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Review

REM sleep atonia: from basic background to clinical application

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Muscle tone is profoundly suppressed during rapid-eye-movement sleep (REMS). Two indices that quantify this muscle activity suppression were introduced; the tonic inhibition index (TII) and the phasic inhibition index (PII). TII expresses the shortness of phasic chin muscle activity, and PII indicates the weakness of rapid eye movements-related phasic chin muscle activity loss. TII increased significantly with age, while PII decreased significantly. These chronological changes were concluded to indicate that the activity of the human nervous systems involved in both tonic and phasic inhibition in REMS increases with age. TII was found to reach the adult level at 12.3 years of age, while PII decreased to the adult value at 0.4 years. According to this difference in age between their maturation, the human nervous systems involved in muscle activity suppression during REMS are hypothesized to comprise at least 2 independent systems. TII and PII are also hypothesized to be affected by the activity of the brainstem inhibitory/facilitatory centers, which might be implicated in the control of muscle activity during wakefulness as well.

Key words: REM sleep, brainstem, tonic inhibition index, phasic inhibition index, development

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Introduction

Muscle tone is profoundly suppressed during rapid-eye-movement sleep (REMS). Brainstem inhibitory/facilitatory centers are considered to have a great contribution to producing this muscle activity loss. In the first part of this review, I would introduce recent knowledge on these functional structures. In order to quantify this muscle activity loss on the routine polysomnographic recording, two indices (the tonic inhibition index, TII; the phasic inhibition index, PII) were designated. In the second part of this review, these two indices are introduced. Since TII and PII were found to reach the adult level at different ages, more than a single system is hypothesized to mediate human REMS atonia. Several reports that support the idea that not a single pathway is involved in the suppression of muscle activity during REMS are also introduced in this section. In the final part, TII and PII values in several neurologically affected patients are summarized. Clinical implications of these two indices are also discussed.

Brain regions responsible for the suppression of muscle activity during REMS

A. Supraspinal control of muscle activity.

In primates, a wide range of movements is maintained in spite of lesions of the pyramidal tract[1], while interruption of the ventromedial brainstem-spinal cord pathways results in severe impairment of axial and proximal-extremity movements[2]. The brainstem plays crucial roles in coordinating posture and movement[3,4]. The outflow from the basal ganglia, which is requisite for movement control and was once believed to be

prepyramidal rather than extrapyramidal[5], was recently re-recognized to travel not only to motor cortical areas via the thalamus (acting as a prepyramidal system) but also to the brainstem[6] through the pedunculopontine tegmental nucleus (PPN)[7]. The brainstem is considered to affect fundamental motor processes[7,8].

Since the introduction of decerebrate rigidity[9], the brainstem has been regarded as a structure contributing excitatory influences to motor outflows. As originally discovered by Magoun and Rhines[10], this decerebrate rigidity was abolished nonreciprocally on stimulation of the midbrain, pontine and medullary reticular formations[11–18]. Disfacilitation might be responsible for this abolition of decerebrate rigidity, however, inhibitory drives are also considered to be involved in this collapse. In fact, inhibitory postsynaptic potentials were produced in motoneurons on electrical stimulation of the brainstem reticular formation in the decerebrate cat[19,20]. Therefore, it is obvious that not only excitatory but also inhibitory drives arise from the brainstem.

For any given movement, the activity of a competing muscle must be inhibited unconsciously to complete the desired movement without interference. A number of spinal inhibitory systems, such as reciprocal inhibition, appears to be insufficient to explain this kind of muscle activity suppression[21]. The actions of the supraspinal neural systems that suppress muscle activity should underlie every movement to make it smooth. The brainstem reticular formation could be one of the sources to suppress muscle activity during voluntary movements[19,20].

B. Brainstem inhibitory centers

Without higher brain structures[22], both the tonic and phasic types of muscle activity loss could be elicited during REMS even in humans[23]. The phasic muscle activity reduction occurs in association with rapid eye movements[22–25]. Brainstem inhibitory centers are postulated to be responsible for the occurrence of these two types of muscle activity loss[26]. Activation of brainstem inhibitory centers is considered to be involved in the cortically-induced reduction of muscle activity through corticoreticular pathways[4]. Some negative motor phenomena, such as cataplexy and a type of atonic seizure, are potentially implicated in brainstem inhibitory centers[27,28]. Recently, positron emission tomography of the brain demonstrated that the human brainstem is activated in REMS[29–31]. The suppression of muscle activity in human REMS is likely to be maintained by the brainstem inhibitory centers. In fact, lesions in the rostral pontine and medial medullary reticular formations disturb atonia during REMS[32–34], including in humans[35,36]. Lesions in the dorsolateral pontine tegmentum was reported to prevent the rapid eye movement-related phasic muscle activity loss in REMS[37].

The brainstem inhibitory centers consist of 3 major sites; the midbrain, pontine and medial medullary reticular formations. The midbrain inhibitory centers include the retrorubral nucleus, ventral paralemniscal tegmental field and the PPN[13]. The pontine inhibitory centers are located in the rostral part of the pontine reticular formation, and the medullary inhibitory centers are distributed in the nucleus reticularis gigantocellularis, nucleus reticularis magnocellularis and nucleus reticularis paramedianus[12,17,38]. Chemical stimulation of these areas suppresses muscle activity[11,12,14,15], which indicates that cellular components in these brainstem regions are responsible for the suppression of muscle activity. In freely moving, awake cats, electrical stimulation of the descending fibers from the pontine to medullary inhibitory centers produces natural postural suppression with termination of ongoing locomotor movements[39]. Also, neurons in the pontine inhibitory centers intervene in the control of the postural adjustments induced by cortical stimulation[40]. Some cells in feline brainstem inhibitory centers were found to exhibit increased firing not only in REMS but also in postural relaxation during wakefulness[41,42]. Recently, the medullary reticular formation has been found to produce a motor inhibition by acting on alpha- and gamma-motoneurons, and on interneurons in reflex pathways in the spinal cord[18]. This finding demonstrates an important contribution of the medullary reticular formation to suppressing muscle activity not only during REMS but also during wakefulness.

C. Brainstem disfacilitatory mechanisms involved in REMS atonia

Serotonin[43] and noradrenalin[44] exert an excitatory effect on motoneurons. The brainstem sources of these neurotransmitters (raphe nuclei for serotonin and the locus coeruleus (LC) for noradrenalin) could be a part of brainstem facilitatory centers. The midbrain locomotor region (MLR, the PPN and the caudal half of the cuneiform nucleus) and the caudal part of the pontine reticular formation (the nucleus reticularis pontis caudalis, NRPc) could also be included in these functional centers. Firing of the neurons in the association cortex exhibits little correlation with phasic muscle activity[45], while unit discharges correlated with phasic

muscle activity (twitches) during REMS are recorded in the NRPc[46] and in the dorsal raphe nucleus[47]. The firing rate of neurons in the raphe nuclei and the LC is highest during wakefulness, decreases during non-REMS, and completely ceases during REMS[48]. Several other evidences revealed that disfacilitatory mechanisms of the serotonergic system play significant roles on diminishing muscle activity during REMS[49,50]. On the noradrenergic system, activation of the oral part of the pontine reticular formation, a part of the former mentioned brainstem inhibitory centers, evoked bilateral suppression of muscle activity as well as the inhibition of unit activity in the LC and MLR[51]. Hypocretin-1, a recently identified excitatory neuropeptide, is reported to enhance the firing rate of neurons in the LC, resulting in the suppression of REMS and in the increase of wakefulness[52]. In addition, during cataplexy, a sudden loss of muscle tone seen in canine narcoleptics, discharge rates of neurons in the LC are as low as or lower than these seen during REMS[53]. Disfacilitatory mechanisms are considered to be involved in the loss of muscle tone in cataplexy[53] and REMS[54]. It is difficult to deny that this disfacilitatory mechanisms involved in the brainstem facilitatory centers are not implicated in muscle activity reduction during wakefulness.

D. Brainstem control of muscle activity in humans.

It is likely that brainstem inhibitory/facilitatory centers are involved in not only REMS atonia but also in the suppression of muscle activity during wakefulness. However, we still have no direct evidence of the activity of these centers during wakefulness in human. If we could assess the outputs from these brainstem centers, this assessment might provide a clue as to the inhibitory/disfacilitatory control of human muscle activity during wakefulness. Needless to say, this assessment means the quantification of REMS atonia.

However, we were unable to record the membrane potential of human motoneurons. Because of the difficulty in quantifying muscle activity loss by simply studying the reduced level of muscle activity during REMS, we have so far had no tool to assess the degree of muscle atonia during human REMS. Recently, the way to quantify muscle activity loss in REMS has been introduced as follows.

Two indices that quantify REMS atonia in humans

Making use of phasic chin muscle activity (PCMA), which is one of the characteristic muscle activities in REMS[26,55], two indices have been introduced to quantify REMS atonia (56-58); TII and PII. Standard polysomnographic recordings[55,59,60] are available for calculating these indices.

A. Definitions (Figs. 1 & 2)

TII is the rate of short PCMA during REMS against the total number of PCMA during REMS[57,58]. PCMA is defined as chin muscle activity lasting less than 2 seconds, with a peak amplitude of at least 50 % above the baseline amplitude (calibration at 50 uV/5 mm; time constant, 0.003). If the peak interval of two PCMAs is 0.25 sec. or more, they are defined as different PCMA. We took the cutoff between long PCMA and short PCMA as the duration of 0.5 sec. TII expresses the shortness of PCMA in REMS regardless of the difference in the definition of the short PCMA [e.g., 0.2 sec[61]] and reflects one kind of, or tonic, suppression of the activity of the antigravity muscle in REMS.

PII reflects the degrees of suppression of the occurrence of PCMA in the period of the burst of rapid eye movements[56,58]. A burst of rapid eye movements is defined as 2 or more consecutive rapid eye movements occurring at intervals of less than 0.5 sec. Rapid eye movements are defined as having a 75 uV or greater amplitude, with calibration at 50uV/ mm (or 50 uV/2.5 mm), a time constant of 2.0 (or 1.5 when calibration was at 50 uV/2.5 mm), and a 50 (70 when calibration was at 50 uV/2.5 mm) or greater angle of rise. PII is the geometric mean of the following 2 values; 1) the percentage of PCMA that occurs in the bursts of rapid eye movements against the total number of PCMA in REMS, and 2) the percentage of bursts of rapid eye movements that appear with PCMA against the total number of bursts. When a part of a period of PCMA was observed between the onsets of the first and last rapid eye movements that formed a burst, we scored the PCMA and burst as occurring simultaneously. This interrelationship was judged by visual inspection.

B. Age-related changes

TII and PII were calculated in 135 polysomnographical recordings obtained for healthy humans, from premature babies to a 77-year-old man[62]. TII and PII showed marked incremental and decremental age variation, respectively, particularly in infancy and childhood (Fig. 3)[63]. Both indices showed small interindividual variations[56,57] and are known to be unaffected by the first night effect[64]. These characters are convenient for clinical usage.

TII reflects the shortness of PCMA in each subject,

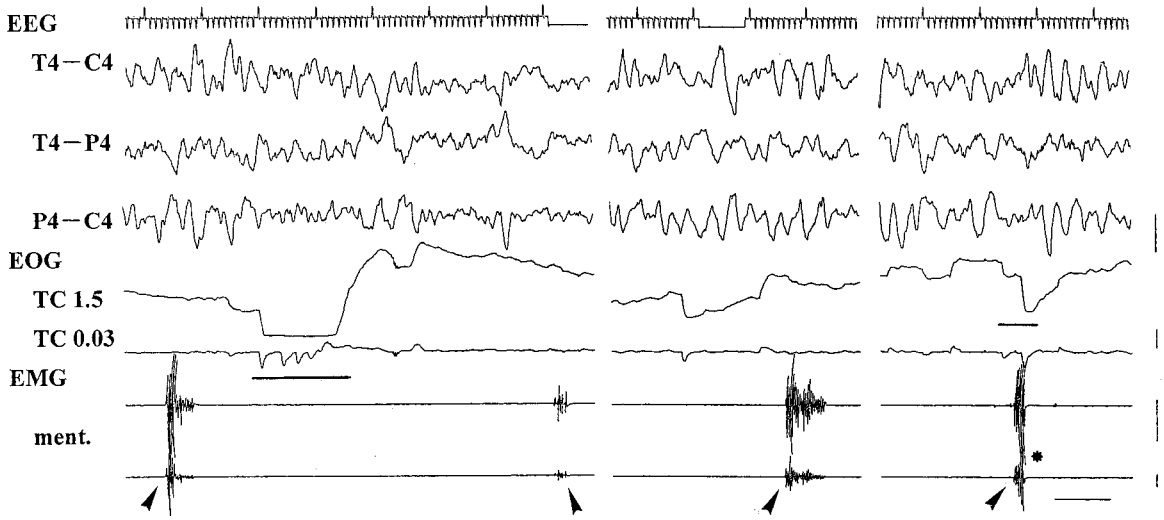

Figure 1. Parts of an actual polygraph of a 18-month-old girl during REMS. The underlinings in the electrooculographic (EOG) tracing indicate bursts of rapid eye movements. Electromyographic (EMG) recording from mental muscle consisted of low and high gain tracing. High gain tracing (upper trace) was performed to confirm the continuity of the muscle activity. Four phasic chin muscle activity (PCMA) can be seen (arrow heads). The PCMA indicated by the asterisk occurred simultaneously with a burst of rapid eye movements. This type of PCMA appearance is uncommon except for in the early phase of life. Calibration, 1 sec, 100 mV; TC, time constant; ment., mental muscle.

$$\text{TII} = \frac{\text{the number of short PCMAs (duration lasting 0.5 sec. or less) during REM sleep}}{\text{the number of all PCMAs during REM sleep}}$$

$$\text{PII} = \sqrt{\frac{\text{the number of PCMAs that occur with RBs}}{\text{the number of PCMAs during REM sleep}} \times 100\,(\%) \times \frac{\text{the number of RBs that occur with PCMAs}}{\text{the number of RBs during REM sleep}} \times 100\,(\%)}$$

PCMAs, phasic chin muscle activities; RBs, rapid eye movements bursts.

Figure 2. Formulae for calculating TII and PII.

although the duration of each PCMA was not measured. Similar to in the study of Fish et al.[65], shortening of PCMA (= elevation of TII with age) is assumed to be produced through relative elevation of inhibitory drives against excitatory ones to the trigeminal motoneurons which control chin muscles[57]. PII standardizes the rate of simultaneous occurrence of a PCMA and a burst of rapid eye movements. The decrease of PII with age is assumed to reflect an increase in the activity of rapid eye movement-related phasic inhibition. The chronological changes in TII and PII have been concluded to indicate that the activity of the human nervous systems involved in both tonic and phasic inhibition in REMS increases with age[62]. The normal lower (TII) and upper (PII) levels in each age group obtained by calculating mean - 2 standard deviations (SDs) for TII and

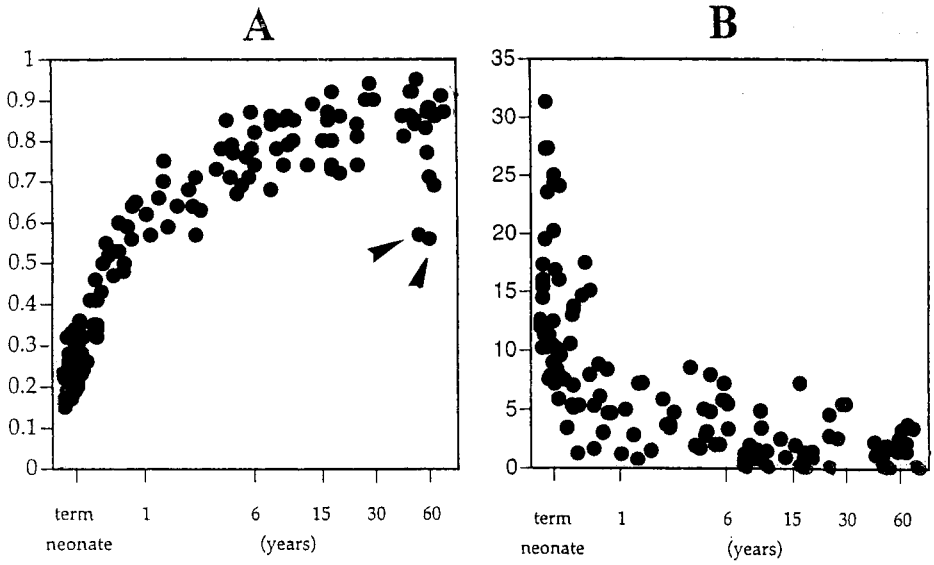

Figure 3. Chronological changes in TII (A) and PII (B) (48) obtained for 135 neurologically unaffected subjects. The horizontal axis expresses age on a logarithmic scale. TII exhibits a rapid increase during childhood, while PII decreases rapidly during infancy. These chronological changes are statistically significant. Arrow heads indicate 2 old men (56- and 64-year-old) who showed low TII values.

Table 1. Normal lower (TII) and upper (PII) levels in each age group (62)

Age group (n)	TII	PII
Preterm babies (11)	0.10	32.3
Term babies (25)	0.16	31.6
< 6 months (15)	0.25	26.2
< 1 year (8)	0.44	12.3
< 6 years (23)	0.55	10.2
< 15 years (17)	0.69	8.3
< 30 years (14)	0.68	9.2
< 60 years (10)	0.79 (n=9)	6.3
60 years ≤ (12)	0.68 (n=11)	4.9

the mean+2SDs for PII are presented in Table 1[62].

In two normal elder subjects, with ages of 56 and 64 years, the TII values were low, being equivalent to the 1-year-old level (arrow heads in Fig. 3). The neuronal systems that determine TII might lose their activities with the normal aging which produces undetectable minor lesions or physiological cell losses[66]. In addition to these 2 subjects, the mean TII and PII values in the eldest age group (60 years ≦) (TII, 0.83; PII, 2.0) were lower for TII and higher for PII than those in the second eldest age group (30-60 years) (TII, 0.88; PII, 1.5)[62]. The normal aging might also affect these indices. Consistently, disturbance of REMS atonia has been reported in healthy elderly subjects[66].

By calculating the age when each regression line (TII = 0.47ln[ln(x-30)] - 0.09, ln(PII + 2) = -1.05lm[ln(x-30)] + 3.44, x: postconceptional weeks of age (in term neonates, it is usually 40)[62]) crossed the lower (TII; mean-2SDs) or upper (PII; mean+2SDs) range of the adult group aged between 30 and 60, TII was found to reach the adult level (0.79) in preadolescence (12.3-year-old), while PII reached it (6.3) in early infancy (0.4-year-old)[62]. According to this difference, TII and PII are suggested to be determined by different systems, respectively. Thus, the human nervous systems involved in the suppression of muscle activity during REMS were hypothesized to comprise at least 2 independent systems[62].

C. TII/PII and the basal ganglia.

The outflow from the basal ganglia is requisite for movement control, and has recently been recognized to travel to the brainstem[7,8]. TII and PII are considered to be affected by the activity of the basal ganglia. Regarding the functional maturation of neuronal systems in the basal ganglia, several findings have been accumulated. TII and PII might also be influenced by these factors.

From the striatum to the substantia nigra pars reticularis/globus pallidus interna, two functional pathways

are postulated; direct pathway and indirect one. The ventral part of the striatum had D1 dopamine receptors and send direct fibers to the substantia nigra pars reticularis/globus pallidus interna (direct pathway), while the dorsal part of the striatum had D2 dopamine receptors, and had indirect connections with the substantia nigra pars reticularis/globus pallidus interna through the globus pallidus externs and the subthalamic nucleus. The direct pathway is known to develop functionally during early stage of life, while the indirect pathway is functionally immature in childhood[67].

The latencies of both visually- and memory-guided saccades during wakefulness reach the adult levels at around 12 years[68]. For the initiation of both types of saccades, the basal ganglia, especially tonic inhibitory influences from the substantia nigra pars reticulata over the superior colliculus, plays a crucial role[69]. However, for the completion of saccades, sensory systems, as well as the interconnection between sensory and motor systems are needed to act properly. It is obscure which components are essential for determinating the maturation of the latencies of saccades during wakefulness.

We found that TII reached the adult level at 12.3 years of age, while PII decreased to the adult value at 0.4 years. If PII were affected by the basal ganglia activity, neuronal systems that are involved in the determination of the PII value are likely to complete their maturation before 0.4 years of age. Further evidences are needed to obtain definitive conclusion.

D. Not a single brainstem pathway is involved in the suppression of muscle activity.

López-Rodriguez et al. proposed that the phasic inhibition in REMS is produced through phasic enhancement of the activity of an inhibitory system that tonically inhibits motoneurons during REMS[24]. On the contrary, Ornitz et al.[70] proposed that the phasic inhibition that occurs with the ocular activity during REMS is mediated through a different system from the system that produces tonic inhibition in REMS. Slow conducting reticulospinal cells (6-8 m/s), that fire specifically during REMS, have been identified in the feline ventral medulla[71]. On the other hand, fast conducting neurons (80-100 m/s) that inhibit motoneuronal excitability have been found in the dorsal medulla in decerebrate cats [38]. By stimulating the brainstem reticular formation in the decerebrate cat, the fast (22.8 m/s $\leqq$) and slow (<22.8 m/s) conducting systems that mediate muscle tone suppression have been identified[17]. Unilateral stimulation of trigeminal sensory fibers reduces the activities of the masseter and temporal muscles bilaterally with short and long latencies (two successive exteroceptive suppressions)[72]. Each component of muscle activity reduction is considered to be relayed by independent circuits[73]. On inhibition of the masseteric reflex, the involvement of glycine in the early phase suppression and that of GABA in the late phase were suggested[74,75]. All these findings support our idea that more than a single supraspinal system mediates the suppression of muscle activity.

By comparing the results in two papers on PGO[FN1] wave-related inhibitory postsynaptic potentials[24,25], it can be calculated that it took 20 to 30 ms for volleys mediating this phasic suppression of motoneuronal activity to be conducted from the brainstem to the lumbar segment of the spinal cord[17]. Taking into account the distance between these two sites (in general, it would be 200 to 300 mm), PGO wave-related phasic inhibitory postsynaptic potentials are likely to be mediated primarily by the slow conducting system[17].

E. Pathophysiology of TII/PII.

The TII value in the baby exposed to methamphetamine was low, while that in the baby exposed to haloperidol was high[58]. Methamphetamine exposure results in exaggeration of monoaminergic action, and haloperidol blocks its transmission. Cholinergic system is profoundly involved in the production of REMS atonia. Then, TII is hypothesized to be elevated by the relative increase of the cholinergic tone against the monoaminergic tone[58]. Interestingly, in these babies, PII values were unaffected.

Around the age when PII has decreased to the adult level (0.4 years), the Moro reflex disappears. The symmetrical extension and abduction of the upper extremities seen in this primitive reflex suggest the participation of the reticulospinal tract as an executive system. In patients with infantile spasms (IS), similar symptoms predominantly involving bilateral proximal muscles are well known. Indeed, it was described in a Japanese classic textbook that IS was sometimes mistaken for the Moro reflex[76]. Interestingly, PII has been reported to be elevated in IS[77]. Rapid eye movement-related phasic suppression of muscle activity is produced through excitement of the putative phasic event generator in the brainstem[23,78,79]. This excitement

Footnote 1. PGO waves, which are the most well known phasic event in feline REMS observed in the pontine reticular formation, lateral geniculate body and posterolateral cerebral cortex (i.e., pontogeniculo-occipital [PGO] wave), accompany rapid eye movements.

was found not only to suppress muscle activity but also to facilitate muscle activity at the same time[23,78,79]. Extrinsic stimuli such as auditory ones can induce the Moro reflex as well as the excitement of the phasic event generator[78]. In patients with IS, unknown intrinsic stimulation might affect the phasic event generator. However, IS patients have a deficit in the mediation of phasic inhibition shown by the elevation of the PII. Insufficient phasic inhibition (= elevation of PII) may produce a relative increase in facilitatory drives from the brainstem (phasic event generator/brainstem facilitatory centers) to motoneurons. This imbalance might produce the Moro reflex in normal infants aged 5 months (0.4 years) or less and spasms in patients with IS[62]. PII is elevated in IS patients, and after ACTH treatment, PII is decreased markedly. Anticholinesterase, which increases the cholinergic activity in the central nervous system, is reported to have a favorable effect on IS[80]. PII is likely to be mainly affected by the putative ACTH-ceptive cholinergic/cholinoceptive system.

Clinical implication of TII/PII

A. Disturbance of TII/PII (Table 2)

Disturbance of rapid eye movements-related phasic inhibition with a normal TII value was reported in patients with IS[76], nocturnal enuresis[81], severe myoclonic epilepsy in infancy[82], autisms[83], and Parkinson disease (PD)[62]. On the contrary, disturbance of TII without an affect on phasic inhibition was found in a patient who subsequently died of suspected sudden infant death syndrome (SIDS)[84], in infants who experienced an apparent life-threatening event[84], in newborn patients with congenital hypothyroidism[85], and in patients with Down syndrome[83]. In patients with group A xeroderma pigmentosum (XP)[86], both TII and PII were found to be affected. In infants who had breath-holding spells, phasic REMS components were reported to be disturbed[87]. Here, TII and PII in these patients are examined, and both of them are found to be impaired (Table 3). So far, corresponding to these findings, pathological changes in the brainstem have been reported in patients with IS[88,89] and SIDS[90], and functional brainstem disturbance has been suggested in patients with nocturnal enuresis[91].

IS patients often develop mental retardation or behavioral difficulties including autistic tendency in addition to convulsions. Interestingly, disturbance of phasic inhibition in REMS has been reported in patients with autism[70,83]. Phasic inhibition might also be a clue for elucidating the mechanism of the higher brain dysfunction in IS patients[92,93].

In PD patients, the occurrence of disturbed REMS atonia is well known[94]. Disturbance of rapid eye movements-related phasic suppression of muscle activity (= an elevation of PII) is observed in a patient with PD of pure akinesia[95], in an idiopathic PD patient[62], and also in PD patients with REMS without atonia (personal communication; Miyamoto M. and Miyamoto T.), although the degree of disturbance varied among patients. PD patients are suggested to have reduced reticulospinal activity[96–98], and also impaired inhibitory inputs to motoneurons[99]. For the occurrence of REMS behavior disorder in patients with PD, degeneration of brainstem neurons that promote REMS with atonia is hypothesized[100]. Consistently, taken together with the abnormal response of the late component in exteroceptive suppression in PD patients[101], the brainstem reticular formation, which is involved in the suppression of muscle activity, might be impaired in PD.

In contrast, infants with jitteriness (JT) showed abnormally higher TII values than in the controls[102] without an affection of PII[58]. JT is a rhythmic tremor of equal amplitude around a fixed axis, and is one of the most common involuntary movements observed in the neonatal period. Its prevalence reaches 41-44% during the first hours of life[103]. Although JT has been found to be associated with a variety of pathologic conditions (e.g., hypoglycemia, hypocalcemia, drug withdrawal syndrome, hypoxic ischemic encephalopathy, etc.), its pathogenesis remains unclear[104]. The elevation of TII in infants with JT is the first neurophysiological finding commonly seen in jittery infants. This finding is considered to reflect the accelerated maturation of nervous systems involved in atonia during REMS. It is obscure as to whether the acceleration of maturation is favorable for the developing brain or not. Relative elevation of the cholinergic systems against the monoaminergic systems are hypothesized to produce this condition[58,63].

B. Conditions with unaffected TII/PII

So far, in the following conditions, both TII and PII have been known to be unaffected; the non-group A XP patients, the patients with epilepsy without brainstem involvement (absence epilepsy, frontal lobe epilepsy[105], localization-related epilepsy, and generalized tonic-clonic seizures without exhibiting a focal abnormality on brain imaging or electroencephalography), neurologically unaffected children who had a cerebral

Table 2. TII and PII in several neurologically affected conditions

Disorders	high PII	normal PII
low TII	group A xeroderma pigmentosum, breath holding spell	an infant who subsequently died of suspected sudden infant death syndrome, infants who experienced an apparent life-threatening event, congenital hypothyroidism, Down syndrome, metamphetamine baby
normal TII	infantile spasms, nocturnal enuresis, severe myoclonic epilepsy in infancy, autism, Parkinson's disease	non-group A xeroderma pigmentosum, rhythmic movement disorder, absence, frontal lobe epilepsy, localization-related epilepsy, etc.
high TII (maturational acceleration?)		infants who had jitteriness during the neonatal period

Table 3. TII and PII in patients who showed breath holding spells

Name	gender	birth (PCA wks)	age of onset (PCA wks)	age at study (PCA wks)	age at the last attack (PCA wks)	TII	PII
BHS 1	M	40w, 3052g	79w	94w	164w	0.47	6.2
BHS 2	M	38w, 2956g	54w	98w	293w	0.46	8.4
BHS 3	F	38w, 2666g	64w	119w	125w	0.47	11.2
BHS 4	M	41w, 4025g	128w	135w	193w	0.43	10.2
BHS 5	F	39w, 3170g	129w	137w	140w	0.47	5.8
BHS 6	M	31w, 1682g	82w	143w	159w	0.45	8.0
T.T.	M	35w, 2540g	48w	156w	– (died at PCA 157w)	0.53	
Control	n=9	mean				0.63	4.0
		SD				0.08	2.6
p value (BHS1-6 vs Control)						0.001	0.004

structural anomaly (a double cortex or a subependymal heterotopia, both of which were found by chance)[63], and patients with rhythmic movement disorder[106].

Conclusion

The neural systems which suppress muscle activity are indispensable for the accomplishment of smooth motor performance[21,107]. TII and PII quantify muscle activity loss in human REMS. Muscle tone suppression in REMS is likely to be maintained by the brainstem inhibitory/facilitatory centers. Thus, TII and PII might reflect the activity of these brainstem centers. Several reports have suggested that these functional brainstem structures play a role in the suppression of muscle activity not only in REMS but also in wakefulness. It is well known that brainstem-spinal cord pathways are

involved in axial and proximal-extremity movements[2]. TII and PII might be valuable for human studies regarding REMS atonia, activity of brainstem control of muscle activity suppression, and movements involved in axial and proximal-extremity muscles not only during REMS but also during wakefulness.

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