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A static handgrip method for distal quantitative sweat measurements

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Abstract

The quantitative sudomotor axon reflex test (QSART) measures sympathetic C fibre function when iontophoresed acetylcholine (Ach) evokes a measurable reliable sweat response. This study tests a novel, simplified method of sweat stimulation which accompanies hand dynamometry. In 34 healthy subjects we compared the standard sudomotor axon reflex test with a simplified method using static handgrip as sweat stimulus and recorded from the distal forearm, thumb and little finger tips. The standard method failed on technical grounds beyond the forearm. At the distal forearm, sweat rates were 313 ± 140 nl/min, representing a four-fold increase from baseline. Static handgrip induced sweat rates of 339 ± 156 (thumb) and 296 ± 139 (little finger) nl/min, representing a 1.7 and 1.6 fold increase from baseline. Static handgrip did not significantly alter distal forearm sweat secretion, and in females handgrip induced significantly less sweating over the thumb than in males. After dynamometry or Ach stimulation, over the three sites (thumb, little finger and forearm), the stimulated sweat secretion volumes were measured at 0.0278 ± 0.021 μl/cm^2/min (thumb), 0.0204 ± 0.020 μl/cm^2/min (little finger), and 0.0503 ± 0.0283 μl/cm^2/min (forearm) after correction. Our study suggests the static handgrip method can be used to stimulate distal sweat production and may be of particular significance in investigating length-dependant neuropathies and assessing distal C fiber function.

Keywords: QSART; Sweat stimulation; Dynamometry; Fingertip; C fiber; Autonomic nervous system

Physiological sweat secretion is the result of sympathetic nerve activation which in humans is triggered via emotion and temperature. Disorders in sweat production often occur in relation to disorders of the autonomic nervous system and are often seen in association with length-dependant polyneuropathies such as diabetic neuropathy [16]. The quantitative sudomotor axon reflex test (QSART) is an established technique for the quantitative assessment of sudomotor activity in a defined skin area [17,7]. The technique depends on two crucial elements: (a) reliable sweat stimulation and (b) accurate measurement of the small volume of sweat produced [9]. The standard stimulus for sweating uses acetylcholine driven by iontophoresis through the skin.

Acetylcholine binds to nicotinic receptors of the postganglionic sympathetic axons and results in axonal activation upon which an impulse travels antidromically to a nerve branchpoint. Here endogenous acetylcholine is released, crosses the neuroglandular junction and binds to M3 muscarinic receptors on eccrine sweat glands to evoke sweat secretion [7]. Recent developments have resulted in the commercial availability of extremely sensitive and reliable sudorometers able to conveniantly analyze and display sweat rates and volumes [9]. Using acetylcholine, sweat secretion commences with a latency of 1–2 min followed by a rapid rise time. Sweat secretion returns to baseline within 5–10 min after cessation of the stimulus. Standard values used to express sweat production are the resting base line sweat rate in nl/min and sweat volumes in μl/cm^2/min [8]. The technique has been used to measure sweat in the forearm, proximal leg, distal leg, and foot. For many of these areas normal values have been published [12,10].

QSART provides a clinically relevant means for diagnosing peripheral nerve disorders such as diabetic neuropathy,

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idiopathic small fiber neuropathy, Fabry disease and familial dysautonomia [1,3–6]. Although QSART is now established as a standardized method for testing C fibre function, the delivery of acetylcholine is disadvantaged by being messy, associated with skin irritation and difficult to apply to distal sites of the extremity. For these reasons we sought an alternative method to stimulate sweat stimulation. Since sweat secretion is a physiological phenomenon accompanying voluntary muscle contraction [15], we investigated the static handgrip method as an alternative to iontophoresed acetylcholine as a sweat stimulus.

Healthy subjects were recruited after informed consent. The project was approved by the Institutional Review Board of National University Hospital of Singapore, the location of the study. To test the effect of age on QSART, subjects were recruited into four 10 year age bands (21–30, 31–40, 41–50, and 51–60; mean age: 38.2, age range 20–60 years, 16 males, 14 females). Coffee and tea could not be taken 2 h prior to testing. Inclusion criteria were no symptoms or signs of any form of nervous disorder, hand injury or pain, any form of weakness and willingness to participate in the research. Exclusion criteria were pregnancy and age below 21. In all volunteers, QSART was performed using the two types of sweat stimulation described below. The two techniques were tested either during the same experimental session or with a gap of up to two weeks. The three areas tested were the skin over the fifth and first digit tip and the skin over the volar forearm just proximal to the wrist crease.

Each subject was acclimated to the test environment by resting seated for 5 min. Air temperature was adjusted by air-conditioning to between 24 and 26 °C and the humidity at 40–60%. Skin temperature over the three assessed areas was determined immediately prior to testing using an infrared no touch thermometer (Exergen®, Raytek). Testing proceeded if the temperature registered between 30 and 33 °C. QSART measuring chambers were placed over the fifth and first digit tip and the skin over the volar forearm. Despite repeated attempts, we failed to attach the iontophoresis capsules to the volar digit tips without leakage of air. As such, we were unable to compare the iontophoretic acetylcholine technique with the dynamometric one over the digit tips.

After a stable baseline recording over 3 min, subjects were asked to lightly grip a standard blood pressure sphygmomanometer cuff inflated to 20 mm Hg with the opposite hand to that being tested for sweat production. Next, subjects were asked to squeeze the cuff, such that the mercury column was maintained at levels above 160 mm Hg (males)/100 mm Hg (females) for 45 s. This level of force was chosen after repeated trials identified it as representing about two-thirds of the maximum contraction force that could be reasonably maintained over 45 s. The level of force applied was visually verified by the tester. The sweat response was recorded until the sweat production rate returned to base line level. Responses were repeated three times and the average response measured and used for calculation purposes.

Standard procedures were used as previosuly described [9]. Briefly, the positive pole of the iontophoresis unit was attached to the medial forearm three quarters of the distance from the ulnar epicondyle to the pisform bone with the negative pole on the volar hand. After recording a stable baseline sweat secretion over 3 min, sweating was stimulated using 10% acetylcholine applied by iontophoresis using a constant current generator with a stimulus of 2 mA for 5 min.

Statistical analysis was performed using SPSS® 13 (Chicago, Illinois 60606). The paired and one sample *t*-test was employed to test for differences between baseline and peak sweat stimulation with the significant threshold set at $P = 0.05$ level. All data were shown as mean ± S.D.

In 34 healthy subjects, the two techniques of QSART were performed and compared. Mean subject height was 165.5 cm, (range 146–182), mean weight 62.8 kg, (range 47–80). Baseline sweat secretion rates over the thumb and little finger were 199 ± 42 and 184 ± 34 nl/min (mean ± S.D.), respectively. After stimulation using dynamometry, mean peak rate sweat secretion values were 339 ± 156 and 296 ± 139 nl/min (mean ± S.D.), respectively. This represented on average a 1.7 and 1.6 fold statistically significant increase in sweat secretion from baseline, respectively ($p < 0.001$). Baseline sweat secretion rate over the forearm was 78 ± 35 nl/min (mean ± S.D.). Acetylcholine stimulation resulted in peak rates of 313 ± 140 nl/min (mean ± S.D.), representing a 4.0 fold increase from baseline sweat secretion. Over the three sites (thumb, little finger and forearm), the stimulated sweat secretion volumes were measured, after dynamometry or Ach stimulation, at 0.0278 ± 0.021 μl/cm^2/min (mean ± S.D., thumb), 0.0204 ± 0.020 μl/cm^2/min (mean ± S.D., little finger), 0.0503 ± 0.0283 μl/cm^2/min (mean ± S.D., forearm) after correction (Fig. 1). This was achieved by subtracting the

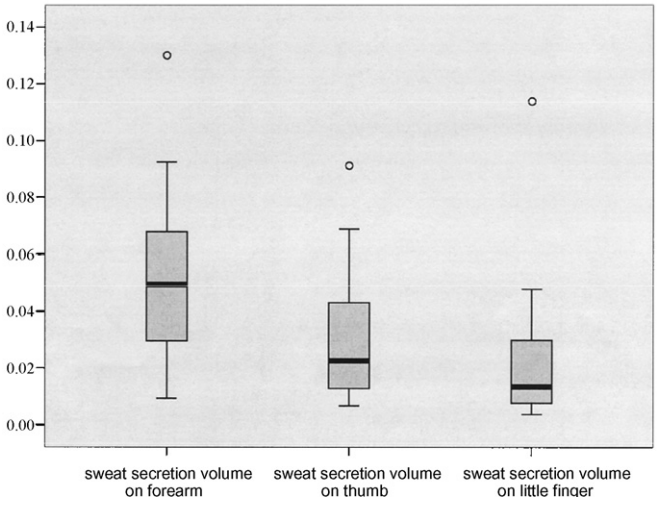

Fig. 1. Mean value of sweat secretion volume on forearm, thumb and little finger after Ach and dynamometry stimulation. Median, 25th and 75th percentiles, minimum, and maximum are shown. Paired *t*-test was used for the statistic analysis of thumb and little finger, respectively: $t = 2.37$, $P = 0.024 < 0.05$ ($n = 34$). One sample *t*-test was used for the mean value of volume on forearm, thumb and little finger compared with the baselines of sweat secretion: $t = 9.717$, $P < 0.001$ ($n = 34$, forearm); $t = 7.470$, $P < 0.001$ ($n = 34$, thumb); $t = 5.439$, $P < 0.001$ ($n = 34$ little finger). The statistic result indicated that there was significant change of the mean value of sweat secretion volume between the thumb and little finger after dynamometry. Also there was significant change of the mean value of volume on forearm, thumb and little finger compared with the baseline (set up by 0). Three outliers (circles) are shown in the testers.