Chapter 4

Archaeal Digoxin and Personality Profiles

The endosymbiotic archaea produces an endogenous membrane Na^+-K^+ ATPase inhibitor, digoxin. Elevated digoxin levels have been described in several neuropsychiatric conditions like bipolar mood disorder and epilepsy. There is no data on digoxin status and membrane Na^+-K^+ ATPase levels in various psychological states. It was therefore considered pertinent to assess serum digoxin levels and membrane Na^+-K^+ ATPase activity in psychological states like - spirituality, bonding and affection, hypo/hyper/homo sexual states, various levels of appetite and sleep, creativity and addiction. The relationship between digoxin secretion and hemispheric dominance was also assessed to find out the psychological correlates of hemispheric dominance. The serum digoxin levels and membrane Na^+-K^+ ATPase activity were measured in left hemispheric, right hemispheric and bihemispheric dominant individuals to assess the relationship between cerebral dominance and personality profiles. The results are presented in this paper.

Results

(1) Serum digoxin levels and RBC Na^+-K^+ ATPase activity was assessed in different psychological conditions

In spiritually inclined individuals, creative individuals, addiction, promiscuous / homosexual individuals, anorexic, insomniac and individuals with reduced bonding and affection and detached behaviour - serum digoxin levels were elevated, RBC Na^+-K^+ ATPase activity reduced and serum magnesium reduced.

In spiritually non-inclined individuals, non-creative individuals, individuals without addictive behaviour, non-promiscuous individuals, individuals with gastronomic tendency, somnolent individuals and individuals with increased bonding and affection - serum digoxin levels were reduced, RBC Na^+-K^+ ATPase activity increased and serum magnesium increased.

(2) Serum digoxin RBC Na^+-K^+ ATPase activity and tyrosine / tryptophan catabolic patterns in right hemispheric dominant, left hemispheric dominant and bihemispheric dominant individuals

Serum digoxin levels were increased and RBC Na^+-K^+ ATPase activity reduced in right hemispheric dominant individuals. Serum digoxin levels were reduced and RBC Na^+-K^+ ATPase increased in left hemispheric dominant individuals. The bihemispheric dominant individuals had intermediate values. The levels of tryptophan, serotonin, quinolinic acid, nicotine and strychnine were elevated and that of tyrosine, dopamine, noradrenaline and morphine decreased in right hemispheric dominant individuals. The levels of tryptophan, serotonin, quinolinic acid, nicotine and strychnine were decreased and that of tyrosine, dopamine, noradrenaline and morphine increased in left hemispheric dominant individuals.

The Hyperdigoxinemic Personality

In the hyperdigoxinemic right hemispheric dominant state, tryptophan and its catabolites are increased and tyrosine and its catabolites are reduced. This could be due to the fact that digoxin can regulate neutral amino acid transport system with preferential promotion of tryptophan transport over tyrosine. In addition to the increased digoxin levels the decrease in membrane Na^+-K^+ ATPase activity in the psychological states of creativity, addiction, spirituality, promiscuity, homosexuality, detached behaviour, anorexia and insomnia as well as right hemispheric dominant individuals could be due to the fact that the hyperpolarising neurotransmitters (dopamine, morphine and noradrenaline) are reduced and the depolarising neuroactive compounds (serotonin, strychnine, nicotine and quinolinic acid) are increased. The schizoid neurotransmitter pattern of reduced dopamine, noradrenaline and morphine and increased serotonin, strychnine and nicotine is common to left handed / right hemispheric

dominant individuals and to all these psychological states and could predispose to their development. Quinolinic acid, an NMDA agonist can contribute to NMDA excitotoxicity reported in schizophrenia. Strychnine by blocking glycinergic transmission can contribute to the decreased inhibitory transmission in schizophrenia. Recent data suggest the initial abnormality in schizophrenia involves a hypodopaminergic state and the low dopamine levels now observed agrees with this. Nicotine by interacting with nicotinic receptors can facilitate the release of dopamine, promoting the dopaminergic transmission in the brain. This can explain the increased dopaminergic transmission in the presence of decreased dopamine levels. The increased serotoninergic activity and reduced noradrenergic outflow from locus coeruleus reported earlier in schizophrenia agrees with our finding of elevated serotonin and reduced noradrenaline levels. In the presence of hypomagnesemia, the magnesium block on the NMDA receptor is removed leading to NMDA excitotoxicity. The increased presynaptic neuronal calcium can produce cyclic AMP dependent phosphorylation of synapsins resulting in increased neurotransmitter release into the synaptic junction and vesicular recycling. Increased intracellular calcium in the post synaptic neuron can also activate the calcium dependent NMDA signal transduction. The plasma membrane neurotransmitter transporter (on the surface of the glial cell and presynaptic neuron) is coupled to a sodium gradient which is disrupted by the inhibition of Na^+-K^+ ATPase, resulting in decreased clearance of glutamate by presynaptic and glial uptake at the end of synaptic transmission. By these mechanisms, inhibition Na^+-K^+ ATPase can promote glutamatergic transmission. The elevated levels of quinolinic acid, strychnine and serotonin can also contribute to NMDA excitotoxicity. Strychnine displaces glycine from its binding sites and inhibits glycinergic inhibitory transmission in the brain. The glycine is free to bind to the strychnine insensitive site of the NMDA receptor and promote excitatory NMDA

transmission. Quinolinic acid and serotonin are also positive modulators of the NMDA receptor. Increased glutamatergic transmission resulting in excitotoxicity has been implicated in primary generalised epilepsy and schizophrenia. Inhibition of Na^{+}-K^{+} ATPase can also result in defective neuronal membrane repolarisation and a paroxysomal depolarization shift resulting in epileptogenesis. Thus in the right hemisphere dominant hyperdigoxinemic state there is upregulated serotoninergic, cholinergic, nicotinergic, strychninergic and glutamatergic transmission and downregulated dopaminergic, glycinergic, morphinergic and noradrenergic transmission. There was an increased tendency for spirituality in hyperdigoxinemic individuals. Temporal lobe epileptic phenomenon has been described in spiritual individuals. Increased glutamatergic transmission is associated with memory and intelligence. This can contribute to increased creativity. They had a tendency towards reduced appetite and eating behaviour. Increased serotoninergic transmission can lead on to reduced appetite. There was also hypersexual behaviour / homosexuality and promiscuity in hyperdigoxinemic individuals. This could be related to increased production of nitric oxide in hyperdigoxinemic individuals consequent to induction of nitric oxide synthase by increased intracellular calcium. Nitric oxide has been related to erectile function. There was an increased tendency to addictive behaviour in hyperdigoxinemic individuals. Endogenous morphine deficiency has been related to addiction. Morphine synthesis is low because of low tyrosine levels. There was tendency to insomnia and reduced sleep. This could be related to reduced levels of morphine. There was less of bonding and affectionate behaviour. Bonding and affectionate behaviour has been related to dopamine and morphine. Dopamine and morphine deficiency in hyperdigoxinemic individuals could contribute to less of bonding and affectionate behaviour.

The Hypodigoxinemic Personality

The results showed that the concentration of tryptophan, quinolinic acid, strychnine, nicotine and serotonin was found to be lower in the plasma of right handed / left hemispheric dominant individuals while that of tyrosine, morphine, dopamine and norepinephrine was higher. In spiritually non-inclined individuals, non-promiscuous individuals, non-creative individuals, individuals with gastronomic tendency, somnolent individuals and individuals with increased bonding and affection similar tryptophan and tyrosine catabolic patterns are probable owing to hypodigoxinemia. Thus there is a decrease in tryptophan and its catabolites and increase in tyrosine and its catabolites in the serum of right handed / left hemispheric dominant individuals and the above described psychological states. This could be due to the fact digoxin can regulate neutral amino acid transport system with preferential promotion of tryptophan transport over tyrosine and that digoxin levels are low in right handed / left hemispheric dominant individuals and in the above mentioned psychological states. In addition to reduced digoxin levels the increase in membrane Na^+-K^+ ATPase activity in left hemisphere dominance and in the above mentioned psychological states (spiritually non-inclined individuals, non-promiscuous individuals, non-creative individuals, individuals with gastronomic tendency, somnolent individuals and individuals with increased bonding and affection) could be due to the fact that the hyperpolarising neurotransmitters (dopamine, morphine and noradrenaline) are increased and the depolarising neuroactive compounds (serotonin, strychnine, nicotine and quinolinic acid) are decreased. The low level of quinolinic acid, serotonin and strychnine can contribute to reduced excitatory glutamatergic transmission as they are all positive modulators of the NMDA receptor. In the presence of hypermagnesemia, the magnesium block on the NMDA receptor is strengthened leading on to reduced NMDA transmission. The decreased

presynaptic neuronal calcium can produce reduced cyclic AMP dependent phosphorylation of synapsins resulting in a decrease in glutamate release into the synaptic junction and vesicular recycling. The plasma membrane glutamate transporter (on the surface of the glial cell and presynaptic neuron) is coupled to sodium gradient, which is activated by the stimulation of Na^+-K^+ ATPase, resulting in increased clearance of glutamate by presynaptic and glial uptake at the end of synaptic transmission. By these mechanisms, stimulation of Na^+-K^+ ATPase can inhibit glutamatergic transmission. Deficiency of serotonin can lead to increased appetite and eating behaviour resulting in bulimia nervosa. Dopamine and morphine has been related to bonding behaviour. Increased morphine and dopamine could lead to increased bonding and affectionate behaviour. Increased synthesis of morphine can also lead on to lack of addictive behaviour. Morphine deficiency has been related to addiction. The reduced glutamatergic transmission noted could be related to the average to normal IQ and creativity noticed. Dementia has also been related to depression and the phenomenon of pseudomentia has been described. Decreased production of nitric oxide can lead on to hyposexual behaviour. Synthesis of NO has been related to erectile function. Low serotonin levels could predispose to depression and obsessive compulsive disorder. Depression and OCD could predispose to the above mentioned psychological states. These behavioural patterns are suggestive of left hemispheric dominance.

References

[1] Kurup RK, Kurup PA. *Hypothalamic Digoxin, Cerebral Dominance and Brain Function in Health and Diseases*. New York: Nova Medical Books, 2009.