conditioning.

Twenty-four hours following conditioning, taste aversion testing occurred. Following the same order in which conditioning was completed, a 15-min, two-bottle preference test (water vs. saline) was administered to all animals[2]. Consumption of both fluids was recorded to the nearest .10 gram.

CHAPTER 3

RESULTS

Experiment 1

To normalize the distribution of scores and allow comparisons with previous shock-elicited aggression studies (e.g., Davis et al., 1995; Davis et al., 1993), the response total for each animal was converted to a $\log_{10}(X_i + 1)$ score prior to analysis. Group mean responses are shown in Figure 1.

Analysis of Variance (ANOVA) of the response data yielded significance for the group factor, $F(2, 22) = 4.90$, $p < .05$. A test for effect size revealed the proportion of variance accounted for by the group effect (η^2) was .3. Subsequent Tukey's post hoc tests determined specific differences among the three groups and indicated Group Grits (M = 1.72, SD = .10) and Group Aspartame (M = 1.69, SD = .15) animals performed non-differentially but made significantly ($p < .05$) more aggressive responses than Group Control animals (M = 1.4, SD = .34).

Analysis of the duration of aggression scores also yielded a significant group effect, $F(2, 23) = 10.10$, $p < .01$. Mean duration scores (s) are presented in Figure 2. A test for effect size demonstrated the proportion of variance accounted for by the group effect (η^2) was .49. Subsequent Tukey's post hoc tests determined specific differences among the three group types and showed Group Grits (M = 57.14, SD = 14.07) and Group Aspartame (M = 63.26, SD = 14.98) animals performed non-differentially but made significantly ($p < .05$) longer aggressive responses than Group Control (M = 31.98, SD = 13.69) animals.

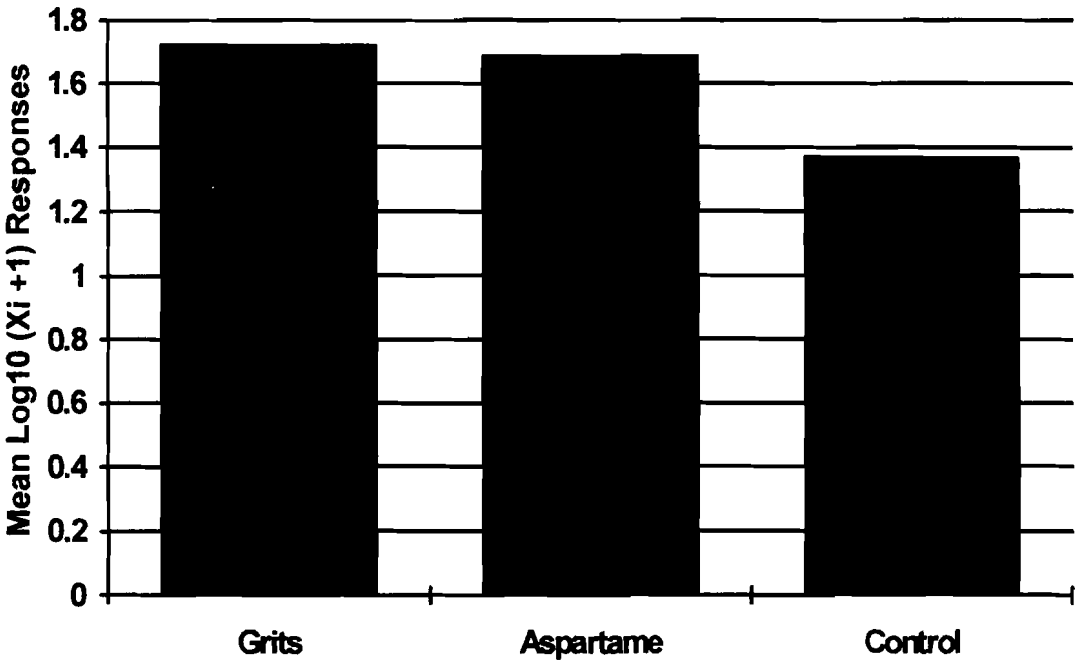

Figure 1. Group mean responses during aggression testing.

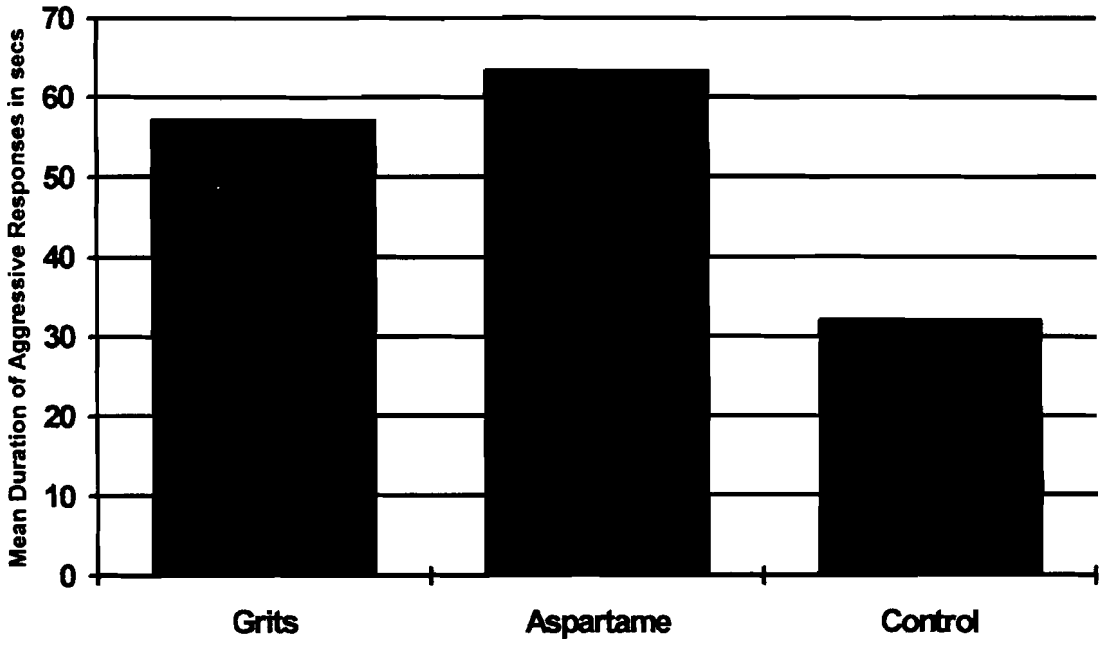

Figure 2. Group mean duration of responses during aggression testing.

Experiment 2

To ensure group comparability in initial fluid consumption, an ANOVA was conducted on intake levels during the conditioning phase. This analysis revealed no significant group differences, $F(2, 21) = 1.26$, $p = .3$. Group mean consumption ratios following taste-aversion conditioning are shown in Figure 3. These ratios were calculated by dividing grams consumed during the testing phase of each fluid by grams consumed at conditioning.

An ANOVA of the consumption ratios of the Grits, Aspartame, and Control animals during testing yielded significance for the group factor, $F(2, 18) = 20.68$, $p < .001$. As shown in Figure 3, Group Grits ($M = .06$, $SD = .02$) and Group Aspartame ($M = .06$, $SD = .03$) consumed less saline during testing than Group Control ($M = .19$, $SD = .06$). A test for effect size revealed the proportion of variance accounted for by the group effect (η^2) was .70. Subsequent Tukey's post hoc tests determined that Grits and Aspartame animals performed non-differentially but consumed significantly less ($p < .01$) saline than did controls.

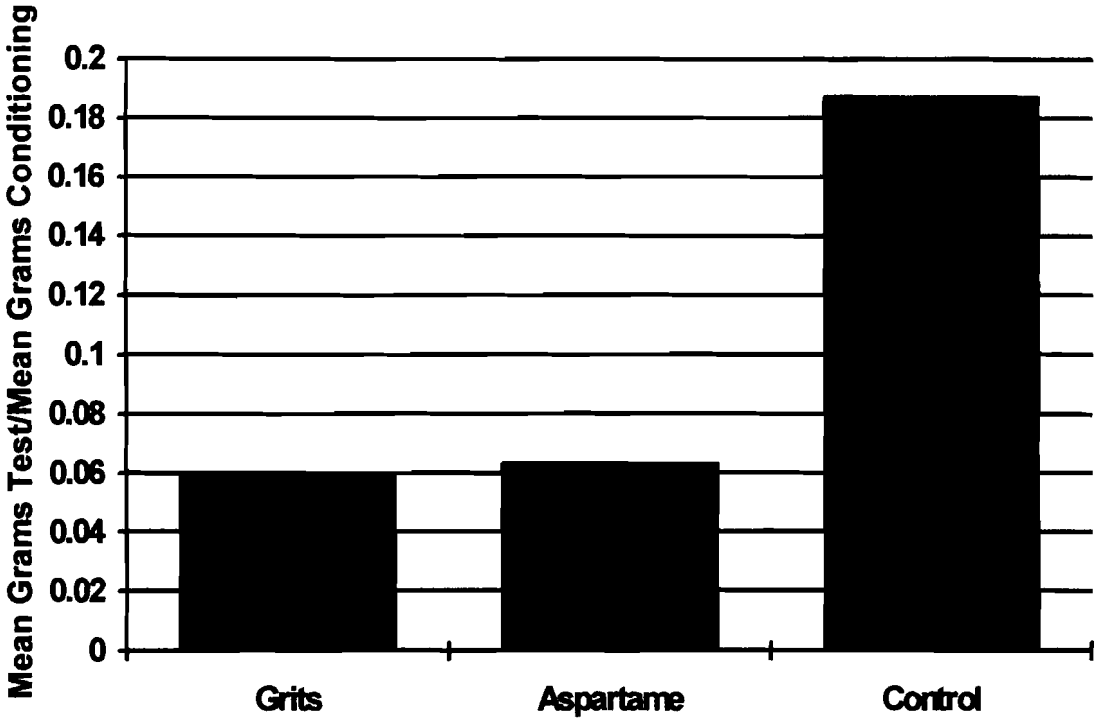

Figure 3. Group mean consumption ratios following taste-aversion conditioning.

CHAPTER 4

DISCUSSION

These two experiments demonstrate rats exposed to a tryptophan-deficient or tryptophan-blocking diet responded more aggressively and exhibited stronger taste aversions than rats exposed to a normal diet. The elevated shock-elicited aggression shown by rats fed only grits corroborates previous research reporting diets high in corn content, which decrease 5-HT synthesis (Lytle et al., 1975), are related to increased levels of aggression in humans and lower animals. These results also establish that animals exposed to aspartame, which prohibits the transfer of tryptophan into the brain, exhibit increased aggression levels. Additionally, predictions based on earlier investigations were supported in Experiment 2 with grits- and aspartame-exposed rats forming stronger aversions to the novel saline taste.

As anticipated, these data also strengthen the hypothesis that 5-HT levels play a major role in an organism's level of reactivity. Obsessive-compulsive disorders, violent and aggressive behavior, and aversions to novel stimuli, all apparently related to 5-HT amounts, involve the common element of a heightened emotional response. The functional nature of this relationship, however, is not clear from the present results. Conceivably, heightened reactivity will peak and begin to decline if brain 5-HT is continually decreased; therefore, expanded study is needed to clarify this functional relationship. To this end, at least three approaches to controlling the 5-HT content of the brain are open to manipulation: a) increasing or decreasing 5-HT production, b) changing the rate of 5-HT destruction, and c) changing the utilization of 5-HT by affecting the

receptors. Corresponding to the first approach, the tryptophan-deficient and tryptophan-blocking diets in the present study reduced the synthesis of 5-HT. However, several more explicit methods are feasible. One approach is to evaluate reactivity against a larger range of aspartame levels. For example, a design incorporating five aspartame-water mixture percentages separated by equal intervals (e.g., .05%, .15%, .25%, .35%, and .45%) would indicate the strength and type of relationship between aspartame (and accordingly 5-HT) and reactivity. Similar data could be obtained using a longer feeding regimen (e.g., 120 days instead of 60), or contrasting the present Groups Aspartame and Grits with a third condition in which rats receive both grits and aspartame. Moreover, dietary manipulations with a wider range of animals is necessary to elucidate the relationship and allow for comparisons with, and generalizations to, previous research. Species suggested include mice (Bronson & Eleftheriou, 1970), cats (Chi & Flynn, 1971), and various monkey and ape species (Hall, 1970; Michael & Zumpe, 1970). Comparing alternative measures of aggression and reactivity with the present measures would also address concerns about the generalizability of this study's results. For example, attacking behavior towards other animals is used as the primary dependent variable in numerous studies on animal aggression (e.g., Azrin, Hutchinson, & Hake, 1969; Flynn, 1974; Robinson, Alexander, & Bowne, 1969).

Related to the second approach of controlling 5-HT levels, one might engage in a series of investigations altering the rate of 5-HT destruction. For example, the administration of monoamine oxidase inhibitors (MAOIs) would demonstrate if increased 5-HT levels produce behavioral results opposite to findings of the present

study (i.e., reduced aggression and reactivity). MAOIs block the enzyme monoamine oxidase (MAO) which metabolizes 5-HT and the catecholomines epinephrine, norepinephrine, and dopamine (Kalat, 1995). Thus, MAOIs yield increased 5-HT and catecholomine levels and allow these neurotransmitters to remain in the synapse longer than usual, increasing their efficacy. However, the simultaneous rise in catecholomine amounts hinders precise evaluation of the behavioral effects of heightened 5-HT, and the connection with the 5-HT-reactivity relationship. A more prudent method to specifically increase 5-HT is the administration of tryptophan. As previously mentioned, tryptophan is transformed into 5-hydroxytryptophan, the sole substrate for 5-HT synthesis.

The third approach involves changing the utilization and function of 5-HT by affecting the receptors. A fruitful line of research lies in the use of antimetabolites, substances that chemically resemble related metabolites (e.g., 5-HT, norepinephrine, acetylcholine) and occupy the receptor site normally reserved for the metabolite. A specific deficiency of the metabolite thus occurs and excludes it from its normal function. As such, administration of anitmetabolites would add credence to the 5-HT-reactivity hypothesis if shown to heighten aggressive behaviors and/or emotional reactions. Early work supports such a possibility. For example, the first evidence for the participation of 5-HT in mental processes was found through the use of antimetabolites (Woolley, 1962). Related studies indicated one antimetabolite of 5-HT, nitroindole, caused profound mental depression in humans. Another, medmain, produced convulsive fits in rats (Woolley). It is also likely several substances in addition to aspartame work to

block tryptophan, thereby decreasing 5-HT production and increasing emotional and aggressive behavior. Identification of such chemicals demands empirical attention.

Although the present results support the proposition that low 5-HT is related to heightened aggression and emotion, they do not indicate why this relationship occurs. Even the suggested empirical extensions would not explain the chemical and/or structural changes that accompany the relationship. However, several speculations are plausible. First, brain structures responsible for overall nervous system function and the relay of sensory information throughout the cerebral cortex contain significant concentrations of 5-HT. Most of the total concentration of 5-HT in the central nervous system is in the brain stem which includes the medulla, pons, and thalamus (Woolley, 1962). Thus, one possible explanation is that in the absence of a stable and high influx of 5-HT, nervous system functions controlled by these structures are diminished. For instance, the medulla and the pons contain the reticular formation and the raphe system; two systems that regulate the overall state of the nervous system. Decreased 5-HT levels may significantly alter these system's functioning and promote a heightened nervous system response to stimuli. In a similar fashion, the thalamus' processing and distribution of sensory information may be altered by inadequate 5-HT levels. Under normal circumstances, sensations from the environment are sent to distinct areas in the cortex for further processing and the formation of appropriate behavioral responses. Decreased 5-HT in the thalamus may cause crucial information to be lost or sent in unmanageable amounts. This latter possibility would explain the increased excitation inherent in heightened reactivity.

Moreover, the thalamus is an integral part of the limbic system: a collection of sub-cortical structures linked to emotional behavior including aggression and anxiety. This connection suggests a second possible explanation for the 5-HT--reactivity relationship involves this system. A particular structure of interest is the hypothalamus as it is related to, among other things, activity levels and aggression (Kalat, 1995). Electrical stimulation of this area elicits attacking behavior in cats (Chi & Flynn, 1971; Levison & Flynn, 1965; Roberts & Kiess, 1976) and a state of dyscontrol and "drunk-like" behavior in humans (Ervin & Mark, 1976). Like the thalamus, the hypothalamus typically contains an appreciable amount of 5-HT (Woolley, 1962). Consequently, a drop in 5-HT levels may diminish this structure's functioning and induce a hypersensitive state of aggressive or anxious reactions.

Presumably, the intricate nature of the limbic system and the brain stem allow for a multitude of possible sources for the 5-HT--reactivity relationship. However, in spite of a solid understanding of the underlying processes, the present results justify several conclusions. Perhaps most readily applicable is the negative role aspartame plays in the relationship. Numerous diet beverages and foods contain significant amounts of aspartame, typically advertised as Nutrasweet®. Additionally, many individuals sweeten their coffee or tea with granular forms of aspartame, such as the popular brand Equal. Although the FDA studied and approved aspartame as an artificial sweetener, research indicates brain tumors in rats and headaches and seizures in humans are related to aspartame (Farber, 1990). Moreover, the literature contains virtually no indication that aspartame's tryptophan-blocking properties were fully examined prior to FDA approval.

Future research is needed to specifically determine how much aspartame is detrimental to humans and whether one's level of aggression and emotional reactivity correlate with their aspartame use. The .15% aspartame-water mixture used in the present study may not parallel actual human aspartame intake levels. Surveying human aspartame use and then imposing similar body weight percentages in an animal population would provide more applicable information on this substance's effect on human aggression. However, because the metabolism process for aspartame in rats may differ significantly from humans, results would be tenuous at best.

In a broader context, the present results indicate investigation of the physiological bases of aggression demand more attention. However, because environmental conditions are relevant and influential, any comprehensive study of aggression and emotional reactivity must address facets of both nature and nurture. Unfortunately, the complexity of the interrelationship between the biological correlates of aggression, and social, cultural, and environmental factors, hinders understanding the phenomenon fully. Nevertheless, science's appreciation of the relationship is a significant first step.

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Footnotes

[1]One of the animals in Group Grits died during the grits-exposure phase. Therefore, this group was comprised of only 7 animals at the time of aggression testing.

[2]A second Group Grits animal died prior to taste-aversion conditioning. Therefore, only 6 animals remained for the duration of Experiment 2.

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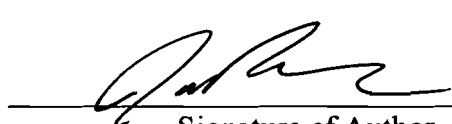

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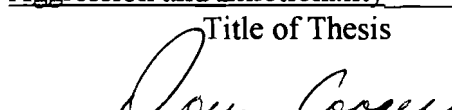

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