Low growth hormone levels linked to memory defects later in life can be prevented with early growth hormone treatment

Scientists have shown that early growth hormone supplementation in rats with growth hormone deficiency can prevent defects in memory developing later in adulthood. The study, published in the *Journal of Endocrinology* is the first to show that memory defects in adults as a result of growth hormone deficiency arising in childhood can be prevented by growth hormone treatment during adolescence.

Growth hormone levels start off low in early life, and peak just before puberty, after which they gradually decline with increasing age. Growth hormone deficiency can be present from birth, or arise during childhood or adulthood as a result of various disorders. Growth hormone deficiency originating in childhood is treated with growth hormone supplementation to increase body size (mainly height) during adolescence. Until now, it has not been clear if or how this treatment directly affects memory in adulthood, or whether it can prevent learning and memory deficits commonly observed in adults with childhood onset growth hormone deficiency.

Professor Michelle Nicolle and colleagues from Wake Forest University School of Medicine and The Reynolds Oklahoma Center on Aging (University of Oklahoma Health Sciences Center), USA studied rats with a genetic mutation that leads them to produce significantly decreased levels of growth hormone, as a model for early-onset growth hormone deficiency. They assessed the animals’ performance in a water maze test designed to measure spatial memory, at either 8 or 18 months of age. To mimic adult-onset growth hormone deficiency, one group was treated with growth hormone for a specific period during adolescence (4-14 weeks old) only; to mimic childhood-onset growth hormone deficiency, one group was treated with a saline control; and a third group was treated with growth hormone from 4 weeks old throughout their lifespan. The above groups were compared to a control group with normal growth hormone levels.

At 8 months old there was no difference between the groups in performance in the water maze task. However, at 18 months of age, the group with childhood-onset growth hormone deficiency performed significantly poorer in the task than all other groups, indicating poorer spatial learning. This suggests that the growth hormone supplementation during adolescence prevented the age-related deficiencies in learning and memory seen in the childhood-onset group. The group treated with growth hormone during puberty (adult-onset) performed equally
well as the group treated with growth hormone into adulthood, indicating no further effect of growth hormone treatment on spatial memory beyond adolescence.

These results show that, in rats, memory impairment in adults as a result of growth hormone deficiency arising in childhood can be reduced or prevented by early growth hormone supplementation. This study highlights the potentially significant role that growth hormone plays in memory function and the importance of further studies with larger sample sizes to determine the mechanisms underlying the effects of growth hormone treatment during adolescence on brain maturation.

**Researcher Professor Michelle Nicolle said:**

*"We carried out this study to investigate the effect of growth hormone supplementation during adolescence on memory function in adults. Our results show that in rats, growth hormone deficiency during adolescence leads to learning and memory deficits in adults. Furthermore, treating growth hormone deficiency by supplementing with growth hormone during puberty prevents this deleterious effect on brain function later in life. This shows that growth hormone replacement during adolescence is important not only for increasing growth but also for brain maturation. This may have important implications for the treatment of patients with growth hormone deficiency and is an aspect of therapy that needs to be taken into account in future clinical growth hormone studies in this key age group."*

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**Notes for editors:**
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ABSTRACT

Early-onset GH deficiency results in spatial memory impairment in mid-life and is prevented by GH supplementation

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GH levels increase to high concentrations immediately before puberty then progressively decline with age. GH deficiency (GHD) originating in childhood is treated with GH supplementation to foster somatic development during adolescence. It is not clear if or how early GH replacement affects memory in adulthood, or whether it can prevent the cognitive deficits commonly observed in adults with childhood-onset GHD. Rats homozygous for the Dw-4 mutation (dwarf) do not exhibit the normal increase in GH at 4 weeks of age when GH levels normally rise and are used to model childhood or early-onset GHD (EOGHD). One group of these rats was injected with GH from 4 to 14 weeks of age to model GH supplementation during adolescence with GHD beginning in adulthood (adult-onset GHD; AOGHD). Another group received GH from 4 weeks throughout the lifespan to model normal lifespan GH (GH-replete). Age-matched, Dw-4 heterozygous rats (HZ) do not express the dwarf phenotype and were used as controls. At 8 and 18 months of age, spatial learning in the water maze was assessed. At 8 months of age all experimental groups were equally proficient. However, at 18 months of age, the EOGHD group had poor spatial learning compared to the AOGHD, GH-replete, and HZ groups. Our data indicate that GHD during adolescence has negative effects on learning and memory that emerge by middle-age unless prevented by GH supplementation.