Clinical Neurophysiology 161 (2024) 59–68

Contents lists available at ScienceDirect

Clinical Neurophysiology

journal homepage: www.elsevier.com/locate/clinph

Review

Neural control of blinking

Matteo Bologna [a,b,*], Giulia Paparella [a,b], Josep Valls-Solé [c], Mark Hallett [d], Alfredo Berardelli [a,b]

[a] Department of Human Neurosciences, Sapienza, University of Rome, Rome, Italy
[b] IRCCS Neuromed, Pozzilli, IS, Italy
[c] Institut d'Investigació Biomèdica August Pi i Sunyer, Barcelona, Spain
[d] National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, MD, USA

HIGHLIGHTS

- Blinking is crucial to protect the eyes and maintain the ocular surface integrity, ensuring optimal conditions for visual inputs.
- Blinking is governed by partially overlapping circuits including cortical, subcortical, and brainstem areas.
- We provide an overview of the anatomical and physiological foundations underlying the control of different blinking types.

ARTICLE INFO

Article history:
Accepted 7 February 2024
Available online 22 February 2024

Keywords:
Blinking
Motor control
Neurophysiology

ABSTRACT

Blinking is a motor act characterized by the sequential closing and opening of the eyelids, which is achieved through the reciprocal activation of the orbicularis oculi and levator palpebrae superioris muscles. This stereotyped movement can be triggered reflexively, occur spontaneously, or voluntarily initiated. During each type of blinking, the neural control of the antagonistic interaction between the orbicularis oculi and levator palpebrae superioris muscles is governed by partially overlapping circuits distributed across cortical, subcortical, and brainstem structures. This paper provides a comprehensive overview of the anatomical and physiological foundations underlying the neural control of blinking. We describe the infra-nuclear apparatus, as well as the supra-nuclear control mechanisms, i.e., how cortical, subcortical, and brainstem structures regulate and coordinate the different types of blinking.

Contents

Abbreviations: M4, caudal cingulate cortex; CMAs, cingulate motor areas; EMG, electromyography; fMRI, functional magnetic resonance imaging; LPMCd, dorsal lateral premotor cortex; LPMCv, ventral lateral premotor cortex; LPS, levator palpebrae superioris; LTD, long-term depression; LTP, long-term potentiation; MCA, middle cerebral artery; OO, orbicularis oculi muscle; M1, primary motor cortex; PD, Parkinson's disease; PSP, progressive supranuclear palsy; Vc/C1, subnucleus caudalis-upper cervical spinal cord; SMA, supplementary motor area; M2, supplementary motor cortex; M3, rostral cingulate cortex; TMS, transcranial magnetic stimulation; Vi/Vc, trigeminal nucleus interpolaris-caudalis transition zone.

* Corresponding author at: Department of Human Neurosciences, Sapienza University of Rome, Viale dell'Università, 30, 00185 Rome, Italy.
E-mail address: matteo.bologna@uniroma1.it (M. Bologna).

https://doi.org/10.1016/j.clinph.2024.02.023
1388-2457/

1. Introduction

The eyelids play a role in protecting the eyes from potential injuries caused by harmful mechanical and chemical stimuli, as well as continuous exposure to light. Additionally, eyelid motion is instrumental in maintaining the integrity of the ocular surface and facilitating efficient lacrimal drainage. The eyelids' dynamic movement helps replenish the pre-corneal tear film and cleanse the eyes. The act of blinking accomplishes all these functions. Blinking is defined as a temporary closure of both eyes, involving movements of the upper and lower eyelids and consisting of three phases: the closing phase, the opening phase, and the inter-phase pause, i.e., the time elapsing between the end of the closing phase and the beginning of the opening phase (Bologna et al., 2013). Blinking is crucial in preventing dryness and discomfort of the corneal surface, ensuring optimal eye health, and providing undisturbed visual inputs.

The study of eyelid movements when blinking offers interesting insights into specific aspects of motor control. Indeed, eyelid movements differ from limb or axial movements since they are more stereotyped and primarily governed by three muscles (Evinger et al., 1991). The first is the orbicularis oculi muscle (OO), which consists of the preseptal, pretarsal, and ciliary parts; it is innervated by motor neurons of the VII cranial nerve originating at the pontine level. The OO primarily controls vertical downward movements, specifically eyelid closure. On the other hand, the levator palpebrae superioris muscle (LPS), innervated by motor neurons of the III cranial nerve originating at the midbrain level, is responsible for the vertical position and upward movements of the eyelid, facilitating eye-opening. Finally, there is also a minor muscle, i.e., the sympathetic dependent tarsal muscle of Muller, which originates from the LPS and inserts onto the upper margin of the tarsal plate, providing an additional upward force on the eyelid (Esteban et al., 2004; Evinger et al., 1991). The OO and the LPS exhibit distinct characteristics in their muscle fiber physiology (Brooke and Kaiser, 1970; Porter et al., 1989). Notably, the OO comprises a significantly larger proportion of fast twitch type I fibers than the LPS. This discrepancy accounts for the classical asymmetric temporal pattern observed in eyelid movement, wherein the closing phase of the OO is considerably faster than its opening phase (Hwang et al., 2011). Other passive forces, mainly represented by the tendon-aponeurotic apparatus of the upper eyelid, as well as other physical factors involving the upper eyelid, such as stiffness and viscosity, also provide an elastic energy contributing to the eyelid closure (Esteban et al., 2004). The distinct muscle features, along with their respective innervation and supranuclear control, form the fundamental basis for eyelid control and contribute to the precise coordination of eyelid movements (Bologna et al., 2013; Esteban et al., 2004; Evinger et al., 1991; Schmidtke and Büttner-Ennever, 1992).

In the following sections, we will first introduce the different blinking types and the methods for their neurophysiological assessment. Then, we will discuss the anatomical pathways and mechanisms responsible for controlling eyelid movements in humans during different types of blinking under normal physiological conditions. We will consider recent advances in our understanding of these processes, primarily based on findings from neurophysiological studies in animals and humans. The relevant findings from the major neuroimaging studies on the topic will be considered. It is important to note that, in addition to primary ocular pathological conditions (Mak et al., 2016; McMonnies, 2021, 2007), blinking abnormalities can occur in various neurological disorders (Agostino et al., 2008; Antelmi et al., 2016; Bologna et al., 2016, 2014, 2013, 2012, 2009; Bologna and Paparella, 2020; Cabib et al., 2014; Deuschl and Goddemeier, 1998; Karson et al., 1984; Kimber and Thompson, 2000; Korosec et al., 2006; Lozza et al., 1997; Manca et al., 2001; de Tommaso et al., 2001; Valls-Sole, 2019; Valls-Solé et al., 1997). These disorders encompass conditions affecting the neuromuscular system as well as those involving the brainstem or basal ganglia, such as movement disorders. Blinking abnormalities may also be observed in disorders of functional origin (Hanzlíková et al., 2019), in psychiatric diseases (Barbato et al., 1993; Caplan and Guthrie, 1994; Karson et al., 1986; Kleinman et al., 1984), and in disorders generated as side effects of the use of drugs such as antipsychotics (Karson, 1983; Keshavan et al., 1983; Lin et al., 2006). Accordingly, when relevant, we will briefly describe the most significant abnormalities in blinking observed in these pathological conditions.

2. Blinking types and their neurophysiological assessment

During blinking, the OO and LPS muscles exhibit reciprocal activation patterns. Prior to and during the activation of the OO, there is an inhibitory modulation of the basal tonic activity in the LPS, which is responsible for eyelid elevation (Cruz et al., 2011; Evinger et al., 1991; Porter et al., 1989). In the pre-blink phase, the activity of the LPS diminishes, while the motoneurons of the face generate a transient, high-frequency burst of activity in the orbicularis oculi. This burst of activity induces a temporary downward movement of the upper eyelids. As the activity in the OO ceases, the LPS reverts to its original tonic activity, resulting in the elevation of the upper eyelid and re-opening of the eye (Aramideh et al., 1994; Bjork and Kugelberg, 1953; Bour et al., 2002; Esteban et al., 2004; Esteban and Salinero, 1979; Evinger et al., 1991, 1984). Thus, during the closing phase, the passive downward force of the LPS sums up to the active burst of the OO, while the opening phase depends almost entirely on the LPS. Consequently, the closing phase usually has a greater mean, peak velocity, and a shorter duration than the opening phase. Finally, while the OO plays a key role in blinking movements, the LPS is likely the only actor in the small saccadic lid movements accompanying vertical saccadic eye movements. For upward saccadic eye movements, increases in LPS muscle activity raise the eyelid, and for downward saccades, the LPS transiently turns off, allowing the upper eyelid to fall (Becker and Fuchs, 1988; Evinger et al., 1991; Van Allen and Blodi, 1962).

Three distinct types of blinking have been delineated in the literature (Table 1). The reflex blink is characterized by its response to abrupt somatosensory, auditory, or visual stimuli. This blink is elicited involuntarily and serves as a protective mechanism in response to potentially threatening or startling stimuli. Spontaneous blink manifests as periodic and unconscious eyelid closures, exhibiting variable rates among individuals. These spontaneous blinks occur without any immediate external stimuli and contribute to maintaining ocular surface lubrication. A voluntary blink is an intentionally performed eyelid movement to close the eyes. Unlike reflex and spontaneous blinks, voluntary blinks are under volitional control and can be employed for various purposes, such as communication or alleviating ocular discomfort. By classifying blinking into these distinct categories, researchers have been able

Table 1
Synopsis of the main features and studies on reflex, spontaneous and voluntary blinking. M1: primary motor cortex, LPMCv: ventral lateral premotor cortex, LPMCd: dorsal lateral premotor cortex. SMA: supplementary motor cortex.

	Methodologies	Main mechanisms /brain areas	Major references
Reflex blinking	Corneal mechanical/electrical stimulation, supraorbital nerve percutaneous electrical stimulation, electrical stimulation of trigeminal branches other than the ophthalmic, visual/acoustic stimuli, high-intensity laser pulses to any trigeminal division, electrical stimulation of a peripheral nerve or the skin of the body or limbs (somatosensory-evoked blink response).	Cutaneous receptors of cornea and face, trigeminal ganglion neurons (Aδ and C type), spinal trigeminal nucleus. Supraorbital nerve Aβ, Aδ and C type fibers, olygo-synaptic pontine circuit and polysynaptic interneurons chain in the pontomedullary reticular area. Influences by the M1, basal ganglia, substantia nigra, superior colliculus, nucleus raphe magnus, and cerebellum.	Accornero et al., 1980; Kimura et al., 1985; Berardelli et al., 1985a; Hori et al., 1986; Schmidtke and Büttner-Ennever, 1992; Basso and Evinger, 1996; Esteban, 1999; Cruccu and Deuschl, 2000; Hirata et al., 2004; Cruccu et al., 2005; Chen and Evinger, 2006; Henriquez and Evinger, 2007; Bologna et al., 2010; Bologna et al., 2013
Spontaneous blinking	Usually recorded for 60-s epochs during a rest condition while participants are asked to relax and look straight at a fixed point. Spontaneous blinking rate, interblink intervals, amplitudes and velocity of the opening and closing phase, duration of the inter-phase pause are considered.	Regulated by the central dopaminergic tone (which increases spontaneous blinking rate), and by the cholinergic and GABA-ergic tones (which decrease spontaneous blinking rate). Influences by the frontal cortex activity, spinal trigeminal complex, parapontine reticular formation, and cerebellum.	Karson, 1983; Karson et al., 1984; Montagna and Zucconi, 1984; Kleinman et al., 1984; Kimber and Thompson, 2000; Doughty, 2001; Kaneko et al., 2004; Naase et al., 2005; Yoon et al., 2005; Agostino et al., 2008; Sforza et al., 2008; Cruz et al., 2011; Kaminer et al., 2011; Bologna et al., 2013; Bologna et al., 2016; Paparella et al., 2020; Ranti et al., 2020; Sanchis-Jurado et al., 2020.
Voluntary blinking	Recorded by asking participants to look at a fixed point and blink as fast as possible after a verbal/sound command. Amplitudes and velocity of the opening and closing phase, and duration of the inter-phase pause are usually considered.	Primary mediated by M1, LPMCv and LPMCd. Influences by the SMA, rostral and caudal cingulate cortices, frontal eye field, supplementary eye field, posterior parietal cortex. The occipital and the cerebellum may also play a role.	Kuypers, 1958; Jenny and Saper, 1987; Schmidtke and Büttner-Ennever, 1992; Bodis-Wollner et al., 1999; Bour et al., 2000; Morecraft et al., 2001; Delgado-García et al., 2003; Sohn et al., 2004; Zadikoff and Lang, 2005; Agostino et al., 2008; Suzuki et al., 2010; van Koningsbruggen et al., 2012; Bologna et al., 2012; Bologna et al., 2013; Valls-Sole, 2019; Sanchis-Jurado et al., 2020.

to elucidate the different physiological and neural mechanisms underlying each type, providing valuable insights into the multi-faceted nature of this fundamental ocular motor behavior (Bologna et al., 2013; Bour et al., 2000; Cruz et al., 2011; Delgado-García et al., 2003; Kofler et al., 2023; Snow and Frith, 1989; Valls-Sole, 2019, 2012; VanderWerf et al., 2003).

Our current understanding of the neural control of the eyelid comes from studies on animals and in healthy human subjects, as well as on human patients with various neurological and psychiatric diseases (Agostino et al., 2008; Bologna et al., 2016, 2014, 2013, 2012, 2009; Bour et al., 2002; Caplan and Guthrie, 1994; Deuschl and Goddemeier, 1998; Hanzlíková et al., 2019; Karson et al., 1986, 1984; Kimber and Thompson, 2000; Kleinman et al., 1984; Korosec et al., 2006; Lozza et al., 1997; Manca et al., 2001; de Tommaso et al., 2001; Valls-Sole, 2019; Valls-Solé et al., 1997). Blinking recording techniques have evolved over the years. In the past, the eyelid motion was registered with mechanical systems that were no longer employed, in which the eyelid was attached to a lever arm connected to a device that registered the lid motion (Cruz et al., 2011). To date, more sophisticated methods are available, which overall provide information on the rate of blinking (blink/min), on the interval of time between two consecutive blinks, namely the interblink interval, on the amplitude (usually expressed in degrees or mm) and velocity (degrees/s or mm/s) of the closing and opening phases, and on the duration of the inter-phase pause (ms) (Bologna et al., 2013; Cruz et al., 2011). Among these techniques, electrooculography measures blinking, placing the electrodes vertically above the eyebrow and on the malar prominence in line with the pupil. In this setting, an eyeblink is defined as a minimal voltage change during a certain period (Denney and Denney, 1984). Electromyographic (EMG) techniques can be used to record and non-invasively analyze the activation of the OO through surface electrodes, whereas the activity of the LPS muscle can only be recorded and analyzed using needle electrodes (Aramideh et al., 1994; Aramideh and Ongerboer de Visser, 2002; Cruccu and Deuschl, 2000; Esteban et al., 2004; Grandas et al., 2020; Van Allen and Blodi, 1962). The search coil technique and optoelectronic motion analyzers can also be used to perform a detailed, objective evaluation of eyelid kinematics during the different types of blinking (Becker and Fuchs, 1988; Bologna et al., 2013; Bour et al., 2002, 2000; Evinger et al., 1991; Paparella et al., 2020; Sforza et al., 2008; Sprenger et al., 2008; VanderWerf et al., 2003). However, since these techniques entail attaching fine wire coils or reflective markers to the upper eyelids and require expensive laboratory equipment, they may be technically challenging and not easily applicable on a large scale. More recently, computer-assisted video acquisition systems (frame rate per second ranging from 4 to 280), suitable for real-time measurement of blinking even in the clinical setting, have been adopted (DeAngelis et al., 2019; Espinosa et al., 2018; Godfrey et al., 2019; Kwon et al., 2013; Lapa et al., 2023; Nousias et al., 2022; Paparella et al., 2022; Sanchis-Jurado et al., 2020; Wambier et al., 2014). Also, infrared reflectance measures blinking by using an infrared LED to illuminate the eye surface and a phototransistor or a photodiode mounted on an eyeglass frame to detect the infrared light reflected from the eye. The blink signal is based on the difference between the light emitted and the light reflected from the eyelid and eyeball (Cruz et al., 2011). Neurophysiological techniques and various experimental methods have also been used, either alone or combined with neuroimaging, to accurately characterize the different types of blinking and shed light on their neural control systems (Casse et al., 2007; Cruccu et al., 2005; Guipponi et al., 2015).

3. Reflex blinking

The reflex control of blinking relies on neural mechanisms that involve visual stimuli converging on the motor effectors at the brainstem level, auditory stimuli mediated by the ventral cochlear nucleus, as well as sensory stimuli from trigeminal or extratrigeminal sources. In fact, startling-like inputs of any sensory modality may activate nuclei of the reticular formation to give rise to a reflex reaction, the smallest expression of which is a blink (Brown et al., 1991; Rimpel et al., 1982; Rothwell et al., 2021).

The coordination of OO and LPS muscle activation during reflex blinking suggests the presence of a premotor neural structure within the brainstem. This structure acts as a generator, integrat-

ing sensory stimuli of various types and connecting them with different motor nuclei, namely the motor nuclei of the VII and III cranial nerves (Schmidtke and Büttner-Ennever, 1992). In contrast to other body parts, the eyelid is characterized by a limited number of proprioceptors since it moves within a relatively constant mechanical load. As a result, reflex eyelid movements exhibit a unique property of being unaffected by monosynaptic stretch reflexes. This peculiarity highlights the distinct nature of the neural control mechanisms governing reflex eyelid movements (Bologna et al., 2013; Delgado-García et al., 2003; Valls-Sole, 2019).

Both visual (photic) and acoustic stimuli can cause a reflex closure of the eyes (Esteban, 1999). In these cases, blinking responses are formed by a single bilateral component of the OO. These responses are characterized by a marked intra- and interindividual latency variation and have been considered equivalent to the second responses of the electrical trigeminal blink reflex (see next paragraphs). The central pathways of photic and acoustic blink reflexes remain uncertain. Due to experimental observations showing preserved photic and acoustic reflexes in animals and humans with temporal and occipital cortical lesions (Hill et al., 1961; Hori et al., 1986; Khater-Boidin and Duron, 1987; Weiskrantz et al., 1974), it is almost certain that the cerebral cortex does not participate. The tentative visual pathway would convey the impulses from the retina throughout the optic nerve, optic tract, lateral geniculate body and pretectum/central tegmental tract (Esteban, 1999). A possible acoustic reflex pathway would include the ventral cochlear nucleus, the superior olivary complex, the lateral lemniscus nuclei and the caudal colliculus (Hori et al., 1986).

Reflex blinking is also induced by somatosensory inputs from the cornea and the cutaneous receptors of the ophthalmic division of the V cranial nerve (Cruccu and Deuschl, 2000). Corneal receptors encode somatosensory stimuli, which are transmitted through primary afferents of the trigeminal ganglion neurons, i.e., thin myelinated (Aδ type) and unmyelinated (C type) fibers, which are in turn located in two spatially distinct regions of the spinal trigeminal nucleus in the lower brainstem, specifically the trigeminal nucleus interpolaris-caudalis transition zone (Vi/Vc) and the subnucleus caudalis-upper cervical spinal cord (Vc/C1) (Hirata et al., 2004, 2003). Vi/Vc Neurons are second-order neurons of the reflex path projecting to OO motoneurons. Recordings of Vi/Vc neurons have revealed two distinct neuron types, i.e., tonic and phasic. The blink amplitude increases with the recruitment of tonic and phasic neurons according to the number of spikes evoked by the corneal stimulus (Henriquez and Evinger, 2007). The neurons located at the Vi/Vc transition also project to the superior salivatory nucleus and mediate tear production in response to irritation caused by the original tear film deficiency or noxious chemical stimulation of the ocular surface (Hirata et al., 2004). The neurons located within the superficial laminae (I-II) of the Vc/C1 transition project to the posterior thalamic nucleus (a central relay of thermal-pain inputs from the face) and are likely to play a prominent role in the sensory-discriminative aspects of corneal nociception. While reflex blinking to corneal stimuli is purely mediated by Aδ fibers, the blink reflex to cutaneous inputs from the face is thought to be mediated by the Aβ afferents that convey touch sensation. They project mechano-sensitive neurons in the medullary laminae III–IV and to the polysynaptic chain of wide-dynamic-range brainstem interneurons in the pontomedullary reticular area, equivalent to the spinal lamina V. The relaying afferent inputs cross the midline and then ascend from the medulla to the efferent branch of the trigeminal-facial reflex, i.e., the facial motor neurons innervating the OO (Aramideh and Ongerboer de Visser, 2002; Cruccu et al., 2005).

In experimental conditions, reflex blinking can be elicited in humans by mechanical or electrical stimulation of the corneal surface, which activates Aδ fibers (corneal reflex) (Accornero et al., 1980; Cruccu et al., 1986) or by the percutaneous electrical stimulation of the supraorbital nerve, which activates Aβ, Aδ, and C type fibers of the nerve trunk (blink reflex) (Aramideh and Ongerboer de Visser, 2002; Bour et al., 2000; Cruccu et al., 2005; Cruccu and Deuschl, 2000; Kimura et al., 1970, 1969; Kofler et al., 2023; Pellegrini et al., 1995; Powers et al., 1997; Rothwell et al., 2021). Afferents from the cornea yield a bilateral late electromyographic response in the OO at a latency of approximately 40 ms but not early responses, even with supramaximal stimulation (Accornero et al., 1980). Inputs from the supraorbital nerve, instead, yield an early ipsilateral R1 response in the OO, observed at a latency of approximately 10 ms, mediated through an oligo-synaptic pontine circuit, and a late bilateral R2 response, which occurs in the OO at a latency of approximately 30–35 ms (Aramideh and Ongerboer de Visser, 2002; Cruccu et al., 2005; Cruccu and Deuschl, 2000; Esteban, 1999; Kimura et al., 1970, 1969). In the human blink reflex, a third component also exists, namely the R3 response, which is bilateral and has a mean onset latency of around 80 ms (Esteban, 1999). Sometimes it can be difficult to distinguish the R3 from the R2 component, especially in pathological conditions, thus the presence of R3 occasionally makes the analysis of the basal reflex excitability rather complicated (Esteban, 1999). Blink reflexes do not differ significantly between males and females. R2 latency may increase with age (Kofler et al., 2013; Peddireddy et al., 2006). It was also reported that when the R2 component of the blink reflex was habituated by repetitive stimuli, stimulation of the cornea still evoked a reflex, but supraorbital stimulation produced only a depressed R2 response (Berardelli et al., 1985a). The fact that the blink reflex to corneal stimuli is less prone to habituation phenomena from low-frequency repetitive stimulation compared with the R2 component of the blink reflex to supraorbital nerve stimuli indicates that the reflex eyelid movements evoked by these various afferent inputs are mediated through different neural substrates (Berardelli et al., 1985a). While inputs from the cornea relay to only a few intramedullary synapses, the afferents contributing to the R2 component of the blink reflex to supraorbital nerve stimuli relay to a polysynaptic chain of interneurons in the pontomedullary reticular area (Berardelli et al., 1985a; Cruccu et al., 2005). Evidence from studies on animals and on healthy humans indicates that high-frequency stimulation of the supraorbital nerve may result in the long-term potentiation (LTP)-like and long-term depression (LTD)-like plasticity mechanisms in the synapses of the blink reflex circuit, as indexed by facilitatory or inhibitory changes of the R2 component area (Bologna et al., 2010; Mao and Evinger, 2001). The data also support the hypothesis that LTP and LTD mechanisms play a role in humans' adaptive modification of reflex blink circuits (Bologna et al., 2010; Mao and Evinger, 2001). Concerning the physiology of the late R3 component, some evidence suggested that nociceptive afferent fibers mainly conduct R3, though is shares some central and peripheral pathways with the R2 component (Esteban, 1999). Alternative evidence suggests that the R3 reflects a somatosensory startle reaction rather than a nociceptive reflex (Ellrich and Hopf, 1996; Kofler and Halder, 2014; Téllez et al., 2009; Versace et al., 2020). The blink reflex may also be elicited by stimulating trigeminal branches other than the ophthalmic (Jääskeläinen, 1995). Furthermore, high-intensity laser pulses directed to any trigeminal division may elicit reflex blinking responses (Romaniello et al., 2003). Finally, the somatosensory-evoked blink response is another type of reflex blinking, which is elicited by electrical stimulation of a peripheral nerve or the skin of the body or limbs (Miwa et al., 1998), and is thought to be the result of the integration of facilitatory and inhibitory mechanisms within the brainstem (Miwa et al., 1998, 1996).

Experimental observations in humans showed that the late component of the blink reflex is depressed in patients with hemi-

spheric cerebral vascular lesions because of damage to corticonuclear projections and slowed transmission of impulses in the brainstem circuits (Berardelli et al., 1983; Catz et al., 1988; Kaplan and Kaplan, 1980; Kimura et al., 1985). Although these changes apply to reflexes evoked by both corneal and supraorbital nerve stimuli, the blink reflex to supraorbital nerve stimuli displays a greater safety factor, as indicated by the fact that it is inhibited in a lower percentage of cases (Berardelli et al., 1983; Kimura et al., 1985). More recently, it has been reported that recovery of the R2 component of the blink reflex in healthy humans is significantly inhibited after low-frequency and sub-threshold repetitive transcranial magnetic stimulation (rTMS) of the primary motor cortex (M1), which thus confirms the existence in humans of cortical facilitatory drive to the brainstem reflex pathways (De Vito et al., 2009). These data provide evidence of crossed facilitation from widespread areas within the cortex and from the sensory representation of the face to the brainstem circuits mediating the blink reflex response.

Neurophysiological studies, mainly performed in the 1980s and 1990s, in patients with movement disorders, like blepharospasm, Parkinson's disease (PD) and dystonia, provided evidence of enhanced excitability of the blink reflex circuits in these conditions, likely resulting from changes of central dopamine activity levels and abnormal basal ganglia influences on brainstem structures which mediate the trigeminal reflexes (Agostino et al., 1987; Antelmi et al., 2016; Berardelli et al., 1985b; Deuschl and Goddemeier, 1998; Miwa et al., 1996; Nakashima et al., 1990; Pauletti et al., 1993; de Tommaso et al., 2001; Valls-Solé et al., 1997). Studies on animals also described the possible circuits sub-serving the basal ganglia modulation of reflex blinking circuits (Basso et al., 1996; Basso and Evinger, 1996). The basal ganglia output via the substantia nigra pars reticulata inhibits neurons in the superior colliculus, which in turn excites tonically active neurons of the nucleus raphe magnus; finally, neurons in the nucleus raphe magnus inhibit spinal trigeminal neurons involved in the reflex blink circuits (Basso et al., 1996; Basso and Evinger, 1996; Gnadt et al., 1997). It has been suggested that noxious stimuli in the face transiently increase the output of the basal ganglia, suppressing orienting behavior to allow unopposed withdrawal or defensive behaviors. In addition to suppressing orienting behavior, data indicate that the basal ganglia output increases the sensitivity of cutaneous reflexes to enhance the protective function of trigeminal reflex blinks (Basso et al., 1996; Basso and Evinger, 1996). As opposite to the demonstrated enhanced blink reflex circuit excitability, however, the kinematics of reflex blinking, including the opening and closing phases, as well as the inter-phase pause duration, were normal in PD (Agostino et al., 2008; Bologna et al., 2013). Conversely, in atypical parkinsonism, e.g., progressive supranuclear palsy (PSP), patients showed a normal closing phase but a prolonged inter-phase pause of reflex blinking (Bologna et al., 2009). In this case, the brainstem damage related to PSP may play a predominant role in lengthening the switching between the closing and opening phases during reflex blinking.

Few data are also available on the role played by the cerebellum in the modulation of normal reflex blinks. Animal studies have shown that two groups of neurons in the interpositus nucleus respond to corneal stimulation. The tonic discharge in pause neurons ceases following stimulation of the cornea, whereas burst neurons display a transient increase in their firing frequency. Cessation of pause neuron activity appears to contribute to the end of the blinks. A delay in the increased tonic discharge rate and cessation of pause neuron activity is accompanied by an increased amplitude and duration of the reflex blinks resulting from blink adaptation. Pause neurons treated with GABA(A) antagonists once again yield an increase in reflex blink amplitude and duration, accompanied by increased tonic activity and a delayed pause. By contrast, burst neurons do not appear to modulate reflex blinks. Burst neuron discharges neither correlate with blink characteristics nor with blink adaptation. These findings indicate that pause neurons affect reflex blinks by providing a tonic excitatory input to facial motor neurons during lid closure and then inhibiting the facial motor neurons from adjusting the termination of lid closure; in contrast, burst neurons appear to play a role in eyelid conditioning (Chen and Evinger, 2006).

In summary, the neural control of reflex eyelid movements is mediated primarily by motor effectors and circuits at the brainstem level. Other supra-segmental structures, including the cerebral hemispheres, basal ganglia, and cerebellum, also modulate the excitability of the blink reflex circuits.

4. Spontaneous blinking

Although spontaneous blinking is one of the most frequent human movements, and an abnormal blink rate is frequently observed in various neurological conditions, the neural mechanisms underlying this movement are unclear.

The rate of spontaneous blinking broadly varies across individuals, being subjected to factors including lighting, time of the day, fatigue, temperature, wind, ocular surface status, level of mental activity, sex and age (Cruz et al., 2011; Doughty, 2001). Spontaneous blinking rate is lower in neonates and infants (from 0.7 to 2.7 blinks/min according to some reports) (Bacher and Smotherman, 2004; Cruz et al., 2011), it increases rapidly in children and adolescents and stabilizes in adults, with a mean value ranging from 10 to 20 blinks/min (Cruz et al., 2011). The spontaneous blinking rate is usually higher in older subjects than younger subjects, as well as in women than men (Ranti et al., 2020). Anxiety, visual fatigue, sleep deprivation, driving, and tasks requiring speech, memory or mental load increase the spontaneous blinking rate (Cruz et al., 2011). Conversely, spontaneous blinking is inhibited during engaged visual attention to minimize blink-induced interruption to visual information (Ranti et al., 2020). The interblink interval is also markedly variable. Subjects with the same spontaneous blinking rate may blink in different ways, and four patterns of interblink interval distribution have been described, including the J-shaped, irregular plateau, bimodal, and symmetrical pattern (Cruz et al., 2011; Naase et al., 2005; Sanchis-Jurado et al., 2020). Finally, spontaneous blinking amplitudes, usually referring to the down phase of the movement, range from less than 10 degrees up to 60 degrees. The mean amplitude decreases in older patients (Sun et al., 1997). Also, young men close their eyes completely (or almost completely) 44% of the time, whereas the eyelid closure of older men and women is less frequently complete (between 25% to 75% of the maximum excursion) (Ranti et al., 2020; Sforza et al., 2008). The peak velocity of the spontaneous blinking movement is always achieved during the down phase, while the up phase is slower. Additionally, the maximum velocity reduces with age during eyelid closure and opening. Women move faster than men (Sforza et al., 2008).

Neuropharmacological and clinical observations and experimental studies in neurological diseases such as PD, atypical parkinsonism and schizophrenia indicate that the neural control of spontaneous blinking is closely related to central dopaminergic activity. Dopamine has, ever since the early 1980s, been known to facilitate the blink rate (Karson, 1983), whereas the central cholinergic and GABA-ergic tone is known to be inversely related to the spontaneous blink rate. Due to the reduced central dopaminergic activity, a reduced spontaneous blink rate is a common finding in parkinsonian syndromes (Agostino et al., 2008; Altiparmak et al., 2006; Bologna et al., 2016, 2014, 2013, 2012, 2009; Demiral et al., 2022; Deuschl and Goddemeier, 1998; Hanzlíková

et al., 2019; Karson et al., 1984; Kimber and Thompson, 2000; Korosec et al., 2006; Valls-Sole, 2019). A progressive reduction in spontaneous blink rate often reflects a worsening clinical picture in these conditions. Dopaminergic replacement stabilizes the spontaneous blinking rate (Bologna et al., 2009; Kimber and Thompson, 2000). Reduced spontaneous blinking rate in PD is also increased by subthalamic nucleus deep brain stimulation (Bologna et al., 2012). Conversely, a significant increase in the blink rate in parkinsonian patients off medication may be an indicator of dystonia (Kimber and Thompson, 2000), also supporting other evidence which showed an increased spontaneous blinking rate in individuals with primary dystonia (Valls-Solé et al., 1997). In atypical parkinsonisms, including PSP, the spontaneous blink rate is strongly reduced (Altiparmak et al., 2006; Bologna et al., 2009), together with the peak velocities and amplitudes of both the closing and opening phases (Bologna et al., 2009). This is thought to reflect the reduced central dopaminergic activity and a primary degeneration of cerebral structures, generating spontaneous blinking, including the mesial cortical areas in the frontal lobe and brainstem (see next paragraph) (Bologna et al., 2013). The increased blink rate in schizophrenia, particularly in medication-naive subjects, lends further support to the important role played by the central dopaminergic neurotransmitter systems in regulating spontaneous blinking (Karson, 1983; Karson et al., 1984; Kleinman et al., 1984). Previous evidence also showed that dopamine plays a role in antinociceptive processes (Rezaee et al., 2020; Wawrzczak-Bargieła et al., 2020). Notably, a recent study demonstrated an increased spontaneous blinking rate during pain stimulation in healthy humans (Paparella et al., 2020), interpreted as reflective of an increased central dopaminergic tone due to pain. Finally, another recent report investigating the possible relationship between spontaneous blinking rate, as a marker of dopamine system functioning, and individual performance during high-incentive conditions demonstrated that people with low spontaneous blinking rate could improve their performance when incentives were at stake; in contrast, people with high basal spontaneous blinking rate were not. These findings are consistent with the idea that suboptimal performance in high-stakes conditions may stem from the neuromodulatory effects of dopamine (van de Groep et al., 2017), further supporting the relationship between dopamine and spontaneous blinking.

Studies in humans based on functional magnetic resonance imaging (fMRI) and the electrooculogram suggest that the mesial areas of the frontal cortex may play a role in generating spontaneous eye blinking (Kaneko et al., 2004; Montagna and Zucconi, 1984; Yoon et al., 2005). More recent data from animal models, however, indicate that the spinal trigeminal complex is another major element in the generation of spontaneous blinking (Kaminer et al., 2011). The spontaneous blink rate is probably controlled by a definable neural system originating in the parapontine reticular formation, which is believed to facilitate spontaneous eye blinking. In this regard, it has been demonstrated that observing patients' spontaneous blinking rate could help to discriminate between vegetative state/unresponsive wakefulness syndrome and minimally conscious state, with the latter showing a significantly higher spontaneous blinking rate as compared to the former (Magliacano et al., 2021). Spontaneous blink rate might, however, also be modulated by influences provided by other structures, like the cerebellum, though its role is unclear. Lastly, spontaneous blinking can be volitionally suppressed, and a few studies demonstrated the involvement of the insular cortex and other brain areas in blinking suppression and the associated sense of urge to blink that comes with it (Berman et al., 2012).

To sum up, studies in humans and animals possibly indicate the existence of a generator of spontaneous blinking in the brainstem, which is subject to numerous influences, including dopamine, as well as to a cortical control, by which spontaneous blinking can be voluntarily suppressed (Berman et al., 2012).

5. Voluntary blinking

The origin and course of cortical projections mediating voluntary control of the eyelid are not yet entirely understood.

Studies on non-human primates revealed that distinct cortical areas are involved in the voluntary control of facial expressions. Animal studies designed to investigate the distribution of corticofacial projections showed that brain areas on frontal lobe convexity, including M1 and the ventral lateral premotor cortex (LPMCv) give rise to the main corticofacial projections. The dorsal lateral premotor cortex (LPMCd) and other areas on the medial surface of the frontal lobe, e.g., the supplementary motor cortex (M2), rostral cingulate cortex (M3) and caudal cingulate cortex (M4), make a further important contribution to muscle innervations of the face. M1, LPMCv, M4 and LPMCd primarily innervate the contralateral lower muscles, whereas M2 and M3 bilaterally innervate the upper face, including the eyelid (Morecraft et al., 2001). This complex innervation explains why the middle cerebral artery (MCA) occlusion usually results in paralysis of the contralateral lower face, but it spares the upper face. As historically assumed, this may be a consequence of the bilateral innervation from M1 that the upper musculature of the face receives compared to the lower face, which is innervated only by the contralateral M1. However, not all studies fully support this classic interpretation (Jenny and Saper, 1987; Kuypers, 1958). As recently emphasized (Morecraft et al., 2001), since the origin of the M3 projection is located within the vascular territory of the anterior cerebral artery, the bilateral sparing of the upper face following superficial MCA occlusion is due, in part, to sparing of anterior cingulate projection to the dorsal and medial regions of the facial nucleus. Moreover, the fact that in animals there is widespread face representation at the cortical level raises the possibility that each face representation may innervate the facial nucleus, preferentially targeting subsectors controlling different groups of muscles, given the musculotopic organization of the primate facial nucleus (Morecraft et al., 2001).

Earlier studies in humans demonstrated that cortical areas regulate the tonic activity in the LPS muscles. Thus, eyelid opening could be evoked by electrical stimulation of cortical areas of the frontal, temporal and occipital cortex, whereas various lesions in the same structures lead to eyelid ptosis. Several dysfunctions of voluntary eyelid control, including the so-called phenomena of 'apraxia' of eyelid opening and closing, are often observed in a variety of neurological conditions characterized by focal or widespread cortical damage (Schmidtke and Büttner-Ennever, 1992; Zadikoff and Lang, 2005). TMS studies on healthy humans have confirmed that the upper muscles of the face are innervated mainly by descending projections arising in the midline frontal region (Sohn et al., 2004). Studies using fMRI revealed that voluntary blinks are associated with activation of frontal, occipital and parietal cortex (Bodis-Wollner et al., 1999, 1997). Another fMRI study focused on the role of the cingulate motor areas (CMAs) in voluntary blinking based on the evidence that in nonhuman primates, CMAs send a preferential projection to the dorsal and intermediate facial subnuclei controlling the OO and frontalis (Morecraft et al., 2001). The authors demonstrated rostral cingulate activity in the cingulate or paracingulate sulcus: one close to the genu of the corpus callosum (anterior part of the rostral cingulate zone) and the posterior part of the rostral cingulate zone during voluntary blinking (Hanakawa et al., 2008). In addition, Suzuki et al., who explored the physiological mechanisms of voluntary eyelid closing/opening using positron emission tomography, concluded that the supplementary motor area (SMA) plays a role in the preparation and pro-

cessing of voluntary eyelid movements, M1 is involved in movement execution whereas the pre-SMA and cerebellum are likely involved in the generation of the eyelid movement rhythm (Suzuki et al., 2010). An fMRI study in healthy subjects showed that all areas of the oculomotor cortex were activated by both left and right winking, including the frontal eye field, the supplementary eye field, and the posterior parietal cortex. Blinking activated the frontal eye field and supplementary eye field, though not the posterior parietal cortex. Both the frontal eye field and posterior parietal cortex were significantly more active during winking than blinking. These results indicate that the frontal eye field plays a crucial role in voluntary unilateral eye closure (van Koningsbruggen et al., 2012).

Early neurophysiological investigations indicate different amounts and characteristics of EMG activity during voluntary and spontaneous blinking in healthy individuals (Valls-Sole, 2019). Kinematic analysis of voluntary blinking also demonstrated different kinematics compared to reflex and spontaneous blinking, further supporting a different supranuclear pathway organization. The blinking pattern is significantly more stable, and the number of complete blinks is higher during voluntary blinking than spontaneous blinking (Sanchis-Jurado et al., 2020). Nevertheless, some subjects may blink occasionally between the two go signals without being instructed to do so (Sanchis-Jurado et al., 2020). This non-instructed blinking may be considered a sporadic response to an insufficient wetting of the ocular surface after the previous blink. The mean and peak velocities and amplitudes are also higher during voluntary blinking than spontaneous blinking, as demonstrated by studies using the search coil technique and high-speed infrared video cameras (Sanchis-Jurado et al., 2020). Kinematic analysis of voluntary blinking has also been conducted in patients with PD (Bologna et al., 2013). These studies overall demonstrated normal velocity and amplitude of the closing and opening phases during voluntary blinking in patients but a longer duration of the inter-phase pause as compared to control subjects, only partially restored by dopaminergic treatment (Agostino et al., 2008; Bologna et al., 2012). The altered switching between the closing and opening phases of voluntary blinking has been interpreted as a consequence of PD's abnormal basal ganglia output, leading to functional deafferentation of the mesial frontal region areas, including the SMA, which subserve sequential movements. Again, deep brain stimulation of the subthalamic nucleus in PD patients prolongs the inter-phase pause duration for voluntary blinking without modifying this parameter during spontaneous and reflex blinking (Bologna et al., 2012). The present finding supports the hypothesis that the basal ganglia and interconnected cortical structures are primarily involved in the abnormal coordination of the timing and reciprocity of the OO and LPS muscle activation in PD.

In summary, studies on animals and neurophysiological and neuroimaging studies on humans indicate that the anatomical framework of the neural control of voluntary eyelid movement is centered on the frontal mesial areas, though other structures are also involved. This complex cortical organization justifies the peculiar features that characterize voluntary blinking in healthy individuals and pathological conditions.

6. Conclusions

Blinking movements are crucial to protect the eyes from potential injuries, maintain the ocular surface's integrity, and ensure optimal conditions for visual inputs. The study of blinking offers valuable insights into specific aspects of motor control. By classifying blinking into three distinct categories, i.e., reflex, spontaneous, and voluntary, researchers have tried to elucidate the main different physiological and neural mechanisms underlying each type of blinking. The evidence indicates that the mutually reciprocal innervation of the OO and LPS muscles during the different types of blinking is controlled by premotor structures at the brainstem level and by partially overlapping circuitries distributed across cortical and subcortical structures (Table 1). Although the neural mechanisms underlying reflex blinking have been well documented, anatomical and neurophysiological studies on both animals and humans are needed to understand better the mechanisms involved in the neural control of spontaneous and voluntary blinking. Moreover, investigations comparing the blink dynamics in healthy subjects and patients with various diseases will likely provide additional information on the neural control of the eyelid.

Competing interest/Financial Disclosure/Conflict of Interest concerning the research related to the manuscript

None of the authors have any relevant conflicts of interest to disclose.

Funding sources for study

This work was supported by the Italian Ministry of Health (Current Research 2024).

CRediT Author Contribution Statement

Matteo Bologna: Conceptualization, Writing – original draft. **Giulia Paparella:** Writing – review & editing. **Josep Valls-Solé:** Writing – review & editing. **Mark Hallett:** Writing – review & editing. **Alfredo Berardelli:** Writing – review & editing, Supervision.

Acknowledgments

The authors wish to thank Dr. Laura Centonze (laura.centonze1987@gmail.com) from the Department of Human Neurosciences, Sapienza University of Rome, for her help in the English-language editing of the manuscript.

References

Accornero N, Berardelli A, Bini G, Cruccu G, Manfredi M. Corneal reflex elicited by electrical stimulation of the human cornea. Neurology 1980;30:782–5. https://doi.org/10.1212/wnl.30.7.782.

Agostino R, Berardelli A, Cruccu G, Stocchi F, Manfredi M. Corneal and blink reflexes in Parkinson's disease with "on-off" fluctuations. Mov Disord 1987;2:227–35. https://doi.org/10.1002/mds.870020401.

Agostino R, Bologna M, Dinapoli L, Gregori B, Fabbrini G, Accornero N, et al. Voluntary, spontaneous, and reflex blinking in Parkinson's disease. Mov Disord 2008;23:669–75. https://doi.org/10.1002/mds.21887.

Altiparmak UE, Eggenberger E, Coleman A, Condon K. The ratio of square wave jerk rates to blink rates distinguishes progressive supranuclear palsy from Parkinson disease. J Neuro-Ophthalmol 2006;26:257–9. https://doi.org/10.1097/01.wno.0000249326.65227.2e.

Antelmi E, Di Stasio F, Rocchi L, Erro R, Liguori R, Ganos C, et al. Impaired eye blink classical conditioning distinguishes dystonic patients with and without tremor. Parkinsonism Relat Disord 2016;31:23–7. https://doi.org/10.1016/j.parkreldis.2016.06.011.

Aramideh M, Ongerboer de Visser BW. Brainstem reflexes: electrodiagnostic techniques, physiology, normative data, and clinical applications. Muscle Nerve 2002;26:14–30. https://doi.org/10.1002/mus.10120.

Aramideh M, Ongerboer de Visser BW, Koelman JH, Bour LJ, Devriese PP, Speelman JD. Clinical and electromyographic features of levator palpebrae superioris muscle dysfunction in involuntary eyelid closure. Mov Disord 1994;9:395–402. https://doi.org/10.1002/mds.870090404.

Bacher LF, Smotherman WP. Systematic temporal variation in the rate of spontaneous eye blinking in human infants. Dev Psychobiol 2004;44:140–5. https://doi.org/10.1002/dev.10159.

Barbato G, Moul DE, Schwartz P, Rosenthal NE, Oren DA. Spontaneous eye blink rate in winter seasonal affective disorder. Psychiatry Res 1993;47:79–85. https://doi.org/10.1016/0165-1781(93)90057-n.

Basso MA, Evinger C. An explanation for reflex blink hyperexcitability in Parkinson's disease. II. Nucleus raphe magnus. J Neurosci 1996;16:7318–30.

Basso MA, Powers AS, Evinger C. An explanation for reflex blink hyperexcitability in Parkinson's disease. I. Superior colliculus. J Neurosci 1996;16:7308–17.
Becker W, Fuchs AF. Lid-eye coordination during vertical gaze changes in man and monkey. J Neurophysiol 1988;60:1227–52. https://doi.org/10.1152/jn.1988.60.4.1227.
Berardelli A, Accornero N, Cruccu G, Fabiano F, Guerrisi V, Manfredi M. The orbicularis oculi response after hemispheral damage. J Neurol Neurosurg Psychiatry 1983;46:837–43. https://doi.org/10.1136/jnnp.46.9.837.
Berardelli A, Cruccu G, Manfredi M, Rothwell JC, Day BL, Marsden CD. The corneal reflex and the R2 component of the blink reflex. Neurology 1985a;35:797–801. https://doi.org/10.1212/wnl.35.6.797.
Berardelli A, Rothwell JC, Day BL, Marsden CD. Pathophysiology of blepharospasm and oromandibular dystonia. Brain J Neurol 1985b;108(Pt 3):593–608.
Berman BD, Horovitz SG, Morel B, Hallett M. Neural correlates of blink suppression and the buildup of a natural bodily urge. NeuroImage 2012;59:1441–50. https://doi.org/10.1016/j.neuroimage.2011.08.050.
Bjork A, Kugelberg E. The electrical activity of the muscles of the eye and eyelids in various positions and during movement. Electroencephalogr Clin Neurophysiol 1953;5:595–602. https://doi.org/10.1016/0013-4694(53)90037-6.
Bodis-Wollner I, Bucher SF, Seelos KC. Cortical activation patterns during voluntary blinks and voluntary saccades. Neurology 1999;53:1800–5. https://doi.org/10.1212/wnl.53.8.1800.
Bodis-Wollner I, Bucher SF, Seelos KC, Paulus W, Reiser M, Oertel WH. Functional MRI mapping of occipital and frontal cortical activity during voluntary and imagined saccades. Neurology 1997;49:416–20. https://doi.org/10.1212/wnl.49.2.416.
Bologna M, Agostino R, Gregori B, Belvisi D, Manfredi M, Berardelli A. Metaplasticity of the human trigeminal blink reflex. Eur J Neurosci 2010;32:1707–14. https://doi.org/10.1111/j.1460-9568.2010.07446.x.
Bologna M, Agostino R, Gregori B, Belvisi D, Ottaviani D, Colosimo C, et al. Voluntary, spontaneous and reflex blinking in patients with clinically probable progressive supranuclear palsy. Brain J Neurol 2009;132:502–10. https://doi.org/10.1093/brain/awn317.
Bologna M, Fabbrini G, Marsili L, Defazio G, Thompson PD, Berardelli A. Facial bradykinesia. J Neurol Neurosurg Psychiatry 2013;84:681–5.
Bologna M, Fasano A, Modugno N, Fabbrini G, Berardelli A. Effects of subthalamic nucleus deep brain stimulation and L-DOPA on blinking in Parkinson's disease. Exp Neurol 2012;235:265–72. https://doi.org/10.1016/j.expneurol.2012.02.004.
Bologna M, Marsili L, Khan N, Parvez AK, Paparella G, Modugno N, et al. Blinking in patients with clinically probable multiple system atrophy. Mov Disord 2014;29:415–20. https://doi.org/10.1002/mds.25830.
Bologna M, Paparella G. Neurodegeneration and sensorimotor function. Brain Sci 2020;10:808. https://doi.org/10.3390/brainsci10110808.
Bologna M, Piattella MC, Upadhyay N, Formica A, Conte A, Colosimo C, et al. Neuroimaging correlates of blinking abnormalities in patients with progressive supranuclear palsy. Mov Disord 2016;31:138–43. https://doi.org/10.1002/mds.26470.
Bour L, Ongerboer de Visser B, Aramideh M, Speelman J. Origin of eye and eyelid movements during blinking. Mov Disord 2002;17(Suppl 2):S30–2. https://doi.org/10.1002/mds.10047.
Bour LJ, Aramideh M, de Visser BW. Neurophysiological aspects of eye and eyelid movements during blinking in humans. J Neurophysiol 2000;83:166–76. https://doi.org/10.1152/jn.2000.83.1.166.
Brooke MH, Kaiser KK. Muscle fiber types: how many and what kind? Arch Neurol 1970;23:369–79. https://doi.org/10.1001/archneur.1970.00480280083010.
Brown P, Rothwell JC, Thompson PD, Britton TC, Day BL, Marsden CD. New observations on the normal auditory startle reflex in man. Brain J Neurol 1991;114(Pt 4):1891–902. https://doi.org/10.1093/brain/114.4.1891.
Cabib C, Llufriu S, Martinez-Heras E, Saiz A, Valls-Solé J. Abnormal control of orbicularis oculi reflex excitability in multiple sclerosis. PloS One 2014;9:e103897.
Caplan R, Guthrie D. Blink rate in childhood schizophrenia spectrum disorder. Biol Psychiatry 1994;35:228–34. https://doi.org/10.1016/0006-3223(94)91253-x.
Casse G, Sauvage J-P, Adenis J-P, Robert P-Y. Videonystagmography to assess blinking. Graefes Arch Clin Exp Ophthalmol Albrecht Von Graefes Arch Klin Exp Ophthalmol 2007;245:1789–96. https://doi.org/10.1007/s00417-007-0611-8.
Catz A, Steinvil Y, Reider-Groswasser I, Costeff H, Luz Y, Solzi P. Blink reflex in stroke: follow-up and correlation with function and CT parameters. Eur Neurol 1988;28:171–3. https://doi.org/10.1159/000116259.
Chen F-P, Evinger C. Cerebellar modulation of trigeminal reflex blinks: interpositus neurons. J Neurosci 2006;26:10569–76. https://doi.org/10.1523/JNEUROSCI.0079-06.2006.
Cruccu G, Agostino R, Berardelli A, Manfredi M. Excitability of the corneal reflex in man. Neurosci Lett 1986;63:320–4. https://doi.org/10.1016/0304-3940(86)90378-2.
Cruccu G, Deuschl G. The clinical use of brainstem reflexes and hand-muscle reflexes. Clin Neurophysiol 2000;111:371–87.
Cruccu G, Iannetti GD, Marx JJ, Thoemke F, Truini A, Fitzek S, et al. Brainstem reflex circuits revisited. Brain J Neurol 2005;128:386–94. https://doi.org/10.1093/brain/awh366.
Cruz AAV, Garcia DM, Pinto CT, Cechetti SP. Spontaneous eyeblink activity. Ocul Surf 2011;9:29–41. https://doi.org/10.1016/s1542-0124(11)70007-6.
de Tommaso M, Sciruicchio V, Spinelli A, Specchio N, Difruscolo O, Puca F, et al. Features of the blink reflex in individuals at risk for Huntington's disease. Muscle Nerve 2001;24:1520–5. https://doi.org/10.1002/mus.1177.
De Vito A, Gastaldo E, Tugnoli V, Eleopra R, Casula A, Tola MR, et al. Effect of slow rTMS of motor cortex on the excitability of the blink reflex: a study in healthy humans. Clin Neurophysiol 2009;120:174–80. https://doi.org/10.1016/j.clinph.2008.09.024.
DeAngelis KD, Rider A, Potter W, Jensen J, Fowler BT, Fleming JC. Eyelid spontaneous blink analysis and age-related changes through high-speed imaging. Ophthal Plast Reconstr Surg 2019;35:487–90. https://doi.org/10.1097/IOP.0000000000001349.
Delgado-García JM, Gruart A, Trigo JA. Physiology of the eyelid motor system. Ann N Y Acad Sci 2003;1004:1–9. https://doi.org/10.1196/annals.1303.001.
Demiral ŞB, Manza P, Biesecker E, Wiers C, Shokri-Kojori E, McPherson K, et al. Striatal D1 and D2 receptor availability are selectively associated with eye-blink rates after methylphenidate treatment. Commun Biol 2022;5:1015. https://doi.org/10.1038/s42003-022-03979-5.
Denney D, Denney C. The eye blink electro-oculogram. Br J Ophthalmol 1984;68:225–8. https://doi.org/10.1136/bjo.68.4.225.
Deuschl G, Goddemeier C. Spontaneous and reflex activity of facial muscles in dystonia, Parkinson's disease, and in normal subjects. J Neurol Neurosurg Psychiatry 1998;64:320–4.
Doughty MJ. Consideration of three types of spontaneous eyeblink activity in normal humans: during reading and video display terminal use, in primary gaze, and while in conversation. Optom Vis Sci 2001;78:712–25. https://doi.org/10.1097/00006324-200110000-00011.
Ellrich J, Hopf HC. The R3 component of the blink reflex: normative data and application in spinal lesions. Electroencephalogr Clin Neurophysiol 1996;101(4):349–54. https://doi.org/10.1016/0924-980x(96)95684-2.
Espinosa J, Domenech B, Vázquez C, Pérez J, Mas D. Blinking characterization from high speed video records. Application to biometric authentication. PloS One 2018;13:e0196125. https://doi.org/10.1371/journal.pone.0196125.
Esteban A. A neurophysiological approach to brainstem reflexes. Blink reflex Neurophysiol Clin Clin Neurophysiol 1999;29:7–38. https://doi.org/10.1016/S0987-7053(99)80039-2.
Esteban A, Salinero E. Reciprocal reflex activity in ocular muscles: implications in spontaneous blinking and Bell's phenomenon. Eur Neurol 1979;18:157–65. https://doi.org/10.1159/000115072.
Esteban A, Traba A, Prieto J. Eyelid movements in health and disease. The supranuclear impairment of the palpebral motility. Neurophysiol Clin Clin Neurophysiol 2004;34:3–15. https://doi.org/10.1016/j.neucli.2004.01.002.
Evinger C, Manning KA, Sibony PA. Eyelid movements. Mechanisms and normal data. Invest Ophthalmol Vis Sci 1991;32:387–400.
Evinger C, Shaw MD, Peck CK, Manning KA, Baker R. Blinking and associated eye movements in humans, guinea pigs, and rabbits. J Neurophysiol 1984;52:323–39. https://doi.org/10.1152/jn.1984.52.2.323.
Gnadt JW, Lu SM, Breznen B, Basso MA, Henriquez VM, Evinger C. Influence of the superior colliculus on the primate blink reflex. Exp Brain Res 1997;116:389–98.
Godfrey KJ, Wilsen C, Satterfield K, Korn BS, Kikkawa DO. Analysis of spontaneous eyelid blink dynamics using a 240 frames per second smartphone camera. Ophthal Plast Reconstr Surg 2019;35:503–5. https://doi.org/10.1097/IOP.0000000000001356.
Grandas F, Traba A, Perez-Sanchez JR, Esteban A. Pretarsal blepharospasm: clinical and electromyographic characteristics. Clin Neurophysiol 2020;131:1678–85. https://doi.org/10.1016/j.clinph.2020.03.016.
van de Groep IH, de Haas LM, Schutte I, Bijleveld E. Spontaneous eye blink rate (EBR) predicts poor performance in high-stakes situations. Int J Psychophysiol 2017;119:50–7. https://doi.org/10.1016/j.ijpsycho.2017.01.009.
Guipponi O, Odouard S, Pinède S, Wardak C, Ben HS. fMRI cortical correlates of spontaneous eye blinks in the nonhuman primate. Cereb Cortex N Y N 1991 2015;25:2333–45. https://doi.org/10.1093/cercor/bhu038.
Hanakawa T, Dimyan MA, Hallett M. The representation of blinking movement in cingulate motor areas: a functional magnetic resonance imaging study. Cereb Cortex N Y N 1991 2008;18:930–7. https://doi.org/10.1093/cercor/bhm129.
Hanzlíková Z, Kofler M, Slovák M, Věchetová G, Fečíková A, Kemlink D, et al. Prepulse inhibition of the blink reflex is abnormal in functional movement disorders. Mov Disord 2019;34:1022–30. https://doi.org/10.1002/mds.27706.
Henriquez VM, Evinger C. The three-neuron corneal reflex circuit and modulation of second-order corneal responsive neurons. Exp Brain Res 2007;179:691–702. https://doi.org/10.1007/s00221-006-0826-7.
Hill K, Gogan DG, Dodge PR. Ocular signs associated with hydranencephaly. Am J Ophthalmol 1961;51:267–75.
Hirata H, Okamoto K, Bereiter DA. GABA(A) receptor activation modulates corneal unit activity in rostral and caudal portions of trigeminal subnucleus caudalis. J Neurophysiol 2003;90:2837–49. https://doi.org/10.1152/jn.00544.2003.
Hirata H, Okamoto K, Tashiro A, Bereiter DA. A novel class of neurons at the trigeminal subnucleus interpolaris/caudalis transition region monitors ocular surface fluid status and modulates tear production. J Neurosci 2004;24:4224–32. https://doi.org/10.1523/JNEUROSCI.0381-04.2004.
Hori A, Yasuhara A, Naito H, Yasuhara M. Blink reflex elicited by auditory stimulation in the rabbit. J Neurol Sci 1986;76:49–59. https://doi.org/10.1016/0022-510x(86)90141-3.
Hwang K, Huan F, Kim DJ. Muscle fiber types of human orbicularis oculi muscle. J Craniofac Surg 2011;22:1827–30. https://doi.org/10.1097/SCS.0b013e31822e8468.
Jääskeläinen SK. Electrophysiological study of blink reflex in humans: differences in mental and supraorbital nerves. Acta Physiol Scand 1995;154:143–50. https://doi.org/10.1111/j.1748-1716.1995.tb09896.x.

Jenny AB, Saper CB. Organization of the facial nucleus and corticofacial projection in the monkey: a reconsideration of the upper motor neuron facial palsy. Neurology 1987;37:930–9. https://doi.org/10.1212/wnl.37.6.930.
Kaminer J, Powers AS, Horn KG, Hui C, Evinger C. Characterizing the spontaneous blink generator: an animal model. J Neurosci 2011;31:11256–67. https://doi.org/10.1523/JNEUROSCI.6218-10.2011.
Kaneko K, Mito K, Makabe H, Takanokura M, Sakamoto K. Cortical potentials associated with voluntary, reflex, and spontaneous blinks as bilateral simultaneous eyelid movement. Electromyogr Clin Neurophysiol 2004;44:455–62.
Kaplan PE, Kaplan C. Blink reflex: review of methodology and its application to patients with stroke syndromes. Arch Phys Med Rehabil 1980;61:30–3.
Karson CN. Spontaneous eye-blink rates and dopaminergic systems. Brain J Neurol 1983;106(Pt 3):643–53. https://doi.org/10.1093/brain/106.3.643.
Karson CN, Burns RS, LeWitt PA, Foster NL, Newman RP. Blink rates and disorders of movement. Neurology 1984;34:677–8.
Karson CN, Goldberg TE, Leleszi JP. Increased blink rate in adolescent patients with psychosis. Psychiatry Res 1986;17:195–8. https://doi.org/10.1016/0165-1781(86)90047-8.
Keshavan MS, Narashimha Rao IV, Narayanan HS. Rate of blinking may predict neuroleptic-induced parkinsonism. Br J Psychiatry J Ment Sci 1983;142:423. https://doi.org/10.1192/bjp.142.4.423a.
Khater-Boidin J, Duron B. The orbicularis oculi reflexes in healthy premature and full-term newborns. Electroencephalogr Clin Neurophysiol 1987;67:479–84. https://doi.org/10.1016/0013-4694(87)90012-5.
Kimber TE, Thompson PD. Increased blink rate in advanced Parkinson's disease: a form of 'off'-period dystonia? Mov Disord 2000;15:982–5. https://doi.org/10.1002/1531-8257(200009)15:5<982::aid-mds1033>3.0.co;2-p.
Kimura J, Powers JM, Van Allen MW. Reflex response of orbicularis oculi muscle to supraorbital nerve stimulation. Study in normal subjects and in peripheral facial paresis. Arch Neurol 1969;21:193–9. https://doi.org/10.1001/archneur.1969.00480140093009.
Kimura J, Rodnitzky RL, Van Allen MW. Electrodiagnostic study of trigeminal nerve. Orbicularis oculi reflex and masseter reflex in trigeminal neuralgia, paratrigeminal syndrome, and other lesions of the trigeminal nerve. Neurology 1970;20:574–83. https://doi.org/10.1212/wnl.20.6.574.
Kimura J, Wilkinson JT, Damasio H, Adams HR, Shivapour E, Yamada T. Blink reflex in patients with hemispheric cerebrovascular accident (CVA). Blink reflex in CVA. J Neurol Sci 1985;67:15–28. https://doi.org/10.1016/0022-510x(85)90018-8.
Kleinman JE, Karson CN, Weinberger DR, Freed WJ, Berman KF, Wyatt RJ. Eye-blinking and cerebral ventricular size in chronic schizophrenic patients. Am J Psychiatry 1984;141:1430–2. https://doi.org/10.1176/ajp.141.11.1430.
Kofler M, Halder W. Alterations in excitatory and inhibitory brainstem interneuronal circuits in fibromyalgia: evidence of brainstem dysfunction. Clin Neurophysiol 2014;125(3):593–601. https://doi.org/10.1016/j.clinph.2013.08.009.
Kofler M, Kumru H, Schaller J, Saltuari L. Blink reflex prepulse inhibition and excitability recovery: influence of age and sex. Clin Neurophysiol 2013;124:126–35. https://doi.org/10.1016/j.clinph.2012.07.001.
Kofler M, Valls-Solé J, Thurner M, Pucks-Faes E, Versace V. In the spotlight: How the brainstem modulates information flow. Clin Neurophysiol 2023;148:52–64. https://doi.org/10.1016/j.clinph.2023.01.013.
van Koningsbruggen MG, Peelen MV, Davies E, Rafal RD. Neural control of voluntary eye closure: a case study and an fMRI investigation of blinking and winking. Behav Neurol 2012;25:103–9. https://doi.org/10.3233/ben-2011-0355.
Korosec M, Zidar I, Reits D, Evinger C, Vanderwerf F. Eyelid movements during blinking in patients with Parkinson's disease. Mov Disord 2006;21:1248–51. https://doi.org/10.1002/mds.20930.
Kuypers HG. Corticobular connexions to the pons and lower brain-stem in man: an anatomical study. Brain J Neurol 1958;81:364–88. https://doi.org/10.1093/brain/81.3.364.
Kwon K-A, Shipley RJ, Edirisinghe M, Ezra DG, Rose G, Best SM, et al. High-speed camera characterization of voluntary eye blinking kinematics. J R Soc Interface 2013;10:20130227. https://doi.org/10.1098/rsif.2013.0227.
Lapa I, Ferreira S, Mateus C, Rocha N, Rodrigues MA. Real-time blink detection as an indicator of computer vision syndrome in real-life settings: an exploratory study. Int J Environ Res Public Health 2023;20:4569. https://doi.org/10.3390/ijerph20054569.
Lin C-L, Shiah I-S, Yeh C-B, Wan F-J, Wang T-S. Amisulpride related tic-like symptoms in an adolescent schizophrenic. Prog Neuropsychopharmacol Biol Psychiatry 2006;30:144–6. https://doi.org/10.1016/j.pnpbp.2005.08.026.
Lozza A, Schoenen J, Delwaide PJ. Inhibition of the blink reflex R2 component after supraorbital and index finger stimulations is reduced in cluster headache: an indication for both segmental and suprasegmental dysfunction? Pain 1997;71:81–8. https://doi.org/10.1016/s0304-3959(97)03342-3.
Magliacano A, Rosenfelder M, Hieber N, Bender A, Estraneo A, Trojano L. Spontaneous eye blinking as a diagnostic marker in prolonged disorders of consciousness. Sci Rep 2021;11:22393. https://doi.org/10.1038/s41598-021-01858-3.
Mak FHW, Harker A, Kwon K-A, Edirisinghe M, Rose GE, Murta F, et al. Analysis of blink dynamics in patients with blepharoptosis. J R Soc Interface 2016;13:20150932. https://doi.org/10.1098/rsif.2015.0932.
Manca D, Muñoz E, Pastor P, Valldeoriola F, Valls-Solé J. Enhanced gain of blink reflex responses to ipsilateral supraorbital nerve afferent inputs in patients with facial nerve palsy. Clin Neurophysiol 2001;112:153–6. https://doi.org/10.1016/s1388-2457(00)00516-2.
Mao JB, Evinger C. Long-term potentiation of the human blink reflex. J Neurosci 2001;21. https://doi.org/10.1523/JNEUROSCI.21-12-j0002.2001 RC151.
McMonnies CW. Diagnosis and remediation of blink inefficiency. Contact Lens Anterior Eye J Br Contact Lens Assoc 2021;44. https://doi.org/10.1016/j.clae.2020.04.015 101331.
McMonnies CW. Incomplete blinking: exposure keratopathy, lid wiper epitheliopathy, dry eye, refractive surgery, and dry contact lenses. Contact Lens Anterior Eye J Br Contact Lens Assoc 2007;30:37–51. https://doi.org/10.1016/j.clae.2006.12.002.
Miwa H, Nohara C, Hotta M, Shimo Y, Amemiya K. Somatosensory-evoked blink response: investigation of the physiological mechanisms. Brain J Neurol 1998;121(Pt 2):281–91. https://doi.org/10.1093/brain/121.2.281.
Miwa H, Yamaji Y, Abe H, Mizuno Y. Evaluation of the somatosensory evoked blink response in patients with neurological disorders. J Neurol Neurosurg Psychiatry 1996;60:539–43. https://doi.org/10.1136/jnnp.60.5.539.
Montagna P, Zucconi M. Cortical potentials related to voluntary, spontaneous and reflex blinking. Electromyogr Clin Neurophysiol 1984;24:583–9.
Morecraft RJ, Louie JL, Herrick JL, Stilwell-Morecraft KS. Cortical innervation of the facial nucleus in the non-human primate: a new interpretation of the effects of stroke and related subtotal brain trauma on the muscles of facial expression. Brain J Neurol 2001;124:176–208. https://doi.org/10.1093/brain/124.1.176.
Naase T, Doughty MJ, Button NF. An assessment of the pattern of spontaneous eyeblink activity under the influence of topical ocular anaesthesia. Graefes Arch Clin Exp Ophthalmol Albrecht Von Graefes Arch Klin Exp Ophthalmol 2005;243:306–12. https://doi.org/10.1007/s00417-004-0990-z.
Nakashima K, Rothwell JC, Thompson PD, Day BL, Berardelli A, Agostino R, et al. The blink reflex in patients with idiopathic torsion dystonia. Arch Neurol 1990;47:413–6.
Nousias G, Panagiotopoulou E-K, Delibasis K, Chaliasou A-M, Tzounakou A-M, Labiris G. Video-based eye blink identification and classification. IEEE J Biomed Health Inform 2022;26:3284–93. https://doi.org/10.1109/JBHI.2022.3153407.
Paparella G, De Biase A, Cannavacciuolo A, Colella D, Passaretti M, Angelini L, et al. Validating a portable device for blinking analyses through laboratory neurophysiological techniques. Brain Sci 2022;12:1228. https://doi.org/10.3390/brainsci12091228.
Paparella G, Di Stefano G, Fasolino A, Di Pietro G, Colella D, Truini A, et al. Painful stimulation increases spontaneous blink rate in healthy subjects. Sci Rep 2020;10:20014. https://doi.org/10.1038/s41598-020-76804-w.
Pauletti G, Berardelli A, Cruccu G, Agostino R, Manfredi M. Blink reflex and the masseter inhibitory reflex in patients with dystonia. Mov Disord 1993;8:495–500. https://doi.org/10.1002/mds.870080414.
Peddireddy A, Wang K, Svensson P, Arendt-Nielsen L. Influence of age and gender on the jaw-stretch and blink reflexes. Exp Brain Res 2006;171:530–40. https://doi.org/10.1007/s00221-005-0300-v.
Pellegrini JJ, Horn AK, Evinger C. The trigeminally evoked blink reflex. I Neuronal circuits. Exp Brain Res 1995;107:166–80. https://doi.org/10.1007/BF00230039.
Porter JD, Burns LA, May PJ. Morphological substrate for eyelid movements: innervation and structure of primate levator palpebrae superioris and orbicularis oculi muscles. J Comp Neurol 1989;287:64–81. https://doi.org/10.1002/cne.902870106.
Powers AS, Schicatano EJ, Basso MA, Evinger C. To blink or not to blink: inhibition and facilitation of reflex blinks. Exp Brain Res 1997;113:283–90. https://doi.org/10.1007/BF02450326.
Ranti C, Jones W, Klin A, Shultz S. Blink rate patterns provide a reliable measure of individual engagement with scene content. Sci Rep 2020;10:8267. https://doi.org/10.1038/s41598-020-64999-x.
Rezaee L, Alizadeh A-M, Haghparast A. Role of hippocampal dopamine receptors in the antinociceptive responses induced by chemical stimulation of the lateral hypothalamus in animal model of acute pain. Brain Res 2020;1734. https://doi.org/10.1016/j.brainres.2020.146759 146759.
Rimpel J, Geyer D, Hopf HC. Changes in the blink responses to combined trigeminal, acoustic and visual repetitive stimulation, studied in the human subject. Electroencephalogr Clin Neurophysiol 1982;54:552–60. https://doi.org/10.1016/0013-4694(82)90040-2.
Romaniello A, Iannetti GD, Truini A, Cruccu G. Trigeminal responses to laser stimuli. Neurophysiol Clin Clin Neurophysiol 2003;33:315–24. https://doi.org/10.1016/j.neucli.2003.10.010.
Rothwell J, Antal A, Burke D, Carlsen A, Georgiev D, Jahanshahi M, et al. Central nervous system physiology. Clin Neurophysiol 2021;132:3043–83. https://doi.org/10.1016/j.clinph.2021.09.013.
Sanchis-Jurado V, Talens-Estarelles C, Esteve-Taboada JJ, Pons ÁM, García-Lázaro S. Non-invasive high-speed blinking kinematics characterization. Graefes Arch Clin Exp Ophthalmol Albrecht Von Graefes Arch Klin Exp Ophthalmol 2020;258:2701–14. https://doi.org/10.1007/s00417-020-04782-w.
Schmidtke K, Büttner-Ennever JA. Nervous control of eyelid function. A review of clinical, experimental and pathological data. Brain J Neurol 1992;115(Pt 1):227–47.
Sforza C, Rango M, Galante D, Bresolin N, Ferrario VF. Spontaneous blinking in healthy persons: an optoelectronic study of eyelid motion. Ophthalmic Physiol Opt J Br Coll Ophthalmic Opt Optom 2008;28:345–53. https://doi.org/10.1111/j.1475-1313.2008.00577.x.
Snow BJ, Frith RW. The relationship of eyelid movement to the blink reflex. J Neurol Sci 1989;91:179–89. https://doi.org/10.1016/0022-510x(89)90086-5.

Sohn YH, Voller B, Dimyan M, St Clair Gibson A, Hanakawa T, Leon-Sarmiento FE, Jung HY, Hallett M. Cortical control of voluntary blinking: a transcranial magnetic stimulation study. Clin Neurophysiol. 2004 Feb;115(2):341-7. doi: http://dx.doi.org/10.1016/j.clinph.2003.10.035. PMID: 14744575.

Sprenger A, Neppert B, Köster S, Gais S, Kömpf D, Helmchen C, et al. Long-term eye movement recordings with a scleral search coil-eyelid protection device allows new applications. J Neurosci Methods 2008;170:305–9. https://doi.org/10.1016/j.jneumeth.2008.01.021.

Sun WS, Baker RS, Chuke JC, Rouholiman BR, Hasan SA, Gaza W, et al. Age-related changes in human blinks. Passive and active changes in eyelid kinematics. Invest Ophthalmol Vis Sci 1997;38:92–9.

Suzuki Y, Kiyosawa M, Mochizuki M, Ishiwata K, Ishii K. The pre-supplementary and primary motor areas generate rhythm for voluntary eye opening and closing movements. Tohoku J Exp Med. 2010 Oct;222(2):97-104. doi: http://dx.doi.org/10.1620/tjem.222.97. PMID: 20877165.

Téllez MJ, Axelrod F, Kaufmann H. The R3 component of the electrically elicited blink reflex is present in patients with congenital insensitivity to pain. Pain 2009;141(1–2):178–80. https://doi.org/10.1016/j.pain.2008.10.030.

Valls-Sole J. Spontaneous, voluntary, and reflex blinking in clinical practice. J Clin Neurophysiol 2019;36:415–21. https://doi.org/10.1097/WNP.0000000000000561.

Valls-Sole J. Assessment of excitability in brainstem circuits mediating the blink reflex and the startle reaction. Clin Neurophysiol 2012;123:13–20. https://doi.org/10.1016/j.clinph.2011.04.029.

Valls-Solé J, Tolosa ES, Nobbe F, Diéguez E, Muñoz E, Sanz P, et al. Neurophysiological investigations in patients with head tremor. Mov Disord 1997;12:576–84. https://doi.org/10.1002/mds.870120415.

Van Allen MW, Blodi FC. Electromyographic study of reciprocal innervation in blinking. Neurology 1962;12:371–7. https://doi.org/10.1212/wnl.12.5.371.

VanderWerf F, Brassinga P, Reits D, Aramideh M, Ongerboer de Visser B. Eyelid movements: behavioral studies of blinking in humans under different stimulus conditions. J Neurophysiol 2003;89:2784–96. https://doi.org/10.1152/jn.00557.2002.

Versace V, Campostrini S, Sebastianelli L, Saltuari L, Valls-Solé J, Kofler M. Threat vs control: potentiation of the trigeminal blink reflex by threat proximity is overruled by self-stimulation. Psychophysiology 2020;57(10). https://doi.org/10.1111/psyp.13626 e13626.

Wambier SPF, Ribeiro SF, Garcia DM, Brigato RR, Messias A, Cruz AAV. Two-dimensional video analysis of the upper eyelid motion during spontaneous blinking. Ophthal Plast Reconstr Surg 2014;30:146–51. https://doi.org/10.1097/IOP.0000000000000031.

Wawrzczak-Bargieła A, Ziółkowska B, Piotrowska A, Starnowska-Sokół J, Rojewska E, Mika J, et al. Neuropathic pain dysregulates gene expression of the forebrain opioid and dopamine systems. Neurotox Res 2020. https://doi.org/10.1007/s12640-020-00166-4.

Weiskrantz L, Warrington EK, Sanders MD, Marshall J. Visual capacity in the hemianopic field following a restricted occipital ablation. Brain J Neurol 1974;97:709–28. https://doi.org/10.1093/brain/97.1.709.

Yoon HW, Chung J-Y, Song M-S, Park H. Neural correlates of eye blinking; improved by simultaneous fMRI and EOG measurement. Neurosci Lett 2005;381:26–30. https://doi.org/10.1016/j.neulet.2005.01.077.

Zadikoff C, Lang AE. Apraxia in movement disorders. Brain J Neurol 2005;128:1480–97. https://doi.org/10.1093/brain/awh560.