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DEVELOPMENTAL VITAMIN D DEFICIENCY (DVD) AND BRAIN DOPAMINE ONTOGENY

D. Eyles[1], X. Cui[2], M. Pelekanos[3], J. Kesby[3], T. Burne[1], J. McGrath[1]

[1]QCMHR, [2]Queensland Brain Institute, [3]University of Queensland, Brisbane, Australia

Our group has pioneered research indicating that Developmental vitamin D (DVD) deficiency (a candidate risk factor for schizophrenia) alters both brain development and function. We have convergent evidence indicating a disturbance in dopamine signalling in this model. 1stly the superior colliculus (the proto-basal ganglia) is the initial site where the vitamin D receptor is expressed in foetal brain; 2ndly we show a reduction in Catechol-O-methyl transferase (a major metabolic enzyme for dopamine) in these foetal brains; 3rdly dopamine metabolites in the DVD deplete neonatal brain reflect this enzymatic change. When we allow these animals to mature under vitamin D normal conditions we repeatedly observe alterations in both spontaneous and psychomimetic enhanced locomotion. Consistent with the theme of persistent changes in dopamine signalling in this model we now present new data showing that dopamine transporter density and/or affinity are altered in DVD deplete female offspring whilst DA 1 receptor density and dopamine cell number are reduced in DVD deplete male offspring (all $P < 0.05$ $n > 8$).
Our most recent studies indicate that Nurr-1, a nuclear transcription regulator important in both bone and dopamine neuron development and survival may be a molecular mediator of these processes. Nurr-1 is upregulated by parathyroid hormone (PTH). PTH levels are 2-3 fold greater in vitamin D deficient Dams across gestation. Most importantly we have just shown that Nurr-1 is dose-dependently upregulated by parathyroid hormone (PTH) in a neuroblastoma cell line.

Conclusions: Our findings strongly suggest that vitamin D directly (or indirectly via PTH) mediates dopamine neuron development

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