Immobilization alters mechanical muscle responses and may alter spindle sensitivity in rats.

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Summary

We found that joint contractures due to immobilization alter the muscle's mechanical and sensory response to stretch. Our findings suggest that increased reflex activity in neuromuscular disorders like cerebral palsy and stroke might not only be due to increased spinal excitability but also be due to alterations in muscle properties and spindle sensitivity.

Introduction

Muscle spindles play a crucial role in the stretch reflex. Muscle spindles fire in response to muscle stretch. Muscle spindle firing can be explained by a linear combination of muscle fiber force and its first time-derivative, yank [1]. This suggests that the muscle's mechanical and neural response to stretch are coupled. This is directly relevant to understand the altered response to stretch in neuromuscular disorders, such as cerebral palsy and stroke, that affect both muscle mechanical properties and the neural response to stretch. To date, it remains unclear how changes in sensory input, the intrinsic sensitivity of the muscle spindle, and increased spinal excitability contribute to increased neural responses to stretch. As a first step towards disentangling different contributions to the altered response to stretch, we compared muscle and spindle responses between rats with altered muscle properties due to immobilization and healthy control rats.

Methods

All procedures and experiments were in strict agreement with the EU regulations and approved by local university ethical committees. We collected *in situ* muscle-tendon length and force, and muscle spindle firing rates during ramp-hold-release stretches with different stretch speeds and amplitudes in immobilized (N=3) and healthy (N=3) rats. In the immobilized rats, the ankle was immobilized in a plantarflexion position for 4 weeks prior to the experiment.

We assessed muscle-tendon forces of the plantarflexors and spindle instantaneous firing rates (IFR) in response to stretch as well as the relation between both. We fitted a previously proposed model that relates IFR to contractile muscle force and its derivative, yank to our data [2]. Non-contractile force was modeled as an elastic force with both exponential and linear stiffness in parallel with the contractile force [2];

$$F_{nc} = k_{lin}(L - L_0) + Ae^{k_{exp}(L-L0)}$$

with F_{nc} non-contractile force, L the entire muscle-tendon length, and L_0 the resting muscle-tendon length. Constants k_{lin}, A, and k_{exp} were estimated across all conditions for each rat by maximizing the contributions of passive force to total force. Non-contractile force was subtracted from recorded muscle-tendon force to estimate contractile force F_c. IFR was modeled as a linear combination of F_c and its derivative Y_c:

$$\widehat{IFR} = F_c * k_F + Y_c * k_Y + C$$

Gains k_F and k_Y describing the sensitivity of the spindle to force and yank, and the offset C were estimated for each stretch and each cell by maximizing the fit between modeled and measured IFR.

Results and Discussion

Data was recorded from 13 afferent cells (range 1-9 per rat) in immobilized rats and 7 afferent cells (range 1-4 per rat) in control rats. Immobilized rats had higher and more variable peak muscle-tendon forces, reflecting higher stiffness after immobilization, and peak instantaneous firing rates (IFR) than control rats (Fig.1). Higher IFRs could be explained by both higher contractile force and yank (sensory input to spindle) and higher gains. Force gain and yank gain were respectively higher in one out of three and all immobilized rats than in control rats (Fig. 1). This might indicate that increases in the muscle's IFR after immobilization are not only due to altered sensory inputs but also due to increased spindle sensitivity.

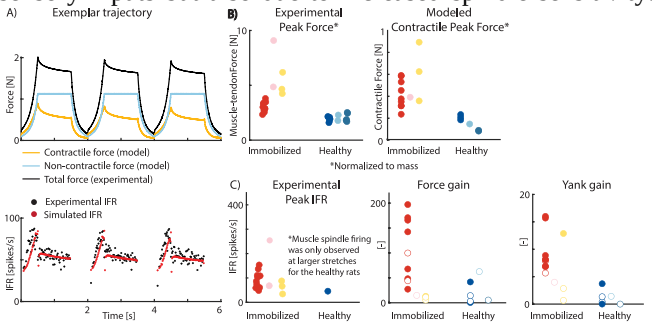

Fig. 1: A) Exemplar trajectory (left) for experimental (black) and simulated (color) force (top) and firing rates (bottom). **B)** Experimental peak muscle-tendon force (left) and modeled peak contractile force (right). **C)** Model parameters for experimental IFR, optimized force and yank gains for each cell (filled dots: type Ia afferents, open dots: type II afferents). Each color represents one rat.

Conclusions

Our preliminary data suggests that joint contractures may affect spindle sensitivity. Hence, the increased reflex activity in response to muscle stretch in many neuromuscular disorders might in part be due to altered sensory input combined with altered spindle sensitivity. We will confirm these results in more rats and add a group of spastic rats with increased spinal excitability to the comparison.

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References

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