Project Details	
Project Code	CMD27Ba Maher
Title	How Does Extreme Muscle Disuse Affect Whole-Body Health?
Research Theme	Cardiometabolic Disease
Project Type	Wet lab
Summary	Loss of muscle activity can happen through injury, illness or periods of hospitalisation. This rapidly disrupts the body's ability to regulate blood sugar and increases long-term health risks. This project will use spinal cord injury as a model of extreme muscle disuse to understand how metabolic health declines over time and identify factors that increase disease risk. It will also test an innovative whole-body electrical stimulation technique designed to mimic the benefits of exercise when movement is limited. The project provides outstanding training in human physiology, clinical trials, metabolic phenotyping, and translational research across the Universities of Bath and Exeter.
Description	Periods of physical inactivity and disuse—arising from critical illness, immobilisation, or neurological injury—are associated with rapid loss in skeletal muscle mass and function, and an increased risk of cardiometabolic disease. As skeletal muscle is the primary site of insulin-stimulated glucose disposal, loss of muscle mass and contractile activity contributes to impaired glycaemic control and insulin resistance. While the adverse metabolic consequences of muscle disuse are well recognised, the trajectory of cardiometabolic decline and determinants of metabolic risk remain poorly defined. Exercise is effective for improving cardiometabolic health, however, most individuals experiencing disuse are unable to participate in conventional exercise because of profound mobility limitations. Alternative strategies are needed to preserve metabolic health in this high-risk population. Neuromuscular electrical stimulation (NMES) is a promising strategy to elicit muscle contractions in the absence of voluntary movement. Previous studies show that lower limb NMES can attenuate muscle loss and enhance glucose utilisation in populations experiencing prolonged disuse. However, the efficacy of whole-body NMES for improving glycaemic control and insulin sensitivity remains largely unexplored. Using spinal cord injury (SCI) as a model of profound and sustained skeletal muscle disuse, this project will characterise the development of cardiometabolic dysfunction and evaluate the therapeutic potential of whole-body NMES. Overall aim: To characterise the emergence, progression, and determinants of cardiometabolic dysfunction in individuals with spinal cord injury (SCI), using SCI as a human model of profound and sustained skeletal muscle disuse, and to evaluate whole-body neuromuscular electrical stimulation (NMES) as a targeted intervention to improve metabolic health. Objective 1: Characterise the development of cardiometabolic dysfunction following severe disuse. The student will establish and contribute to a longitudinal observational study using spinal cord injury (SCI) as a model of profound disuse and sustained muscle inactivity. Participants at different stages post injury beginning at discharge from specialist rehabilitation will undergo detailed cardiometabolic phenotyping to include body composition,

	tissue morphology, blood/plasma-based cardiometabolic risk markers, blood pressure and free-living continuous glucose monitoring. Participants will be followed every 3 months for the first year and annually thereafter to map cardiometabolic decline from the early post injury period(~6-months) into the chronic stage. The student will establish a prospective longitudinal cohort that will continue beyond the lifetime of the PhD, generating the first longitudinal dataset describing early cardiometabolic changes following SCI and a resource for future investigation of longer-term outcomes. These findings will inform future intervention strategies, including NMES, by identifying key metabolic impairments and optimal windows for intervention. The student will coordinate with NHS partners across specialist spinal rehabilitation centres for recruitment. Following training, they will take ownership of cohort development, data collection, and refinement of phenotyping protocols. Objective 2 (University of Bath): Determine the acute effects of whole-body neuromuscular electrical stimulation (NMES) on postprandial glycaemic control. The student will conduct acute experimental studies to test whether whole-body NMES can improve glycaemic control in individuals experiencing severe disuse compared to a SHAM control condition. Unlike traditional NMES protocols targeting isolated muscle groups, whole-body NMES will activate multiple muscle groups simultaneously, providing a substantially greater metabolic stimulus. Participants will complete: • Whole body NMES (60-min) delivered during a 3-hour oral glucose tolerance test (OGTT) compared to a SHAM control condition. • Serial measurement of fasting and postprandial glycaemic control over 3 hours (circulating glucose, insulin, c-peptide). • Assessment of whole body metabolic responses (e.g., energy expenditure, substrate utilisation) Glucose and insulin responses will be used to derive iAUC, ISI-Matsuda and HOMA-2 indices of insulin sensitivity, insulin resistance and β-cell function. Energy expenditure and substrate oxidation rates will be assessed using repeated indirect calorimetry. This objective will determine whether whole-body NMES acutely enhances postprandial glucose handling. The student will lead optimisation of NMES protocols (electrode configurations, stimulation parameters, etc). Objective 3 (University of Exeter): Determine the effects of a two-week whole-body NMES intervention on insulin sensitivity and metabolic function. The student will conduct a two-week home-based intervention study to determine whether repeated exposure to whole-body NMES improves glycaemic control and insulin sensitivity in individuals with SCI. Participants will complete two daily NMES sessions, with one session performed following a standardised breakfast. Participants will complete: • Baseline and follow-up OGTT using the same metabolic outcomes described in Objective 2. • Two weeks of home-based whole-body NMES.

	• Continuous glucose monitoring throughout the intervention period to assess changes in mean glucose concentration, glycaemic variability, postprandial glucose excursions, and time spent within target glucose ranges. A subset of participants will undergo additional metabolic phenotyping at the University of Exeter before and after the intervention. This will include hyperinsulinaemic-euglycaemic clamps and skeletal muscle biopsies to investigate adaptations in insulin sensitivity and metabolic signalling pathways. The student will lead intervention delivery, participant monitoring, and protocol refinement. They will receive advanced training in hyperinsulinaemic-euglycaemic clamp methodology, skeletal muscle biopsy analysis, and molecular techniques used to investigate insulin signalling and glucose metabolism.
Can be completed part time?	No
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