Localized Muscle Fatigue (LMF) is a complex, multifactorial phenomenon that involves exercise-induced decrements in the ability to generate force or power. LMF can adversely affect performance and may increase the risk of work-related musculoskeletal disorders (WMSDs), and is thus of contemporary occupational relevance. Despite considerable progress in understanding and predicting muscle fatigue, there are many uncertainties and unresolved issues that are principally associated with the physiological complexity of LMF and the diverse mechanisms that underlie LMF development. This research thus aimed to address some of the theoretical and practical issues related to muscle fatigue and recovery. Regarding the theoretical aspects, two specific MFMs were directly compared and some important differences in their predictions were identified. These differences were used, in part, as a basis for developing testable hypotheses and designing associated experiments. Further theoretical evaluations were conducted to explore the sensitivity of these models to the model parameters and their ability to predict endurance time in both prolonged and intermittent exertions. Sensitivity to inherent model parameters was quantified, which was relatively high in conditions involving lower to moderate levels of effort. Further assessments indicated substantial variability related to model recovery parameters, which might be related to the inability of these MFMs in simulating the recovery process. From a practical viewpoint, the effect of cycle time on the development and consequences of LMF was determined during intermittent isometric exertions. A shorter cycle time led to less fatigue development as reflected by rates of change in perceived discomfort, performance, and muscle capacity. Lastly, the dependency of muscle recovery on these different histories of fatiguing muscle contractions was explored. How a muscle recovers appeared to depend only on the state from which it starts to recover, though not the exertion history that led to that state. In summary, results of these studies may help in enhancing our understanding of fatigue and recovery processes, and in improving existing models of muscle fatigue and recovery. More accurate predictions of LMF development may help in enhancing muscle performance and in reducing the risk of musculoskeletal injuries and their associated healthcare costs.