



# Growth hormone increases ALAS2, the rate-limiting enzyme of Hbb in male rat hippocampus

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## ➤ Background

Growth hormone (GH) has neuroprotective properties. Hypophysectomy (hx) completely abolishes circulating endocrine GH and decreases the expression of neuronal (non-erythrocyte) haemoglobin beta chain (Hbb) in the hippocampus. GH infusions (GH inf) and injections (GH x 2) robustly increase the levels of Hbb approximately 2-4-fold in male rat hippocampus<sup>1</sup>.

Hbb protein is present in mitochondria of the mammalian brain and it is thought that the expression is linked to neuroprotective potential against insults<sup>2,3</sup>.

To investigate the signalling pathway between GH and Hbb, we investigated the transcript levels of delta-aminolevulinate synthase 2 (ALAS2), a mitochondria specific rate-limiting enzyme of the heme synthesis, in the hippocampus of male rats.

To further study the signalling pathways involved in neuroprotection, we also included delta-aminolevulinate synthase 1 (ALAS1) and hypoxia-inducible factor 1-alpha (HIF1a) in male rat hippocampus.

## ➤ Material & Method

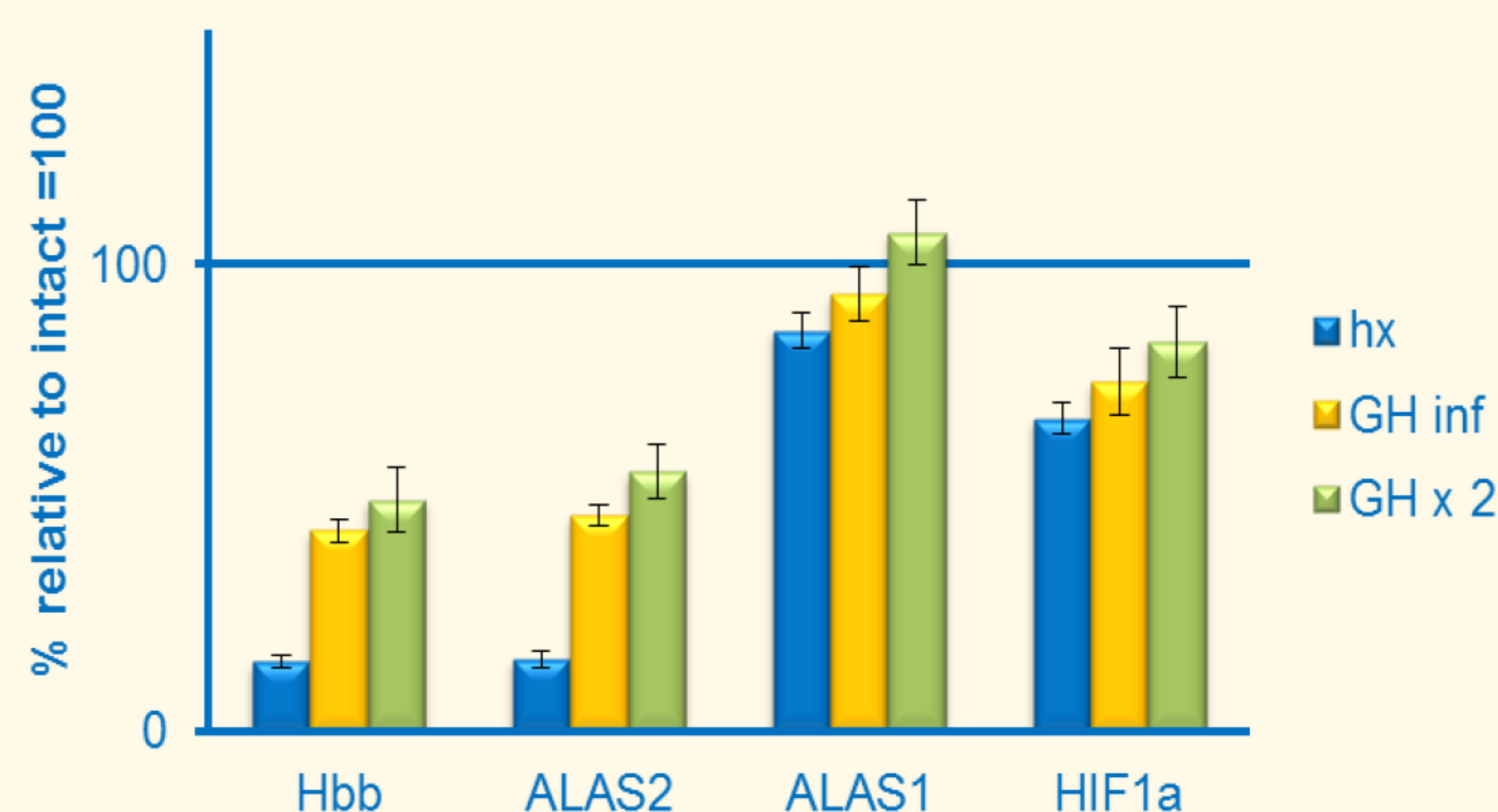
Seven days of GH administration as a continuous infusion (GH inf) or as two daily injections (GH x 2) in hx male rats aged 50 days at the beginning of the experiment.

The expression of Hbb, ALAS2, ALAS1 and HIF1a in response to GH administration in the hippocampus were assessed by Q-RT-PCR using TaqMan assays.

## ➤ References

1. Walser, M., et al., J Endocrinol, 2014. 222(2): p. 181-90.
2. Horng, L.Y., et al., British Journal of Pharmacology, 2015. 172(19): p. 4741-4756.
3. Shephard, F., et al., Mitochondrion, 2014. 14(1): p. 64-72.

## ➤ Results of Hbb, ALAS2, ALAS1 and HIF1a in male rat hippocampus



Levels of neuronal haemoglobin beta (Hbb), delta-aminolevulinate synthase 2 (ALAS2), delta-aminolevulinate synthase 1 (ALAS1) and hypoxia-inducible factor 1-alpha (HIF1a) in hippocampus as analysed by Q-RT-PCR.

Intact levels (non hx) = 100%. Data are presented as mean ± SEM. (n=5)

There are significant differences between hx:

- versus Hbb and ALAS2 for both GH inf and GH x 2 (p<0.001)
- versus ALAS1 for GH x 2 (p=0.028)

Hypophysectomy decreased Hbb and ALAS2 to a greater extent than ALAS1 and HIF1a. The levels of all four transcripts had a tendency to normalise in both treatment groups with GH x 2 having a higher effect.

## ➤ Conclusion

The robust response on Hbb after GH administration in the hippocampus of male rats may have relevance for a neuroprotective action of GH. Administration of GH affects Hbb abundance probably by increasing the level of ALAS2.

Although ALAS1 and HIF1a are less robustly affected by GH, they are both affected in the same manner, with GH injections x 2 giving higher response. This supports the notion that infusions/injections may have different effect of magnitude on the neuroprotective capacity of male hippocampi.

