ORIGINAL ARTICLE

Brainstem Excitability is Increased in Subjects with Palmomental Reflex

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Background/Purpose: The palmomental reflex (PMR) is a brief contraction of the mentalis muscles caused by a scratch over the thenar eminence, i.e. a brainstem reflex to afferents of upper limb. Using electrophysiologic methods, we studied the characteristics of brainstem excitability in PMR subjects.
Methods: Ten healthy PMR subjects were included in the study. Brainstem excitability was assessed with electrical stimulation at the trigeminal nerve, median nerve, ulnar nerve, and sural nerve with recordings at the mentalis muscles. A comparison was made by the probability between the mechanical scratch and the electrical stimulation to evoke the visible muscle contraction of mentalis.
Results: An electrical stimulus was able to elicit mentalis muscle responses ($MMR_{electrical}$) in all the subjects if the stimulus was of sufficient strength. Using electrical stimulation, the median nerve at the wrist was the best site to evoke $MMR_{electrical}$. However, in PMR subjects, the probability of $MMR_{electrical}$ to median nerve stimulation was less than that of $MMR_{scratch}$, i.e. the clinical findings of PMR. Significantly lower thresholds and higher amplitudes were noted in PMR subjects only when the median nerve was stimulated. The onset latency did not show any difference between the two groups despite the stimulation sites.
Conclusion: The facial motor neurons to median nerve stimulation are more sensitive in PMR subjects. In healthy PMR subjects, this indicates that the excitability increases only in the specific neuronal circuits between the lower cervical spinal cord and the facial motor nucleus in the rostral medulla. $MMR_{electrical}$ is a physiologic phenomenon, and PMR is a sign of increased brainstem excitability. [*J Formos Med Assoc* 2007;106(8):601–607]

Key Words: brainstem excitability, facial motor neuron, median nerve, palmomental reflex

The palmomental reflex (PMR) is a brief contraction of the mentalis muscles, usually unilateral and ipsilateral to the stimulated thenar eminence, resulting in a unilateral pouting expression. It is a polysynaptic reflex that is served by neuronal circuits extending from the lower cervical spinal cord to the facial motor nucleus in the rostral medulla.[1] PMR is present in the earliest stages of ontogenetic development.[2] It gradually disappears as the brain matures, but may reappear in old age or in patients with cortical deterioration.

The reflex may be present in healthy people of all ages but is more common in patients with neurologic diseases such as stroke, multiple sclerosis, motor neuron disease, severe head injuries, Down syndrome, AIDS, and cerebral tumors.[3] However, habituation is more frequent in healthy groups than patient groups.[4,5] The clinical value

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of PMR is still controversial. Most studies show that the reflex does not correlate with functional ability in cases of neurologic disorders, but the reflex is increasingly prevalent with advancing stages of HIV disease and the degree of akinesia in Parkinson's disease.[6,7] The mechanism of PMR is under speculation and remains uncertain. In parkinsonian syndrome, it is inferred that PMR may result from disinhibition of brainstem reflex responses related to abnormal striatal output.[7,8] Another proposal is that cortical inhibition of reflex and decussating brainstem pathways is lost with aging and disease states.[9,10]

PMR is a mentalis muscle response (MMR) to cutaneous stimulation to the palm. It is elicited in normal subjects by mechanical stroke over the palm,[9] and by electrical stimulation over the median nerve at the wrist and also at other body surfaces.[11–13] Different methods may account for the wide range of latencies in these studies.[9,13] The common afferent pathway consists of the cutaneous and muscular receptors of the thenar eminence and the median nerve. The common efferent pathway involves the motor nuclei of the facial nerve. PMR and MMR both reflect the balance of excitatory and inhibitory influences on the facial motor neurons in the brainstem.

Electrophysiologic method may help to quantify MMR and brainstem excitability to somatic afferents.[11–13] Therefore, we studied the characteristics of brainstem excitability of healthy PMR subjects.

Patients and Methods

To exclude the variable of disease entity, we selected healthy PMR subjects for study. The PMR group consisted of six men and four women (mean age, 71.3 ± 5.5 years; age range, 64–80 years). None of them had prior neurologic diseases (such as stroke, Parkinson's disease, amyotrophic lateral sclerosis, dementia), and their neurologic examinations did not reveal any significant signs. The control group consisted of 24 healthy volunteers (16 men, 8 women; mean age, 67.0 ± 7.8 years; age range, 51–78 years) without PMR. Two neurologists verified the positive PMR. PMR was provoked by scratching the thenar eminence in a proximal to distal direction using the fingernail of the examiner. A visible contraction of the mentalis muscle was considered to be a positive reaction. If there was disagreement between these two neurologists, the subject was neither included in the PMR group nor the control group. The probability of PMR was studied in a series of 10 trials in each PMR subject. The interval was at least 2 minutes between trials. All subjects were studied after informed consent had been given.

Brainstem excitability

MMR

Electrical stimuli were delivered to the trigeminal nerve at the supraorbital notch ($MMR_{trigeminal}$), the median nerve at the wrist (MMR_{median}), the ulnar nerve at the wrist (MMR_{ulnar}), and the sural nerve at the ankle (MMR_{sural}) in a random sequence. The duration of the stimulus was 0.2 ms. Short trains of stimuli were given, typically eight pulses at 200 Hz. The preliminary stimulus intensity was the median-nerve threshold that induced a compound muscle action potential (≥ 50 μV) in the thenar muscle. If such a stimulus did not induce any MMR_{median}, the intensity was progressively increased. It was difficult to consistently evoke $MMR_{electrical}$. Therefore, when the intensity was able to evoke ≥ 3 similar MMR_{median} patterns in 10 consecutive trials, it was defined as the MMR_{median} threshold.

The MMR threshold of each nerve stimulated was based upon the MMR_{median} threshold and was progressively increased until there were ≥ 3 similar MMR patterns in 10 consecutive trials. The working intensity was 1.5 times the MMR threshold of each nerve. The probability of MMR of each nerve was studied at the working intensity of MMR_{median}. The percentage probability was calculated as

$$\text{Percentage probability} = 100 \times (\text{the number of responses obtained/the number of stimuli})$$

To increase the probability and to avoid habituation, the interval between trials was at least 2 minutes. $MMR_{electrical}$ was considered positive when a burst of electromyographic activity, with an amplitude ≥ 50 μV and a duration ≥ 10 ms, appeared consistently at a latency compatible with a reflex response (i.e. earlier than a voluntary reaction). Electromyographic activity was recorded from the mentalis muscles with pairs of surface electrodes. The active recording electrodes were placed on the lateral aspect of the chin for the mentalis.

In each subject, three MMR responses were selected. The mean onset latency and the mean peak amplitude were measured in each subject. As facilitation occurred in conditions of mild voluntary contraction, all subjects were asked to relax themselves to the best of their ability with the aid of audio- and visual electromyographic feedback.

A visual analog scale (VAS; 10 = most severe pain, 0 = no pain) was used to assess these two methods, i.e. scratch over palm for PMR and electrical stimulation for $MMR_{electrical}$.

Blink reflex to trigeminal nerve

The blink reflex responses to single electrical stimuli and the blink reflex excitability recovery curve to paired stimuli were induced with interstimulus intervals of 100–800 ms in steps of 100 ms. Electrical stimuli were applied to the trigeminal nerve, at the supraorbital notch, at an intensity giving rise to a stable R2 response with single stimuli, usually three to five times the sensory threshold. In the responses elicited by single stimuli, we measured the onset latencies and peak-to-peak amplitudes of R1 and R2. The area of R2 responses was obtained by multiplying the peak-to-peak amplitude by the duration of the response. In the responses obtained with paired stimuli, we calculated the percentage of excitability recovery as

$$\text{Excitability recovery (\%)} = 100 \times (\text{area of R2 response to test stimulus}/\text{area of R2 response to conditioning stimulus})$$

The data of interstimulus intervals of 200 ms were taken as the recovery index.[8]

Data analysis

The Wilcoxon rank sum test was used to analyze the differences between the PMR and control groups. All data were considered significant when the p value was less than 0.05.

Results

MMR

Our study showed that an electrical stimulus was able to elicit $MMR_{electrical}$ in all the subjects if the stimulus was of sufficient strength. At the intensity of 1.5 times the MMR threshold, the majority of subjects perceived the stimulus as uncomfortable. Median nerve stimulation usually evoked MMR bilaterally with higher amplitudes on the side of stimulation. The data ipsilateral to stimulation were collected for analysis. Significant findings between PMR and control groups were noted only when the median nerve was stimulated (Table). The consistency of $MMR_{electrical}$ had difficulty achieving 100%, even when the intensity was up to 1.5 times the MMR threshold. Using electrical stimulation at the working intensity of MMR_{median}, median nerve stimulation had the highest probability in both groups (PMR—median 60.0%, trigeminal 47.0%, ulnar 12.0%, sural 6.0%; control—median 52.5%, trigeminal 45.0%, ulnar 9.6%, sural 6.7%) (Figures 1 and 2). For group comparison of electrical stimulation, significant difference in probability was noted in the median nerve ($p = 0.0292$) but not in the trigeminal ($p = 0.7367$), ulnar ($p = 0.3764$), or sural ($p = 0.7528$) nerves. However, in PMR groups, scratching over the thenar eminence had a higher probability of producing visible muscle contraction of the mentalis than electrical stimulation at the median nerve or thenar eminence (i.e. MMR_{thenar}) ($MMR_{scratch}$ 67.0%; MMR_{median} 60.0%; MMR_{thenar} 5.0%; $p < 0.0001$ between $MMR_{scratch}$ and MMR_{median}; $p < 0.0001$ between $MMR_{scratch}$ and MMR_{thenar}; $p < 0.0001$ between MMR_{median} and MMR_{thenar})

Table. Mentalis muscle response to electrical stimuli in subjects with and without palmomental reflex*

	Trigeminal	Median	Ulnar	Sural
Subjects with PMR ($n=10$)				
Threshold (mA)	12.2 (1.1)	10.9 (1.4)†	15.4 (3.6)	20.2 (4.0)
Latency (ms)	71.3 (6.9)	75.6 (4.8)	79.3 (5.9)	116.0 (7.7)
Amplitude (μV)	144 (53)	229 (42)†	98 (28)	68 (14)
Subjects without PMR ($n=24$)				
Threshold (mA)	13.3 (1.9)	13.1 (2.0)	15.7 (2.4)	19.2 (3.9)
Latency (ms)	72.8 (5.0)	76.8 (7.7)	78.8 (5.5)	117.2 (8.5)
Amplitude (μV)	155 (52)	159 (47)	102 (28)	74 (17)

**Data are presented as mean (standard deviation); †significant difference between palmomental reflex and control groups with $p<0.05$. PMR = palmomental reflex.*

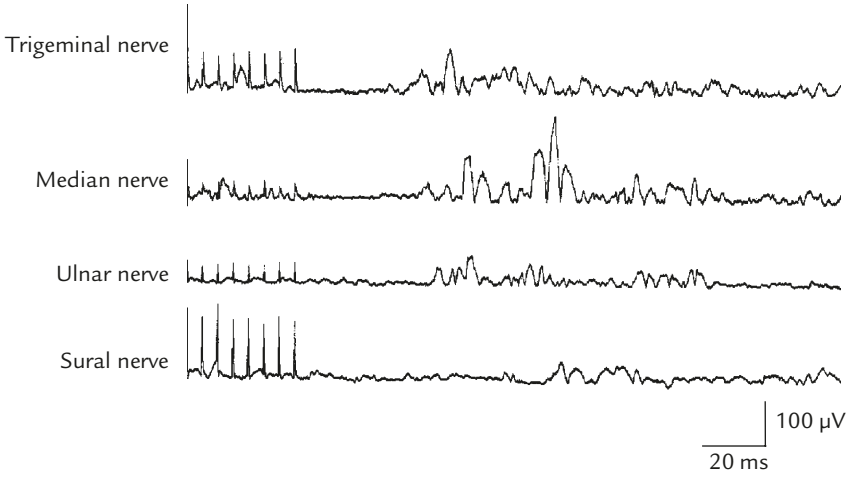

Figure 1. Mentalis muscle responses to electrical stimulation at the same intensity in a subject with palmomental reflex.

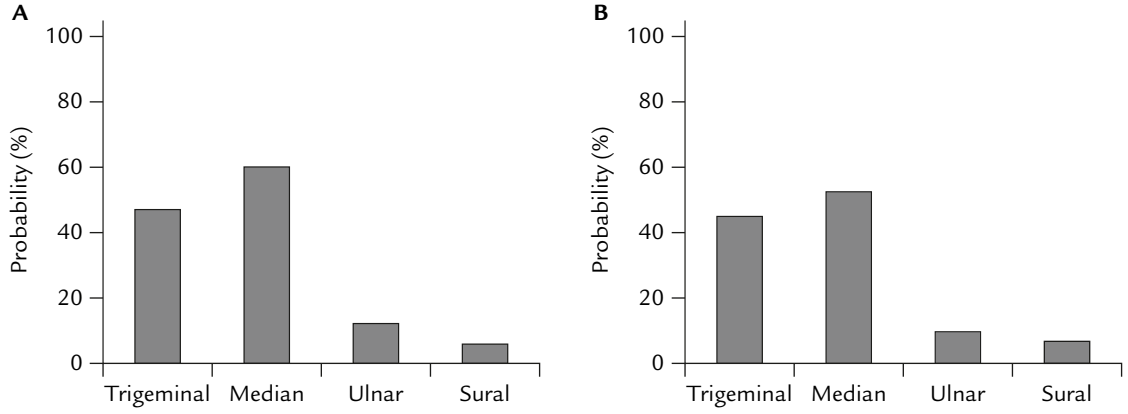

Figure 2. Electrical stimulation was able to elicit mentalis muscle responses in all the nerves sampled. Using the same intensity of stimulus, the median nerve was the most sensitive site to evoke the reflex. (A) Subjects with palmomental reflexes; (B) subjects without palmomental reflexes.

(Figure 3). VAS showed that electrical stimulation at 1.5 times the MMR_{median} threshold produced much more pain than scratching (VAS—electrical stimulation 6.7 ± 0.9, scratching 1.2 ± 0.4; $p<0.0001$).

In the PMR group, the threshold for $MMR_{electrical}$ was 12.2 ± 1.1 mA to trigeminal nerve (control, 13.3 ± 1.9 mA; $p=0.1081$), 10.9 ± 1.4 mA to median nerve (control, 13.1 ± 2.0 mA; $p<0.0022$),

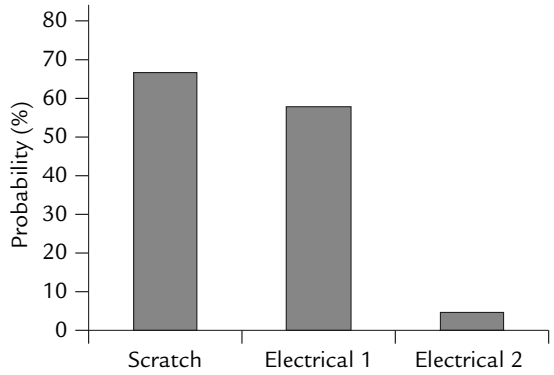

Figure 3. In healthy subjects with palmomental reflexes, a comparison of visible muscle contraction of the mentalis was made among the stimuli of scratch over the thenar eminence, electrical stimulation of the median nerve at the wrist (Electrical 1), and electrical stimulation over the thenar eminence (Electrical 2).

15.4 ± 3.6 mA to ulnar nerve (control, 15.7 ± 2.4 mA; $p = 0.6872$), and 20.2 ± 4.0 mA to sural nerve (control, 19.2 ± 3.9 mA; $p = 0.5406$).

In the PMR group, mean onset latency of the MMR was 71.3 ± 8.4 ms to trigeminal stimulus (control, 72.8 ± 8.6 ms; $p = 0.6231$), 75.6 ± 7.6 ms to median nerve stimulation (control, 76.8 ± 7.4 ms; $p = 0.7195$), 79.3 ± 6.9 ms to ulnar nerve stimulation (control, 78.8 ± 7.4 ms; $p = 0.8947$), and 116.0 ± 9.2 ms to sural nerve stimulation (control, 117.2 ± 8.7 ms; $p = 0.8798$).

In the PMR group, the peak amplitude of $MMR_{electrical}$ was 144 ± 53 μV (control, 155 ± 52 μV; $p = 0.3663$) to trigeminal nerve stimulus, 229 ± 42 μV (control, 159 ± 47 μV; $p < 0.0001$) to median nerve stimulation, 98 ± 28 μV (control, 102 ± 28 μV; $p = 0.0759$) to ulnar nerve stimulation, and 68 ± 14 μV (control, 74 ± 17 μV; $p = 0.0759$) to sural nerve stimulation (Figure 1).

Blink reflex

In the study of blink reflex to single trigeminal nerve stimulation, the mean values of the onset latencies of R2 (PMR, 30.5 ± 2.2 ms; control, 30.8 ± 1.9; $p > 0.05$) and the peak amplitudes of R2 (PMR, 527 ± 90 μV; control, 534 ± 83 μV; $p > 0.05$) were not significantly different between PMR and control subjects. The R1 amplitude was usually facilitated at interstimulus intervals < 100 ms and returned to baseline level later. The R2 amplitude was usually inhibited at interstimulus intervals of 100–200 ms. The percentage of excitability recovery of the blink reflex to paired stimuli at interstimulus intervals of 200 ms was similar between PMR and control groups (PMR, 17.2 ± 2.9%; control, 17.6 ± 3.5%; $p > 0.05$).

Discussion

Our results show that mentalis muscle is more sensitive than orbicularis oculi to median nerve stimulation in PMR subjects. Similar findings were also noted in patients with progressive supranuclear palsy.[8] It seems that not all the brainstem conditions can be interpreted by the blink reflex to trigeminal nerve. Therefore, an add-on with another facial reflex will distinguish some pathologic conditions, although the recovery curve of blink reflex is usually taken as an index of brainstem excitability.[8]

Trigeminal and upper limb afferents follow different pathways to facial motor neurons and do not exactly share the same mechanism in the cranial muscle reflex.[8] Further evidence is the clinical observation of PMR. A scratch over the palm usually evokes responses only at the mentalis muscles, but not at the orbicularis oculi. Therefore, PMR is not a spreading phenomenon of blinking. In an animal study of monkeys, limb afferents projected more specifically onto the lower facial motor neurons through the corticonuclear tract, while the direct cortical innervation of the upper facial muscles was scant.[14] In the cat, trigeminofacial reflexes follow a relatively direct pathway through the lateral pontomedullary reticular formation.[15] This circuit may not involve the nucleus reticular pontis caudalis, which is located at a more medial and ventral position.[16] This could be the reason why the mentalis motor neurons are more sensitive to limb afferents than the orbicularis oculi.

It is hypothesized that lateral reticular formation has a system to control polysensory information, such as acoustic, visual and somatic

inputs.[17] These sensory inputs usually compete at the sensory pool of the brainstem before they reach the facial motor neurons.[17–19] The control system selects relevant sensory information and then produces a specific reflex.[19] If PMR is a reflex specific to cutaneous stimulation, it would explain why it is easier for scratch to evoke PMR than electrical stimulation. Electrical stimulation at the wrist or thenar eminence usually evokes many different sensory modes. A competition of different sensory modes will reduce the specific cutaneous effect on the facial motor neurons at brainstem.

From the viewpoint of receptive field, PMR has a more specific area than $MMR_{electrical}$. PMR cannot be elicited by scratch over the wrist or the index fingertip of our PMR subjects, even though both areas are innervated by the median nerve and the density of tactile receptors is greater at the index tip. There is no doubt that the thenar eminence is the specific receptive field for PMR. Most superficial reflexes are also triggered by specific receptive fields, such as abdomen reflex to the skin near the bellybutton, gag reflex to the oropharyngeal area, cremasteric reflex to the medial thigh, and Babinski's sign to the lateral aspect of the sole etc. It seems that the neural code for superficial reflex is related to the receptive field and the stimulating mode but not the intensity and the receptor number.

Using electrical stimulation, the probability of MMR_{median} increased with higher intensity of stimulus. Most of the stimuli were painful, indicating that $MMR_{electrical}$ had nociceptive and startle components. This is supported by animal and human studies. Somatic afferents may evoke startle facial response in cats and human subjects with hyperekplexia.[20,21] Otherwise, PMR is usually observed in awake subjects. Startle and wakefulness are both mediated by circuits involving the brainstem reticular formation. This could account in part for why $MMR_{electrical}$ is easily suppressed or rapidly habituated during the probability test.

When stimulus is of sufficient strength, electrical stimulation is able to elicit MMR in subjects without PMR.[11–13] This leads to the thought that electrical stimulation is a powerful tool to explore the subclinical physiologic phenomenon of PMR.[11,12,22] However, our probability study showed that electrical stimulation was not more effective than scratching to evoke muscle contraction of the mentalis in PMR subjects. VAS study also showed that scratching was always more comfortable than electrical stimulation, and indicated that the specific receptive field of the thenar eminence and tactile afferents had a more important role in the PMR mechanism. It is clear that both $MMR_{electrical}$ and $MMR_{scratch}$ reflexes did not exactly share the same mechanism to produce muscle responses.

In conclusion, our study proves that brainstem excitability increases in response to afferents of the upper limbs in healthy PMR subjects, but $MMR_{electrical}$ should not be taken as a synonym of PMR, the clinical observation. The increase in excitability may be due to the brainstem itself or due to decreased cortical inhibition. A further study of transcranial magnetic stimulation would help to explore the role of the cortex in the mechanism of PMR.

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