Stretch Activation and the Myosin Converter Domain Influence *Drosophila* Muscle Power Generation

by

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ABSTRACT

Mechanisms by which *Drosophila* regulate muscle mechanical power output were investigated. First, we examined how variation in calcium concentration in muscle could influence power output for flight. Our results revealed that *Drosophila* indirect flight muscle (IFM) power output increased with increasing calcium concentration beyond pCa 5.8 and reached maximum at pCa 5.25. Over a 2-fold calcium concentration range where power varied most between pCa 5.7 and pCa 5.4, power output varied 2-3 fold and myosin kinetics varied 1.2-fold. These results are consistent with previous aerodynamic measurements in which a 2-fold variation in calcium led to a 1.2-fold change in wing beat frequency and a 2-fold change in aerodynamic power during flight. Stretch activated tension showed the same calcium dependency as power and contributed 4-fold more than calcium tension to total tension generation, suggesting that *Drosophila* may modulate power during flight by varying calcium concentration to modulate the stretch activation response. Second, we investigated the role of the converter, a myosin structural domain suggested to be important in setting muscle function. Disrupting the interaction between the converter and relay domain by a single point mutation R759E reduced muscle power production by 58% and myosin kinetics by 31%. Flies harboring the mutation showed decreased flight ability and wing beat frequency. The functions of the converter domain were studied by creating transgenic flies in which the IFMs express myosin with exon 11d, an embryonic converter. The mutant 11d fibers showed a 41% reduction in power and 63% decrease in myosin kinetics when compared to wild type fibers. The decrease in total tension of 11d fibers was due to the decrease in passive tension. Further investigation into the conditions for maximum power production revealed that increased strain amplitude of 11d fibers compensates for the reduction in oscillating frequency to enable greater power output. We conclude that the myosin converter domain is a critical region for modulating muscle power output and kinetics.