Shortening-induced force depression is primarily caused by cross-bridges in strongly bound states

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INTRODUCTION

Force depression has been defined as the decrease in steady-state isometric force following shortening of an active muscle compared to the steady-state force obtained for purely isometric contractions at the corresponding length (Edman *et al.*, 1993). In previous studies, force depression has been shown to depend on the force and magnitude (and thus the work) of shortening (Herzog and Leonard, 1997), and has been associated with a decrease in stiffness in single fiber preparations (Sugi and Tsuchiya, 1988). Therefore, force depression has been thought to be associated with a decrease in the proportion of attached cross-bridges which might be caused by an inhibition of cross-bridge attachment following shortening contractions (Maréchal and Plaghki, 1979). However, it is not clear if all cross-bridges contribute to force depression equally, or if force depression affects specific states in the cross-bridge cycle.

The purpose of this study was to investigate if force depression affects so-called weakly and strongly bound cross-bridges to the same degree. Specifically, we hypothesized that active muscle shortening inhibits cross-bridge binding to the same degree for all cross-bridge states. In order to address this specific hypothesis, tests were performed with normal fibers and fibers exposed to 2,3-butanedione monoxime (BDM) which biases cross-bridges towards the weakly bound state. If our hypothesis is correct, then the amount of force depression relative to the isometric reference values and decrease in stiffness should be the same for the fibers in normal Ringer's and the experimental BDM solution.

METHODS AND PROCEDURES

Single fibers (n = 9) were dissected from frog lumbrical muscles and suspended between a motor arm and a force transducer inside an experimental chamber. Isometric reference contractions were performed at a length corresponding to the length following the shortening step in the experimental contractions (i.e., optimal length in this study). Test contractions consisted of an isometric contraction that was immediately followed by active shortening with magnitudes of 10 or 15% of the optimal length at a speed of 13% optimal length/s. Each contraction lasted 5s and stiffness was measured using a quick stretch (1% optimal length over 1ms) just before deactivation. Experiments were performed in Ringer's solution (pH=7.2), and following that were repeated after exposure to 7.5mM BDM. Force depression was measured as the median of force over a 0.3s period starting 4.5s following the onset of activation. Force was normalized to fiber cross-sectional area and stiffness was calculated by dividing force by elongation.

RESULTS AND DISCUSSION

Average isometric force decreased by 42% and stiffness by 25% when fibers were exposed to BDM. The absolute amount of force depression was decreased while the relative amount was the same in the BDM exposed (10.7%) compared to the normal fibers (12.3%; Fig.1, table1). The absolute amount of force depression was strongly correlated to the work performed by the fibers during shortening for both the BDM exposed and normal fibers (Fig. 2, *p*~0).

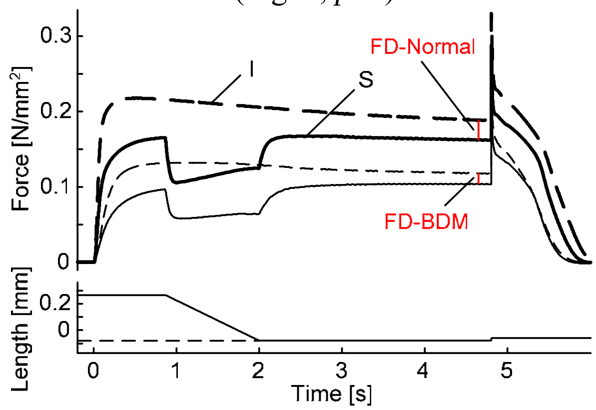

Figure 1. Raw force (top) and change in length (bottom) time histories of active shortening (solid, S) and isometric reference contractions at the corresponding final length (dashed, I) in normal (thick) and BDM (thin) conditions. Force depression with normal (FD-Normal) and BDM exposed fiber (FD-BDM) are indicated in red.

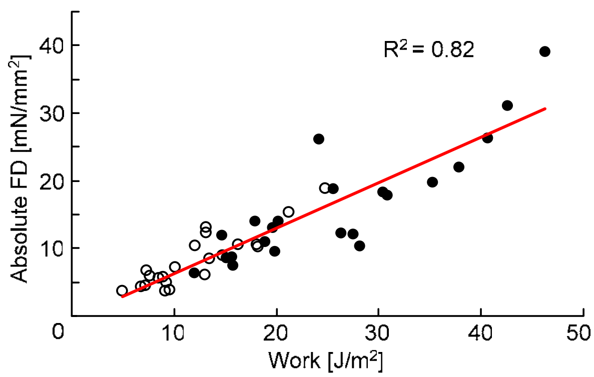

Figure 2. Work vs. absolute force depression with normal (●) and BDM (○) exposed fibers.

The average decrease in stiffness was smaller in the BDM exposed fibers (6.7%) than the normal fibers (16.8%; table1). The results of this study confirm previous findings in that force depression was strongly correlated to the amount of work performed during active muscle shortening and that force depression was nearly proportional to the decrease in stiffness in fibers exposed to normal conditions. New to the literature is the result that force depression in fibers biased towards weakly bound cross-bridge states (BDM) showed the same amount of relative force depression as normal fibers but had a much reduced decrease in stiffness. These results support the idea that force depression through active muscle shortening is primarily produced by cross-bridges in the strongly bound states while cross-bridges in the weakly bound states are unaffected.

CONCLUSIONS

From the results of this study we conclude that active muscle shortening affects cross-bridges in different ways depending on their states. Strongly bound cross-bridges are inhibited and so contribute to the observed force depression, while weakly bound cross-bridges remain largely unaffected.

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Table 1. Force (relative and absolute) and stiffness depression (mean±SE, * sig. level, *p*<.01).

Condition	Relative FD [%]*	Absolute FD [mN/mm^2]*	Stiffness Depression [%]*
Normal	12.3 ± 1.0	16.3 ± 1.8	16.8 ± 1.2
BDM	10.7 ± 0.8	8.2 ± 0.9	6.7 ± 1.1