

Decreases in Core Temperature and Sweating Onset During Whole-body Heating in Individuals with Multiple Sclerosis Following Administration of 4-aminopyridine

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ABSTRACT

Multiple sclerosis (MS) is a progressive neurological disease of the central nervous system that can result in impairments in thermoregulatory function. 4-aminopyridine (4AP), a voltage-gated K⁺ channel blocker, has been postulated to improve conduction in demyelinated axons and improve MS related disabilities. The aim of this study was to test the hypothesis that administration of 4AP would improve sudomotor function in individuals with MS during passive whole-body heating (WBH). Eleven subjects (8 females, 3 males; 39±7 years; 78.6±24.0 kg; 170±9 cm; 8±4 years since diagnosis) with relapsing-remitting MS participated in this study. A randomized single-blinded 2-week crossover design was utilized with 4AP and placebo (PBO) including a 1-week washout period between drugs. Subjects were outfitted in a tubelined water perfusion suit and exposed to a normothermic (NT) baseline (34 °C water) and WBH (48 °C water; increase in internal temperature of ~0.8 °C) condition. Core body temperature (telemetric pill) and sweat rate at the dorsal forearm (capacitance hygrometry) were continuously measured. Baseline NT core body temperature while on 4AP was lower compared to placebo (4AP: 37.3±0.2 °C vs. PBO: 37.5±0.2 °C, p=0.002). Core body temperature at the onset of sweat was also lower while on 4AP compared to placebo (4AP: 37.4±0.2 °C vs. PBO: 37.6±0.3 °C, p=0.0006). However, sweat rate (Δ from NT) on 4AP was similar compared to placebo during WBH (4AP: 0.7±0.3 mg/cm²/min vs. PBO: 0.8±0.4 mg/cm²/min, p=0.49). These initial findings suggest K⁺ channel blockers may have protective benefits for people living with MS by lowering resting core temperature and the sweat onset core temperature threshold. Thus, administration of 4AP may improve heat sensitivity in MS by expanding the range for core temperatures increases prior to symptom worsening.

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