Pulling the Brakes — "Catch Down Growth"
A phenomenon for achieving mid parental height centile after acquired, all-cause brain injury

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Introduction Objectives

- **Of any pituitary dysfunction following brain injury, growth hormone (GH) deficiency (GHD) is the most prevalent.**
- **The cut-off point for defining GHD has been placed at 7 ng/mL, representing optimum test performance.**
- **We hypothesised this cut-off may be set too low for genetically taller children with an acquired brain injury, notably brain tumours, who demonstrate severe growth failure but repeatedly fail to meet diagnostic thresholds for GH replacement until several centiles have been crossed downward over time; this treatment delay may ultimately compromise metabolic status and post-injury wellbeing.**
- **We reviewed the possibility that this cut-off, and its undifferentiated applicability to a broad variety of taller children with clear longitudinal growth failure, requires re-consideration for this cohort, according to their midparental height (MPH) and body mass index (BMI)**

Methods

We reviewed retrospectively the parental heights, longitudinal growth records and charts of 50 children diagnosed with a brain tumour (47) or traumatic brain injury (3) and noted, at intervals, height, weight, Tanner stage and peak GH (pkGH) to dynamic provocation at first onset of growth failure and at any subsequent re-test for persistent growth failure. BMI, BMI SDS, height SDS and midparental target height SDS (MPHSDS) were calculated.

Patients were categorised into three respective groups according to how many times (once, twice or thrice) they required testing for persistent growth failure before meeting diagnostic criteria for GH deficiency (GHD) for the first time. Data are shown as Mean and 95% C.I. and one-way ANOVA was used for between cohort comparisons.

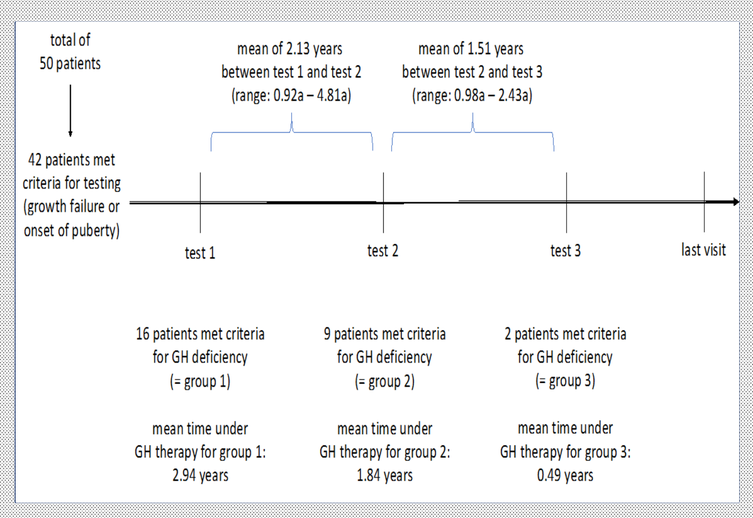

Figure 1: Patient Cohort - 50 patients undergoing one or more dynamic GH provocation tests for persistent decline in height velocity before meeting diagnostic criteria for GHD

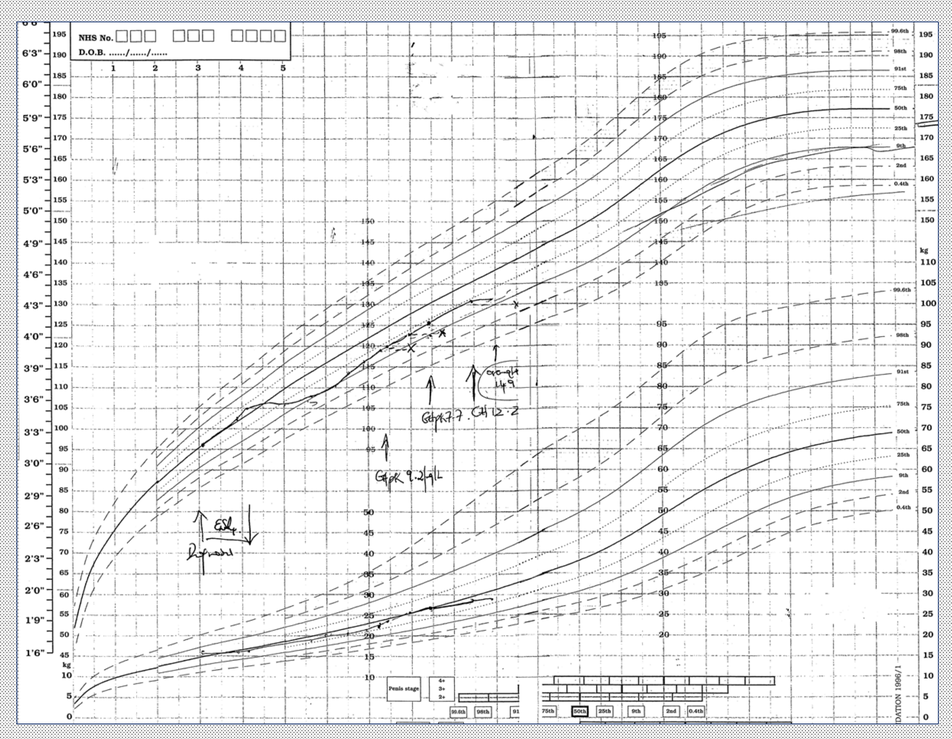

Figure 2: Representative growth chart of a patient failing GH tests thrice

At the time of this patient's brain tumour diagnosis, his height SDS was 0.39 and his midparental target height SDS was -0.41. At his first GH test, 3.52 years later, his growth had decelerated to a height SDS of -0.76 and he remained prepubertal .

However, with a pkGH of 9.2 ng/mL, he did not yet meet diagnostic criteria for GHD. Neither did he at his second test (pkGH 7.7 ng/mL) 0.92 years later, when height SDS was still -0.77. Even at his third GH test (0.98 years later), he did not meet criteria for GHD (pkGH 12.7ng/ml). His height SDS was still -0.77.

Results

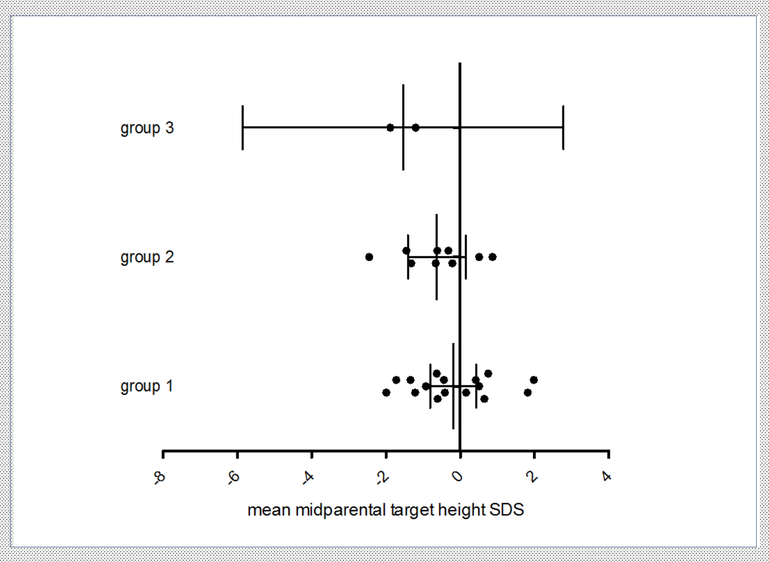

Figure 3: Mean midparental target height SDS by group

The (midparental) target height SDS for all three patient groups was not significantly different from the norm and one-way ANOVA revealed no difference between groups.

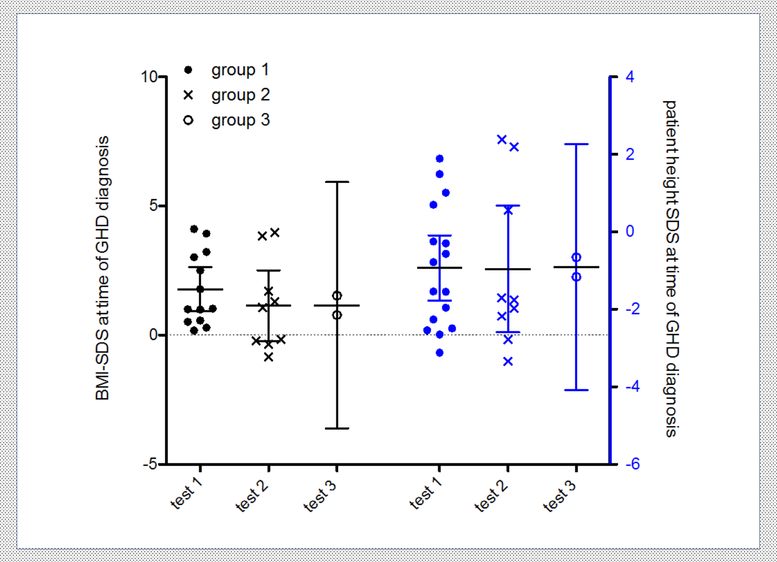

Figure 4: Mean patient BMI-SDS and height SDS by group

Children with growth failure diagnosed as GHD (pkGH < 7ng/mL) at first test, (group 1) had a slightly higher BMI-SDS than those undergoing repeated testing (groups 2 and 3). In all groups, children had reached a similar height SDS when they eventually met diagnostic criteria for GH-deficiency.

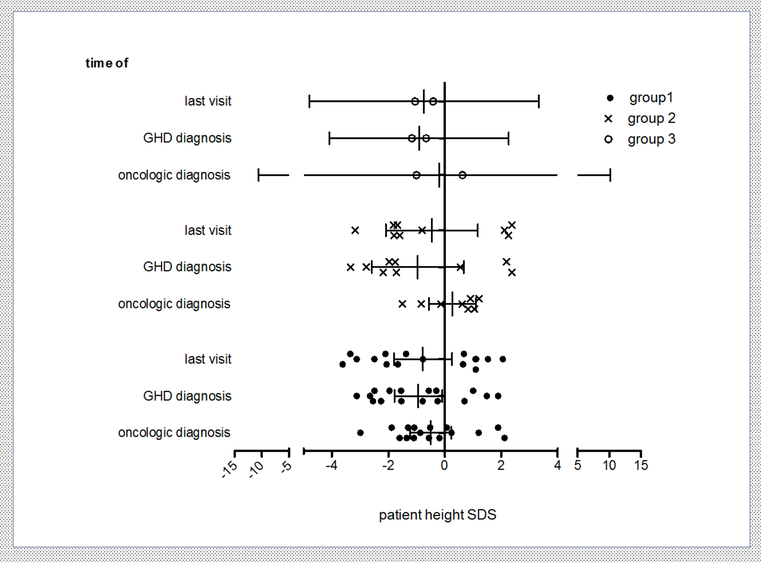

Figure 5: Patient height SDS at the time of brain tumour diagnosis, GHD diagnosis and latest visit

All children showed a decrement in height SDS between their tumour diagnosis and eventual diagnosis of GH-deficiency, which was greatest in groups 2 and 3. This decrement was only partially reversible with GH replacement therapy over a mean treatment time of 2.9y (group 1), 1.8y (group 2) and 0.5y (group 3), respectively.

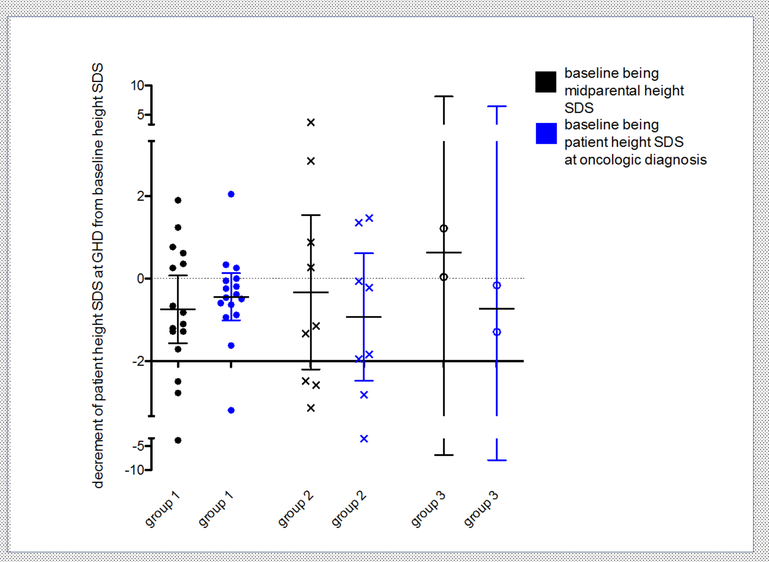

Figure 6: Decrement of patient height SDS at GHD diagnosis either from mean parental height SDS (black) or from height SDS at oncologic diagnosis (blue)

Patients diagnosed first (group 1) had a greater decrement from their mean parental height SDS than those who took longer to diagnose (group 2 and 3). In contrast, group 2 and 3, showed a higher decrement from their height SDS at the time of oncologic diagnosis than group 1.

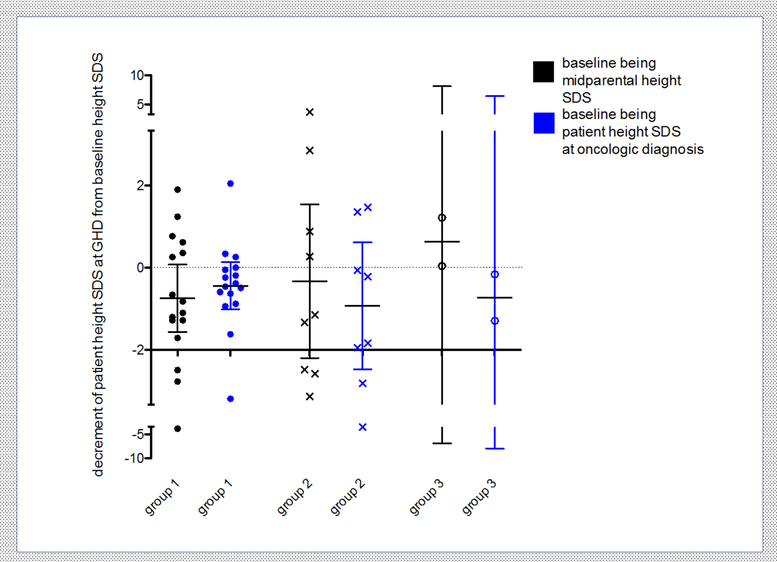

Figure 7: Decrement of patient current height SDS either from midparental height SDS (black) or from height SDS at oncologic diagnosis (blue)

At the time of their last follow-up (2.9y, 1.8y and 0.5y, respectively, after start of GH therapy), only patients who had been diagnosed GH deficient at their first GH test showed a height SDS lower than their midparental target height. Patients that took longer to diagnose as GHD (group 2 and 3) had a mean height SDS above their midparental height SDS. However, it was still below their initial height SDS at oncologic diagnosis.

CONCLUSIONS

Our data before GH treatment do not suggest that a midparental target height above average or an increment of BMI-SDS impairs diagnostic validity of current pkGH.

Instead this may represent a physiological 'catch-down growth' towards MPHSDS, not requiring immediate GH treatment.

Severe GHD may ensue, which requires continuous monitoring after recanalization into the mid-parental centile and at the onset of puberty.

A post-treatment review is still required to ensure that these children achieve their innate growth potential without compromise.

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Growth and syndromes (to include Turner syndrome)

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