Co-firing of levator palpebrae and masseter muscles links the masticatory and oculomotor system in humans

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Abstract

Simultaneous co-firing of the levator palpebrae (LP) and pterygoid muscles were recorded in Marcus Gann Syndrome (MGS) patients in early clinical studies. "Release hypothesis" proposed an intrinsic masticatory oculomotor neural circuit and this kind circuit, which, however, has been observed only in amphibian. On the other hand, congenital miswiring hypothesis has overwhelmed other interpretations. However, the same phenomenon visualized in MGS cases was unveiled in human subjects without any sign of congenital oculomotor disorder. To further study co-firing of the upper eyelid and jaw muscles, we applied non-invasive EMG recording of the upper eyelid and ipsilateral masseter muscle belly in nine healthy volunteers. LP activity was determined initially by looking upward and active retraction of upper eyelid with head fixed. Then, dual channel inputs from upper eyelid and masseter muscle was recorded during tooth occlusion motivated by isometric masseter muscle contraction without jaw and face moving. The EMG recorded from upper eyelid when the subjects retracted eyelid with head fixed exhibited the same pattern as that collected during tooth occlusion, but the pattern was completely different from EMG of active eye closure. This reflects tooth occlusion evoked LP activity. Then, simultaneous co-firing of the LP and masseter muscle was recorded simultaneously during tooth occlusion without jaw movement. Finally, the aforementioned co-firing was recorded when the subjects conducted rhythmic occlusion and synchronous EMG from both muscles was acquired. In conclusions, humans may also have an intrinsic masticatory oculomotor circuit and release hypothesis may apply, at least, to some cases of MGS.

Keywords: Marcus Gann Syndrome, healthy human, EMG, upper eyelid, tooth occlusion.

Introduction

Marcus Gunn syndrome (MGS) is an oculomotor disorder characterized by abnormal eye movements, most notably eyelid retraction elicited by jaw movements1-4. It has been hypothesized to be caused by aberrant neural regeneration, specifically peripheral misdirection of regenerated axons of the trigeminal motor root into the extraocular muscles after neuropa-
thy or head trauma\textsuperscript{[5]}. However, this hypothesis has been proven anatomically impossible as axon regeneration is undertaken inside of the endoneurium\textsuperscript{[6-7]}. The "release hypothesis"\textsuperscript{[3-4]}, on the other hand, postulates the presence of a primitive masticatory oculomotor reflex that is normally suppressed in humans but released pathologically. In \textit{Xenopus toad}\textsuperscript{[8]}, the central processes of the temporal muscular afferent mesencephalic trigeminal nucleus (Vme) neurons project directly to the oculomotor nucleus (III) and trochlear nucleus (IV), adding substantiation to the "release hypothesis". Luo \textit{et al.} provided additional evidence for Vme neuronal projections to the oculomotor system in rats, implying the presence of a primitive masticatory oculomotor reflex pathway\textsuperscript{[9]}. However, it remains undocumented whether there is a similar neural pathway in humans.

In the present work, we sought to investigate whether the masticatory oculomotor reflex pathway was present in humans by simultaneous electromyographical (EMG) recording from both the levator palpebrae (LP) and masseter muscle of healthy human volunteers.

### Materials and methods

#### Subjects

We studied nine healthy adults aged 20 to 56 years. The study protocol was approved by the local institutional review boards at Shaanxi Provincial Eye Research Institute and Eye Hospital and written informed consent was obtained from the study subjects.

#### EMG Recording

The upper eyelid recording electrode was placed at the middle of the upper eyelid and the reference electrode was positioned at the middle of the forehead above the skin (Fig. 1A). LP EMG activity was recorded when the subject looked upward or actively lifted the eyelid with the head fixed. The electrode was adjusted to obtain optimum EMG signals upon active upper eyelid retraction. The discharge of the orbicularis oculi muscle (OOM) was recorded from the same upper eyelid electrode when the subjects actively closed the eyes. A third recording electrode was placed on the skin above the belly of the masseter muscle (Fig. 1A; Fig. 2A and D). The subjects were asked to forcefully occlude the teeth with minimal movement of the jaw. EMG signals from the upper eyelid recording electrode were then obtained and analyzed. Thereafter, EMG signals from both the upper eyelid and the masseter muscle belly were recorded simultaneously during occlusion through dual-channel input. The subjects were also trained to conduct rhythmic voluntary isometric contraction with little isotonic contraction of the jaw closing muscles and co-firing EMG from both the upper eyelid and the masseter muscle belly was recorded. A NTS-2000 EMG-EEG dual-channel amplifier upgraded with NTS-2000-A12 software and USB outlet (Pukang Electronic Tech, Shanghai, China) was applied to record EMG activities, with one channel receiving the upper eyelid inputs and the other channel conducting jaw closing muscular signals.

#### Results

**Comparison of EMG signals during active eye closure, eyelid retraction and tooth occlusion**

OOM activities of the upper eyelid during eye closure are illustrated in Fig.1B (the upper panel).
Representative LP EMG signals when the subjects looked upward with the head fixed or actively retracted upper eyelid are shown in the middle panel of Fig. 1B. Representative LP EMG signals recorded during forceful tooth occlusion are shown in the lower panel of Fig. 1B. We found that the EMG waveforms during tooth occlusion highly resembled that of upper eyelid activity, suggesting that forceful tooth occlusion elicited LP activity. In contrast, OOM activity waveform was completely different from the EMG waveform generated by forceful tooth occlusion.

**Co-firing of LP and jaw closing muscles during static and rhythmic forceful tooth occlusion**

EMG signals from the LP elicited by voluntary isometric contraction of jaw closing muscles with tooth occlusion were detected in all nine subjects (Fig. 2 B and E). The co-firing of the LP and the jaw muscles during static occlusion is represented in Fig. 2. In addition, EMG of the LP and jaw closing muscle in responses to rhythmic tooth occlusion with minimum jaw movement (Fig. 3A) was recorded (Fig. 3B). They showed a clear rhythmic co-firing of the two muscular groups (Fig. 3B).

**Discussion**

In the present work, we recorded EMG activities from the LP, OOM and the masseter muscle during active eyelid retraction, eye closure and forceful tooth occlusion. We observed that EMG signals during active eyelid lifting are unequivocally analogous to those of tooth occlusion, and completely different from EMG activities evoked by eye closure. This suggests that tooth occluding behavior probably initiates the discharge of the LP, possibly including activity of the superior rectus. In the study, the subjects performed isometric contraction of the jaw closing muscles and minimized jaw and face movement that may cause skin stretch. In addition, synchronous co-firing of the upper eyelid and jaw closing muscle discharges was recorded during static and rhythmic tooth occlusion in circumstance of isometric jaw closing muscle contraction that minimized jaw and face movement. These results imply an intrinsic linkage between the masticatory and oculomotor system.

Actually, simultaneous co-firing of LP and pterygoid muscles was recorded in MGS patients in early clinical studies[4,11], furthermore, stimulation of the pterygoid muscle nerve elicited ipsilateral eyelid retraction, and section

![Fig. 2 Co-firing of muscles on upper eyelid and masseter muscle](image)

A and D, subjects were performing tooth occlusion by isometric contraction without jaw and face movement. B and E, EMG was recorded from the upper eyelid. C and F, EMG was collected from electrode on masseter muscle belly. Use of the photograph was permitted by the subject.
of this nerve from the trigeminal motor root relieved eyelid EMG activity and eliminated jaw-winking synkinesis\[^{12}\]. However, congenital miswiring and aberrant regeneration hypothesis\[^{5}\] has been the dominant theory in MGS pathogenesis for nearly a century although aberrant regeneration of the trigeminal motor root into the oculomotor nerve seems impossible anatomically\[^{6-7}\].

Congenital peripheral miswiring is still used to interpret abnormal oculomotor synkinesis\[^{13-15}\] because congenital miswiring between the oculomotor and abducens nerve was observed\[^{19}\]. MGS is also categorized into these congenital miswiring disorders\[^{15-16}\]. Accordingly, simultaneous co-firing of LP and masticatory muscles observed in the MGS patients is probably a consequence of miswiring.

However, retraction of the upper eyelid was evoked by electrical stimulation of the trigeminal motor root, and LP EMG was also recorded during this stimulation in a recent clinical study on subjects without any sign of congenital miswiring\[^{17}\]. Our current results of upper eyelid and masticatory co-firing is consistent with the aforementioned report. Some MGS cases show trigemino-oculomotor synkinesis only temporarily in life\[^{11}\]. While other MGS patients exhibit a pattern of alternative healing and relapse\[^{11}\]. Hence, a “release hypothesis” derived to explain the MGS as a pathophysiologic release of a primitive reflex that is depressed normally\[^{4,11,10}\]. Consistently, a central process of the temporal muscle spindle afferent Vme neurons has been demonstrated directly projecting to nucleus III and IV in amphibians\[^{8}\]. This neuronal circuit may help an amphibian focus its eyes on its prey when the animal targets to the prey and opens mouth widely\[^{8}\].

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**Fig. 3** Rhythmic co-firing of muscles on the upper eyelid and masseter muscle. A, a subject was carrying out rhythmic biting as if chewing, but the jaw and face did not move with only isometric contraction of jaw closing muscles (arrows). B, a clear rhythmic co-fire of muscles on upper eyelid and masseter muscle during rhythmic occlusion driven by rhythmic isometric contraction of the masseter muscle without jaw and face movement. Use of the photograph was permitted by the subject.
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