INTRODUCTION AND REVIEW OF LITERATURE

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The term "basal ganglia" is used in different ways by clinicians and classical amatomists. Anatomists tend to include all of the non-cortical grey matter of the telencephalon, that is the caudate nucleus, the lentiform (putamen and globus pallidus), the claustrum, the amygdala, the substantia innominata and the nucleus accumbens septi. Clinicians tend to restrict the term basal ganglia, on functional grounds, to the two nuclear elements of the corpus striatum, the caudate and the lentiform nuclei (Graybiel and Ragsdale, 1978).

The basal ganglia are large subcortical nuclear masses located in the forebrain. The corpus striatum constitutes the largest part of the basal ganglia and is divided into two parts:

I. The Neostriatum:

This comprises the caudate and putamen nuclei. The caudate nucleus appears as an inverted comma-shapped nucleus intimately related to the lateral ventricle. It is embedded in the forebrain and is separated from the cerebral cortex by the corpus callosum. It consists of a head, body and tail. The head of the caudate nucleus forms part of the lateral wall of the anterior horn of the lateral ventricle and constitutes

the largest and most rostral part of the caudate nucleus. The rostroventral part of the head of the caudate nucleus is continuous laterally with the putamen. Its body extends caudally along the dorsolateral surface of the thalamus. Its tail is the long, attenuated caudal extension from the body. It curves ventrally and rostrally into the temporal lobe and comes into relationship with the amygdaloid nuclei complex. The putamen is embedded deeply in the telencephalon. It has a convex lateral surface, separated from the claustrum by the capsula externa. It is separated medially from the pallidum by the external medullary lamina and from the caudate nucleus and thalamus by the internal capsule. Together with the pallidum it forms a biconvex nucleus called the lentiform nucleus. There are no anatomical features that differentiate the two components of the neostriatum from each other. Striatal tissue can be defined by the following characteristics that apply equally to the caudate and putamen nuclei (Graybiel and Ragsdale, 1978):

- More than 95% of striatal cells are small and rounded in shape (12-18 μm in diameter). They are of homogeneous distribution without lamination or special grouping. Among these are scattered large

cells (20-30 μm in diameter), the ratio of the large to the small neurones being 1:20.

- The striatum is unique among the other regions of the forebrain, as it contains an extremely high concentration of acetylcholinestrase (Jacobwitz and Palkovits, 1974) and dopamine (Ungerstedt, 1971) almost in the same regions.
- The neostriatum receives nearly all of the afferents of the corpus striatum. These are from the cerebral cortex, the intralaminar thalamic nuclei, the dorsal raphe nuclei and the substantia nigra pars compacta, but have a limited efferent distribution, projecting only to the globus pallidus and substantia nigra.

In human and high primates, the caudate and putamen are separated from each other by the internal capsule, while in rodents, the caudate and putamen constitute a single huge mass called the "caudate-putamen" or simply the striatum as the internal capsule is not developed.

II. The Paleostriatum or Globus Pallidus:

It is further subdivided, in human and high primates, by a thin lamina of nerve fibres, into

medial and lateral pallidal segments. In lower mammals the globus pallidus constitutes a single mass that corresponds to the lateral pallidal segment in man (Fox, Hillman, Seigesmund and Sther, 1966) while the medial pallidal segment is represented by a collection of neurones called the entopeduncular nucleus. The globus pallidus forms the smaller and medial segment of the lentiform nucleus. It is separated from the putamen by the external medullary lamina and it is subdivided into outer larger and inner smaller segments by the internal medullary lamina. many bundles of myelinated fibres traverse the pallidum. The pallidum represents the output segment of the basal ganglia, as most of its afferents come from the striatum and it gives multiple efferent projections.

The precise role of the basal ganglia is not fully understood. However, they are considered as motor centres involved with the integration relating the initiation and control of voluntary and involuntary movements. Although the basal ganglia and related nuclei play an important role in motor functions, none of these nuclei project direct fibres to the spinal cord, and the mechanisms and pathways

that mediate their functional role at a spinal level remain obscure.

Zinc as a Trace Element and Effects of its Deficiency:

Trace elements are of singular significance in the dynamics of nutrition. There are ten elements known to be essential in trace amounts to good health; copper, zinc, iron, iodine, manganese, cobalt, molybdenum, selenium, chromium and tin (Underwood, 1971). Possible future candidates for essential status appear to be nickel, arsenic, cadmium, barium, flourine, vanadium, bromine and strontium. Functioning primarily as catalysts in enzyme systems in the cells, trace elements perform a role in enzymatic reactions ranging from weak ionic strength effects to highly specific associations known as metalloenzymes (Prasad, 1976).

The presence of zinc in living organisms and its role as an essential nutrient for plants and animals has been recognized since it was shown by Raulin (1869) to be necessary for the growth of Aspergillus niger. its occurrence in biological matter was first described by Lechartier and Bellamy (1877). In the same year, Raoult and Berton described the presence of

zinc in human liver. Difficulties in methodology limited most investigations to qualitative efforts. Lutz (1926) found that zinc was present in all organs of the rat, cat and man. Todd, Elvehjem, and Hart (1934) were the first to demonstrate that zinc was required for normal growth and development in the rat. However, it was not until 1955 when Tucker and Salmon showed similar requirements in the pig, that greater attention was paid to this nutrient. The discovery of zinc in many highly purified enzymes (Vallee, 1955) has revealed the diversity of its functions in protein and carbohydrate metabolism. Zinc is known to be an integral part of at least 70 enzymes and it is now established that this element has a central role in nucleic acid and protein synthesis (Prasad, 1976).

The adult human body contains about 2.5 gm zinc. Normal serum zinc averages 121 $\pm$ 19 µg/100 ml. The whole blood content varies from 700-800 µg/100 ml. Analyses performed on serum and plasma are equivalent. There are no seasonal or diurnal variations, nor do there appear to be differences between the sexes. In blood serum, zinc exists in two fractions; firmly bound zinc which amounts to about 34% and loosely bound zinc about 66% of the total zinc content

(Vallee, 1959).

The recommended dietary requirement for zinc is 15 mg/day for adults with a higher requirement during growth and development (Harper, 1973). The main source of the dietary zinc intake is meat. Red meat having the highest zinc content. Fish also has a relatively high zinc content. Most other food items that constitute the daily diet have variable amounts of zinc (Osis, Kramer, Wiatrowski and Spencer, 1972). Although the dietary intake of zinc may be adequate, the utilization of this zinc intake may be inadequate, and therefore the retention of zinc may be borderline or low. This may be due to impaired intestinal absorption of zinc because of the unavailability of zinc for absorption. Phytate has been shown to inhibit the absorption of zinc and this inhibition is more accentuated in the presence of a high calcium intake (Oberleas, Muhrer and O'Dell, 1966 and O'Dell, 1969). This decrease in zinc absorption was associated with a decrease of the plasma zinc level and an increase of the fecal zinc excretion (Reinhold, Nasr, Lahimgarzadeh and Hedayati, 1973). Food items such as soya products, which contain phytic acid phosphorus, are not a desirable source of dietary zinc

(Spencer, Osis, Kramer and Norris, 1972) other factors have been documented to affect zinc homeostatis. These include, alcoholic beverages, blood loss, malabsorption, prolonged intravenous fluids, fasting , infection, nephrosis, chelating agents, myocardial infraction, surgery, cirrhosis, hormones, other heavy metals, pregnancy and lactation (Prasad, 1976). Only that zinc which is transported to the cell, whether as an enzyme cofactor or bound to a membrane or other metabolically active form, is of any significant value to the body. Considerable zinc is not absorbed or if absorbed is not efficiently utilized by the body and is quickly excreted.

Once absorbed, zinc is excreted primarily in the gastrointestinal and pancreatic secretions. Urine contains about 0.5 mg. per day. Studies in the rat, indicated that -in contrast to iron- the body stores of zinc are not readily mobilized and hence, there is an unusual dependence upon a regular exogenous supply of the element particularly during periods of growth.

The effect of zinc deficiency, through nutritional deprivation experiments on many different animal species has been studied. They have all shown major

clinical findings of stunted growth, anorexia, hair loss, dry hyperkeratotic skin with various dermatosis, delayed wound healing and congenital malformations in maternal zinc deficiency (Prasad, 1966 and Underwood, 1971).

The total protein content of various tissues of zinc-deficient rats was lowered compared to that of zinc-supplemented control animals (Macapinlac, Pearson, Barney and Darby, 1968; Somers and Underwood, 1969a; Sandstead, Terhune, Brady, Gillespie and Hollaway, 1971 and Prasad et al., 1971). Somers and Underwood (1969) demonstrated that zinc-deficient rat testes contain a higher level of non protein nitrogen. In lambs, the retention of dietary amino acids was reduced, as indicated by an increased urinary excretion of nitrogen and sulfur when compared to that of control animals. Biochemical changes in protein metabolism are also indicated by abnormalities in the protein pattern of plasma and serum (Fox and Harrison, 1965; Miller et al.,1968 and Tao and Hurley, 1971). Zinc deficiency is associated with abnormalities in amino acid metabolism (Hsu and Anthony, 1971).

The biochemical changes brought about by zinc

deficiency in animals may be so extensive that they are indicated by gross alterations in the cellular composition of certain tissues. Thus, testes and connective tissue of zinc deficient rats were found to contain significantly less RNA and DNA than those of control animals (Macapinlac et al., 1968; Somers and Underwood, 1969 and Fernandez-Madrid, Prasad and Oberleas, 1973). The brain of zinc deficient rats was found to contain less RNA, DNA and protein than control animals (Sandstead et al., 1971; Sandstead, Fosmire, Mckenzie and Halas, 1975; Fosmire, Ubaidi and Sandstead, 1975; Moynahan, 1976; Eckhert and Hurley, 1977; Buell, Fosmire, Ollerich and Sandstead, 1977 and Pfeiffer and Braverman, 1982).

There are numerous studies showing that zinc deficiency in animals impairs the incorporation of labelled thymidine into DNA (Fujioka and Lieberman, 1964; Sandstead and Rinaldi, 1969; Swenerton, Shrader and Hurley, 1969; Weser, Seeber and Warnecke, 1969; Williams and Chesters, 1970; Dreosti, Grey and Wilkins, 1972; Grey and Dreosti, 1972; Hsu and Hsu, 1972; Sandstead, Gillespie and Brady, 1972; Fernandez-Madrid et al., 1973; Stephan and Hsu, 1973 and Prasad and Oberleas, 1974).

Besides, the various studies by Vallee (1959) have shown that zinc is a constituent of a number of metalloenzymes. Hence, in zinc deficient rats, the activity of various zinc-dependent enzymes as judged by histochemical techniques was reduced in testes, bones, oesophagus and kidneys, when compared to their controls (Prasad, 1966 and Prasad and Oberleas, 1971). These results were correlated with the clinical manifestations of testicular atrophy, reduced growth rate and oesophageal parakeratosis. Studies of tissue homogenates of pigs showed that the zinc content was significantly reduced in liver, kidney, pancreas and bone in zinc-deficient animals as compared with their controls (prasad et al., 1971).

The activity of alkaline phosphatase enzyme was found to be significantly decreased in serum of zinc deficient rats, pigs, dairy cows, calves and chicks (Macapinlac et al., 1966; Luecke and Baltzer, 1968 and Luecke, Olman and Baltzer, 1968). However, Guttikar, Panemangalore and Rao (1970) found that alkaline phosphatase was not affected by calorie intake. In zinc deficient rats the activity of the enzyme decreased before any sign of lowered food intake or reduced growth rate were evident. The activity of the

enzyme was found to be reduced in bones from zinc-deficient rats, pigs, cows, chicks, turkey poults and quail (Prasad, 1976). Iqbal (1971) and Williams (1972) found that intestinal alkaline phosphatase decreased as early as 3 days after rats were given a zinc-deficient diet.

Activity of lactate dehydrogenase was reduced significantly in tissues of zinc deficient rats and pigs (Prasad, Oberleas, Wolf and Horwitz, 1967; Prasad, Oberleas, Wolf, Horwitz, Miller and Luecke, 1969a and Prasad, Oberleas, Wolf and Horwitz, 1969b).

Zinc dependent NADH diaphorase also showed lower levels during zinc deficiency (Prasad et al., 1967).

Two enzymes of importance in protein digestion are the pancreatic carboxypeptidase A and B. A loss of activity of the pancreatic carboxypeptidase A in zinc deficiency is a consistent finding (Hsu, Anilane and Scanlan, 1966).

Carbonic anhydrase activity was reduced in blood, stomach and intestine (Miller and Miller, 1962; Ott, Smith, Stob, Parker, Harrington and Beeson, 1965;

Iqbal, 1971 and Prasad, 1976).

Alcohol dehydrogenase was reduced after zinc deficiency in the liver, bones, testes, kidneys and oesophagus of rats and pigs (Prasad et al., 1967; Kfoury, Reinhold and Simonian, 1968; Prasad et al., 1969a; Prasad et al., 1969b; Prasad and Oberleas, 1971 and Prasad et al., 1971).

Glutamic dehyrogenase tended to have lower activities in both liver and kidneys of zinc deficient rats (Kfoury et al., 1968).

In addition, histopathological changes were recorded in various tissues. Thus sections of the testes of zinc deficient rats revealed a marked decrease in the cellularity of all the cells (Follis, Day and McCollum, 1941; Macapinlac et al., 1966; Prasad et al., 1967 and Diamond and Hurley, 1970). In the prenatal and developing brains, the number of cells in the forebrain and cerebellam was reduced (Fosmire et al., 1975; McKenzie et al., 1975; Moynahan, 1976; Stephen, Fosmire, Ollerich and Sandstead, 1977 and Dvergsten, Fosmire, Ollerich and Sandstead. 1983) and the cytoplasmic nuclear ratio was

increased, besides an increased blood flow to the brain. The oesophagus showed hyperkeratosis, parakeratosis and vacuolar changes of the squamous epithelial cells. The kidneys revealed minimal hyaline necrosis of the proximal and distal convoluted tubules (Follis et al., 1941; Macapinlac et al., 1966 and Prasad et al., 1967).