IMCL is Increased in Adolescent Type 1 Diabetics - comparison with both age matched and adult controls

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Introduction

Controversy exists over whether IMCL levels, measured using ^{1}H spectroscopy, are higher in Type 1 Diabetics (T1D) compared to age matched controls [1,2]. Unlike previous studies [1,2], which used subjects in their late 20s, adolescents were chosen in our study in order to determine if IMCL is increased at an early age in T1D subjects. Sinha et.al. [3] has reported IMCL levels that are lower in lean adolescents compared with adult controls [4], but concluded that a true comparison was not possible due to differences in the methodology. Here we approach this matter by also comparing our IMCL values in adolescents with adult controls.

Method

10 T1D subjects (7 male, 3 female), 9 age matched controls (3 male, 6 female), and 11 adult controls underwent a hyperinsulinaemic euglycaemic clamp and DEXA scan to assess insulin sensitivity corrected for lean body mass (M-LBM).

IMCL measurement:
A ^{1}H spectrum was obtained from a voxel, of cube length 1.5cm, in the soleus muscle of the right leg using PRESS on a Bruker 3.0T scanner. The voxel was positioned to avoid fasciae lines and visible fat. Good shimming on the voxel was obtained by first using FASTMAP [5] on a 6cm cube before shimming the individual voxel. Water suppressed data was acquired with a TE=35ms, TR=5s and 64 averages. The spectra were analysed in jMRUI [6,7] and fitted using the AMARES [8] algorithm and then IMCL was quantified relative to creatine. All statistics were performed in SPSS.

Results

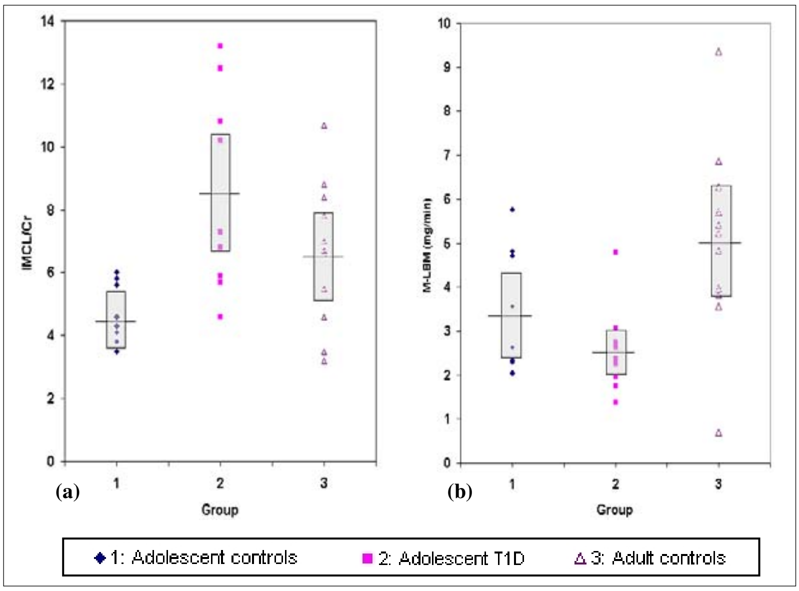

Fig 1. (a) IMCL and (b) M-LBM measurements in adolescent controls and T1D as well as adult controls. Each dot corresponds to one persons data. The horizontal line represents the mean and the vertical bar the ± 2SE. Note that in (a) there are two points superimposed at 3.5 in the control (group 1) and two points at 7.3 in the T1D (group 2).

	Adolescent			Adult
	Controls	**T1D**	**T-test p-value**	**Controls**
IMCL	4.58±0.99	8.43±3.01	0.003	6.62±2.30
M-LBM (mg/min)	3.36±1.41	2.53±0.94	0.063	5.07±2.19
Age (yrs)	16.9±0.90	18.0±3.80	0.391	24.2±3.70

Table 1. Comparison of controls with T1D. Values are means ± SD.

IMCL is significantly higher in the adolescent T1D compared to the age matched controls (Fig 1a, Table 1). The IMCL was also significantly elevated in the adult control group (p=0.024) compared with the adolescent controls. The mean of the T1D was higher than the adults but this increase was not statistically significant. Although the age of the adult controls was young, it was still significantly higher than the T1D (p=0.001).

Figure 1b shows a lower M-LBM value in the T1D (compared to the the adolescent controls), suggesting they are more insulin resistant, but this just fell outside the 5% significance level (Table 1). This we may expect as adolescent controls are known to be insulin resistant (and this is also shown by the decreased M-LBM in the adolescent controls compared with the adults). The T1D were significantly insulin resistant compared with the adults (p=0.003).

Within the diabetic group IMCL correlated significantly with body fat (Spearman's rho, ρ=0.637, p=0.048). In the control group significant correlations were found between M-LBM and exercise (ρ=0.958, p=0.003), M-LBM and IMCL (ρ=-0.917, p=0.001), and IMCL and body fat (ρ=0.667, p=0.050) after the IMCL was adjusted for exercise (as trained athletes have high IMCL, the IMCL values were weighted slightly depending on the amount of vigorous exercise each subject performed per week). Within the adult control group IMCL correlated significantly with M-LBM (ρ=-0.673, p=0.012) and also body fat (ρ=0.691, p=0.009). However, no correlation of M-LBM with exercise was found in the adults, which may be possibly due to the smaller variability in vigorous exercise values found in the adult group.

Within each group there was no significant effect of age, body mass index, gender or weight on IMCL nor M-LBM. However, when collecting the two control groups together (thereby extending the age range), a significant correlation was found between IMCL and age (ρ=0.652, p=0.002).

Conclusion

Results highlight a significant increase in IMCL at an early age in T1D compared with age matched controls (Table 1), with a mean that is above the adults (not statistically significant). IMCL in the adult controls was significantly higher than the adolescent controls (p=0.024). The T1D have a lower M-LBM value (but not statistically significant) than their age matched controls, which we may expect as adolescent controls are insulin resistant. The correlation of M-LBM with exercise is plausible and the correlations of M-LBM with IMCL and IMCL with body fat in the control groups are consistent with previous findings[3,9].

References

[1] Perseghin, G et.al., 2003, A*m J Physiol Endocrinol Metab*, **285**, E1174-E1181.
[2] Bernoider, E et.al., 2005, *J Clin Endo & Metab*, **90**, 5559-5565.
[3] Sinha, R et.al., 2002, *Diabetes*, **51**, 1022-1027.
[4] Krssak, M et.al., 1999, *Diabetologia*, **42**, 113-116.
[5] Gruetter, R, 1993, *MRM*, **29(6)**, 804-811.
[6] Naressi, A et.al., 2001, *MAGMA*, **12**, 141-152.
[7] http://www.mrui.uab.es/mrui/
[8] Vanhamme, L et.al., 1997, *J. Magn. Reson.*, **129**, 35-43.
[9] Machann, J et.al., 2004, *Diabetes Obes. Metab*., **6**, 239-248.

Acknowledgments

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