Evidence for a Biological Basis of Infantile Autism

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Early infantile autism is a severe and little-understood childhood behavior disorder which is characterized primarily by extreme self-isolation and an anxiously obsessive desire for the preservation of sameness. Since 1943, when it was first described by Kanner, a large body of literature on autism has accumulated, and the distinctive features of the syndrome have been well defined by a number of researchers (Chambers, 1969; Rimland, 1964; Wing, 1966) but, as yet, its cause remains unknown.

Although there is general agreement as to the symptoms associated with autism, there is considerable controversy regarding the nature of the basic defect and the important etiological factors. Kanner (1943) originally suggested that the condition was primarily an inborn disturbance of affective contact. However, most investigators have taken exception to this position since they have found it difficult to see how the observed abnormalities of vision, hearing, and speech could be derived from a symptom such as social withdrawal, especially when the disturbance often begins in the first few months of life before social attachments are formed. Some have argued that autism is due to an abnormality of physiological arousal, but whether the autistic condition involves "un-der-arousal" (Rimland, 1964; Schopler, 1965) or "over-arousal" (Hutt, Hutt, Lee, and Oun-sted, 1965) is a matter of dispute. Others have emphasized cognitive and perceptual abnormalities, the defect in the integration of sensory stimuli, and the language or coding problem (Ornitz and Ritvo, 1968; Rutter, 1968). The fact remains, however, that there is no specific biological hypothesis to explain the basic pathologic mechanisms underlying the deficits.

It is the purpose of this paper to suggest that the capacity to respond to social stimulation may be largely a function of the responsiveness and excitability of the nervous system, and that factors which increase the level of excitability without enhancing the level of aggressiveness may lead to the development of early infantile autism in a genetically vulnerable child. The possible role of hyper-vitaminosis A in precipitating pathological development is pointed out.

Adrenal Cortical Activity and the Autistic Syndrome

Kanner was the first to point out that the parents of true cases of autism were likely to be above average in intelligence, educational attainment, and occupational level (Kanner and Eisenberg, 1955). This observation has been confirmed by a number of researchers in the ensuing years (Lotter, 1967; Treffert, 1970), but they have scarcely mentioned that, among the highly intelligent, one finds two contrasting personalities (Gillispie, 1968; Hudson, 1966). In general, individuals with

interests in the more abstract areas of knowledge tend to be unemotional and guarded in their feelings; whereas those inclined to move towards the more human aspects of culture tend to be emotionally open and spontaneous. Kanner laid great stress on the fact that the parents of autistic children seemed to be "inhibited," "introverted," "objective," and "unemotional," although he concluded that autism might be partly a psychogenic disorder because of this emotional frigidity. However, when one stops looking for faulty parents and looks instead for faulty genes, then one finds that the personality traits of the parents explain far more about the possible origins of autism than is presently realized.

Within the last decade a series of studies has demonstrated that pituitary-adrenal cortical activity is a sensitive indicator of the individual's response to a wide variety of stimuli, and that the degree of arousal or threat experienced is highly correlated with personality structure. The more one reacts emotionally, the higher the level of 17-hydroxycorticosteroids (17-OHCS), and the more that control is exercised over feelings, the lower the level of 17-OHCS (Fox, Murawski, Bartholomay, and Gifford, 1961). Individuals that are unemotional and guarded in their feelings, and whose characteristic personality traits are like those of the parents, have consistently been found to have low rather than high 17-OHCS levels (Rahe and Arthur, 1968). Since these neuroendocrine patterns most likely represent genetic or constitutional factors (Fox, Gifford, Valenstein, and Murawski, 1965), it is conceivable that autistic children may have a similar pattern. Moreover, because males ordinarily have higher 17-OHCS levels than females (Rahe and Arthur, 1968), the complex feedback system which involves the interaction of the endocrine and the nervous system might be more readily disturbed in the male infant than in the female infant if the levels were unusually low.

Henkin's study (1970) of the relationships between adrenal cortical hormone activity and perception points up the crucial role played by carbohydrate-active steroids in the manner by which sensation and perception take place. Carbohydrate-active steroids, now known to cross the blood brain barrier and enter the tissues of the central and peripheral nervous system, normally act as a negative feedback system which inhibits incoming stimuli to allow maximal neural integration of the sensory information which does reach the central nervous system. The absence of these adrenal cortical steroids leads to an increase in neural excitability which, in effect, lowers the threshold for each major sensory modality. Therefore, sensory signals normally rejected or inhibited produce a neural response. With the loss of normal inhibition, there is a significant impairment in sensory perception or integration ability which, in turn, leads to a functional information loss. Coincident with the reciprocal changes in sensory detection and perception found when insufficient amounts of carbohydrate-active steroids are present in neural tissue, there is ". . . an alteration in the manner by which neural impulses are conducted along axons and across synapses . . . This results in a marked change in the timing by which neural stimuli from the periphery reach the higher integrative centers of the nervous system (p. 103)." It is believed this may be the mechanism for the loss of perceptual ability.

The above evidence suggests that many of the manifestations of autism which are explicable in terms of cognitive and perceptual defects could arise from a deficiency of carbohydrate-active steroids; even the language deficit could be largely due to a deficiency of these same hormones. Henkin observed that untreated adrenal cortical insufficiency leads to a significant impairment in the ability to recognize or integrate auditory information in spite of the fact that signals normally considered "subthreshold" can be detected. This impairment involves a decrease in the dynamic range of auditory responsiveness, and losses of ability to understand speech, localize tonal stimuli, and judge bilateral

equal loudness.

Although a high degree of association exists between the speech and the behavior patterns in true cases of early infantile autism (Rimland, 1971), the speech symptoms are not unique to children who are classically autistic. Several researchers have called attention to the often striking similarities in the abnormalities of speech of children with developmental aphasia and children with autism (Wing, 1966). Moreover, a substantial number of upper-middle-class parents and a high male-female ratio have been reported for both groups of children (Wing, O'Connor, and Lotter, 1967). Whittam, Simon, and Mit-tler (1966) found that 12 percent of the normal siblings of the 43 psychotic children they studied showed some delay in language development. This seemed to point to a possible familial link between speech disorders in psychotic children and speech delay in otherwise normal children. Perhaps of interest in this regard is the unusually high number of children in the group that had been affected by pyloric stenosis. There are observations in the literature which indirectly suggest that a relationship may exist between pyloric stenosis and hypofunction of the adrenals during early life (Barbour, 1936; Jaudon, 1948).

While a growing number of studies have described altered behavioral states with changes in adrenal cortical activity, systematic investigations of the autistic syndrome have not been undertaken. However, in view of the multiplicity and the kinds of effects produced by a deficiency of car-bohydrate-active steroids, it is quite evident that a deficiency, especially if present from birth, could serve to explain a great deal of the symptomatology of autism. The fact that plasma concentrations of corticosterone have been found to be low in excessively submissive mice that no longer interacted with other members of the group (Pearson, 1964) tends to support this conclusion. Nevertheless, there may be a disturbance in steroid metabolism over and above that of a simple deficiency of glucocorticoids. We suggest as a working hypothesis the possibility that the diversity of symptoms manifested by autistic children may be due to a disproportion between androgens and glucocorticoids.

Fleminger (1955) reported that cortisone produced a measurable increase in the amount of speech and social behavior of a patient who at the outset had a high 17-ketosteroid (17-KS) output and flat glucose tolerance curve. (No 17-OHCS estimate was made). This patient exhibited, but to a lesser degree, the two outstanding symptoms which must be clearly evident for a diagnosis of infantile autism, i.e. extreme self-isolation and an obsessive desire for the preservation of sameness. From early childhood she had preferred solitude and had been taciturn and undemonstrative. She was unusual, too, in being exceptionally clean and orderly, and in being quickly angered if her belongings were moved out of place. Cortisone, which reduced androgen secretion, improved her behavior. On the other hand ACTH, which elevated 17-KS levels, accentuated the symptoms which could be considered autistic-like. Fleminger suggested that the patient's mood was influenced" . . . not by the absolute levels of individual adrenocortical products, but by changes in the relative proportions of circulating androgens and cortisone or its equivalent (p. 129)."

Extreme emotional withdrawal, isolation, disinterest in others and the environment, and cessation of previously acquired speech have been observed in children ill with acrodynia, or pink disease (Asperger, 1961; Cheek, 1953; Leys, 1950; Rohmer, 1956). Although this represents a form of mercury poisoning, and as such there should be no close relationship with autism, the very distinctive psychic behavior of the children is quite unlike that of children ill with most other diseases, and bears a striking resemblance to that seen in children with autism. Studies of steroid metabolism in acrodynia have shown a significant rise in 17-KS excretion but failed to demonstrate an elevation of glucocorticoids (Cheek, 1959).

Fox and associates (1965) compared the urinary 17-OHCS and 17-KS levels of 18 individual male subjects with those of nine pairs of monozygotic male twins. They found that the pairs of twins with unusually high 17-KS and low 17-OHCS were relatively guarded and inhibited in their emotional awareness and lacked the capacity for close personal relationships, while those with higher 17-OHCS and lower 17-KS were more emotionally perceptive and seemed to have an unquestioning acceptance of the twinship or a need to emphasize their close relationship. Moreover, as a group the twins had significantly lower 17-OHCS values but higher 17-KS values than the non-twins. The latter point is of considerable interest in view of the crucial role of carbohydrate-active steroids in normal neural function. Rimland (1964) pointed out there is an overloading of monozygotic twins in the total number of cases of autism as well as an overloading of monozygotic as compared to dizygotic twins with autism. The possible importance of this point is further emphasized by the report that male monozygotic twins obtain lower scores on verbal ability than female monozygotic twins, male or female like-sexed dizygotic twins, or single-born controls (Koch, 1966).

Neural Excitability as a Determinant of Social Responsiveness

In recent years, infant research has shown that consistent individual differences in muscle tension and activity level, or motility, emerge very early in life. These differences are relatively independent of maternal and environmental influences and remain stable over long periods of time (Birns, Barten and Bridger, 1969; Schaffer, 1966). Since muscle tension and activity level appear to be directly correlated with the level of central nervous system excitability (Duffy, 1962; Krushinskii, 1962), the relationship of these traits to differences in sociability are of particular interest.

Judging from the literature, children that exhibit a greater degree of bodily activity and muscle tension respond to social stimulation in a manner which is quite different from children who are less active. Moreover, the pattern of behavior seen in highly active children resembles to some extent the pattern of children with early infantile autism suggesting, therefore, that autism may be the extreme end point of a continuum of differences in social responsiveness.

Duffy (1930) pointed out some time ago that the greater responsiveness to stimulation which presumably characterizes the child who reaches a high level of arousal might well affect social reaction to others. She found that nursery school children with greater muscle tension were more excitable than those with less muscle tension, and that a negative relationship appeared to exist between tension scores and the number of physical contacts on the playground, especially between contacts judged to be intentional. In addition, there was some indication of an association between high scores for muscle tension and being below average in weight, using fewer words, and using small muscle groups more often than large (Duffy, 1932).

More recently, Schaffer and Emerson (1964) noted activity level may have considerable influence on personality development and the manner in which interpersonal behavior is shaped. They found one could reliably isolate two groups, those who accepted close contact and those who actively resisted it. This basic posture of sociability emerged very early in life, and seemed to be related to genetically-determined differences in activity or motility rather than maternal treatment.

Similar tendencies have been observed by Escalona (1963) who found that social stimulation was a necessary condition for relatively mature behavior patterns to emerge in the more inactive infants. On the other hand, the markedly active infants excelled when left to their own devices. She noticed that, unlike the inactive infants, the active infants seemed to have a very low threshold to stimuli and appeared to be unable to protect

themselves from the disruptive influences of overstimulation, particularly when it was social in nature. Whereas strongly stimulating conditions led the less active infants to produce fairly complex behavior, such conditions caused the more active infants to fall back on simpler schemata. Of special interest is Escalona's report that, when the infants were talked to and offered a variety of toys in such a way that they could not settle into stereotyped activities, the more active infants were unable to be involved with people and things at the same time, and they became unresponsive to the social aspects of the situation. Her observations strongly suggest that an inverse relationship exists between the responsiveness and excitability of the nervous system, and the capacity to respond to social stimulation.

Both Rheingold (1961) and Schaffer (1963) hold that the need for social attachment has its origin in a generalized need for stimulation. Their studies of social responsiveness and attachment behavior indicated the infant readily learns that social objects are more stimulating than inanimate objects in the environment, and commences to show indiscriminate attachment behavior to all human beings because of their relatively high arousal value. With social objects the infant is unable to control either the manner or the rate of stimulation; not only are social objects physically intense because of their contour and complexity, but they move, and often very rapidly, thus enhancing their effective intensity. It seems likely, therefore, that the greater the neural excitability and responsiveness to stimuli, the greater would be the tendency of the infant to relate to inanimate or low-input objects in the environment. This could readily account for the observation that while autistic children ". . . are remote from affective and communicative contact with people, they develop a remarkable and not unskilled relationship to the inanimate environment (Kanner, 1965, p. 412)."

Intrinsic Level of Aggressivity

Several writers have reported extreme social withdrawal in children abnormally sensitive to a wide variety of stimuli. Bergman and Escalona (1949) described five young children who showed unusual sensitivities in several, if not all, sensory modalities, and who seemed unable to enter into meaningful relationships with other human beings. At least four of the five cases were diagnosed as childhood psychoses. Unusual sensitivities have also been noted by Russian investigators in infants who became psychotic (Bridger, 1961).

However, it may not be solely a marked degree of neural excitability which leads to the complete autistic syndrome. Experimental work with animals suggests that it may be the coupling of heightened behavioral reactivity and reduced aggressivity potential that is crucial. Welch (1967) administered a monoamine oxidase inhibitor and DOPA, separately and in combination, in an effort to enhance natural aggressiveness in pre-isolated and pre-grouped mice. In isolated mice that had been highly excitable and aggressive, the drugs almost completely inhibited normal aggressive activity while in grouped mice that had been less emotionally reactive and non-aggressive, the drugs increased motor activity and irritability, and again failed to enhance aggressiveness. But, unlike the effects in the pre-isolated animals, the drugs caused the pre-grouped animals to become "exquisitely sensitive" to tactile and auditory stimuli, and to develop a perceptual blindness, or agnosia, to social stimuli. The mice were largely oblivious of their cage-mates unless they accidentally bumped into each other. It is noteworthy that autistic children are often painfully sensitive to stimuli and act as if oblivious or "blind" to the presence of other persons.

Recently a series of studies have reported unusual elevations of serotonin in autistic children (Boullin, Coleman, O'Brien, and Rimland, 1971; Ritvo, Yuwiler, Geller, Omitz, Saeger,and Plotkin, 1970), but the meaning of these findings is not understood. In view of the emphasis on the significance of these observations, Welch's experimental results are

of special interest since the drugs he administered increase the level of nervous system activity and general arousal, and alter the levels of brain amines.

Welch (1967) has proposed that the neurophysiological factors which underlie the differences in aggressiveness between isolation-adapted and group-adapted mice are basically the same as those which underlie the differences in aggressiveness between dominant and subordinate mice. If this is so, then it can be inferred that factors which increase neural excitability and responsiveness to stimuli may lead to a pathological response to social stimuli when aggressivity potential is virtually nonexistent.

In both human and non-human species, one of the most widely shared signs of submission and lack of aggressiveness is looking away. This behavior is "a persistent and characteristic feature" in children with infantile autism (Hutt and Ounsted, 1966); in fact, peripheral vision is almost always used in preference to central vision. A derangement of the normal relations between peripheral and central vision may have more far-reaching consequences than is presently realized.

Kluver (1936) found, when studying the effects of bilateral occipital lobe ablation in monkeys, that if only those portions of the afferent visual pathway and visual center instrumental to peripheral vision were preserved, the animal no longer communicated with other animals or showed any vocal response when handled. In fact, it never uttered a sound during the entire first year after the operation. When another monkey was introduced into the cage, it shrank from contact with the other animal; moreover, noises and even forms of stimulation the experimenter was not aware of at the time seemed to throw it into a state of maximal tension. When turned loose in a room, it would climb to some high place above the floor and remain there until disturbed. About 10 weeks after the operation the animal acquired the habit of sitting most of the time with a sack pulled over its head.

The behavior of autistic children closely resembles the behavior Kluver observed in the monkey. The children, too, are mute, avoid contact with other individuals, react to noises and other forms of stimulation which for normal children would be subliminal, and persistently climb on anything available. In addition, they often use their hands to cover their eyes, or will sit for long periods with their head covered by clothing or a blanket. There is also a resemblance between their behavior and the marked disorders of perception (Luria, Pravdina-Vinarskaya, and Yar-buss, 1963) which originate from bilateral occipital lobe brain injury in humans. Both "walk over" and "through" other persons, behave as if blind despite the fact they at times show excellent vision, and seem to be unable to perceive the relation of details to the whole. These similarities suggest that children with infantile autism might suffer from neuronal damage in specific areas or pathways of the visual system. However, Schechter and associates (1969) found that, after periods ranging from 40 to 74 days in a milieu of sensory isolation, the three autistic children they studied made increasing eye-contact, became closely involved with the therapist, and were able to transfer this increased ability to interact socially to other individuals. Hence, the symptoms may be due to a biochemical defect which is reversible rather than structural brain damage.

Very little importance has been attached to the fact that autistic children show little or no aggressive behavior, or that their persistent gaze aversion is an appeasement posture indicating submissiveness. But aggressivity may be an essential component of attachment behavior; without it, a child may be unable to form "the usual biologically provided affective contact with people." Nichtern (1957) reported the results were "interesting and encouraging" when Prostigmine (neostigmine methylsulfate) was administered over a period of time to a small group of children who demonstrated autistic features and were unable to relate to others. All appeared less autistic, more alert, and in

better contact with their environment. Recently, researchers have shown Prostigmine can activate an innate system which elicits aggressive behavior and killing in rats {Smith, King and Hoebel, 1970). Perhaps cholinergic mechanisms are involved in the autistic child's disturbance of affective contact.

Hypervitaminosis A as a Possible Cause of Infantile Autism

Although the capacity to respond to social stimulation may be largely a function of the responsiveness and excitability of the nervous system, overall, the evidence strongly suggests that early infantile autism may develop only if aggressivity potential is virtually nonexistent. This view is further supported by the fact that behavioral changes analogous to those of infantile autism have been reported in animals fed a high vitamin A diet. Excess vitamin A increases activity level (Hellebrandt, 1940) and central nervous system excitability (Chauchard, 1954). Furthermore, it can lower the level of aggressivity.

Calhoun (1967) studied the effects of varying dietary intakes of vitamin A in rats subjected to above-optimum amounts of social stimulation. He observed that a level only four times greater than that available in the animal's natural food produced a perceptual blindness to behavioral stimuli and consistently reduced aggressiveness and involvement in social status interaction. Concomitant with reduced aggression was "... a reduction in the capacity for involvement in, or execution of, complex behaviors (p. 41)." He also noted that those animals which spent the least amount of time in areas where they would encounter other animals and become involved in social interaction were markedly different from those that exhibited less social withdrawal. The withdrawn rats appeared to have developed an agnosia to social stimuli. They gave little evidence of being aware that other animals were nearby, and moved among them "as if they were just so many sticks and stones." These findings suggest that, at least in some children, the predisposition to autism may be a threshold phenomenon with hypervitaminosis A precipitating the pathologic development.

The interplay between neuroendocrine components and vitamin A may be particularly important. It has been observed in animals that cortisone produces a rapid loss of A from the liver (Moore, 1964). Consequently more vitamin A might be retained if Cortisol levels were unusually low. In addition, since large amounts of vitamin A increase 17-KS output (Matteini and Cuisti, 1952; Ray, Ray, and Sadhu, 1965), supplementing the diet with A might further accentuate any disproportion between androgens and glucocorticoids. Klaiber and associates (1967) have presented evidence indicating that androgens inhibit brain monoamine oxidase activity. Therefore it can be postulated that, by raising androgen levels, excess vitamin A might also produce effects which are similar to those of monoamine oxidase inhibitors.

Hypervitaminosis A could be a factor contributing to the unusually high incidence of autism in Jewish families, as their traditional high fat diet (Abrahamson and Pezet, 1964) would cause greater amounts of the vitamin to be stored in the liver (Thompson, 1965) and more of it to be passed on to the fetus during gestation (Thorbjarnarson and Drum-mond, 1938). Since blood (Moore, 1964) and liver levels (McLaren, 1966) are higher in males than in females, vitamin A could be a factor in the high male-female ratio as well. Furthermore, because an excess can lead to deficiencies of ascorbic acid (Moore, 1967) and the B vitamins (Millen and Woolam, 1958; Moore, 1945), hypervitaminosis A could help to explain why children with severe mental disorders have shown considerable improvement in sociability and speech when given ascorbic acid, niacin, and other B vitamins in doses much larger than those required by normal children (Rimland, 1973). That ascorbic acid (Kayahan, 1952), and possibly niacin (Bryson, Samuels, and Goldthorpe, 1950), may alter the androgen Cortisol ratio considerably is a point which should be considered.

Discussion

One of the most intriguing aspects of the autistic syndrome is the fact that the characteristic behaviors of autism closely resemble the behaviors which can compensate for above-optimum increases in group density. When social stimulation becomes too intense, a decrease in all behavior patterns which elicit social awareness of an individual by others or increase the likelihood of contact has much the same effect as decreasing the total number of individuals in the group (Calhoun, 1964). Vocalizations should occur less frequently or not at all; sense organs which extend the individual's perception of others should become less effective; and the individual will occupy areas not normally used, or initiate activity while others are resting. A marked decrease in the same communication-enhancing or contact-producing factors is observable in children with autism. They are mute or use only a peculiar non-communicative kind of language, seem functionally blind in many respects, often are not aware of sound, climb onto anything available, and tend to reverse their day-night sleep-waking pattern.

Because of the potential threat of crowding now facing the human population, increasing interest is being shown in the effects of density on social behavior. Considerable data has been gathered from field and laboratory studies on mammalian populations, and it is now well-documented that changes in population density can profoundly alter hormone and brain amine levels which in turn change behavior. Many investigators argue that the mechanisms seen in non-human species are probably not directly operative on humans. However, there are several lines of evidence, in addition to the previously cited experiments of Welch (1967) and Calhoun (1967), which point to the possibility that density-dependent biological mechanisms may be important in the etiology of early infantile autism. First, when animals are grouped in numbers which exceed those to which the species is best adapted, the young are dwarfed and often develop diarrhea (Ratcliffe, 1968). Similarly, autistic children are retarded in height, weight, and skeletal maturity (Simon and Gillies, 1964) and frequently have chronic diarrhea (Rimland and Meyer, unpublished data). Second, in confined populations at low densities the characteristic behavioral traits of the individual animals are not readily apparent. However, at higher densities a pronounced change occurs and the several classes of animals become spatially separated (Snyder, 1968), but only a few members of the population become functionally withdrawn. Infantile autism is also a rare disorder (Treffert, 1970). Third, in a more recent study, where the population pressure increased to a maximum of 18 times the optimum and diet was not a primary feature in any of the pathological behavior which developed, Calhoun (1971) found that the ultimate outcome was not stressed animals, but instead unstressed animals who exhibited no socialization at all. The intense crowding led to "social death" in nearly all of the group. He also observed that the intense crowding resulted in "masculinely aggressive females." Animal research has shown that exposure to an excess of androgenic hormones at a critical period in development leads to a masculine pattern of behavior in the adult female (Money, 1965; Phoenix, 1966). Moreover, there is growing evidence that fetal androgens may have a favorable influence on potential intelligence in humans (Dalton, 1968; Ehrhardt and Money, 1967; Masica, Money, Ehrhardt, and Lewis, 1969). In view of the lack of emotionality which so often characterizes the highly intellectual person, and especially the parents of autistic children, Calhoun's findings suggest that the biological determinants of human intelligence may be intimately related to the basic biological mechanisms which have permitted man to adapt to ever-increasing population pressure. It is conceivable that these pressures may now be of sufficient intensity that the child with infantile autism could indeed by "the mutant of especially intelligent progenitors."

If density-dependent mechanisms are

operating in the human species, then it seems likely that the incidence of autism may rise as human crowding increases. However, factors other than the genetic mechanisms set in motion by high-population stress probably influence the incidence of autism. The evidence strongly suggests that any factor which increases the responsiveness and excitability of the nervous system, but fails to enhance or actually lowers the level of aggressivity, may cause early infantile autism to develop. Whether this occurs will, of course, depend on the genetic or constitutional nature of the child. Children with unusually low Cortisol levels may be particularly vulnerable.

Although the subject of considerable controversy, a substantial body of scientific evidence has accumulated in the last few years to show that mentally ill persons may have a greatly altered metabolism with regard to certain vitamins. It is possible that the physiological effects of increasing population pressures may be such that a level of vitamin A not toxic under normal conditions may have a number of adverse effects when social stress is intense. If, in fact, this should be the case, it is likely that the concentration of vitamins needed for normal functioning of the brain could be different under conditions of intense social stimulation, since hyper-vitaminosis A produces certain other hypovitaminoses as secondary phenomena (Nieman and Klein Obbink, 1954).

A deficiency of vitamin A suppresses the biosynthesis of steroid hormones (Juneja, Murthy, and Ganguly, 1966), especially androgenic hormones that may favorably influence potential intelligence. On the other hand, an excess of vitamin A may have detrimental effects on emotional and social behavior (Calhoun, 1967). Our knowledge of an individual's requirements and ability to maintain an optimum level of vitamin A is extremely limited, and nothing is known about how these factors might be affected by differences in density of the human population. Considering the current increases in population pressures, it would appear to be extremely important that this set of relationships be determined.

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