Localized ^{31}P saturation transfer reveals differences in gastrocnemius and soleus rates of ATP synthesis in-vivo.

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Introduction

We have previously demonstrated that basal muscle energy production is impaired in elderly and diseased subjects (1,2), using ^{31}P saturation-transfer MRS to assess rates of ATP synthesis, *in-vivo*. Given that there are significant differences in function, metabolic activity and the effects of aging and potentially disease between muscle groups (3), it is highly likely that there are muscle-group specific differences in basal ATP synthesis in healthy subjects and in the modulation of energy production by aging/disease. In these experiments we demonstrate that muscle-specific rates of ATP synthesis can be measured at 4T using adiabatic ISIS-localized ^{31}P saturation-transfer MRS, and that there are significant differences in the basal rates of ATP synthesis between the soleus and gastrocnemius muscle groups in healthy subjects.

Methods

All experiments were performed on a 4T Bruker Medspec system. Slice-selective ^{31}P spectra were acquired in 5 subjects using an 8 x 5cm elliptical surface coil positioned underneath the soleus/gastrocnemius muscle complex of the calf. The unidirectional rate of ATP synthesis in either the soleus or gastrocnemius muscle groups was measured by the saturation-transfer technique in conjunction with adiabatic 1D-ISIS localization using a custom-written pulse sequence. The slice of interest for each muscle group (Fig 1) was positioned with reference to gradient-echo scout images obtained with a coplanar ^{1}H surface coil and was selected to contain solely the muscle of interest (gastrocnemius) or have minimal infiltration from other muscle groups (soleus). ^{31}P spectra were acquired with frequency-selective saturation of the γATP peak or with saturation at a downfield frequency equidistant from P_i, using the following parameters: 2.5msec AHP excitation pulse (centered between P_i and γATP), 4msec AFP ISIS pulse, 15sec 'soft' saturation pulse, sweep width = 10kHz, 4096 complex points, effective T_R = 15sec, 32 transients. The T_1 of P_i under conditions of γATP saturation (T_1') was measured in each muscle using a custom adiabatic inversion-recovery sequence (5msec AFP inversion) with 1D-ISIS localization. Fully relaxed 1D-ISIS spectra (T_R = 35sec, 16 transients) were obtained to determine ^{31}P metabolite concentrations, assuming a constant [ATP] of 5.5 μmol/g in both muscle groups (4). The ordering of the experiments was randomized to prevent any effect of the duration of the study on resting metabolic function.

Results

A scout image of the lower leg from one subject is shown in Fig 1; the shaded areas indicate the typical placement of the gastrocnemius (blue) and soleus (red) slices for localized ^{31}P MRS. Representative 1D-ISIS spectra from each slice are shown in Fig 2 – consistent with literature data, the gastrocnemius (blue spectrum) is characterized by slightly higher PCr content and lower P_i, compared to soleus (red spectrum). The data from the saturation-transfer experiment are summarized in Table 1. Although the rate constant for $P_i \rightarrow$ ATP flux (k') is similar between the different muscle groups, the soleus exhibits a significantly higher rate of ATP synthesis (V_{ATP}) than the gastrocnemius, driven by the higher concentration of P_i.

Fig 1.

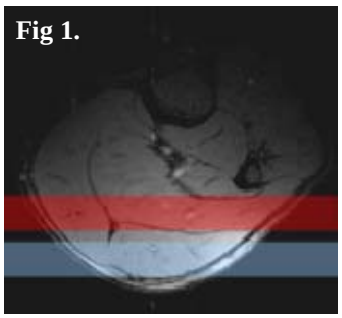

Fig 2.

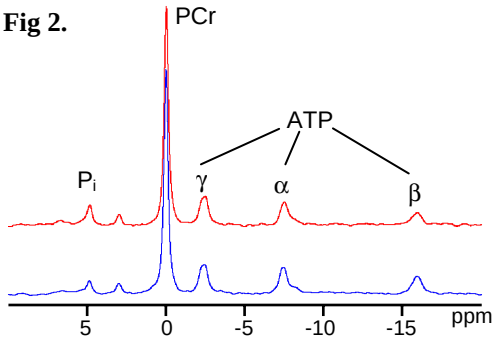

Table 1.

	Gastroc (n = 5)	Soleus (n = 5)
k' (sec^{-1})	0.057 ± 0.012	0.059 ± 0.007
T_1' (sec^{-1})	2.47 ± 0.23	3.90 ± 0.19*
[Pi] (μmol/g)	1.45 ± 0.09	2.35 ± 0.21*
V_{ATP} (μmol/g/min)	4.97 ± 1.08	8.12 ± 0.86*

* $p < 0.05$

Conclusions

Muscle-specific energy production can be measured at 4T using adiabatic ISIS-localized ^{31}P saturation-transfer MRS. Rates of ATP synthesis in two distinct muscle groups can be measured within a reasonable time-frame (< 4 hours). In healthy human muscle the resting rate of ATP synthesis was significantly faster in the soleus than the gastrocnemius, potentially reflecting their differing functional roles: postural (soleus) vs locomotion (gastrocnemius).

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