Altered cellular Ca^{2+} handling in skeletal muscle fatigue

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Acute exercise results in impaired muscle function; that is, fatigue develops. The impaired muscle function in fatigue may be due to central (in the central nervous system) and/or peripheral (within the muscle) factors. My research group studies mechanisms of peripheral fatigue with a special interest in changes in sarcoplasmic reticulum (SR) Ca^{2+} handling. Experiments are performed on intact single muscle fibres obtained from mice and rats; all experiments are approved by the Stockholm North local ethics committee. Central fatigue is often assessed with the twitch interpolation technique, where electrical stimulation is superimposed on an ongoing voluntary contraction and the resulting change in force is measured. We have mimicked this stimulation pattern in single fibre experiments and observe a force increase that could be interpreted as central fatigue; the underlying principles will be discussed. SR Ca^{2+} release is decreased in later stages of fatigue. This decrease has been attributed to changes in energy metabolites but recent data indicate that it also depends on the phosphorylation status of proteins involved in the release mechanisms. Force recovery after fatiguing stimulation may be slow, especially at low stimulation frequencies. Recent data from our laboratory show that two different mechanisms can cause this prolonged force depression: decreased SR Ca^{2+} release and reduced myofibrillar Ca^{2+} sensitivity. The relative importance of these two mechanisms appears to depend on the production of different reactive oxygen species.