Chapter 12

Sphincter EMG for Diagnosing Multiple System Atrophy and Related Disorders

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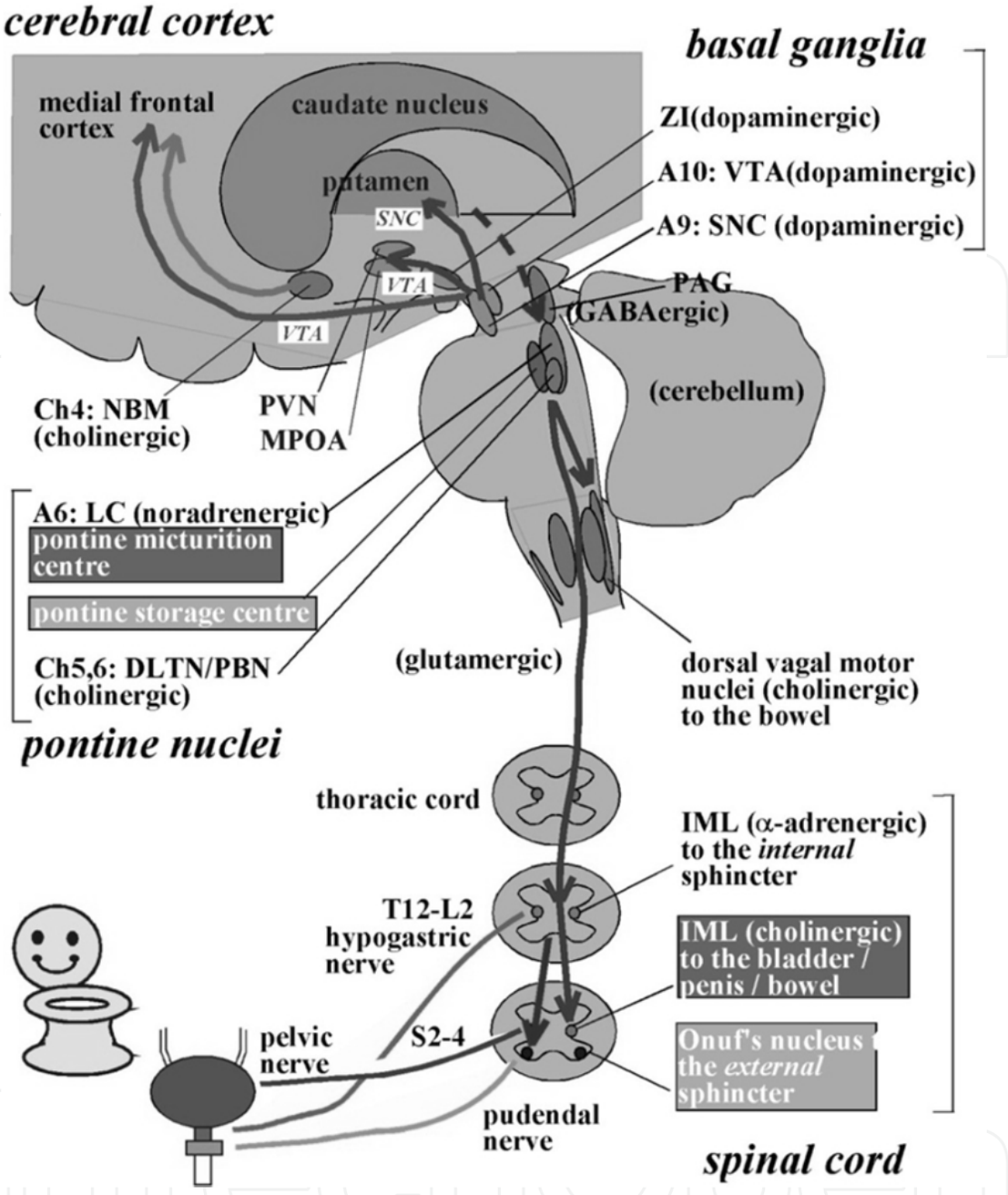
1. Introduction

One of the hallmarks in the pathology of multiple system atrophy (MSA) is neuronal loss in the sacral Onuf's nucleus[11,33,37]. Onuf's nucleus plays a key role in urinary and fecal continence[12]. Neurons in this nucleus receive not only cortical inputs, but also noradrenergic and serotonergic facilitatory inputs via interneurons from various brainstem structures, including the pontine urine-storage center[57,68]. External anal sphincter (EAS)-electromyography (EMG) is an established method to detect neurogenic change in motor unit potentials (MUP), which mostly reflects denervation and reinnervation of the sphincter muscle[30]. The significance of the EAS-EMG in MSA has been well known[30,69,74]. Physiologically, external urethral sphincter (EUS) and EAS share sacral pudendal innervation from Onuf's nucleus[20]. In this article, we review the normal physiology and pathophysiology of the lower urinary tract and the lower gastrointestinal tract briefly, the current methods and interpretations of EAS or EUS-EMG, and sphincter EMG in autonomic disorders.

2. Physiology and pathophysiology of the lower urinary tract

The lower urinary tract consists of two major components, the bladder and urethra. The bladder is abundant with muscarinic M2,3 receptors (contraction) and adrenergic beta 3 receptors (relaxation)[12]. The urethra is abundant with adrenergic alpha 1A/D receptors (contraction) and nicotinic receptors (contraction) **(Fig. 1)**. The storage and emptying functions need an intact neuraxis that involves almost all parts of the nervous system[48]. This is in contrast to postural hypotension, which arises due to lesions below the medullary circulation center[56].



The lower urinary tract consists of two major components, the bladder and the urethra. The bladder is mainly innervated by the parasympathetic pelvic nerve. The urethra is innervated by the sympathetic hypogastric nerve and somatic pudendal nerve, respectively. Urinary storage is dependent on the reflex arc of the sacral spinal cord. The storage reflex is thought to be tonically facilitated by the brain, particularly the pontine storage center. The storage function is thought to be further facilitated by the hypothalamus, cerebellum, basal ganglia, and frontal cortex. Central cholinergic fibers from the nucleus basalis Meynert (NBM, also called the Ch4 cell group) seem to facilitate urinary storage. Micturition is dependent on the reflex arc of the brainstem and spinal cord, which involves the midbrain periaqueductal gray (PAG) and the pontine micturition center (located in or adjacent to the locus coeruleus [LC]). The voiding function is thought to be initiated by the hypothalamus and prefrontal cortex, which overlap the storage-facilitating area.
PVN: paraventricular nucleus, MPOA: medial preoptic area, A: adrenergic/noradrenergic, ZI: zona incerta, VTA: ventral tegmental area, SNC: substantia nigra pars compacta, DLTN: dorsolateral tegmental nucleus, PBN: parabrachial nucleus, IML: IML cell column, GABA: γ-aminobutyric acid, T: thoracic, L: lumbar, S: sacral
(cited from ref. 41)

Figure 1. Neural circuitry relevant to micturition.

Urinary storage is dependent on the autonomic reflex arc of the sacral cord[12]. This reflex is tonically facilitated by the brain, particularly the pontine storage center,[7,57] hypothalamus, cerebellum, basal ganglia, and frontal cortex[25]. In contrast, micturition is dependent on the autonomic reflex arc of the brainstem and spinal cord[12]. This reflex involves the periaqueductal gray[12,32,78] and the pontine micturition center (PMC)[6,7,12,54,63]. The PMC facilitates the sacral bladder preganglionic nucleus by glutamate[35], while inhibiting the sacral Onuf's nucleus by γ-amino-butyric acid (GABA) and glycine[8]. This reflex is regulated by the hypothalamus and prefrontal cortex[16,25].

Bladder (detrusor) overactivity is the major cause of urinary urgency/frequency and urgency incontinence[66]. In lesions above the brainstem, detrusor overactivity is considered an exaggerated micturition reflex[66]. This is in line with the fact that detrusor overactivity appearing after experimental stroke requires mRNA synthesis in the PMC[83]. The exaggeration of the micturition reflex might be brought about not only by decreased inhibition of the brain (by central cholinergic and D1 dopaminergic mechanisms); that is, it might be further facilitated by glutamatergic and D2 dopaminergic mechanisms[82]. Underactive detrusor (or bladder weakness) is the major cause of voiding difficulty in autonomic disorders. Underactive detrusor results from lesions in either upper or lower neurons innervating the bladder muscles, but typically occurs from lower neuron lesions.[1,48]

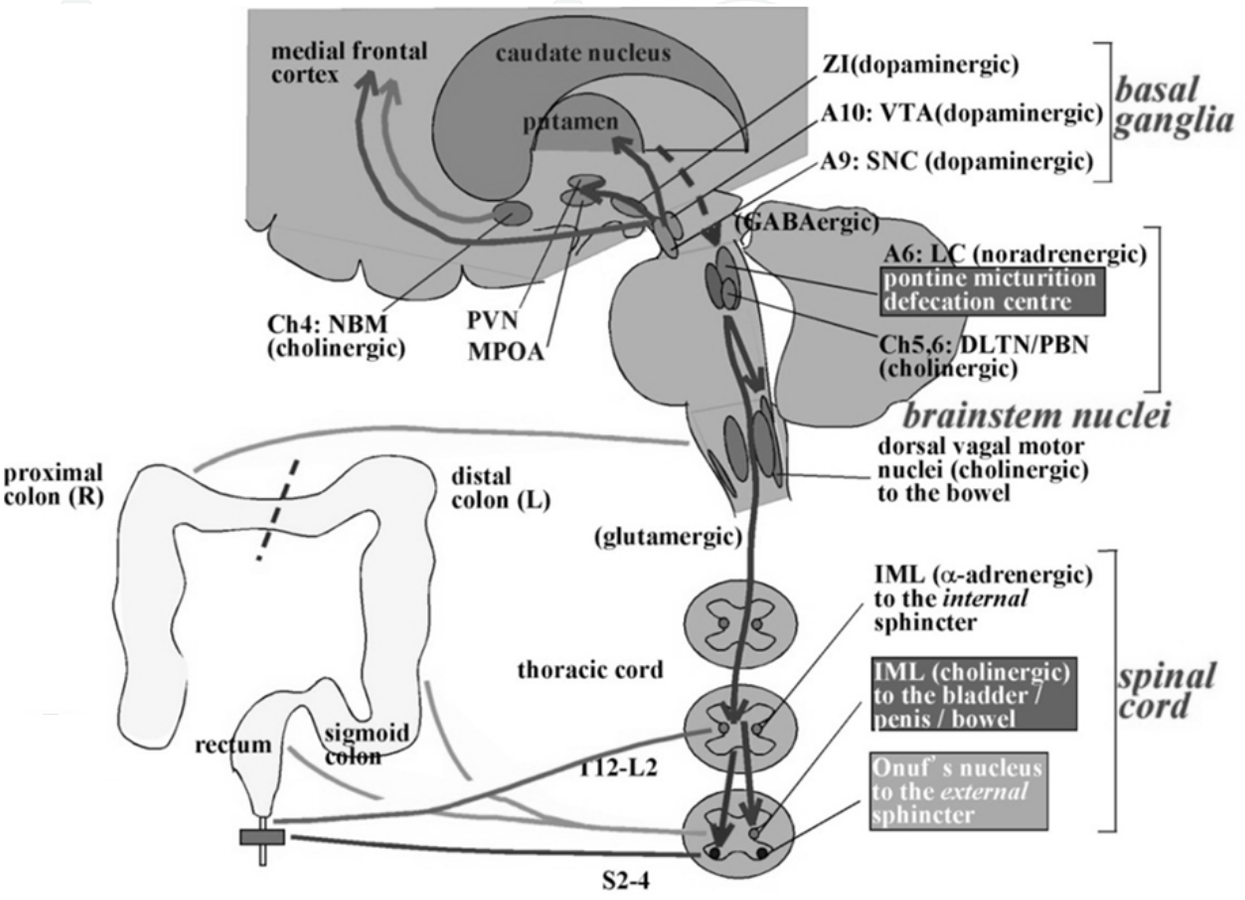
Urinary urgency incontinence and voiding difficulty in MSA result mostly from detrusor overactivity and underactive detrusor, respectively.[1,48] Patients with MSA often have a combination of detrusor overactivity in the filling phase and underactive detrusor in the voiding phase; this is called detrusor hyperactivity with impaired contractile function (DHIC). DHIC presumably reflects multiple lesions in both the storage-facilitating areas (the basal ganglia, pontine storage center) and the voiding-facilitating areas (the PMC, sacral preganglionic neurons in the intermediolateral [IML] cell columns) of this disorder.[23,79] In MSA, incomplete emptying is thought to be secondary to IML involvement.

Sphincter dysfunction contributes to voiding difficulty and urinary incontinence in autonomic disorders, although less commonly than over- or underactive detrusor does. When the urethral sphincter does not relax properly during voiding bladder contraction, it is called detrusor-sphincter dyssynergia.[1] Since a coordinated micturition reflex (bladder contraction with sphincter relaxation) needs an intact brainstem–sacral cord axis,[12] disruption of the axis (such as lesions affecting the cervical/thoracic spinal cord) may lead to detrusor–sphincter dyssynergia. Sphincter weakness is a cause of urinary incontinence. Sphincter weakness occurs from lesions in the sacral motoneurons (Onuf's nucleus), and typically appears in women with MSA as severe stress incontinence[49] or continuous urinary incontinence[34].

3. Physiology and pathophysiology of the lower gastrointestinal tract

The enteric nervous system plays the most important role in regulating the peristaltic reflex of the lower gastrointestinal tract[20]. Two types of myoelectrical activity or pressure changes in the colon are documented. Slow phasic pressure waves are the most common manometric

phenomenon[26], and in humans are measured as spontaneous phasic rectal contraction[9,22]. The peristaltic reflex can be evoked by surface stroking or by circumferential stretching.[20] The reflex consists of two components: ascending contraction (mediated by cholinergic fibers) oral to the stimulus site, and descending relaxation (mediated by non-adrenergic, non-cholinergic fibers) caudal to the stimulus site[2].



The function of the lower gastrointestinal tract is thought to depend on the brain and spinal cord, although less significantly than the lower urinary tract (LUT) does. Whereas the small intestine and ascending colon are innervated by the vagus nerves originating in the medulla, the descending colon, sigmoid colon, and rectum primarily share sacral innervation of the LUT (Figure 1). Both the sacral cord and the vagus nuclei receive projecting fibers from Barrington's nucleus (the pontine micturition/defecation center). Bowel function seems to be modulated by the higher brain structures, including the frontal lobe, the hypothalamus, and the basal ganglia; the main action of the latter on the bowel seems to be inhibitory.
NBM: nucleus basalis Meynert, Ch: cholinergic, PVN: paraventricular nucleus, MPOA: medial preoptic area, ZI: zona incerta, A: adrenergic/noradrenergic, VTA: ventral tegmental area, SNC: substantia nigra pars compacta, LC: locus ceruleus, DLTN: dorsolateral tegmental nucleus, PBN: parabrachial nucleus, PAG: periaqueductal gray, IML: IML cell column, GABA: γ-aminobutyric acid, T: thoracic, L: lumbar, S: sacral
(cited from ref. 41)

Figure 2. Neural circuitry relevant to defecation.

Other types of pressure changes in the colon include giant motor complexes[20]. A giant motor complex is a cyclic contractile activity with a periodicity of 20 to 30 min, and is perhaps analogous to the migrating motor complex of the small intestine[26]. A combination of slow

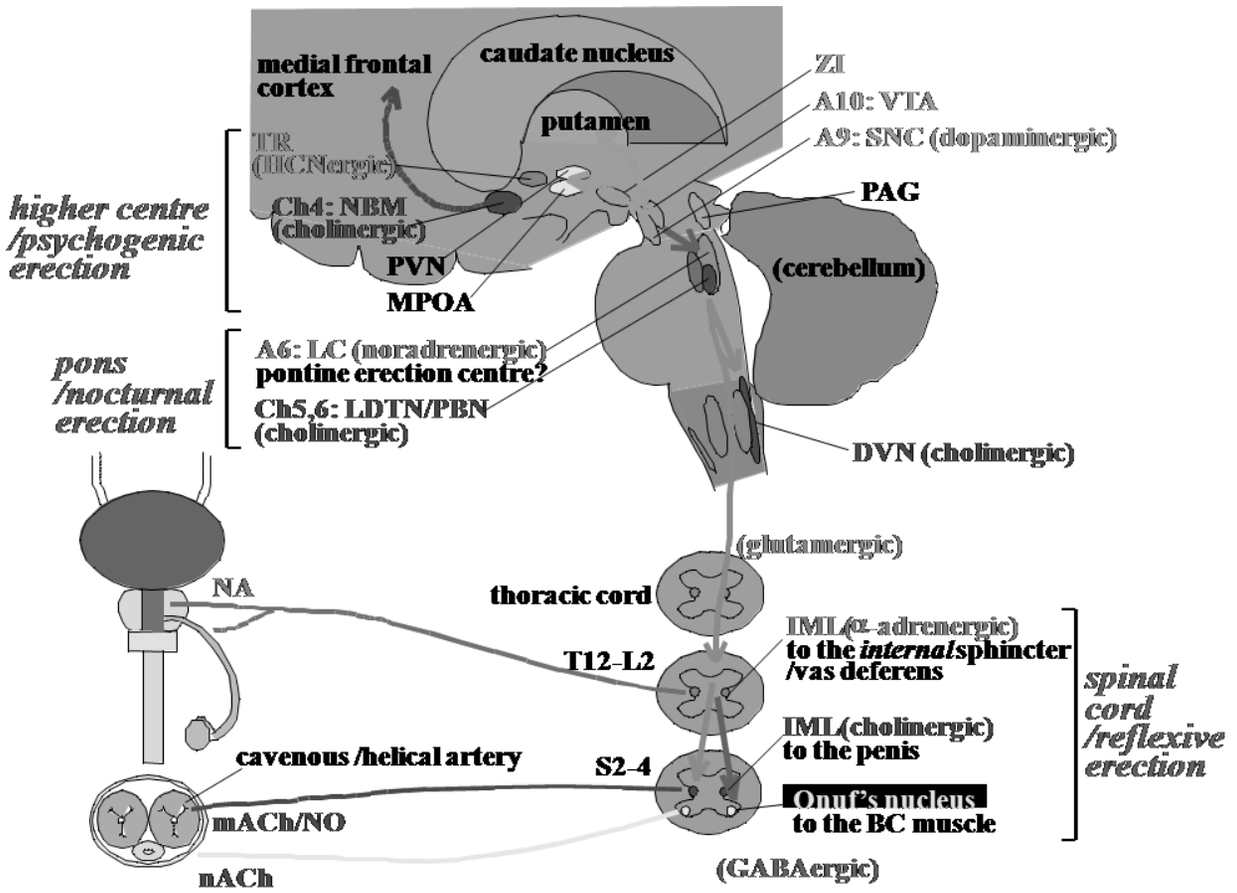
waves and giant motor complexes is thought to promote bowel transport, which in humans is measured by colonic transit time[4]. The strength of cholinergic transmission in the enteric nervous system is thought to be regulated by opposing receptors; serotonin 5-HT4 receptor-mediating excitation[31,73] and dopamine D2 receptor-mediating inhibition[76].

Whereas the rostral lower gastrointestinal tract is innervated by the vagus nerves originating in the medulla, extra-enteric innervation of the caudal lower gastrointestinal tract primarily shares the innervation of the lower urinary tract **(Fig. 2)**[12,22]. The lower urinary tract and lower gastrointestinal tracts perform similar functions of storage and emptying. However, they differ profoundly with regard to anatomy (closed bag versus open-ended tube, respectively), luminal contents (liquid versus half-solid), and physiology (dysfunctional transport, rare ureter versus common bowel; smooth muscle contraction, bladder contraction only on emptying versus persistent spontaneous phasic rectal contraction; abdominal strain, minimal on urination versus strong on defecation)[22]. In addition, while the lower urinary tract requires an intact neuraxis for storage and emptying[12], it has not been entirely clear to what extent the lower gastrointestinal tract needs the extra-enteric nervous system.

Constipation in MSA most probably results from slow colonic transit, decreased phasic rectal contraction, and weak abdominal strain.[58] Some patients also have paradoxical sphincter contraction on defecation (PSCD).[58] The sites responsible for this dysfunction seem to be both the central and peripheral nervous systems, which regulate the lower gastrointestinal tract. Slow colonic transit and decreased phasic rectal contraction most probably reflect peripheral enteric nervous system lesions, whereas weak abdominal strain and PSCD may reflect central lesions.[61] In contrast, fecal incontinence results mostly from a weak anal sphincter due to denervation.[58]

4. Physiology and pathophysiology of the genital organ

The genital organ primarily shares lumbosacral innervation with the lower urinary tract. Erection is a vascular event[3]; occurring secondarily after dilatation of the cavernous helical artery and compression of the cavernous vein to the tunica albuginea[3]. Helical artery dilatation is brought about by activation of cholinergic and nitrergic nerves; this activation facilitates nitric oxide secretion from the vascular endothelium. Ejaculation is brought about by contraction of the vas deferens and the bladder neck, in order to prevent retrograde ejaculation, by activation of adrenergic nerves **(Fig. 3)**. Sacral Onuf's nucleus innervates the bulbocavernosus muscle; and is thought to participate in erection and ejaculation. Sexual intercourse in healthy men can be divided into 3 phases[65]: a) desire (libido), b) excitement and erection, and c) orgasm, seminal emission from the vas deferens, and ejaculation from the penis. Erection can be further classified into 3 types by the relevant stimulation: 1) psychogenic erection (by audiovisual stimulation), 2) reflexive erection (by somatosensory stimulation), and 3) nocturnal penile tumescence (NPT) (associated with rapid eye movement [REM]-sleep). 'Morning erection' is considered the last NPT in the nighttime.



PAG, periaqueductal gray; LC, locus coeruleus; NBM, nucleus basalis Meynert; PVN, paraventricular nucleus; MPOA, medial preoptic area; A, adrenergic/noradrenergic; ZI, zona incerta; VTA, ventral tegmental area; SNC, substantia nigra pars compacta; DLTN, dorsolateral tegmental nucleus; PBN, parabrachial nucleus; IML, intermediolateral nucleus; GABA, γ-aminobutyric acid; T, thoracic; L, lumbar; S, sacral; NA, noradrenaline; Ach, acetylcholine; NO, nitric oxide. See text.

Figure 3. Neural circuitry relevant to erection.

Among the 3 types of erection, reflexive erection requires an intact sacral cord, particularly the intermediolateral (IML) cell columns. Pathology studies have shown that involvement of the IML nucleus is common in MSA, whereas it is uncommon in Parkinson's disease. Therefore, reflexive erection can be affected in patients with MSA. In patients with a supra-sacral spinal cord lesion, reflexive erection might be preserved, whereas psychogenic erection is severely disturbed because of a lesion in the spinal pathways to the sacral cord. Libido and erection are thought to be regulated by the hypothalamus; particularly the medial preoptic area (MPOA) and the paraventricular nucleus (PVN).[13,72] Recent neuroimaging studies have shown that penile stimulation or watching pornography activated these areas in humans[70]. NPT[15] seems to be regulated by the hypothalamic lateral preoptic area,[21] raphe nucleus, and locus ceruleus. Oxytocinergic neurons in the hypothalamic PVN are thought to facilitate erection by projecting directly to the sacral cord,

and by projecting to the midbrain periaqueductal gray and the Barrington's nucleus (identical to the PMC).

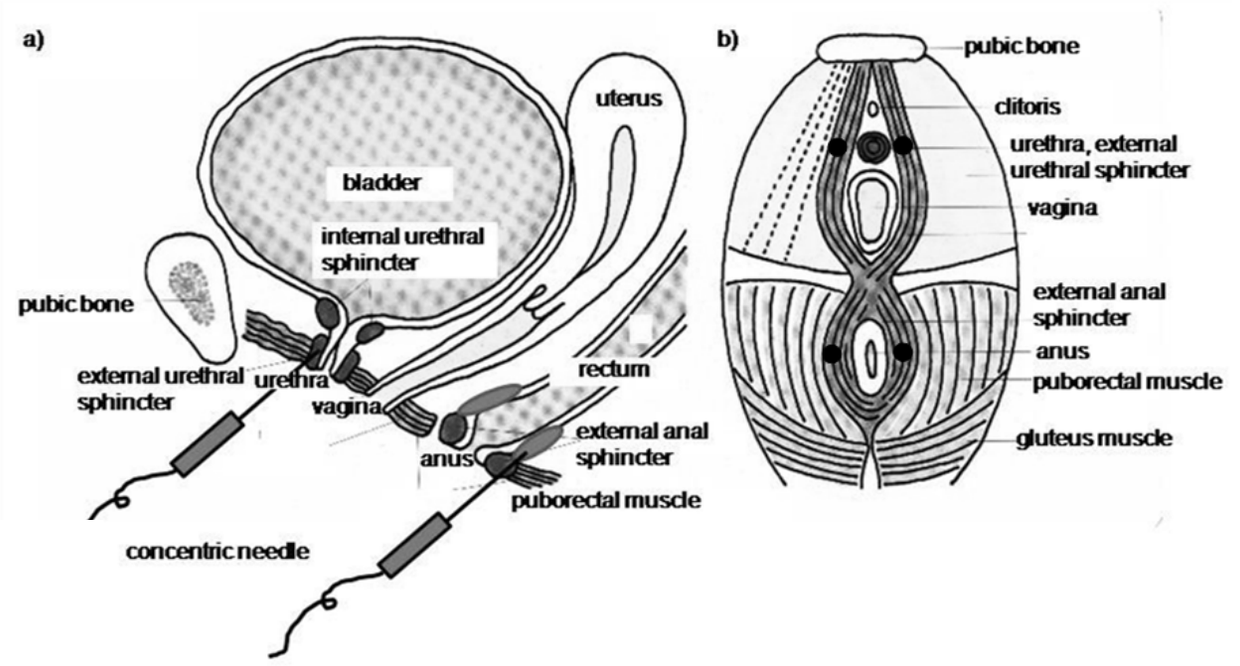
In experimental animals, dopamine is known to facilitate erection and mating behaviors[13]. The MPOA/PVN receives projections from the nigral dopaminergic neurons. Prolactinergic neurons are thought to be inhibitory in sexual function. Prolactin-producing pituitary tumors often cause gynecomastia and erectile dysfunction in male patients. Hyperprolactinemia occurs after the use of sulpiride, metoclopramide, and chlorpromazine (all dopamine receptor antagonists). Therefore, dopaminergic neurons seem to facilitate oxytocinergic neurons whereas they inhibit prolactinergic neurons.

5. Methods and interpretations of sphincter EMG

In humans, the EUS and EAS share sacral pudendal innervation from Onuf's nucleus.[12,20] The EAS lies around the anal canal and forms an 8-shaped sphincter system on the pelvic floor **(Fig. 4)**. Although injury to the peripheral nerves may lead to the dysfunction of the EUS alone, lesions of the sacral Onuf's nucleus affect both the EAS and EUS. For this reason, we use EAS-EMG to assess urinary incontinence, as it is easier to perform and less painful than EUS-EMG. For the same reason, few studies have utilized EUS-EMG.[14,17] In women, the EUS muscle can be examined using a perineal approach. Examination of this muscle is more difficult in men; we can approach it with the fingers by feeling for the prostate within the rectum. However, EUS should be chosen in cases exhibiting a decelerating burst ('whale noise') with complex repetitive discharge in Fowler's syndrome.[24]

The EAS can be divided into a deep part (thick; around the rectal neck to the anal canal) and a subcutaneous part (thin; around the anus). The deep EAS is a major constituent in the generation of anal pressure to hold feces in when the rectum is full. The normal range of static anal pressure is more than 40 cmH_2O, and that of anal squeeze pressure is more than 50 cmH_2O.[22] The former is thought to reflect hypogastric adrenergic innervation, whereas the latter reflects somatic Onuf's nucleus innervation.[22] The subcutaneous EAS is easy to examine. It is reached by inserting a needle about 1 cm from the anal orifice, to a depth of 3–6 mm.[43]

Although the EAS is a skeletal muscle, it usually fires continuously during both waking and sleeping states. To assess EAS, an EMG computer with quantitative, template-operated MUP analysis software is recommended. The commonly used amplifier filter setting is 5–10 kHz. The tip of a concentric needle usually monitors an area approximately 500 micrometers in diameter, which includes approximately 20 MUPs. To assess acute denervation, insertion and spontaneous activities are checked as with the evaluation of other skeletal muscles. When the muscle is completely denervated, the EMG becomes silent. After an interval of 10–20 days, the insertion potentials become prolonged and abnormal spontaneous muscle activities, e.g., fibrillation potentials and positive sharp waves, appear. However, in the EAS, due to the continuous firing activities, it is not easy to see denervation potentials. In such cases, examination of the bulbocavernosus muscle has been recommended[44].



This figure illustrates where to insert concentric needles to measure external sphincter EMG.

Figure 4. The external anal sphincter and the external urethral sphincter.

A normal MUP usually has a 50–500 microV amplitude, a 3–8 msec duration, and 2–4 phases. In order to assess reinnervation, usually 10–20 single MUPs are recorded, which are automatically provided by an EMG computer. To ascertain single MUP, we still check each wave manually and adjust the onset and offset of each wave. It is particularly important to include late components (satellite potentials) to measure the duration of each unit.[42] When the muscle is chronically denervated, an intact nerve tends to innervate the adjacent denervated muscle fibers. As a result, MUPs become of high amplitude, of long duration, and polyphasic. Among various EMG parameters, the use of duration, MUP area, and number of turns is recommended for optimal diagnostic power (sensitivity and specificity) in the EAS muscle.[45] In addition, the results are dependent on the methods used; e.g., including or excluding late components. Palace et al. proposed that either of two criteria is sufficient to diagnose neurogenic changes in the EAS-EMG: (*a*) more than 20% of MUPs have a duration > 10 msec, or (*b*) the average duration of MUPs > 10 msec, particularly including the late components.[38] When satellite potentials were excluded, the duration of MUPs did not differ significantly between Parkinson's disease and MSA.[48] When lower motor neuron-type abnormalities are not apparent, it is reported that abnormal MUP recruitment pattern suggests pyramidal tract involvement.[18] In addition to MUP analysis in the external sphincter muscles, other neurophysiologic tests, e.g., pudendal nerve conduction, sacral reflexes, somatosensory evoked potentials and cranial magnetic stimulation, and urodynamic studies, can be of particular value in the study of autonomic patients.[29,40,41]

6. Sphincter EMG in autonomic disorders

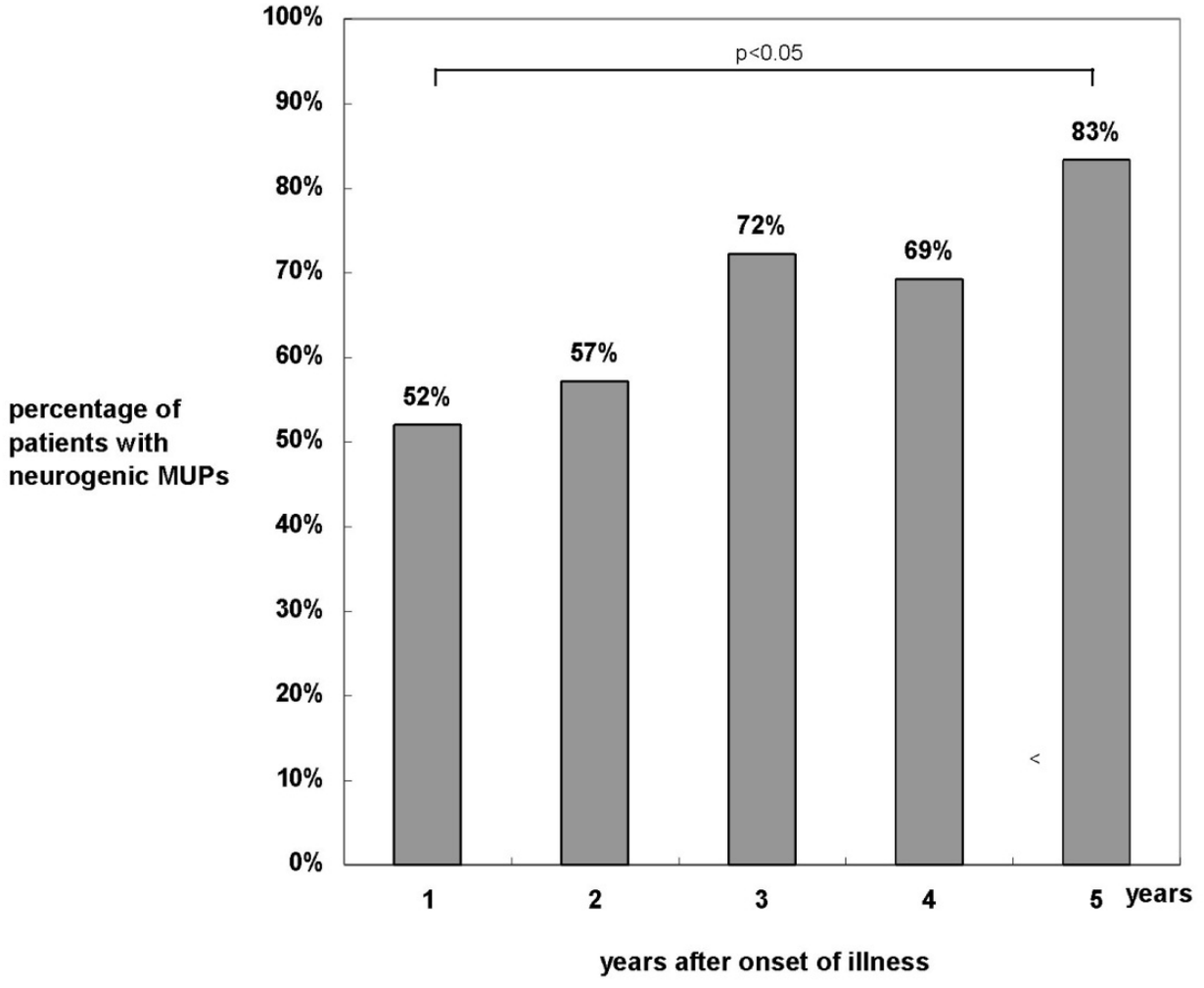
6.1. MSA

Cardiovascular autonomic failure in MSA is thought to derive from neuron loss in the thoracolumbar intermediolateral (IML) cell columns of the spinal cord and the medullary circulation center. In contrast, lower urinary tract disorder in MSA is thought to reflect multiple lesions in the basal ganglia and the pontine storage center (storage-facilitating areas), as well as in the pontine micturition center in or adjacent to the locus ceruleus and the sacral IML cell columns (voiding-facilitating areas).[11] In addition, a distinguishing pathology in MSA is neuronal cell loss in the sacral Onuf nucleus.[33,37]

The first reports on neurogenic changes of EAS-EMG in MSA are attributed to Sakuta et al. (1978).[62] Since then, EAS-EMG results for over 500 MSA patients have been reported, with abnormality rates of more than 70% in many studies[5,30,36,38,47,53,62,64,71]. EAS-EMG is better tolerated and yields identical results to those from EUS investigation[5]. Abnormalities have also been recorded in the bulbocavernosus muscles in MSA.[67] In a larger study, Beck et al. (1994) reported that all (100%) 62 MSA patients with urological symptoms had abnormalities in both EAS and EUS-EMG.[5] Palace et al. (1997) reported abnormal EAS-EMG in 103 (82%) of 126 patients with MSA[38]. Chandiramani et al. (1997) found abnormal EAS-EMG in 49 (94%) of 52 patients with MSA[10]. Kirchhof et al. (1999) found abnormal EAS-EMG in 89 (91%) of 98 patients with MSA[28]. Sakakibara et al. (2000) found an abnormal EAS-EMG in 53 (74%) of 71 MSA patients[52]. These abnormalities correspond to selective loss of ventral horn cells and astrogliosis; the loss is particularly severe in the second and third sacral segments (Onuf's nucleus) in MSA[11]. Sphincter EMG has been proposed as a means of distinguishing between MSA and idiopathic Parkinson's disease (as described below), since the anterior horn cells of Onuf's nucleus are not affected in idiopathic Parkinson's disease.[10] In contrast, there have been debates about whether or not sphincter EMG can be used to distinguish MSA from idiopathic Parkinson's disease. In a study of 13 patients with idiopathic Parkinson's disease and 10 patients with MSA, Giladi et al. (2000) found significant overlap in all EMG parameters (presence of fibrillation potentials, MUP duration, presence of satellite potentials, percentage of polyphasic potentials)[19]. However, the durations of MUPs in both the MSA and Parkinson's disease groups were longer than in other studies.

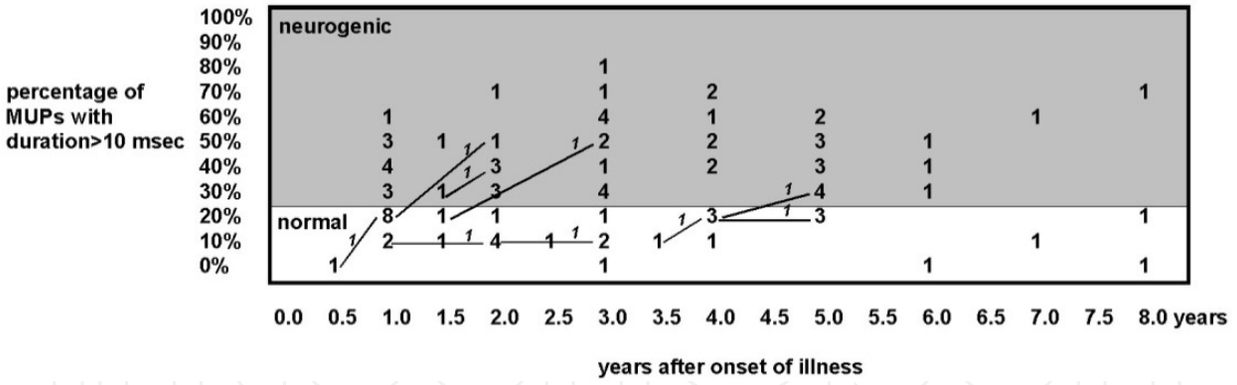
It is reported that EAS-MUP abnormalities can distinguish MSA from idiopathic Parkinson's disease in the first 5 years after disease onset.[30,69,74] However, the prevalence of such abnormalities in the early stages of MSA has not been well known. In our recent study of 84 probable MSA cases, 62% exhibited neurogenic change.[80] The prevalence was relatively low presumably because up to 25% of our patients had a disease duration of 1 year or less. In such early cases, the diagnosis of MSA should be made with extreme caution. In addition to the clinical diagnostic criteria, we usually add an imaging study and we perform gene analysis to the extent possible. The prevalence of neurogenic change was 52% in the first

year after disease onset, which increased to 83% by the fifth year ($p<0.05$) **(Fig. 5)**. Among the patients who underwent repeated studies, many had normal to mild abnormality at the initial examination, which turned into marked abnormality during the course of illness **(Fig. 6)**. Therefore, as expected, it is apparent that the involvement of Onuf's nucleus in MSA is time-dependent. In the early stages of illness, the prevalence of neurogenic change in MSA does not seem to be high. In 2 patients who underwent repeated studies, the EAS-EMG findings tended to remain normal. We do not know whether some MSA patients never develop neurogenic change during the course of their illness. However, Wenning et al. (1994) reported 3 patients with normal EAS-EMG and a postmortem confirmation of MSA.[77] Therefore, a negative result cannot exclude a diagnosis of MSA. More recently, Paviour et al. (2005) reported that among 30 sets of clinical data and postmortem confirmation in MSA cases with a duration of more than 5 years, 24 (80%) had abnormal EAS-EMG, 5 (17%) had a borderline result, and only 1 had a normal EMG.[39]



The prevalence of neurogenic sphincter EMG increased during the course of illness.
MUP: motor unit potential
(cited from ref. 74)

Figure 5. Neurogenic sphincter EMG and duration of illness.



Percentage of MUPs with duration > 10 msec: one of two categories for neurogenic sphincter EMG.
straight figures: the number of patients
oblique figures: the number of patients who underwent the study repeatedly
MUP: motor unit potential
(cited from ref. 74)

Figure 6. Percentage of MUPs with duration > 10 msec and duration of illness.

The prevalence of neurogenic change also increased with the severity of gait disturbance ($p<0.05$) in our study. However, neurogenic change was not related to postural hypotension (reflecting adrenergic nerve dysfunction); erectile dysfunction in men (presumably reflecting cholinergic and nitrate oxidergic nerve dysfunction); detrusor overactivity (reflecting the central type of detrusor dysfunction); constipation (presumably reflecting both peripheral and central types of autonomic and somatic dysfunction); or gender **(Table 1)**. The neurogenic change in EAS-MUP was slightly more common in those with detrusor-sphincter dyssynergia (reflecting the central type of sphincter dysfunction). It has been reported that neurogenic change does not correlate directly with a clinically obvious functional deficit.[74] Patients with marked abnormalities in EAS-MUP may have no faecal incontinence,[77] although, in such patients, anal sphincter weakness is not uncommon.[58] In our study, the prevalence of neurogenic change slightly increased with the severity of storage disorder (incontinence). The most common type of urinary incontinence in MSA is urgency incontinence, which results mostly from detrusor (bladder) overactivity. However, we noted urinary incontinence in 17 patients without detrusor overactivity or low-compliance detrusor; in those cases, the urinary incontinence may have had a sphincter etiology. Urinary incontinence was more severe in the patients with neurogenic change than in those without it ($p<0.05$).

We recently retrospectively analysed 445 case records of EMG cystometry with pressure flow studies, single motor unit potential (MUP) analysis in patients with parkinsonian syndrome, e.g., MSA: n=267, Parkinson's disease (PD): n=129, Dementia with Lewy bodies (DLB): n=25, and progressive supranuclear palsy (PSP): n=24. We carried out receiver operating characteristics (ROC) analysis, revealing that an area under the ROC curve (AUC) in differentiating MSA from other parkinsonian syndrome was 0.70 in duration, 0.62 in phase and 0.51 in amplitude, respectively, with statistically significance. Therefore, duration of MUPs is most sensitive for the differentiation of MSA among MUPs parameters.

	Patients with neurogenic sphincter EMG			Patients with neurogenic sphincter EMG		
	No	%		No	%	
Male	27/42	65	Female	25/42	59	NS
Age <60 years	22/39	56	Age >60 years	30/45	66	NS
MSA-C	29/50	58	MSA-P	23/34	68	NS
Independent walking (1–3*)	11/23	48	Wheelchair bound(6–7*)	9/11	82	p<0.05
Postural hypotension −	30/48	63	Postural hypotension +	22/36	60	NS
Constipation −	40/66	61	Constipation +	12/18	67	NS
Erectile dysfunction −	4/5	80	Erectile dysfunction +	19/30	63	NS
Continent	15/25	59	Incontinent	37/59	63	NS
RU <200 ml	36/62	58	RU >200 ml	16/22	73	NS
Detrusor overactivity −	14/26	55	Detrusor overactivity +	38/58	65	NS
UD/AD −	29/52	56	UD/AD +	20/32	63	NS
DSD −	44/73	60	DSD +	8/11	73	NS

*International cooperative ataxia rating scale, walking capacities subscale.
AD, acontractile detrusor; DSD, detrusor sphincter dyssynergy; MSA, multiple system atrophy; RU, residual urine volume; UD, underactive detrusor.

MSA: multiple system atrophy, RU: residual urine volume, UD: underactive detrusor, AD: acontractile detrusor
DSD: detrusor-sphincter dyssynergia
*: International Cooperative Ataxia Rating Scale, walking capacities subscale
(cited from ref. 74)

Table 1. Neurogenic sphincter EMG and clinical variables other than duration of illness.

6.2. Lewy body diseases

6.2.1. Idiopathic Parkinson's disease (IPD)

Several reports of "supposed IPD" have shown severe bladder dysfunctions, e.g., large post-void residuals or neurogenic change in the EAS-EMG. However, some of these reports were published before a definition of MSA was established. Recent studies have reported almost normal EAS-EMG in patients with typical IPD[38,47,53,67]. Stocchi's study (1997) is important, since EMG in patients with IPD and MSA was performed by researchers blinded to the diagnosis.[67] Pathological studies of IPD have shown a degenerative lesion in the spinal parasympathetic PGN[75], although the lesions are much less developed than those in MSA. No Lewy bodies were found in Onuf's nucleus innervating the anal sphincter in IPD.[75] In contrast, Libelius and Johansson (2000) described neurogenic change in EAS-EMG in PD after a disease duration of more than 5 years.[30] This remains a matter of controversy; on the other hand, some patients with DLB may show abnormal EAS-EMG, as described below.

6.2.2. Dementia with Lewy bodies (DLB)

DLB is characterized as dementia with fluctuating cognition and visual hallucination, with (sometimes atypical) parkinsonism. Cardiovascular and urinary autonomic failure is

another feature. We performed urodynamic studies in 7 patients with DLB, and performed EAS-EMG in 3. Two of those 3 patients exhibited neurogenic changes in MUPs.[55]

6.2.3. Autonomic failure with Parkinson's disease (AFPD)

AFPD is an intermediate entity that describes a combination of autonomic failure and IPD, but without dementia. We performed urodynamic studies in 7 patients with AFPD and performed EAS-EMG in 4. Three of those 4 patients exhibited neurogenic changes in MUPs[55].

6.2.4. Pure autonomic failure (PAF)

Earlier studies reported normal EAS-EMG in small groups of patients with PAF. However, Ravits et al. (1996)[46] found abnormal EAS-EMG in 2 of 7 patients with PAF, although both of them were multiparous women. Sakakibara et al. performed urodynamic studies in 6 patients with PAF and EAS-EMG in 4. Three of those 4 patients exhibited neurogenic changes in MUPs.[51] In PAF, parkinsonism may appear after a 10-year interval.[81] Therefore PAF can be listed in the differential diagnosis of degenerative parkinsonism. To sum up, in all three Lewy body diseases (DLB, AFPD, PAF), the frequency of neurogenic changes seemed higher in EAS-EMG than in IPD but lower than in MSA. This suggests the involvement of the sacral Onuf's nucleus or its fibers in the external sphincter in these diseases. The prevalence of neurogenic changes in EAS-EMG seems to be: **MSA >> DLB = AFPD = PAF >> PD (Table 2)**. However, these assumptions require confirmation with a larger study. The results seem to be in accordance with the fact that 29% of the DLB patients undergoing EMG-cystometry had a low-compliance detrusor, indicating a pre-ganglionic lesion of the pelvic nerves. The bethanechol test showed that both of these patients had denervation supersensitivity of the detrusor, indicating a post-ganglionic lesion of the pelvic nerves. The results of physiological studies and metaiodobenzylguanidine (MIBG) cardiac scintigraphy suggested post-ganglionic abnormalities in DLB.

Disease	LUT symptoms	Urinary incontinence (storage dysfunction)	PVR > 100 ml (voiding dysfunction)	No. of patients	Reference	Detrusor overactivity (central type)	Low compliance (preGGL type)	Bethanechol supersensitivity (denervation) (postGGL type)	Neurogenic change of sphincter MUPs (denervation) (Onuf's nucleus)	No. of patients	Reference
MSA	96%	63%	52%	121	9	56%	31%	19%	93%	121	9, 11
DLB	100%	91%	27%	11	–	71%	29%	2/2	2/3	7	–
AFPD	100%	43%	29%	7	19	86%	14%	1/3	4/4	7	19
PAF	100%	33%	33%	6	17	67%	33%	2/3	¼	6	17
PD	53–70%	25–28%	0%	115	18	81%	0%	Not performed	5%	21	11

AFPD, autonomic failure with Parkinson's disease; DLB, dementia of Lewy body type; GGL, ganglion; LUT, lower urinary tract; MSA, multiple system atrophy; MUP, motor unit potential; PAF, pure autonomic failure; PD, Parkinson's disease; PVR, post-void residual.

MSA: multiple system atrophy, DLB: Dementia with Lewy bodies, AFPD: Autonomic failure with Parkinson's disease
PAF: Pure autonomic failure, PD: Parkinson's disease, GGL: ganglionic
(cited from ref. 78)

Table 2. Comparison of lower urinary tract function in DLB, AFPD, PAF, PD and MSA. See text.

6.3. Other parkinsonian disorders

6.3.1. Progressive supranuclear palsy (PSP)

We performed urodynamic studies in 9 patients with PSP and performed EAS-EMG in 4. Two of these 4 patients exhibited neurogenic changes in MUPs.[50] Abnormal sphincter EMG was also reported in 5 of 12 patients by Valldeoriola et al. (1995)[71], and in 2 of 8 patients by Palace et al. (1997)[38]. Libelius and Johansson (2000) also described anal sphincter EMG abnormalities in 2 of 3 patients with PSP.[30]

6.3.2. Corticobasal degeneration (CBD)

We performed urodynamic studies in 6 patients with CBD and EAS-EMG in 5 of them. However, none of the 5 patients showed neurogenic changes in the MUPs.[60] There is a considerable overlap in the clinical presentation of the parkinsonian form of MSA (MSA-P) and that of PSP. Therefore, we should be cautious in interpreting sphincter EMG in these disorders.

6.4. Cerebellar ataxia

6.4.1. Spinocerebellar ataxia 3 (SCA3)/Machado-Joseph disease

We performed urodynamic studies in 11 patients with spinocerebellar ataxia 3 (SCA3) and performed EAS-EMG in 9. Six of the 9 patients showed neurogenic changes in MUPs.[59]

6.4.2. Late cortical cerebellar atrophy (LCCA):

We performed urodynamic studies in 7 patients with LCCA, which is a pure cerebellar ataxia without heredity, and EAS-EMG in 3 of them. However, none of the 3 patients exhibited neurogenic changes in the MUPs.

6.4.3. Spinocerebellar ataxia 6 (SCA6)

We performed urodynamic studies in 9 patients with spinocerebellar ataxia 6 (SCA6) and performed EAS-EMG in 8. Five of the 8 patients showed neurogenic changes in MUPs.

6.5. Other diseases

Sakuta et al. performed EAS-EMG in 30 patients with amyotrophic lateral sclerosis (ALS).[62] None of them exhibited neurogenic changes in the MUPs, which contrasted with common neurogenic changes in the limb muscles in this disorder. These EMG findings correspond to the postmortem selective sparing of sacral Onuf's nucleus, which contrasts with severe loss of anterior horn cells innervating the limbs, tongue, and bulbar muscles[2]. Neurons in Onuf's nucleus demonstrate some morphological differences from the anterior horn cells innervating limb muscle [33]. However, more recent studies have shown abnormalities in the

Onuf's nucleus in most advanced cases with ALS[27], particularly in patients under mechanical ventilation.

7. Conclusions

We have reviewed the normal physiology and pathophysiology of the lower urinary tract and the lower gastrointestinal tract, the current methods and interpretations of sphincter EMG, and the application of this technique to various autonomic disorders. Sphincter EMG makes it easier to distinguish MSA from idiopathic Parkinson's disease in the first 5 years after disease onset, reflecting the significant involvement of the sacral spinal cord in MSA. However, abnormal sphincter EMG is also seen in some, though not many, patients with DLB or PSP. It is noteworthy that sphincter denervation leads to severe urinary and fecal incontinence in some female patients with MSA, which severely affects their quality of life. Sphincter EMG and relevant sacral autonomic tests are good diagnostic tools in autonomic disorders.

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