Chapter 5

Neurology of Family Bonding Behaviour

Introduction

Archaeal metabolonomics and synthesis of endogenous membrane Na^+-K^+ ATPase inhibitor digoxin are involved in bonding behaviour. The endogenous opioid peptides are involved in the phenomena of mammalian separation distress. The isolation or separation call, sometimes called the distress vocalization, is the most prominent and reproducible aspect of the separation response. In rats, infant distress vocalizations are most potently reduced by morphine and this effect is reversible with naloxone. Separation distress is also attenuated in dogs and non-human primates when opiates are administered.

In addition to separation distress vocalizations, other behaviors used as indicators of social cohesion and attachment are known to be affected by opioids and opiates. Monkey social grooming and the seeking of close social contact and rat social play are other examples of such behaviors. A reduction in central nervous system opioid activity is most often associated with emotional fluctuations that represent more social neediness and/or diminished social support and comfort. Recently it was proposed that the endogenous opioid system serves as a proximate reward mechanism for kin selection. The kin selection theory holds that individuals behave differently towards conspecifics who are genetically related. Proximate mechanisms are postulated to help the individual with discrimination of what is good or bad for him. Opioids are now known to be involved in reinforcement mediation especially when social bonding and emotion are involved. Kin interaction is an adaptive condition which is reinforced by endogenous opioid release.

Endogenous morphine synthesis has been demonstrated in the mammalian brain from the neutral amino acid, tyrosine. Endogenous digoxin which functions as a regulator of membrane Na^+-K^+ ATPase have also been demonstrated in the human brain. Studies from our laboratory have demonstrated the synthesis of

endogenous digoxin by the isoprenoid pathway. Digoxin can regulate the neuronal membrane transport of neutral amino acids - tyrosine and tryptophan. Therefore it is plausible that endogenous digoxin may regulate morphine synthesis. The present paper deals with changes in the isoprenoid pathway related cascade in individuals with contrasting familial affection and bonding behaviour. Since digoxin can regulate multiple neurotransmitter systems, it could also play a role in the genesis of hemispheric dominance. Therefore the isoprenoid pathway related cascade and digoxin synthesis was also assessed in individuals with differing hemispheric dominance to find out the role of hemispheric dominance in familial bonding behaviour.

Results

(1) The results showed that people who tended to have increased familial bonding had decreased HMG CoA reductase activity and serum digoxin as well as increased RBC Na^+-K^+ ATPase activity and serum magnesium levels. The results showed that people who tended to have decreased familial bonding had increased HMG CoA reductase activity and serum digoxin levels with reduced RBC membrane RBC Na^+-K^+ ATPase activity and serum magnesium levels.

(2) The results showed that people who tended to tended to have increased familial bonding had increased levels of tyrosine and its catabolites - dopamine, noradrenaline, morphine and reduced levels of tryptophan and its catabolites - serotonin, quinolinic acid, strychnine and nicotine. The results showed that people who tended to have decreased familial bonding had decreased levels of tyrosine and its catabolites - dopamine, noradrenaline, morphine and increased levels of tryptophan and its catabolites - serotonin, quinolinic acid, strychnine and nicotine.

(3) 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.

Discussion

Archaeal Digoxin and Membrane Na^+-K^+ ATPase Inhibition in Relation to Family Bonding Behaviour

The archaeaon steroidelle DXP pathway and the upregulated pentose phosphate pathway contribute to digoxin synthesis. The results showed that people who tended to have increased familial bonding had decreased digoxin synthesis and increased membrane Na^+-K^+ ATPase activity with increased serum magnesium levels. The low levels of digoxin could be due to its reduced synthesis. Studies from our laboratory have demonstrated the synthesis of endogenous digoxin by the isoprenoid pathway. Low levels of digoxin can stimulate membrane Na^+-K^+ ATPase activity. Membrane Na^+-K^+ ATPase stimulation can lead to an increase in intracellular magnesium and a reduction in intracellular calcium.

Archaeal Digoxin and Regulation of Neurotransmitter Synthesis and Function in Relation to Family Bonding Behaviour

The archaeaon neurotransminoid shikimic acid pathway contributes to tryptophan and tyrosine synthesis and catabolism generating neurotransmitters and neuroactive alkaloids. The low level of digoxin is responsible for the increased neuronal tyrosine load and reduced neuronal tryptophan load in these groups of patients. Digoxin promotes neutral amino acid tryptophan transport over tyrosine. The individuals with increased family bonding had elevated levels of tyrosine catabolites - dopamine, noradrenaline and morphine. Previous studies have demonstrated synthesis of endogenous morphine from tyrosine. Dopamine and morphine are concerned with bonding behaviour. Therefore elevated level of dopamine and morphine contributes to increased familial bonding and stable families. The individuals with increased family bonding had decreased levels of tryptophan catabolites - serotonin, strychnine and nicotine. Studies from our laboratory have demonstrated the synthesis of endogenous strychnine and nicotine from tryptophan. An element of obsessive neurosis is associated with bonding behaviour. Serotonin depletion is associated with obsession. The low level of serotonin consequent to its reduced synthesis from tryptophan contributes to the obsessive features in these groups of individuals. The reduced synthesis of strychnine and nicotine is also significant. Strychnine blocks the glycinergic inhibitory transmission in the brain. Reduced glycinergic inhibitory transmission can probably lead to increased familial bonding. This has not been reported before. Also, there is decreased synthesis of nicotine which promotes cholinergic transmission. Reduced cholinergic transmission could also be associated with this behavioural pattern.

In the presence of hypermagnesemia, the Mg block on the NMDA receptor is strengthened leading to reduced NMDA transmission. The decreased presynaptic neuronal Ca can produce decreased cyclic AMP dependent

phosphorylation of synapsins resulting in decreased neurotransmitter release into the synaptic junction and vesicular recycling. Decreased intracellular Ca^{++} in the post synaptic neuron can also inhibit the Ca^{++} dependent NMDA signal transduction. The plasma membrane neurotransmitter transporter (on the surface of the glial cell and presynaptic neuron) is coupled to a Na^{+} gradient which is stimulated by the activation 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 membrane Na^{+}-K^{+} ATPase can inhibit glutamatergic transmission. The low levels of quinolinic acid, strychnine and serotonin can also contribute to NMDA excitotoxicity. Quinolinic acid, strychnine and serotonin are also positive modulators of the NMDA receptor. Strychnine displaces glycine from its binding sites arid 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. Decreased glutamatergic transmission can lead to increased familial bonding. Decreased cholinergic transmission is also associated with increased familial bonding as noted from the study. Familial bonding is more common with people having a normal IQ than in those with intellectual excellence consequent to increased glutamatergic and cholinergic transmission. Glutamatergic and cholinergic transmission is associated with memory and intelligence.

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 elevated dopamine, morphine and noradrenaline and reduced serotonin, strychnine and nicotine is associated with left hemispheric dominance. Left hemispheric dominant individuals may have an increased

predilection for familial bonding. Right hemispheric dominant individuals tend to be detached and unaffectionate with less family bonding. This is because of the elevated digoxin synthesis and reduced levels of dopamine and morphine associated with bonding behaviour in right hemispheric dominant individuals. Hypothalamic archaeal digoxin and hemispheric dominance may regulate bonding behaviour.

References

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