Muscle disorders are regularly encountered by neurologists and clinical neurophysiologists. Nerve conduction studies are either normal or reveal reduced compound muscle action potential (CMAP) amplitudes. Needle electromyography (EMG) may reveal spontaneous activity (fibrillations or positive sharp waves), myopathic motor units and abnormal recruitment patterns. Structural muscle changes (variation in fibre size and a predominance of smaller fibres) contribute to the ‘myopathic’ EMG. Some muscle disorders however are due to muscle fibre membrane ion channel dysfunction. Increased muscle fibre membrane excitability may result in spontaneous discharges, clinically manifesting as myotonia or stiffness. Reduced excitability may cause slowing or failure of action potential propagation, which may manifest as weakness or paralysis. In a similar way to nerve excitability studies, the pathophysiological consequences of ion channel mutations on muscle membrane function can be assessed using neurophysiological techniques, complementing advancing knowledge of the genetic and molecular defects and of clinical phenotypes.

For muscle contraction to occur, conduction of action potentials along the muscle fibre membrane is dependent upon normal membrane excitability. Depolarisation is mediated by the Na1.4 Na+ channel, product of the SCN4A gene. Calcium ions are subsequently released from the sarcoplasmic reticulum mediating excitation-contraction coupling. Chloride channels (encoded by CLCN1), which have high conductance near the resting membrane potential, stabilise it in the resting and post-excitation state. Assessments of CMAP morphology, muscle fibre conduction velocity (MFCV) and short and long exercise tests can all be helpful in assessing membrane function. Action potential propagation velocity along the muscle fibre membrane (MFCV) can be estimated by cross-correlation potential propagation velocity along the muscle fibre membrane. Action potential propagation velocity along the muscle fibre membrane (MFCV) can be estimated by cross-correlation of surface recorded EMG³ or invasive methods.¹²

In myotonia, exercise can trigger, relieve or aggravate symptoms, so it can be used as a neurophysiological functional test, to aid diagnosis. The short exercise test, first described by Streib et al is useful in investigating myotonic syndromes. Repeated brief exercises are followed by rest and serial supramaximal CMAP recordings. The long exercise test, described by McManis et al is useful for the assessment of suspected periodic paralysis.³

To illustrate the potential utility of EMG techniques the following will describe recent work relating to the non-dystrophic myotonias and critical illness myopathy, where these investigations have been used.

Myotonias
Muscle fibre hyperexcitability is the fundamental abnormality in myotonia, resulting in spontaneous trains of action potentials, which with contraction coupling results in delayed relaxation. Myotonic discharges arise from single muscle fibres. They show rapid firing, waxing and waning of frequency and amplitude, and may be facilitated by mechanical stimuli. However, myotonic discharges are not diagnostically distinctive according to cause. In the absence of prominent clinical myotonia, electrical myotonia is observed in, amongst others, acid maltase deficiency, congenital myopathies, hypothyroidism and polymyositis. These conditions may also possess motor unit and recruitment abnormalities on EMG.

Routine assessment of myotonia relies upon needle EMG revealing myotonic discharges. Neurophysiological provocative tests including repetitive nerve stimulation,² short and long exercise tests, can help distinguish the main phenotypes.

Broadly divided into two groups, variants of myotonia congenita (MC) are caused by dominant or recessive mutations of the chloride channel gene (CLCN1). Myotonia increases after periods of rest and declines with repetition of exercise (warm up phenomenon). Mutations of the alpha subunit of the voltage gated skeletal muscle sodium channel gene (SCN4A) have been found to cause paramyotonia congenita (PC), where myotonia conversely is induced by exercise or cold. Clinical history and examination is frequently enough to be able to guide genetic testing, however it is sometimes unreliable or the phenotype unclear, for example, some SCN4A mutations produce myotonia without an increase after exercise, mimicking MC.²

Recent studies have addressed the utility of the short and long exercise tests in the non-dystrophic myotonias and have found them to be helpful in supporting the diagnosis and guiding genetic testing. Fournier et al studied patients with identified ion channel mutations, using a modified form of the short exercise test.²⁶ Instead of the originally described 10 minute rest period between tests, they used three brief exercise periods separated by only 1 minute each. In patients with myotonia congenita, Fournier, like Strieb previously, noted an initial decline in CMAP amplitude following exercise which gradually improved with further exercise, similar to the clinically recognised warm-up effect. Based on the findings they defined five electrophysiological groups, which distinguished between sodium, chloride and calcium channel mutations and also between subgroups of sodium channelopathies. The first three groups related to myotonic syndromes, which were distinguishable using repeated short exercise tests. The reported sensitivity of the repeated short exercise test was about 85%. Further work studying 54 patients with myotonia identified sodium or chloride channel mutations, describing increased sensitivity (approaching 90-100%) of the short exercise test when combined with muscle cooling.²⁶

The pathophysiological and clinical consequences of ion channel dysfunction can be assessed using neurophysiological techniques.
depending upon the degree of depolarisation.\textsuperscript{11-13} Cooling induces membrane depolarisation by slowing ion channel kinetics; hence in PC, cold has a depolarising effect, causing myotonia and then inexcitability.\textsuperscript{14,15} At room temperature almost all MC patients with recessive chloride channel mutations displayed a transient decrease in the CMAP when the short exercise test was performed after rest, which improves after short exercise test repetition, akin to the warm-up phenomenon. However, those with dominant mutations generally (86%) did not show this reduction following exercise under normal conditions but the majority (75%) did once there had been exposure to cold.

Fournier et al suggested that EMG can guide specific ion channel gene testing and that combining exercise tests with cold exposure improves the sensitivity. Prospective studies testing this hypothesis should be performed. Studies should also look at reproducibility and at the usefulness of such testing in patients with these mutations but milder phenotypes.

Critical illness myopathy (CIM)

In contrast to hyperexcitability causing myotonia, muscle inexcitability has been demonstrated in critical illness myopathy.\textsuperscript{6,11} Differentiating between a myopathy and neuropathy can be challenging in the intensive care unit. The differential diagnosis in ICU also includes Guillain Barré syndrome and myasthenia gravis for example. In a series of 92 patients with neuromuscular disorders acquired in the ICU, a myopathy consistent with CIM was three times as common as axonal polyneuropathy and is increasingly recognised.\textsuperscript{16,17} Careful neurophysiological examination can differentiate these conditions. The ratio of the CMAPs recorded following direct muscle stimulation and motor nerve stimulation has been used to distinguish myopathy and neuropathy in ICU patients, this is however only semi-quantitative and has potential disadvantages.\textsuperscript{17,18} Early in CIM paralysis there are fibrillation potentials and positive sharp waves on EMG. Recruitment and motor unit potentials appear myopathic. Subsequently the muscle becomes inexcitable. Myosin loss demonstrated on biopsy cannot explain muscle fibre membrane inexcitability and its loss lags behind the development of weakness.\textsuperscript{20,21}

We recently demonstrated acquired dysfunction at the level of the muscle fibre membrane in critical illness myopathy, akin to that seen in some inherited channelopathies.\textsuperscript{22,23} We found that in 90% of CIM patients, compared to controls, the CMAP duration recorded from either abductor hal- lucis (AH) or abductor pollicis brevis (APB) was significantly prolonged, exceeding the control mean + 2 SD in either or both the median or tibial responses. The morphology of the abnormal CMAP is also distinctive, being smoothly contoured and the positive phase is often replaced by a characteristic. Weaker patients have lower MFCV or inexcitable fibres on biopsy cannot explain muscle fibre membrane inexcitability and its loss lags behind the development of weakness.\textsuperscript{20,21}

Further work should address reliability and reproducibility, and should investigate the interplay between genetics, neurophysiology and phenotypes. Understanding the precipitants of dysfunction also requires clarification. Our understanding and ability to accurately diagnose both common and rare muscle disorders related to sarcolemmal hyperexcitability or hypexcitability is improving. The neurophysiological assessment can play an important role in this respect, providing accurate and timely diagnosis in the ICU and by directing genetic testing, which is more expensive and time consuming.
Neurophysiology Article

References

National clinical guideline for stroke Third edition

Prepared by the Royal College of Physicians Intercollegiate Stroke Working Party co-chaired by Professor Derick Wade and Dr Tony Rudd

The third edition of these world-renowned stroke guidelines provides the reader with the most comprehensive coverage of stroke care to date, encompassing the whole of the stroke pathway from acute care through to longer-term rehabilitation and secondary prevention. It informs health professionals about what should be delivered to stroke patients and how this should be organised, with the aim of improving the quality of care for everyone who has a stroke, regardless of age, gender, type of stroke, or location. The recommendations have been completely revised to include the most up-to-date evidence published since the last edition in 2004.

New features included in this guideline
• Recommendations from the new guideline by the National Institute for Health and Clinical Excellence on the initial management of acute stroke and transient ischaemic attack.
• A new guide for commissioners of stroke services to help ensure that a population receives an integrated high-quality service.
• An updated information booklet for stroke patients and their carers.
• A section on mental capacity and how it influences stroke management.
• Updated sections, on acute care, rehabilitation, longer-term care, and secondary prevention.
• Profession-specific concise guides for nurses, dietitians and therapy professionals.
• A driving section (in relation to UK driving law).
• A laminated concise guide for convenience.

The guidelines are written in a clear and holistic way. They are an essential resource for everyone involved in stroke care, prevention and rehabilitation, as well as commissioners of stroke services, patients and carers.

Contents
• Commissioning
• Systems underlying stroke
• Acute-phase care
• Secondary prevention
• Recovery phase – rehabilitation
• Late phase

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