

Chapter 2

Neurology of Human Creativity

Introduction

Creativity is a human faculty associated with the creation of works of art, literature and science. Creative individuals tend to have a higher incidence of temporal lobe epilepsy and psychiatric disorders like schizophrenia. Studies from our laboratory have demonstrated increased synthesis of the endogenous membrane $\text{Na}^+\text{-K}^+$ ATPase inhibitor, archaeal digoxin, in seizure disorder and schizophrenia. Archaeal digoxin is a steroidal glycoside synthesized by the isoprenoid pathway. It was therefore considered pertinent to study the digoxin status and the isoprenoid pathway related cascade in creative individuals. Digoxin can regulate the neuronal membrane amino acid transport and can thus modulate multiple neurotransmitter systems. It could thus play a role in the genesis of cerebral dominance. The digoxin status and the isoprenoid pathway related cascade was also studied in individuals of differing hemispheric dominance in order to find out the role of hemispheric dominance in creativity.

Results

- (1) The results showed that creative individuals had increased HMG CoA reductase activity and serum digoxin as well as decreased RBC $\text{Na}^+\text{-K}^+$ ATPase activity and serum magnesium levels. The results showed that non-creative individuals had decreased HMG CoA reductase activity and serum digoxin levels with increased RBC membrane RBC $\text{Na}^+\text{-K}^+$ ATPase activity and serum magnesium levels.
- (2) The results showed that non-creative individuals had increased levels of tyrosine and its catabolites (dopamine and noradrenaline and morphine) and reduced levels of tryptophan and its catabolites (serotonin, quinolinic acid, strychnine and nicotine). The results showed that creative individuals had decreased levels of tyrosine and its catabolites (dopamine,

noradrenaline and morphine) and increased levels of tryptophan and its catabolites (serotonin, quinolinic acid, strychnine and nicotine).

- (3) Serum digoxin levels were increased and RBC $\text{Na}^+\text{-K}^+$ ATPase activity was reduced in right hemispheric dominant individuals. Serum digoxin levels were reduced and RBC $\text{Na}^+\text{-K}^+$ 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 while that of tyrosine, dopamine, noradrenaline and morphine decreased in right hemispheric dominant individuals. The levels of tryptophan, serotonin, quinolinic acid, nicotine and strychnine decreased while that of tyrosine, dopamine, noradrenaline and morphine increased in left hemispheric dominant individuals.

Discussion

Archaeal Digoxin and Membrane $\text{Na}^+\text{-K}^+$ ATPase Inhibition in Relation to Human Creativity

The archaeon steroidelle DXP pathway and the upregulated pentose phosphate pathway contribute to digoxin synthesis. The results showed that creative individuals had increased digoxin synthesis and decreased membrane $\text{Na}^+\text{-K}^+$ ATPase activity with decreased serum magnesium levels. The increased levels of digoxin could be due to its increased synthesis. Studies from our laboratory have demonstrated the synthesis of endogenous digoxin - a steroidal glycoside by the isoprenoid pathway. Digoxin can inhibit membrane $\text{Na}^+\text{-K}^+$ ATPase activity. Membrane $\text{Na}^+\text{-K}^+$ ATPase inhibition can lead to an increase in intracellular calcium and a reduction in intracellular magnesium.

The increase in serum digoxin levels in creativity is significant. Digoxin, a membrane $\text{Na}^+\text{-K}^+$ ATPase inhibitor probably regulates conscious perception. The elements of conscious perception include perceptual binding, focused attention and short-term memory. The evidence of increased hypothalamic archaeal digoxin points to a role for the hypothalamus. The hypothalamus is connected to the thalamus by the mamillothalamic tract and digoxin may play a role in regulating these synapses. There are two-way connections between the cerebral cortex and the thalamic nucleus. There are also two-way connections between the cerebral cortex and hypothalamus and digoxin may possibly regulate these synapses also. The hypothalamus - thalamus - cerebral cortex reverberatory circuit would play a role in mediating conscious perception.

Perceptual binding important in consciousness occurs when all the neurons associated with any one object's perceptual map in layer 5 of the cerebral cortex, fire in bursts and in a synchronised pattern but out of sync with those representing other objects. When an object is perceived there is a simultaneous activation of the cerebral cortex-hypothalamic two-way connections and liberation of digoxin from the hypothalamus to stimulate the widely dispersed cerebral cortical neurons receiving the incoming perception and their resultant synchronised burst-firing. Digoxin, by the sodium potassium ATPase inhibition it produces, can lead to a paroxysmal depolarisation shift resulting in sustained synchronised burst firing of cerebral cortical neurons.

Short-term memory important in conscious perception depends on the hypothalamic-thalamic-cerebral cortex reverberatory circuit as well as the phenomena of sustained synchronised burst-firing of neurons in layer 5 of the cerebral cortex. Sustained synchronised burst firing produced by digoxin can temporarily strengthen the relevant synapses so that this particular pattern of firing is recalled quickly; a type of short term memory. Transient synaptic changes of this type are due to an alteration in the presynaptic neuronal calcium

produced by digoxin. The thalamic-cerebral cortex reverberatory circuit mediating short term memory is glutamatergic and digoxin could amplify the circuit by its inhibitory effect on glial uptake of glutamate and increasing synaptic glutamate content.

All axons that pass either way between the cerebral cortex and thalamic nucleus must go through the thalamic reticular nucleus and all give off collateral excitatory glutamatergic branches that innervate the reticular nucleus. The reticular nucleus in turn provides an inhibitory GABAergic innervation back to the thalamic nucleus that provides the input. The reticular nucleus is involved in mediating selective attention by intensifying or detaching a particular active thalamic input into the cortex. The amplification or focusing and detachment of attention occurs by digoxin's effect in promoting glutamatergic transmission in the collaterals to the reticular nucleus by inhibiting the glial uptake of the glutamate and increasing its synaptic content. The back projections from the cerebral cortical perceptual map of the external world to the hypothalamus decides whether hypothalamic archaeal digoxin should act on the glutamatergic collaterals to the reticular nucleus and thus, focus or detach attention.

The increased secretion of archaeal digoxin in creative individuals produces a hyperconscious state with increased focused attention, perceptual binding and short-term memory.

Archaeal digoxin could also possibly mediate quantal or extrasensory perception. Intuitive phenomena are common in creative individuals and could form the basis of the creative achievements. The perceived element in quantal or subliminal perception which could play a role in creativity could be the quanta of light, sound, vibration pressure and matter-dependent electric and magnetic fields. The brain functions as a quantum computer with the quantum computer memory elements comprised of superconducting quantum

interference devices (the SQUIDS which can exist as superpositions of macroscopic states).

Bose condensation, the basis of superconductivity, is achievable at room temperature in the Frohlich model in biological systems. The dielectric protein molecules and polar sphingolipids of the neuronal membrane; nucleosomes which are a combination of basic histones and nucleic acid and cytoplasmic magnetite molecules; are excellent electric dipole oscillators which exist under a steep neuronal membrane voltage gradient. The individual oscillators are energised with a constant source of pumping energy from outside, by digoxin binding to membrane sodium potassium ATPase and producing a paroxysmal depolarisation shift in the neuronal membrane. This prevents the dipole oscillators from ever settling into thermal equilibrium with the cytoplasm and the interstitial fluid which is always kept at constant temperature. There are connections between the hypothalamus and cerebral cortex, and digoxin may serve as a neurotransmitter for these synapses. Bose condensed states produced by a digoxin mediated dielectric protein molecular-pumped phonon system could be used to store information which might be encoded (all within the lowest collective frequency mode) by appropriately adjusting the amplitudes of and phase relations between the dipole oscillators. The external world sensory impressions exists in the cortical dipole oscillators as probabilistic multiple superimposed patterns; the U phase of quantum mechanics.

The part of the incoming quantal data maps of the external world built by subliminal perception in logical sequence and corollary to the cerebral cortical external world maps built by conscious perception was chosen. Hypothalamo-cerebral cortical connections mediated by digoxin acting on the neuronal membrane help to magnify the chosen map to I graviton criteria and to the threshold required for the neuronal network to fire and consciousness. It is then integrated into the cerebral cortical conscious perceptual external world

map. A comparison is found by a quantal non-local quasicrystal tiling effect which mediates the activation and deactivation of synapses through the contraction and growth of dendritic spines.

This model of quantal perception provides a mechanism for extrasensory or subliminal perception. The increased digoxin level produces increased efficiency of the quantal of subliminal perception in creative individuals. The R part of quantal subthreshold perception is not deterministic and it introduces a completely random element into the time evolution, and in the operation of R there might be a role for free will, an important component of conscious perception.

Archaeal Digoxin and Regulation of Neurotransmitter Synthesis and Function in Relation to Human Creativity

The archaeon neurotransminoid shikimic acid pathway contributes to tryptophan and tyrosine synthesis and catabolism generating neurotransmitters and neuroactive alkaloids. There is an increase in tryptophan and a reduction in tyrosine and their catabolites in the serum of spiritually inclined individuals. This could be due to the fact that digoxin can regulate neutral amino acid transport systems with preferential promotion of tryptophan transport over tyrosine. The decrease in membrane $\text{Na}^+\text{-K}^+$ ATPase activity in spiritually inclined 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. Studies from our laboratory have demonstrated the synthesis of endogenous morphine from tyrosine and endogenous strychnine and nicotine from tryptophan.

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 glutamate release into the synaptic junction and vesicular recycling. Increased intracellular calcium in the postsynaptic neuron can also activate the NMDA signal transduction in the postsynaptic neuron. The membrane glutamate transporter (on the surface of the glial cell and presynaptic neuron) is coupled with a sodium gradient which is disrupted by the inhibition of $\text{Na}^+\text{-K}^+$ ATPase; resulting in decreased clearance of glutamate by presynaptic and glial uptake at the end of synaptic transmission. By these mechanisms, inhibition of $\text{Na}^+\text{-K}^+$ ATPase can promote glutamatergic transmission. Glutamatergic transmission has been related to long-term potentiation (LTP), which is important in learning and memory. Increased glutamatergic transmission could thus lead to increased creativity. Glutamate excitotoxicity is important in epileptogenesis, common in creative individuals.

Creative individuals had reduced dopaminergic, morphinergic and noradrenergic transmission, but they had increased serotonergic, strychninergic and nicotinergic transmission. Nicotine promotes cholinergic transmission. Increased cholinergic transmission in the cerebral cortex could contribute to increased memory, intelligence and creativity. Strychnine levels are increased in creative individuals. The blocking of glycinergic inhibitory transmission may lead to increased creativity. Both nicotine and strychnine are CNS stimulants.

The schizoid neurotransmitter pattern of reduced dopamine, noradrenaline and morphine and increased serotonin, strychnine and nicotine is seen in creative individuals and could be predisposed to its 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 that the initial abnormality in schizophrenia involves a hypodopaminergic state

and the low dopamine levels now observed agrees with this. Nicotine by interacting with nicotine 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 serotonergic activity and reduced noradrenergic outflow from locus coeruleus reported earlier in schizophrenia agrees with our finding of elevated serotonin and reduced noradrenaline levels. A schizophreniform neurotransmitter pattern contributes to the development of human creativity. Inhibition of $\text{Na}^+ - \text{K}^+$ ATPase can also result in defective neuronal membrane repolarisation and a paroxysmal depolarization shift resulting in epileptogenesis. Temporal lobe epileptic phenomena are common in creative individuals.

Archaeal Digoxin and Hemispheric Dominance in Relation to Family Bonding Behaviour

The archaeaon related organelle - steroidelle, neurotransminoid and vitaminocyte contribute to hemispheric dominance. The neurotransmitter patterns of reduced dopamine, morphine and noradrenaline and increased serotonin, strychnine and nicotine is associated with right hemispheric dominance. Right hemispheric dominant individuals may have an increased predilection for creative tendencies. Right hemispheric perception and memory is of the telescopic form, where you see the wood as a whole but not the discrete trees. The right hemisphere is concerned with intuition. Creative pursuits are intuitive and impulsive. There is no logic in creative pursuits. The right hemisphere is also the site for perception of music, dancing and painting pursuits. It is the seat of geometric constructions. This all contributes to creativity. Left hemispheric dominant individuals have reduced digoxin levels, increased levels of dopamine, noradrenaline and morphine and reduced levels of strychnine, nicotine and serotonin. These neurotransmitter patterns and hypodigoxinemia could be related to lack of creativity in non-creative individuals.

References

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