

Safety of Head Down Tilt 15° (HDT15°) in experimental intracerebral haemorrhage: relevance for gravity-based modulation of collaterals in acute stroke

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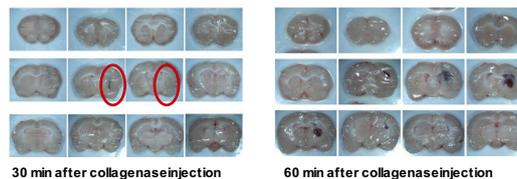
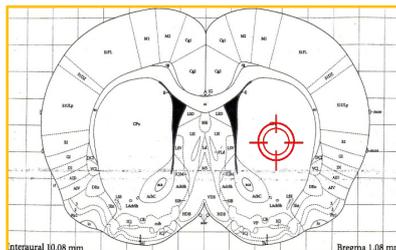
Background

Intracranial collaterals are dynamically recruited after arterial occlusion and are emerging as a strong determinant of tissue outcome in both human and experimental ischemic stroke. Head down tilt 15° (HDT15°) has been shown to be a very effective and safe “collateral therapeutic” in an experimental ischemic stroke model, applied with a therapeutic time window of 30 min. The aim of the present study was to investigate the safety of HDT15° in experimental intracerebral haemorrhage (ICH), which is a compulsory requirement for the translational development of HDT15° as a hyperacute collateral therapeutic for pre-hospital application in suspected ischemic stroke.

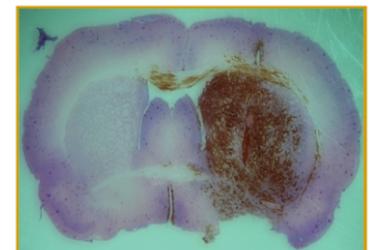
Methods

Intracerebral haemorrhage was produced by stereotaxic intrastriatal injection of collagenase (type IA-S; 0.4 CDU) in adult male Wistar rats (n=64). A **randomized non-inferiority trial design (non-inferiority limit 15%)** was used to randomize rats to HDT15° for 60 minutes or usual flat body position. HDT15° was applied from 60 to 120 minutes after collagenase injection, which corresponds to a time window of hematoma expansion in this model.

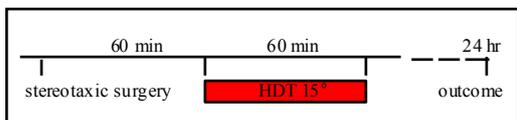
Primary outcome was hematoma expansion at 24 hours, secondary outcomes were mortality at 24 hours and neurobehaviour assessed by Garcia sensorimotor neuroscore.



hematoma volume expansion
(30 min, 60 min, 120 min, 24 hours)



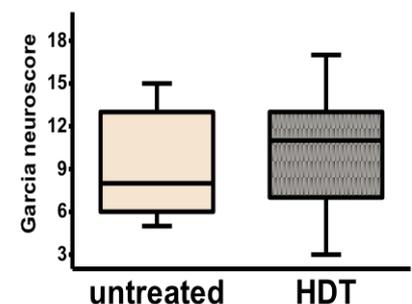
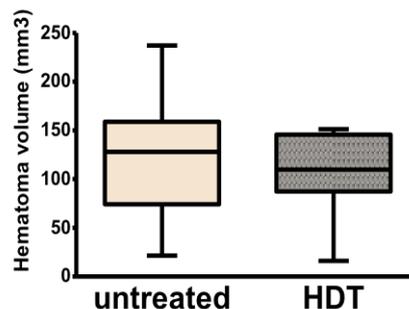
24 hours after collagenase injection



study design (randomized non-inferiority trial)

- 32 animals per group (15% non-inferiority limit; 80% power, 5% alpha)
- **primary outcome:** hematoma volume at 24 hours
- **secondary outcomes:** mortality, neurobehaviour

sample size estimate



Results

HDT15° achieved the specified criteria for non-inferiority in hematoma volume (HDT15° 97±17 mm³ versus flat position 116±23 mm³). Mortality at 24 hours was identical in the two groups (7 animals in HDT15°; 7 animals in flat position). Neurobehaviour showed no difference between flat positioning and HDT15°.

Conclusions

Our findings indicate that HDT15° does not worsen hematoma expansion if applied in the hyperacute phase of experimental intracerebral haemorrhage.

Further research is needed to effectively develop a HDT15°-based gravitational therapy for enhancing cerebral collateral flow in suspected hyperacute ischemic stroke.