Nutritional Influences on Aggressive Behavior

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Introduction

The aggressive behavioral syndrome is marked by restlessness, irritability, impulsivity and a proneness to violence. Diagnostically, it overlaps the DSM III-R diagnoses of Attention-deficit Hyperactivity Disorder, Conduct Disorder, Oppositional Defiant Disorder and Antisocial Personality Disorder. When the syndrome is attributed to organic factors, it would frequently be classified as an Organic Personality Syndrome.[1]

Constitutional factors, including genetics and the effects of disease and physical trauma, are known to play a major role in determining proneness to overaggressive behaviors. The importance of psychological factors is also well known. By contrast, the contribution of nutritional factors to such behaviors is often unrecognized, and therefore not properly addressed.

Nutritional factors are neglected for a number of reasons. Much of the literature on nutritional treatments has yet to evolve beyond the early stages of scientific investigation. Physicians learn so little about nutritional medicine during their training that they feel too uninformed to include it in their practices. Sub-optimal nutrition is generally believed to be rare in industrialized societies — even though up to 50% of the population may fail to ingest the Recommended Dietary Allowance for one or more vitamins or minerals.[2]

In regard to behavioral syndromes, nutritional factors are neglected, in part, because marginal nutritional deficiencies are not believed to affect behavior despite growing evidence to suggest that that belief may be false. (For example, subtle neuropsychological impairment has been documented by EEG recordings of older subjects in association with any of a number of marginal nutritional deficiencies.[3])

Literature Review

1. Vitamins

Deficiencies of several vitamins are known to be associated with irritability. These include niacin,[4] pantothenic acid,[5] thiamine,[6] vitamin B_6[7] and vitamin C.[8] In industrialized societies, the classic vitamin deficiency diseases are rare, although marginal vitamin nutriture due either to inadequate intake or to vitamin dependency appears to be fairly common. Moreover, under laboratory conditions, adverse behavioral changes precede specific clinical findings in a number of vitamin deficiencies.[9]

It is not known how frequently overaggressive behaviors are a manifestation of marginal vitamin nutriture. While little has been published to prove a relationship between the aggressive behavioral syndrome in humans and marginal vitamin nutriture, Lonsdale and Shamberger, writing in *The American Journal of Clinical Nutrition,* reported on twenty people eating "junk food" diets who were found to have biochemical evidence of marginal thiamine deficiency. Their subjects, and particularly the adolescents, were impulsive, highly irritable, aggressive and sensitive to criticism.

Following thiamine supplementation, their behavior improved concurrent with laboratory evidence of improved thiamine nutriture, suggesting that marginal thiamine deficiency may have contributed to their aggressive behavioral syndrome.[6] Hopefully, well-controlled studies will eventually provide a clearer picture of the importance of marginal vitamin deficiencies in promoting overaggressive behaviors.

2. Minerals

Note: for the sake of completeness, minerals which do not function as nutrients are included in this review.

Iron

The most common nutritional deficiency in industrialized societies, 10% of American

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males and 3% of American females are overtly iron-deficient (ferritin less than 10 mg/mL.[10] A deficiency of iron is known to interfere with proper brain function. Dopamine is a major neurotransmitter in the brain, iron is highly concentrated in the dopamine pathways, and animal studies have shown that iron deficiency may cause learning deficits and consequent behavioral impairment by diminishing dopamine neurotransmission.[11] Iron is also needed as a co-factor for the enzymes which metabolize not only dopamine, but also serotonin and norepinephrine, which also have a potent influence on behavior.

Evidence is now emerging that iron deficiency may be an important contributor to the aggressive behavioral syndrome. Among adolescent males, iron deficiency has been shown to be directly associated with aggressive behavior (Conduct Disorder).[12] Moreover, in a population of incarcerated adolescents, the prevalence of iron deficiency was nearly twice that found in their non-incarcerated peers.[13]

Lithium

There is considerable evidence that pharmacologic doses of lithium, which has no known essential function, can reduce abnormal aggressive behaviors including self-mutilation.[14] Lithium has been used successfully with treatment-resistant hospitalized children with diagnoses of Conduct Disorder, Aggressive Type,[15] as well as with brain-injured[16] and mentally retarded[17] patients with aggressive, combative or self-destructive behavior.

While often effective, lithium at pharmacologic doses (generally 900,000 micrograms or more daily) has serious limitations. It suffers from many potential side effects, some of which are common. Because it becomes toxic at a serum level which is not much higher than the therapeutic range, serum lithium levels must be tested periodically. For these reasons, patients must be under medical supervision so long as they are taking the drug.

It is possible that lithium may exert a powerful effect on overaggressive behaviors at far lower levels of intake. Using data from 27 Texas counties, Schrauzer and Shrestha found that the incidences of suicide, homicide and rape were significantly higher in counties whose drinking water supplies contained little or no lithium than in counties with higher water lithium levels, even after correcting for population density. Corresponding associations with the incidences of robbery, burglary and theft were also significant, as were associations with the incidences of arrests for possession of opium, cocaine and their derivatives. Only the incidences of arrests for possession of marijuana, driving under the influence of alcohol, and drunkenness failed to correlate with the water lithium level.[18]

While the effect of low-dose lithium supplementation on overaggressive behaviors has not been reported, results of an uncontrolled study suggest that low-dose lithium derived from vegetable concentrates may have a powerful effect on mental state and behavior. Thirteen depressed patients with bipolar disorder were treated with natural lithium derived from vegetable concentrates. All improved in about ten days and there were no adverse effects. After six weeks, they were taken off of lithium and all regressed to their former depressed state within three days. Two days after lithium was resupplied, their depressions lifted again.[19]

If we assume that a person consumes about one liter of water daily from municipal supplies, it is striking that the level of lithium provided from the vegetable concentrates approximates that consumed by residents of the Texas counties with higher lithium levels: "Natural" lithium dosage - 150 micrograms daily; Lithium level of drinking water in the Texas counties with higher levels[18] - 70-170 micrograms per liter.

Magnesium

Rodent studies suggest that magnesium has a complex relationship with aggressive behaviors. Magnesium deficiency reduces offensive aggressive behavior but increases defensive aggressive behavior.[20] Lower levels of magnesium supplementation increase the number of attacks on intruders while higher levels have the opposite effect.[21]

In humans, magnesium deficiency, which enhances catecholamine secretion and sensitivity to stress, may promote aggressive behavior. Increased catecholamines, in turn, induce intracellular magnesium losses and, eventually, increased urinary losses of magnesium.[22] It has been suggested that the Type A behavior pattern — which is associated with chronic stress and aggressive behavior — may both cause and be caused by magnesium deficiency.[22] Also, suicide attempts, which are violently aggressive acts against the self, have been correlated with lowered magnesium levels in the cerebrospinal fluid.[23]

Manganese

Manganese is an essential trace mineral. Massive overexposure produces "manganese madness" which may initially be marked by violence, criminal acts and a state of mental excitement; later, neurological impairment slowly develops, with signs and symptoms which resemble Parkinson's disease.

The behavioral effects of marginal levels of manganese toxicity have not been described. Recently, Gottschalk and his associates consistently found elevated hair manganese in a population of violent male offenders, suggesting that marginal manganese toxicity may be associated with violent criminal behavior. Compared to the hair manganese levels which they found, people exposed to levels of manganese pollution which are known to be toxic possess hair values that are two to six times higher.[24]

Elevated hair manganese levels have also been reported in hyperkinetic children,[25, 26] and men with a history of childhood hyperactivity have an increased rate of antisocial and drug use disorders.[27] In rats, chronic manganese exposure initially produces hyperactivity with an increased tendency to fight.[28] While any hypothesis concerning the behavioral effects of marginal manganese toxicity in humans is highly speculative, these findings suggest that marginal manganese toxicity may promote overaggressive behaviors in adults.

Heavy Metals

Brain damage due to toxic metal exposure may promote aggressive, antisocial and violent behaviors. Lead exposure is known to cause learning and behavioral problems, problems which are found in a substantial portion of juvenile delinquents.

The strongest evidence to date that lead exposure increases the frequency of aggressive behaviors comes from the Edinburgh Lead Study which included over 500 children between the ages of 6 and 9. After taking 30 possible confounding variables into account, the investigators still found a significant relationship between the log of blood lead levels and teachers' ratings of the childrens' behavior on an "aggressive/antisocial" scale and on a "hyperactive" scale, but not on a "neurotic" scale. As in other studies on the relationship between lead exposure and brain damage, a dose-response relationship was found between blood lead and behavior ratings, with no evidence of a threshold.[29]

Pihl and associates have addressed the relationship of lead exposure and violent behavior in adults. Hair lead levels from 19 violent criminals were found to be elevated as compared with those of 10 nonviolent criminals.[30] This study was repeated 8 years later by the same research team with essentially the same results. However, their results were contradicted by those of the recent Gottschalk study on hair manganese levels; in that study, no significant differences were found between hair lead levels of 104 violent criminals, prison guards and local townspeople.[24]

As with lead, studies comparing hair cadmium levels of violent male offenders to matched controls have had conflicting results. One study published in the *Journal of Learning Disabilities* looked at hair cadmium levels of 40 apparently normal young men entering US Navy recruit training and found a highly significant relationship between hair cadmium levels and the number of demerits each recruit had received. Moreover, the three recruits who had the highest cadmium levels all displayed serious behavior difficulties during training.[31]

Exposure to aluminum may also contribute to overaggressive behaviors. Hair aluminum levels of a group of 22 juvenile offenders,[32] as well as of another group of 10 severely delinquent, psychotic or prepsychotic adolescent boys,[33] were elevated. However, both studies compared aluminum levels to laboratory norms rather than to matched controls; thus other differences between the groups could account for the findings.

3. Amino Acids

Tryptophan

Serotonin, a major neurotransmitter, has been found to play an important role in modulating aggressive behavior. Impulsive, violent and suicidal behaviors have repeatedly been shown to be associated with a reduction in serotonergic activity in the central nervous system.[34]

Tryptophan, an essential amino acid, is the dietary precursor to serotonin, and several lines of evidence have suggested that the amount of tryptophan in the diet relates closely to aggressive behavior. For example, rats given a diet almost lacking in tryptophan develop aggressive behavior towards mice.[35]

Tryptophan must compete with other large neutral amino acids to cross the blood-brain barrier; therefore the ratio of the amount of tryptophan to the amount of competing amino acids (the tryptophan ratio) may provide a rough indication of the availability of tryptophan in the brain for conversion into serotonin. Kitahara has calculated the dietary tryptophan ratio for 18 European countries to attempt to relate it to homicide rates. While initially no correlation was found between low tryptophan ratios and homicide, once social and cultural differences were controlled for, low tryptophan ratios were found to be associated with high homicide rates.[36]

A more direct method of examining the relationship between the tryptophan ratio and aggression is by measuring the actual ratio in the blood plasma. When a group of depressed alcoholics was evaluated in this manner, those with a history of aggression, including suicide attempts, also had the lowest tryptophan ratios.[37]

If a low ratio of tryptophan to competing amino acids is associated with aggressive behavior, will tryptophan supplementation reduce that behavior? Dietary tryptophan was manipulated in social groups of vervet monkeys by providing them with amino acid mixtures that were tryptophan-free, nutritionally balanced, or excessively high in tryptophan. These mixtures were shown to have a marked effect on plasma tryptophan levels. During spontaneous activity, the only effect of the different mixtures was increased aggression in the males on the tryptophan-free mixture. During competition for food, however, while the tryptophan-free mixture continued to increase male aggression, the high-tryptophan mixture reduced aggression in both males and females.[38] These data suggest that tryptophan supplementation may be most effective in reducing aggression during times of stress.

When hospitalized male schizophrenics were given tryptophan, only those patients with high levels of hostility and a high lifetime frequency of aggressive incidents benefited; these patients showed a lessening of hostility and depression, a reduction in ward incidents and improvement on a standardized psychiatric rating scale.[39] In another study of twenty aggressive patients, 6 g of tryptophan daily for one month failed to reduce the number of violent incidents, although it significantly reduced the need for potent medications to control violent or agitated behavior.[40]

The rate of firing of serotonergic neurons in the brain increases as the level of behavioral arousal increases; thus increased serotonin levels would be more likely to influence brain function at higher levels of arousal. Indeed, this fact probably explains why the vervet monkeys only responded to tryptophan supplementation when they were put under competitive stress. It also may explain why altered tryptophan levels failed to affect aggression in a study of normal human males, while overaroused, hostile and aggressive psychiatric patients responded well.

In the conversion of tryptophan to serotonin, the intermediate step is its conversion to 5-hydroxytryptophan. Surprisingly, supplementation with 5-hydroxytryptophan may *increase* aggressive behavior, apparently because, while tryptophan appears to enhance the serotonergic system exclusively, 5-hydroxytryptophan also appears to enhance the catecholaminergic system.[41]

4. Reactive Hypoglycemia

There is early evidence that hypoglycemia during glucose tolerance testing is related to hostile, aggressive behavior such as that seen in habitually violent and impulsive criminals.[34] Virkkunin, for example, found that a group of habitually violent adult criminals had lower basal glucose levels during glucose tolerance testing than controls.[42] Even in the normal population, there is evidence of a relationship between hypoglycemic tendencies and both frustration and hostility.[43]

Assuming that there is an association between hypoglycemia and the aggressive behavioral syndrome, the question of whether hypoglycemia causes the syndrome remains. One method of investigating the issue of causality is by changing the amount of sugar in the diet and examining the behavioral effects. Since dietary sugar provokes insulin production which may cause a reactive hypoglycemia, a change in behavior following a change in sugar intake would be consistent with the hypothesis that dietary sugar influences that behavior.

In a series of increasingly sophisticated double-blind studies, Schoenthaler addressed this question by reducing the sugar intake of thousands of incarcerated juvenile offenders in different locations around the United States. Compared to offenders on a placebo diet, he found a significant reduction in various forms of antisocial behavior (such as assaultiveness, fighting, self-injury and suicide attempts) in offenders restricted to a minimal amount of sugar in their diet — but only for the males.[44]

While Schoenthaler's work suggests that dietary sugar may influence behavior, he did not examine blood sugar levels; it thus fails to address the role of reactive hypoglycemia in the aggressive behavioral syndrome. The finding that only males responded may either be because males are more likely to engage in aggressive behaviors, or because males are more sensitive to nutritional influences on aggression. (Remember that the lack of tryptophan in the diet only increased aggression during spontaneous play in the male monkeys.) Further studies are needed to address these important questions.

5. Food Sensitivities

It appears that overaggressive behaviors can be provoked by a reaction to common foods. Reactions range from irritability to a psychotic aggressive reaction. Children who improved after food eliminations had previously been irritable, fretful, quarrelsome and could not get along with others. Often they had to be taken out of school as they upset the classes and were considered incorrigible. After food eliminations, however, their personalities dramatically changed, and they became happy and social.[45]

A study reported in the *Lancet* suggests that food sensitivities may be quite common among behaviorally-disturbed children. Eighty-one out of a group of 140 children with behavior disorders (almost two-thirds) experienced significant improvement following the elimination of certain foods along with food additives. When they were challenged with the specific foods which had been eliminated, their behavior problems returned. Moreover, 75% of these children reacted to a double-blind challenge with salicylates but not to placebo.[46] The following case study, reported in *Psychology Today,* illustrates how food sensitivities may affect aggressive behavior:

When he was five years and one month old, G.L. was seen because of uncontrollable temper tantrums. He was believed aphasic because of poor speech development, and was too uncomfortable to do initial IQ testing. The EEG showed 14-per-second spikes, large amounts of sharp activity in the motor leads, temporal single, polyphasic sharp waves, and a long run of sharp waves in the right temporal area. Allergy tests revealed strong reactions to milk, chocolate and yeast.

He was placed on a diet free of milk, chocolate, and cola drinks. Seven and one half months later, his EEG was normal. Six months after the repeat EEG, he was learning better and his behavior was much improved. He was challenged again with the suspected foods for one week, during which time his behavior again became uncontrollable.

The EEG now showed two-and-one-half to six-per-second activity on the right, greater in the mid-temporal and parietal leads, accentuated by drowsiness. Light cerebral dysfunction was diagnosed.[47]

Adults may also display overaggressive behaviors due to food sensitivities. For example, MacKarness has written of a woman who had been hospitalized thirteen times for violent behavior and depression; after common foods were eliminated from her diet, she no longer became violent or depressed. Instead she felt fine and obtained a regular job.[48]

While the research literature suggests that any commonly ingested food or food additive may be responsible for provoking pathological psychological and behavioral reactions, milk may be a special case. Schauss and Simonsen found that chronic juvenile delinquents consumed much more milk than matched controls without a history of delinquency. The male offenders consumed an average of a gallon of milk daily compared to a little less than a quart a day for the controls, and the females showed similar differences.[49]

Schauss believes that overconsumption of milk causes antisocial behavior. He has reported that, when several Michigan detention centers reduced their inmates' milk consumption, the incidence of antisocial behavior declined; when they permitted milk consumption to increase again, antisocial behavior also increased.[50]

Discussion and Summary

The literature offers numerous clues, but little scientific verification, consistent with the hypothesis that the aggressive behavioral syndrome can be prevented and treated by manipulating nutritional factors. Epidemiological studies have repeatedly found associations between overaggressive behaviors and deficiencies of several essential nutrients: niacin, pantothenic acid, thiamine, vitamin B_6, vitamin C, iron, magnesium and tryptophan. While repletion of frank deficiencies is likely to be beneficial, the benefit of correcting marginal deficiencies remains to be proven.

Not an essential nutrient, lithium has been proven effective in reducing overaggressive behaviors when provided at massive pharmacologic dosages. Moreover, even the relatively tiny daily lithium intake from municipal water supplies has been found to be negatively correlated with measures of the aggressive behavioral syndrome. In an open trial, supplementation with such natural levels of lithium appeared to be effective in treating bipolar depression. These findings suggest that natural lithium supplementation may be effective in the management of the aggressive behavioral syndrome, a hypothesis which remains to be explored experimentally.

There is some evidence that overaggressive behaviors may be promoted by the toxic effects of aluminum, cadmium and lead. Exposures to these elements (especially cadmium and lead) should be avoided; it is unknown whether treatments designed to chelate these metals in order to remove them from the brain are effective in reducing overaggressive behaviors.

Reactive hypoglycemia may be more common among people displaying the aggressive behavioral syndrome and, in an open study, reducing sugar consumption was followed by a reduction in antisocial behavior. Whether treating documented reactive hypoglycemia reduces overaggressive behaviors remains unknown.

Finally, sensitivities to foods and food additives appear capable of inducing overaggressive behaviors. Most of the evidence remains anecdotal; however, salicylates have been shown to provoke behavioral disturbances under double-blind conditions.

Despite the relative paucity of scientific evidence from controlled studies, clues from case reports, open trials, observational (correlational) studies and animal studies suggest that attention to nutritional factors may reduce overaggressive behaviors and the devastation resulting from them. Those clues, plus the safety of most nutritional interventions, argue that a nutritional approach should be considered in the treatment of the aggressive behavioral syndrome.

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