Figure 2. Relationship between plasma neurotensin and degree of BP fall after glucose ingestion in the patients with autonomic failure.

Figure 3. Changes of MSNA (muscle sympathetic nerve activity) after glucose ingestion in the controls and in the patients with autonomic failure.

References


4. Diseases Affecting Sudomotor Function

Mikihiro KIHARA and Mitsuo TAKAHASHI

Key words: sudomotor function, multiple system atrophy (MSA), amyotrophic lateral sclerosis (ALS), Parkinson, diabetes mellitus (DM)

Autonomic consideration

There are two types of sweat glands, eccrine and apocrine. Apocrine glands are located on the axilla, the anogenital zone, the areola mamma, and the external auditory meatus. In contrast to eccrine secretion, which is abolished by sympathectomy, the apocrine gland has no evidence of secretory inhibition after sympathectomy and is, therefore, less important neurologically than the eccrine gland. Humans have 2 to 4 million eccrine sweat glands. The major function of the eccrine glands which are located throughout the whole body surface exclusive of the palms, soles, and facial skin, is thermoregulation. Eccrine glands receive sympathetic cholinergic innervation and come
Diseases Affecting Sudomotor Function

in contact with sudomotor neural impulses of central origin.

**Sudomotor function test** (1, 2)

Tests of sudomotor function differ in the mode of stimulation and the recording of the evoked response. These stimuli consist of warming and the use of pharmacological agents such as acetylcholine (Ach), and thyrotropin releasing hormone (TRH). Clinical tests of sudomotor function include the thermoregulatory sweat test (TST), quantitative thermoregulatory sweat test (Q-TST), sympathetic skin response (SSR), silastic imprint test (SIT), and skin sympathetic nerve activity (SSNA).

Q-TST is performed using the ventilated capsule method. A plastic capsule is attached to the skin surface (15 cm² recording area), and connected to a plastic tube. Air of low humidity is passed at a constant flow rate through the capsule, and changes of relative humidity are measured by a capacitance hygrometer. Q-TST not only measures the local sweat rate but also analyzes sweat expulsion which is caused by sympathetic sudomotor impulses from the thermoregulatory center in the hypothalamus. There is a positive linear relationship between body temperature and the frequency of sweat expulsion (FsW). Heat stimulation and the TRH enhance frequency of sweat expulsion and increase the local sweat rate. TRH acts as a stronger stimulant than heat in evoking sweat response, when infused at a rate of 0.1 mg/min. In normal controls, the frequency of sweat expulsion increases to 1.5 times that of the resting rate. There is also a linear relationship between the local sweat rate and the frequency of sweat expulsion and thus relating the rate of frequency provides an index of unit volume, which is an indicator for postganglionic sudomotor function. Q-TST, however, can only be used when some sudomotor function is retained. The other disadvantage is that the sampling area is small.

The QSART (quantitative sudomotor axon reflex test) is a sensitive and reliable test of postganglionic sudomotor function described by Low et al (3). This test is based on the principles of the axon reflex. One population of sweat glands is stimulated by acetylcholine iontophoresis using a constant current generator. Impulses pass antidromically along sympathetic C fibers to the branch point then travel orthodromically along other sympathetic C fibers to evoke a sweat response. One population of eccrine sweat glands is stimulated by the iontophoresis of 10% acetylcholine with 2 mA for 5 minutes and then sweat output by a second population of sweat glands is quantitated using a sudomotor for 5 minutes. A low-humidity stream of nitrogen evaporates the sweat droplets and gas of altered humidity is analyzed. The disadvantage of this test is that QSART can only measure a small area and does not detect central or preganglionic lesions reliably.

SART was modified from Minor’s method by Kihara et al (4). Iodine-alcohol-caster oil application is applied to dry skin. A rubber band is tied around the patient’s arm or thigh and then nicotine (10⁻⁴g/ml) is injected subcutaneously, distal to the band. The nicotine is unable to diffuse across the rubber band. Sweat droplets always appear over the rubber band within 5 minutes except in the absence of axon reflex sweating where sweat droplets do not appear. Skin temperature must be maintained at below the thermal threshold (33–34°C). The major advantage of the SART is its simplicity so that it can be used at bedside. The disadvantage is that it is a semi-quantitative test and also does not reliably detect a central or preganglionic lesion.

**Disease affecting sudomotor function**

**Multiple system atrophy (MSA)** (4)

Sudomotor dysfunction is known to occur in the majority of patients with MSA. We investigated the sudomotor function in MSA patients using Q-TST and SART. We concluded that in MSA, thermoregulatory sudomotor dysfunction was more severe in the lower extremities compared with the upper extremities. Frequency of sweat expulsion increased with heat stimulation and TRH. These results suggest that the central thermoregulatory center in MSA retains their function. Results of SART indicate that more than half of moderate MSA patients had a preganglionic lesion and the severe MSA patients had pre- and postganglionic, or postganglionic lesion. We propose that in moderate and presumably early MSA, the lesion is mainly in the intermediolateral cell mass. In severe, presumably later MSA, the lesion is also postganglionic. The initial lesion in the intermediolateral neurons will explain the impaired TST and intact SART with normal or near normal central thermoregulatory function. Later, transsynaptic failure of the postganglionic axon presumably occurs in MSA.

**Parkinson’s disease (PD)** (5)

In early PD patients, there are no local sweat or Fsw differences when compared with control subjects. These results strongly suggest that thermal sweating function is near normal in early PD patients. However, TRH infusion resulted in poor sweating response in PD patients. This result suggests that TRH does not activate the sympathetic nervous system in PD patients and PD patients may have widespread TRH-related metabolic abnormalities.

**Amyotrophic lateral sclerosis (ALS)** (6)

ALS patients have the same pattern of sudomotor impairment as seen in MSA. In ALS and MSA, there was impairment of thermoregulatory and postganglionic sweating over the thigh and TRH increased both sweating and Fsw. The changes in ALS and MSA differ in severity, being more pronounced in MSA. Thus the sudomotor dysfunction of ALS might be due to secondary degeneration of autonomic nerves with motor paralysis in the lower extremity.

**Diabetic neuropathy** (7)

Diabetic neuropathy commonly involves sweat dysfunction. Most patients (65%) exhibited a distal distribution of hypohidrosis and anhidrosis. In 58% of diabetic neuropathy patients, the QSART response was reduced or absent on the foot. We recently performed the silastic imprint test for the axon-reflex response and found that male subjects and patients with mild neuropathy have an enlarged droplet size. Whether the increase in size is due to multi-innervation or receptor alteration is currently not known.
Cerebral infarction (CI) (8)

The sweating dysfunction in CI of the cortex, showed a different pattern which depended on the stage of the disease. In the early stage which means within 10 months after the stroke, sweating dysfunction might occur by central sudomotor impairment and in the sub-acute stage which means more than 10 months after the stroke, dysfunction is influenced by peripheral mechanism such as the prolonged change of skin temperature in the paretic side.

References


5. Micturitional Disturbance

Takamichi HATTORI

Key words: micturitional disturbance, urinary incontinence, urodynamic study

Micturitional disturbances are not rare among patients with various medical diseases, however, these patients often do not complain of symptoms to their doctor even though they are suffering considerably. The reasons why they do not complain of their symptoms are due to shyness, or the patients considers their symptoms to be untreatable or not a disease but rather an aging process. Therefore it seems important for the physician to inquire of the detailed symptoms (1).

Micturitional disturbances are divided into two different phases, storage and expulsion. During the storage phase the bladder accommodates increasing volumes of urine by relaxation of the detrusor muscles and contraction of the urethral sphincter. On the other hand, during the expulsion phase contraction of the detrusor muscles and relaxation of the urethral sphincter occurs. These lower urinary tract functions are totally dependent on the nervous system controls. Three different peripheral nerves innervate the lower urinary tract, the pelvic nerve, pudendal nerve and hypogastric nerve (2). The pelvic nerve is a parasympathetic nerve originating from the intermediolateral cell column of lower thoracic and upper lumbar spinal cord, which innervates the smooth muscles of the bladder and urethra. The main function of the pelvic nerve is for urine expulsion, and that of the hypogastric nerve is for urine storage. Sensory fibers from the bladder and urethra pass centripetally in these three peripheral nerves. The integrative micturition center is situated in the pontine tegmentum which also receives neural controls from the higher central nervous system such as hypothalamus, thalamus, cerebellum, limbic system and frontal lobe. The frontal lobe is regarded as the voluntary control micturition center. Therefore, diseases affecting the nervous system at any levels from the frontal lobe to the peripheral nerves can cause micturitional disturbance.

There are various micturitional symptoms which can be divided into irritative and obstructive as shown in Table 1. Diurnal urinary frequency is defined as 8 or more urination during the day time. Nocturnal urinary frequency is two or more urinations during the night sleep. Urgency is a sensation of strong desire to micturate. Incontinence of urine is an involuntary loss of urine which has several different types such as stress incontinence, urge incontinence, overflow incontinence and reflex incontinence. Stress incontinence is an incontinence caused by the maneuver which increases abdominal pressure.