Potential Role of Cholesterol in the Migration of Neurons Containing Gonadotropin-Releasing Hormone

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Introduction

- Signaling by Sonic Hedgehog (Shh) is instrumental in the development of midline facial and forebrain structures
- Signaling by Shh can be dependent upon conjugation with cholesterol. Structural abnormalities related to cholesterol depletion may be a result of a failure of Shh signaling
- Disorders resulting in cholesterol depletion are often characterized in part by developmental malformations, including holoprosencephaly
- Neurons that synthesize gonadotropin releasing hormone (GnRH; controls the reproductive axis) originate in the nasal compartment and migrate into the brain along a route that may depend upon proper Shh signaling
- The current study was conducted to assess whether cholesterol-depleted enzyme Dhcr24-/- mice would affect the unique migration of GnRH neurons as they migrate to the brain

Methods

Heads from fetuses at embryonic day 16 & 18 were immersion fixed. Dhcr24 knockout (-/-) and heterozygous (+/-) mice were used and neurons containing GnRH were labeled via immunocytochemistry. Immunoreactive neurons were counted in the brain versus nasal compartment.

Conclusions

- Cholesterol depletion produced mice with fewer GnRH neurons in the nasal compartment and more in the forebrain
- Cholesterol depletion did not influence the total number of GnRH neurons. Thus, migration out of the nasal compartment may have increased
- Fibers that guide GnRH neurons were fully intact and there was no evidence of holoprosencephaly or midline defects
- Alternative roles for cholesterol in signaling during development may be based on its utilization in plasma membrane lipid rafts or in signaling through alternative and selective pathways
- These results suggest that in the GnRH migratory pathway, signaling to GnRH neurons that may require cholesterol may play a role in a normal inhibition of the migration of GnRH neurons

Future Analyses

- Finer analysis of GnRH neuron location in brain regions
- Additional analysis of tissue condition between KO and control sections

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References


