IN VIVO CHARACTERISATION OF SKELETAL MUSCLE METABOLISM IN GROWTH HORMONE DEFICIENT ADULTS USING ^{31}P MAGNETIC RESONANCE SPECTROSCOPY

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Background

- Adults with growth hormone deficiency (GHD) experience fatigue and reduced energy levels[1]. Although these symptoms improve with GH replacement, their pathophysiology is poorly understood.
- Fatigue can be classified as central or peripheral in origin.
- GH parameters have been reported to be associated with skeletal muscle mitochondrial capacity in adult men[2].
- Phosphorus-31 magnetic resonance spectroscopy is a non-invasive tool used to assess skeletal muscle mitochondrial oxidative capacity and pH recovery (proton handling) *in vivo* following exercise.
- There have been no detailed investigations into the role of GH in functional muscle metabolism and its link with fatigue. Phosphorus-31 magnetic resonance spectroscopy is a technique that may provide insight into skeletal muscle pathophysiology in the GH-deficient state.

Aims

- To characterise and compare *in vivo* skeletal muscle metabolism in **untreated GHD adults** with **treated GHD adults** and **healthy controls.**
- To compare perception of fatigue using specific domains within QoL-AGHDA, a GHD specific well-being assessment tool, across the 3 groups.

Untreated GHD | Treated GHD | Healthy controls

Methods

- Cross-sectional study.
- 22 untreated GHD, 23 treated GHD & 20 healthy controls (matched for age, gender and physical activity) were recruited.
- All subjects underwent ^{31}P MRS, biochemical, auxological and body composition assessment. They also completed Qol-AGHDA questionnaires.
- REC approval obtained.
- Statistical tests as described (Minitab v16).

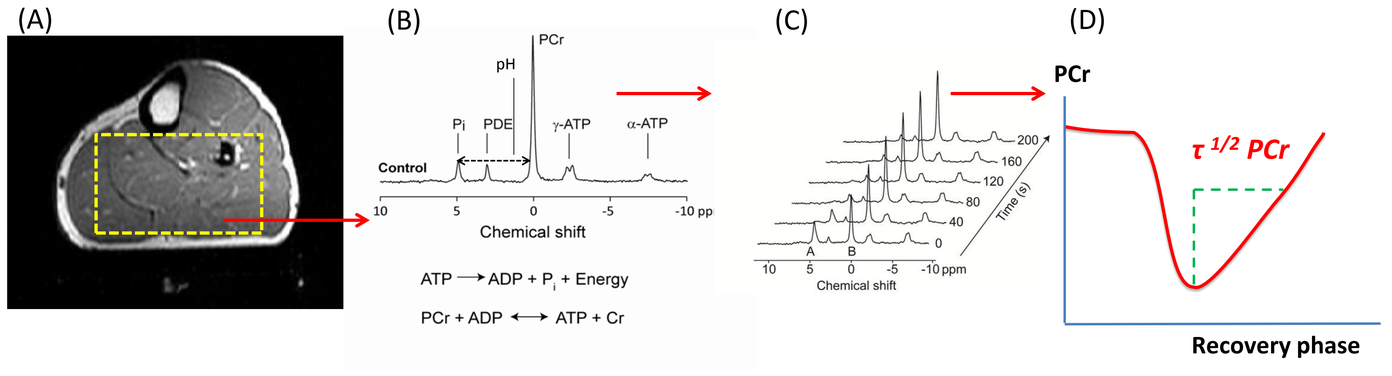

Fig 1: The phosphorus spectrum (B) from the gastro-soleus compartment (A) showing relative concentrations of (Pi)inorganic phosphate,(PCr)phosphocreatine and ATP. Serial spectra (C) were acquired following dynamic exercise during the recovery phase. Exponential fits of the recovery data (D) were made to estimate half-times for recovery to equilibrium ($\tau^{1/2}$PCr), a measure of mitochondrial oxidative phosphorylation.

Results

Mean ±SD	OFF GH	ON GH	Controls	P value
Total No	22	23	20	
Age	27.85±9.34	29.76±10.07	31.05±7.93	0.54
Sex ratio	59.2% males	65.2% males	60% males	
Aetiology of GHD:				
MPHD / Isolated GHD	17/5	20/3	NA	0.40
Childhood /Adult onset	18/4	15/8	NA	0.21
Surgery	14	9	NA	0.48
Radiotherapy	16	8	NA	0.48
Chemotherapy	6	1	NA	0.48
Endocrine parameters:				
IGF-1 (nmol/L)	14.0±11.2	38.1±19.9	30.7±9.5	<0.001
Thyroxine fT4 (pmol/L)	18.2±3.7	19.0±3.9	16.3±2.1	0.09
Testosterone (nmol/L)	20.6±9.5	15.9±7.9	20.7±5.5	0.25
25OHD (nmol/L)	57.9±34.42	53.9±20.2	44.2±29.4	0.42

Table 1: above shows the subject characteristics including aetiology and endocrine profiles

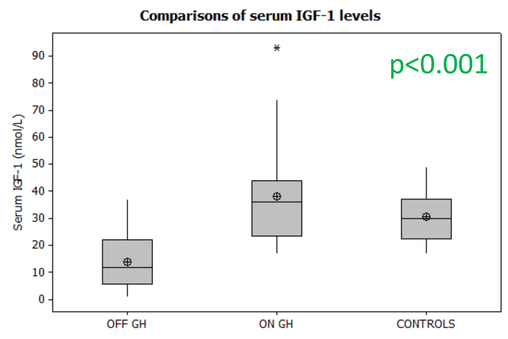

Fig 3: Comparison of serum IGF-1 levels across the three groups showing lower levels in the untreated GHD group (ANOVA)

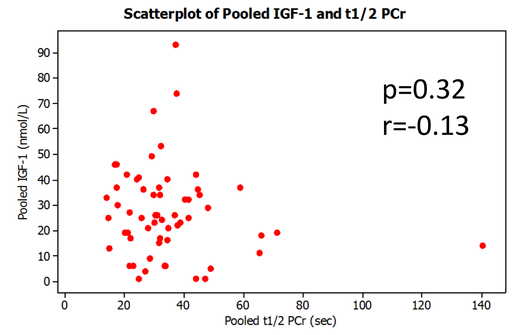

Fig 4: Regression for pooled IGF-1 and pooled $\tau^{1/2}$ PCr showing no correlation between IGF-1 and mitochondrial function (Linear regression)

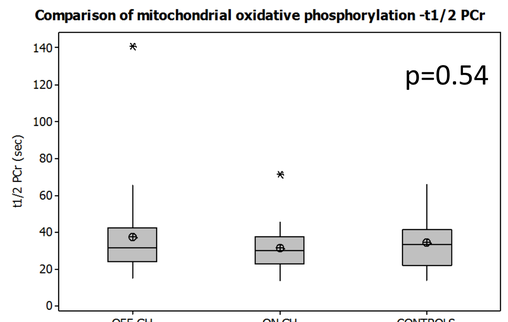

Fig 5: The plot above shows no difference in mitochondrial oxidative function between the 3 groups (ANOVA)

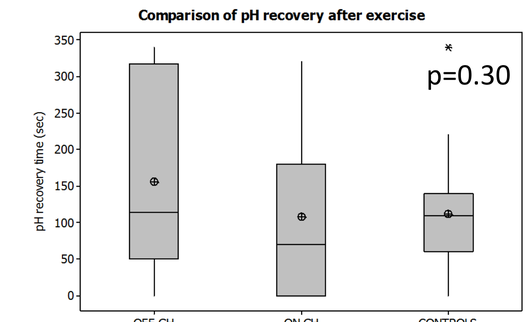

Fig 6: The plot above shows no difference in pH recovery times between the 3 groups (ANOVA)

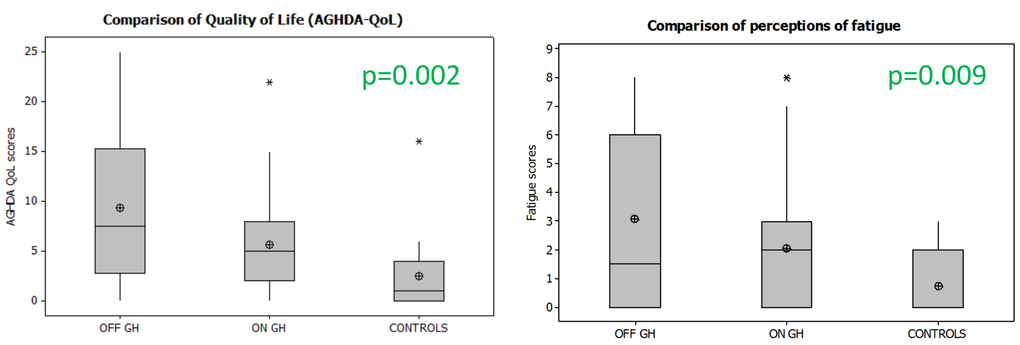

Fig 2: The individual value plots above shows that the highest perception of fatigue (A) and impaired QoL (B) was reported by the untreated GHD group and the least fatigue and normal QoL was reported by the healthy controls (ANOVA)

Conclusions

- We found no evidence to suggest that GH status or IGF-1 modulates skeletal muscle mitochondrial oxidative capacity.
- Although untreated GHD adults experience problematic fatigue compared with treated GHD adults and volunteers, they do not demonstrate any persistent abnormalities in skeletal muscle metabolism (mitochondrial oxidative function nor pH recovery), thereby indicating a likely central component in the pathophysiology of fatigue in GHD.

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References:

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2. Makimura et al, The association of growth hormone parameters with skeletal muscle phosphocreatine recovery in adult men. J Clin Endocrinol Metab, 2011. **96**(3): p. 817-23

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