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Sensorimotor trigeminal unbalance modulates pupil size

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ABSTRACT

We studied whether the patients affected by Temporo-Mandibular Disorder (TMD) showing asymmetric electromyographic (EMG) activity of masticatory muscles display asymmetries also in the pupils size in order to detect a possible tonic trigeminal control on autonomic centres. In 30 pain free TMD patients, we found a highly significant, positive correlation between left-right differences in EMG and pupils size. The asymmetry in the pupils size was likely induced by the asymmetric sensorimotor signals arising from the oro-facial region, as the pupils asymmetry decreased significantly after application of a cusp bite. Moreover, cusp bite wearing bilaterally increased the mydriasis induced by performing haptic tasks. Finally, unbalancing the occlusion by a precontact increased the diameter of the ipsilateral pupil and abolished the mydriasis induced by haptic tasks. In conclusion, trigeminal sensorimotor signals may exert a tonic control on autonomic structures regulating the pupils size at rest and during haptic tasks. Since task-associated mydriasis is correlated with task performance and is strictly proportional to the phasic release of noradrenaline at cerebral cortical level, present findings suggest that unbalanced trigeminal activity influences brain processes not directly related to the orofacial region.

Key words

Elevator muscles • Occlusion • Proprioceptive trigeminal signals • Autonomic control • Pupil size • Locus Coeruleus

Introduction

Occlusal muscles dysfunctions may lead to Temporo-Mandibular Disorders (TMD, Cooper et al., 1991) characterized by pain, enhanced sympathetic activity and increased daytime cortisol levels (Korszun et al., 2002; Light et al., 2009), likely depending on nociceptive trigeminal inputs (Sato and Schmidt, 1973; Bartsch et al., 2000). Moreover, a disregulation of the sympathetic activity in TMD has been recently proposed on the basis of pupillometric findings (Monaco et al., 2012). Finally, recent case reports showed that asymmetric sensorimotor trigeminal signals are associated with asymmetries in the activity of autonomic centres controlling vertebral arteries haemodynamics and the pupil size (De Cicco, 2012a). In this instance, correction of the occlusal unbalance, which reversibly modified the left-right asymmetry in the masseter electromyographic (EMG) activity, reduced pupils size asymmetries. The latter findings suggest that trigeminal centres exert a tonic control on autonomic structures and, thus, asymmetric trigeminal activity may create an unbalance in the activity of autonomic centres.

In order to go deeper into the relation between trigeminal and autonomic activity, we have studied whether 1) pain free TMD patients showing an asymmetry in the EMG activity of left and right

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masseter muscles displayed also asymmetries in the pupil size, and whether 2) a reduction of the EMG asymmetry by application of a cusp bite affected also pupil size asymmetry, thus indicating that sensorimotor trigeminal signals tonically modulate the activity of the autonomic structures controlling the pupil size. Finally, we assessed whether EMG asymmetries influenced the mydriasis associated with a sensorimotor task. In fact, the pupil size correlates with the changes in the neural activity occurring during task-associated "arousal" (Bradshaw, 1967; Bradley et al., 2008) and "mental effort" (Hess and Polt, 1964), as well as with task performance (Rajkoski et al., 1993).

Methods

Subjects

The study protocol was in line with the declaration of Helsinki and was approved by the ethical committee of the San Domenico Clinics, (Rome, Italy). All participants signed an informed consent. Experiments were performed in 30 patients (age 25-45 years, 10 males and 20 females) affected by TMD (Dworkin et al., 1992), showing an asymmetric activity of masseters during clenching, and not exhibiting tooth loss and pain symptoms of any origin. Participants under medication or reporting neurological, psychiatric, metabolic, endocrine symptoms, or orthopaedic problems were not included in the study.

Preliminary evaluation and cusp bite manufacturing

Patients were studied at least 2 hours after the latest caffeine containing beverages and cigarettes smoking. In a preliminary session, evaluation of the EMG activity of masseter muscles (and mandibular kinematics) was performed during swallowing and clenching. Only subjects showing an asymmetry in EMG activity higher than 15% (quantified as the ratio between the left-right difference and the left-right mean) (see Fig. 1A) were further investigated. Then, a fifteen-minutes transcutaneous electrical nerve stimulation (TENS) of trigeminal motor branches (Noaham and Kumbang, 2008), which activates muscles by direct stimulation of motor axons (Gomez and Christensen, 1991), was performed (Fig. 1B). Stimulation was administered through four couples (cathode/anode) of electrodes (1600 mm^2 of surface) applied at the level of incisura sigmoidea and of the submental region of both sides. Biphasic (cathodal/anodal) current pulses (0.54 msec duration, 21-25 mA intensity) were delivered by two I.A.C.E.R. stimulators (Martellago, Venice, Italy) leading to repeated contractions of masseters and mandible depressor muscles. The intensity of the left and right stimulation was adjusted in order to obtain a symmetric muscle activation (evaluated by EMG recording). Low frequency stimulation (0.618 Hz) was utilized for elevator muscles and higher frequency (40 Hz) for depressor muscles. In this way, alternated contraction and relaxation were observed in masseters, while mandible depressor muscles were tonically contracted, giving rise to small amplitude mandibular movements (1 mm). Following TENS, the mandibular resting posture was lowered and a dental impression was obtained in the new relative position of the arches by placing a self-hardening material between them. This dental impression was used to manufacture a cusp bite (Dao et al., 1994) modeled on the inferior dental arch. Cusp bite placement reduced the myoelectric unbalance, which decreased to less than 15% in all patients (Fig. 1C).

Experimental procedure

The experimental procedure is illustrated in Fig 2. At time 0 (t0), patients were studied at first in the habitual occlusal condition (without cusp bite, Bite OFF). The following measurements were made:

1. EMG activity of masseters during clenching effort;
2. pupils size at rest, with the dental arches touching each other;
3. pupils size during performance of an haptic, sensorimotor task (TanGram), with the dental arches touching each other.

All measurements were repeated during cusp bite wearing (Bite ON).

Subjects were tested again after 90 days (t 90) of continuous cusp bite wearing (bite was taken off only during meal and teeth cleaning) in Bite ON condition. The following variables were studied:

1. EMG activity of masseters in resting state;
2. pupils size in resting state;
3. pupils size during TanGram performance.

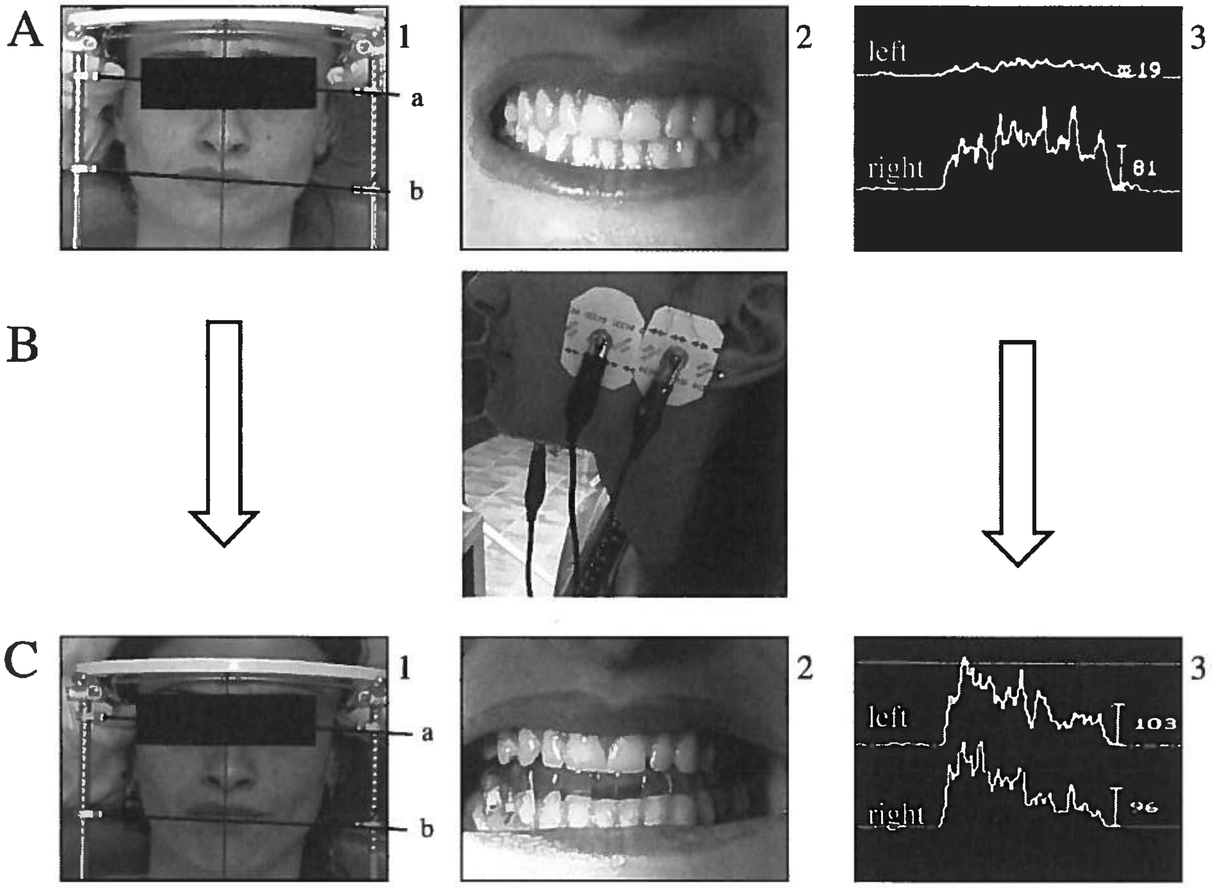

Fig. 1. - Clinical evaluations of asymmetries in masseter activity and their correction by cusp bite. A) Patient in habitual occlusion (1). During clenching a left-right asymmetry in masseter EMG activity was observed (2). Calibration is indicated by vertical white lines and related numbers. B) Soon after the evaluation displayed in A the patient was submitted to transcutaneous electrical nerve stimulation (TENS, see text for further details), thus achieving a new mandibular resting posture. The picture illustrates the positioning of stimulating electrodes. A cusp bite appropriate for maintaining arches in this new position was prepared. C) One week following the initial session the patient was wearing the cusp bite prepared as indicated in B. The positioning of the cusp bite between the arches is shown in 1. Note that during clenching the masseter EMG activity was now more symmetric (2). The numbers on EMG traces represent the amplitude of the calibration bar (white vertical line).

Pupil size (2-3), but not EMG activity (1), was recorded again in Bite OFF condition and Bite ON condition.

At this point a new test was administered to evaluate the effects possibly elicited by the induction of an occlusal deficit on the pupils size. For this purpose, after a further baseline evaluation of the pupils size (Bite OFF) at rest and during haptic task, zircon crystals were applied to the vestibular surface of the inferior canine tooth, on the side of the highest EMG activity (where the pupil was larger, see Fig. 4), in order to produce a pre-contact between the tooth face and the palatal side of the upper canine. In this condition, pupil size measurements were performed both at rest and during haptic task.

Haptic task

At the beginning of the experimental session, patients were instructed to perform a haptic task, which was practiced only once. The haptic task used in the present study was based on Tan Gram, consisting of a puzzle of triangular, square and parallelogram-shaped forms. A piece of the puzzle (the parallelogram) was removed by the experimenter

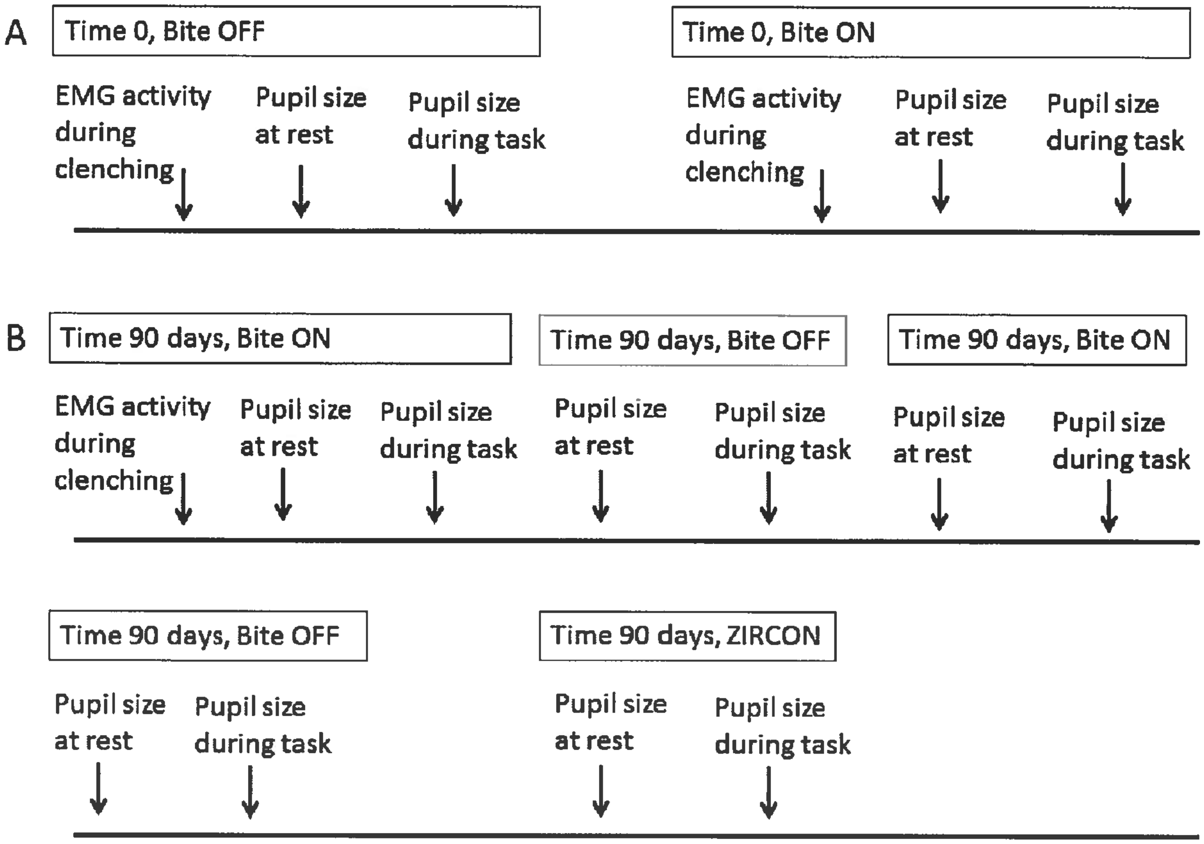

Fig. 2. - Flow chart of the experimental procedure. A. First experimental section (time 0). B. Second experimental section (time 90 days). The Black arrows mark the temporal order of the different tests performed. See text for further explanation.

and placed in the right hand of the subject, who had to reposition it in its original place without looking at his/her hand. Patients performed the task with their head placed in the pupillometer and the pupil size was monitored as soon as they began to explore the puzzle surface.

Data acquisition

Pupil size measurements (mm) were performed in the same day time in all subjects and in standard condition of artificial lighting by using a corneal topographer-pupillographer (MOD i02, with chin support, CSO, Florence, Italy) made up of a standard illuminator (halogen lamp, white light), a camera sensor CCD1/3", with a 56 mm working distance. The operator monitored the iris image by the camera, which had an acquisition time of 33 msec. Measurements were performed for both eyes in photopic conditions (40 lux) and values were displayed online on the computer screen.

The EMG activity of masseter muscles was recorded by Duo-trode surface Ag/AgCl electrodes (interelectrode distance 19,5 mm, Myo Tronics, Seattle, WA, USA). Electrodes were placed on the masseters belly, along an axis joining the orbit corner to the mandibular gonion, two cm far from the latter. The lead axis was parallel to the longitudinal axis of muscle fibres. Data were acquired at the sampling rate of 720 Hz by using an integrated system for EMG activity and mandibular movement recording (K6-I; Myo Tronics). EMG signals were acquired with a lower cutoff frequency of 15 Hz, filtered with a notch (50 Hz), full-wave rectified and displayed on the instruments monitor. The instrument provided the mean value of the rectified EMG bursts produced during clenching. Recording was allowed by the instrument software only when the resistance of the two recording leads was comparable, which allows to minimize possible bias in the asymmetry evaluation due to the different size of the EMG signal of the two sides.

Statistical analysis (SPSS.13)

Analysis was performed by repeated measures ANOVA. For the size of each pupil and absolute left-right size differences a 2 time (t0, t90) x 2 condition (bite on, bite off) x 2 task (resting, haptic task) experimental design was used, while a single factor design (condition or time) was used for EMG activity values and absolute left-right differences recorded during clenching. In addition a 2 condition (bite off, zircon) x 2 task (resting, haptic task) design was performed a t90 for pupils size. Finally, a 2 time (t0, t90) x 2 condition (bite on, bite off) analysis was performed for the increase in pupil size induced by the haptic task. The Greenhause-Geisser ε correction was used when requested. Correlations between variables were assessed by linear regression analysis. Significance was set at $p < 0.05$

Results

A preliminary analysis excluded significant gender effects.

Effects of orthotic correction on pupil size and EMG activity at time 0

During the first experimental session (t0), in habitual occlusion (bite OFF), all patients showed clear asymmetries of EMG activities (absolute left-right difference (mean ± SD = 50.9 ± 17.2, μV) and pupils size (0.326 ± 0.214, SD, mm). The distribution histograms of the corresponding left (L)-right (R) differences was bimodal, with positive (L > R) and negative (R > L) values (Fig. 3). As shown in Fig. 4, the pupil size asymmetry was highly correlated with the corresponding asymmetries in the

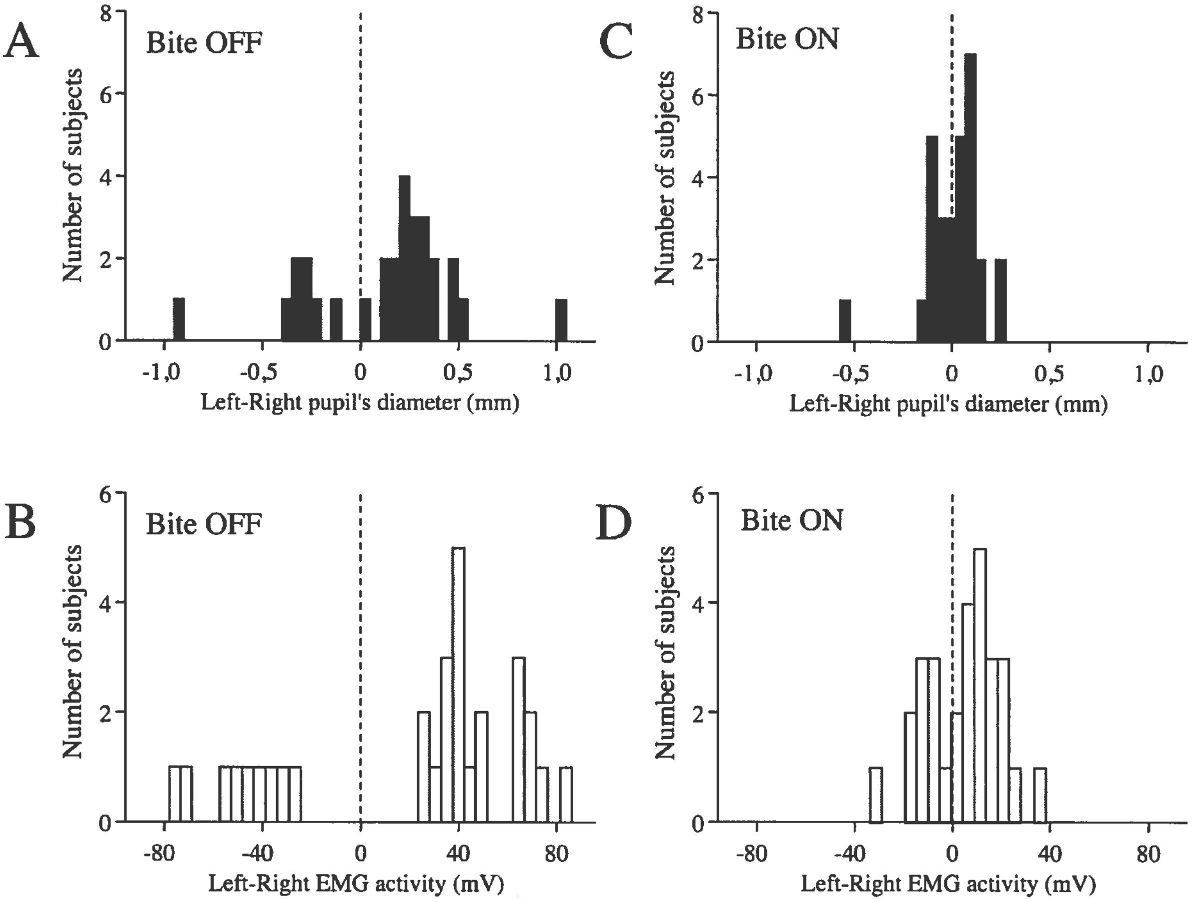

Fig. 3. - Changes in the distributions of left-right differences in EMG activity and pupil size induced by bite correction. Distribution of the differences between left and right pupil size (in mm) and masseter EMG activity (in μV) have been shown in the upper and lower row, respectively. Data obtained during normal occlusion (Bite OFF) and following bite correction (Bite ON) have been shown in A-B and C-D, respectively.

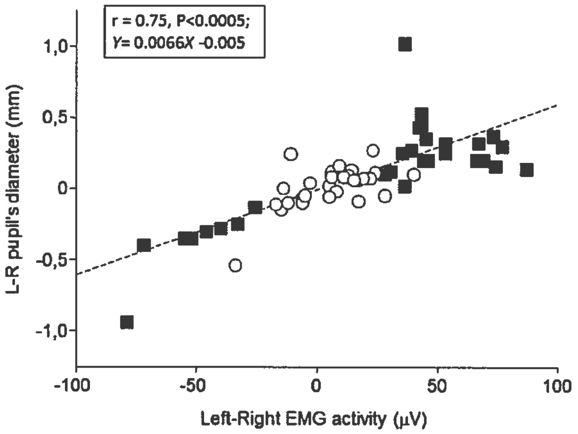

Fig. 4. - Correlation between left-right side differences in pupil size and EMG activity. Scatter plot of left-right differences in pupil size and masseter EMG activity. Black squares and open circles represent subjects in normal occlusion (Bite OFF) and following bite correction (Bite ON), respectively. Positive and negative values on the abscissa and ordinate indicate predominance of the left and right side values, respectively. The regression line plotted on the graph is relative to data obtained in the Bite OFF condition and it is virtually indistinguishable from that obtained for Bite ON data. Its equation has been plotted in the rectangular box together with the value of the coefficient of correlation (r) and statistical significance.

EMG activity ($r = 0.75$, $p < 0.0001$; $Y = 0.0066 X - 0.005$). In all instances, the side showing the largest EMG activity showed also the larger pupil size. The difference between the larger and smaller pupil size was highly significant (EMG activity: $F(1,28) = 254.6$, $p < 0.0001$; pupil size: $F(1,28) = 67.46$, $p < 0.0001$). Wearing the cusp bite reduced significantly the asymmetry in EMG activity (from 50.9 ± 17.2 to 14.1 ± 8.9 µV, $F(1,28) = 125.8$, $p < 0.0001$); as a consequence, the corresponding histogram became unimodal (Fig. 3C-D). The statistical analysis performed on the asymmetry in pupils size (and on the corresponding values) is shown in Table I. Decomposition of the significant time x condition x task interaction indicated that cusp bite reduced significantly the pupils asymmetry at rest (from 0.326 ± 0.214 to 0.11 ± 0.10 mm, $p < 0.0001$). The asymmetries in EMG activity and pupils diameters were still significantly correlated ($r = 0.62$, $p < 0.0005$), although greatly reduced. The correlation between the two variables was similar to that observed before bite wearing ($Y = 0.006 X - 0.007$).

As shown in Table II, the reduction in the asymmetry of masseter EMG was due to a significant increase in the activity of the less active masseter muscle, whereas the reduction of the pupil asymmetry was due to a significant reduction in the diameter of both pupils, although larger in the largest one.

Time, bite and task effects on the pupils size and asymmetry

Decomposition of the significant time x bite x task interaction illustrated in Table I indicated that a both t0 and t90 cusp bite wearing greatly decreased the asymmetry in pupils size at rest, due to significant reductions in the diameters of both pupils (see Table II). On the other hand, on both occasions, the haptic task significantly increased the pupils size independently of bite conditions. During the haptic task, at variance with what observed at rest, bite correction increased the size of both pupils. As a consequence, cusp bite wearing significantly amplified the mydriasis observed during the haptic task, as indicated by decomposition of the significant time x condition effect observed for this parameter variable (larger pupil: $F(1,28) = 8.63$, $p < 0.007$, smaller pupil: $F(1,28) = 33.1$, $p < 0.0001$), with post-hoc comparison indicating significant differences between Bite OFF and Bite ON conditions for both pupils at t0 (largest pupil, $p < 0.0001$; smaller pupil, $p < 0.0001$) and t90 (largest pupil, $p < 0.0001$; smaller pupil, $p < 0.0001$) (Fig. 5, Table II). The larger task-associated mydriasis observed in Bite ON with respect to Bite OFF condition is illustrated in Fig. 6 for a representative patient.

After the 90 days period elapsing from the first experimental session, in Bite ON condition both pupils showed a significantly smaller diameter at rest with respect to the first experimental session and a larger diameter during the haptic task. In Bite OFF condition the only significant difference concerned the larger pupil, which showed a smaller diameter at rest with respect to the first session. As a consequence of the latter change, in Bite OFF the pupils asymmetry observed at rest was smaller in the second experimental session with respect to the first one (t0: 0.33 ± 0.21; t90: 0.21 ± 0.20 mm, $p < 0.0001$). In this condition, the left-right differences in the pupil size measured at t90 was significantly correlated with that observed at t 0 ($r = 0.952$, $Y = 0.738 X - 0.023$, $p < 0.0005$).

Effect of malocclusion on pupil size

The study of the effect of zircon crystal application showed a significant condition (Bite OFF/zircon) x task interaction ($F(1,28) = 75{,}09$, $p < 0.0001$) whose

Table I. - Summary of significant results.

Variable	Smaller pupil effect (df = 28)	Larger pupil effect (df = 28)	Pupils asymmetry effect (df = 28)
time	F = 5.33*	F = 42.2***	F = 8.14**
task	F = 236.2***	F = 211.5***	F = 7.10*
bite	ns	ns	F = 45.09***
time x task	F = 33.84***	F = 122.8***	F = 5.83*
bite x task	F = 33.8***	F = 88.8***	F = 4.11, p = 0.052
time x bite x task	F = 33.1	F = 8.6**	F = 29.77***
	time 0		
	F(1,28) = 65.4***,	69.3***	F = 4.19*
	Bite OFF		
	r < haptic, t = 8.9***	r < haptic, t = 0.06***	ns
	Bite ON		
	r < haptic, t = 14.3***	r < haptic, t = 13.76***	r < haptic, t = 2.52*
	Bite ON vs. OFF		
	resting, OFF > ON, t = 2.7*	resting, OFF > ON, t = 4.99***	resting, OFF > ON, t = 7.15***
	haptic, OFF < ON, t = 6.3***	haptic, OFF < ON, t = 3.87**	haptic, OFF > ON, t = 5.33***
	time 90 days		
	F(1,28) = 129.2***	F = 105.5***	F = 13.98**
	Bite OFF		
	r < haptic, t = 8.1***	r < haptic, t = 9.84***	r < haptic, t = 4.01***
	Bite ON		
	r < haptic, t = 19.16***	r haptic, t = 17.4***	r < haptic, ns
	Bite ON vs. OFF		
	resting, OFF > ON, t = 4.47***	resting, OFF > ON, t = 5.82***	resting, OFF > ON, t = 3.95***
	haptic, OFF < ON, t = 7.29***	haptic, OFF < ON, t = 4.20***	haptic, OFF > ON, t = 6.07***
	time 0 vs. time 90 days		
	Bite ON		
	resting, t0 > t90, t = 5.256***	resting, t0 > t90, t = 9.86***	resting, ns
	haptic, t0 < t90, t = 4.98***	haptic, t0 < t90, t = 5.11***	haptic, ns
	Bite OFF		
	resting, ns	resting, t0 > t90, t = 7.78***	resting, t0 > t90, t = 7.05***
	haptic, ns	haptic, ns	haptic, ns

*** = p < 0.0001; ** = p < 0.01; * = p < 0.05

decomposition indicated that the zircon-induced malocclusion increased significantly the pupil size in the resting condition (from 4.29 ± 0.79 to 5.06 ± 0.76, $p < 0.0001$), but not during the haptic task performance (Bite OFF: 5.05 ± 0.79; zircon: 5.14 ± 0.77, NS). As a consequence, malocclusion abolished the pupil dilation elicited by the task owing to the placement of a zircon crystal, which made the pupil size at rest as large as that observed during task performance with normal occlusion.

Discussion

Changes in basal pupil size: functional considerations

The results of the present study indicate that the presence of an asymmetric EMG activity of masticatory muscles during clenching is highly predictive of an asymmetry of the same sign in the pupils size. EMG asymmetries during clenching did not arise from asymmetries in the electrodes resistance and

Table II. - Mean values of recorded variables.

Time	Time 0						Time 90 days					
Condition	Bite OFF			Bite ON			Bite OFF			Bite ON		
Task	Rest	Haptic	Haptic-Rest	Rest	Haptic	Haptic-Rest	Rest	Haptic	Haptic-Rest	Rest	Haptic	Haptic-Rest
larger pupil	4.42 ± 0.82	5.04 ± 0.78		3.96 ± 0.69	5.33 ± 0.71		4.29 ± 0.79	5.05 ± 0.77		3.77 ± 0.62	5.38 ± 0.70	
smaller pupil	4.09 ± 0.72	4.70 ± 0.68		3.85 ± 0.63	5.16 ± 0.64		4.08 ± 0.70	4.68 ± 0.72		3.70 ± 0.58	5.24 ± 0.63	
larger pupil mydriasis			0.62 ± 0.42			1.37 ± 0.54			0.60 ± 0.39			1.61 ± 0.50
smaller pupil mydriasis			0.60 ± 0.36			1.31 ± 0.48			0.76 ± 0.43			1.54 ± 0.42
EMG activity (hypertonic side)	162.3 ± 45.8			150.7 ± 31.2						137.4 ± 25.4		
EMG activity (hypotonic side)	111.4 ± 40.8			140.6 ± 28.5						146.9 ± 25.8		

The table reports the mean ± standard deviation values obtained for pupil size, EMG activity and task-related mydriasis, at time 0 and 90 days, during normal occlusion (Bite OFF) and while subjects weared a cusp bite that reduced the difference in EMG activity between left and right masseter (Bite ON).

placement. They were strongly reduced by cusp bite placement and reappeared as soon as the cusp bite was removed. The asymmetric EMG activity is likely due to an asymmetry in proprioceptive signals deriving from muscle spindles/periodontal receptors and/or in the efference copies of trigeminal motor signals. Present findings indicate that this sensorimotor unbalance exerts a tonic influence on sympathetic activity related to the control of the pupils size. In fact, the reduction/abolition of the muscle asymmetry (and, as a consequence of the asymmetry in sensory and/or motor trigeminal signals) by bite correction is immediately coupled to a drastic reduction in the asymmetry observed in pupil size. The remarkable stability of these effects was documented by the fact that they could be observed also 90 days after the first session. We may conclude that the development of a left-right asymmetry in the trigeminal sensory and/or motor signals induces a corresponding unbalance in the activity of left and right autonomic structures involved in the control of pupil size.

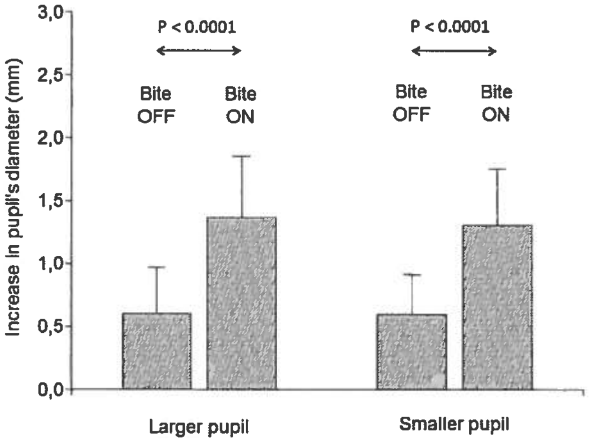

Fig. 5. - Average increase in pupil size elicited by the haptic task in Bite ON and OFF conditions. The height of the columns represents the mean of the differences in pupil size observed between sensorimotor task and resting condition for all the subjects tested (n = 29). The error bars correspond to the standard deviation of the corresponding values. Data have been evaluated separately for the larger and smaller pupil, both in normal occlusion (Bite OFF) as well as following bite correction (Bite ON).

Our findings can be accounted for by the fact that trigeminal afferents may affect the dilatator pupillae muscle by controlling the activity of preganglionic neurons located within the superior cervical ganglion (Bartsch et al., 2000). It is known that trigeminal afferents are the origin of pathways running through well-known autonomic structures, such as the nucleus tractus solitarii, the ventrolateral medulla, the A5 area, the ventrolateral part of the parabrachial nucleus and the Kolliker-Fuse nucleus (Panneton et al., 2000). Moreover, the peritrigeminal area surrounding the trigeminal motor nucleus is connected to the parvicellular reticular formation (Bourque and Kolta, 2001; Notsu et al., 2008), a structure mediating autonomic reflexes (Esser et al., 1998). In addition, preganglionic parasympathetic neurons located within the Edinger-Westphal nucleus, which induces miosis, receive afferents from the reticular formation and vestibular nuclei (Breen et al., 1983), which

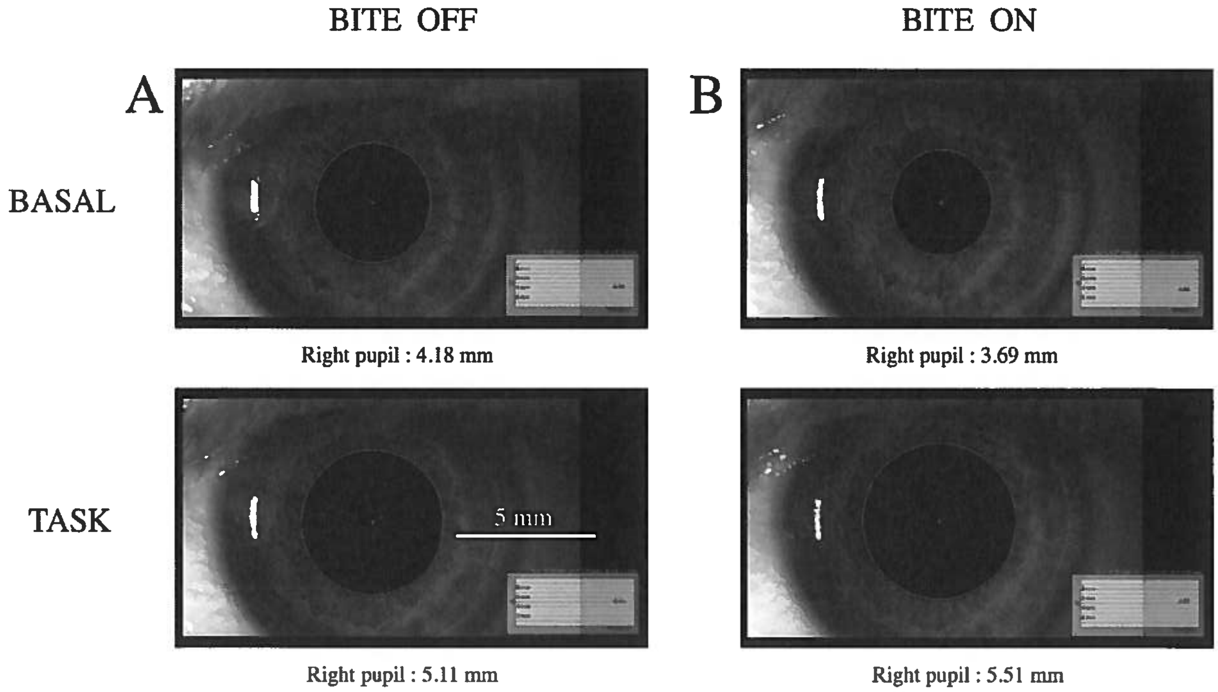

Fig. 6. - Effect of wearing the cusp bite on the mydriasis associated to the haptic task. In a representative subject, photographs of a pupil have been taken in resting state (basal, upper row) and sensorimotor task (task, lower row) in both Bite OFF (A) and Bite ON (B) conditions.

are known to receive trigeminal signals (Shammah-Lagnado et al., 1992; Diagne et al., 2006). Finally, trigeminal input may reach the *Locus Coeruleus* (LC), which is regarded as "an autonomic ganglion" (Van Bockstaele and Aston-Jones, 1995) and is activated in parallel with the autonomic nervous system by several sensory stimulations (Elam et al., 1986; Bradley et al., 2008), probably through the paragigantocellularis (PGi) nucleus (Elam et al., 1986). In this respect, LC neurons may respond to trigeminal stimulation, as shown by transcutaneous electrical stimulation of the hamster's pinna (Zhang and Guan, 2007); moreover, LC seems to receive afferents from the trigeminal mesencephalic nucleus, or at least from a brain region included between the LC and the latter structure (Cedarbaum and Aghajanian, 1978).

Noradrenergic LC neurons inhibit the preganglionic parasympathetic neurons of the Edinger-Westphal nucleus (Szabadi and Bradshaw, 1996). This inhibition is necessary to increase the pupil size, as the tonic activity of the iris constrictor would prevent pupil enlargement by dilatator pupillae (Wilhelm et al., 2001). This is probably the reason why, in monkeys, modifications in the pupil size show an impressive covariation with the changes in the discharge of LC noradrenergic neurons (Rajkoski et al., 1993; Sterpenich et al., 2006). Compelling evidence indicate that the same occurs in humans (Gilzenrat et al., 2010: Murphy et al., 2014).

Thus, the unbalance in the pupils size induced by asymmetric trigeminal sensory and/or motor signals may develop in parallel to an unbalance in the activity of LC neurons. This hypothesis is consistent with the fact that occlusal disharmony increased the release of noradrenaline in the hypothalamic paraventricular nucleus and that such an increase was abolished by the lesion of the ascending noradrenergic bundle arising from LC (Yoshihara and Yawaka, 2011). It can be proposed that bite correction, which reduces the asymmetry in trigeminal signals, also reduces the asymmetries in LC neurons activity.

Changes in the pupil's diameter modulation by the haptic task

Cusp bite and zircon crystal placement did not change only the basal pupil size, but also the mydriasis induced with the haptic task. Mydriasis depends on the participants' involvement in the performed task (Rajkoski et al., 1993) and is strictly proportional to the parallel task-related phasic release of noradrenaline at cerebral cortical level (Gabay et al., 2011). This release originates from the activation of LC, which modulates cortical arousal, (Carter et al., 2010; Samuels and Szabadi, 2008) and sensorimotor excitability (Matsutani et al., 2000).

It is known that phasic LC activity improves task performance, while high tonic activity is detrimental (Rajkoski et al., 1993; Gilzenrat et al., 2010). Given the relation observed between pupil size and LC discharge (Rajkoski et al., 1993; Sterpenich et al., 2006, Murphy et al., 2014), it can be proposed that bite correction, which decreases pupil size during rest and increases the task associated mydriasis, improves task performance. In contrast, the zyrcon-induced malocclusion, which induces opposite effects, should deteriorate task performance.

On the basis of the present findings we propose that rebalancing the activity of trigeminal afferents decreases the tonic, but enhances the phasic release of norepinephrine at brain level during a sensorimotor task, improving the task performance. On the other hand, unbalancing the occlusion by zircon crystals increased basal pupil size but almost canceled the mydriasis associated with a sensorimotor task, probably being detrimental to integrative neural processes underlying the task.

Present results suggest that an asymmetry in trigeminal input would affect sensorimotor performance

A case report concerning a patient affected by a neurodegenerative diseases (De Cicco, 2012b) is in line with these observations, which are also consistent with the fact that asymmetric sensory stimulations attenuate the deficits following asymmetric brain lesions. In fact, in humans, lesions of the right posterior parietal lobe induce neglect of the contralateral part of body and space (Vallar et al., 1990; Karnath et al., 1993; Rorsman et al., 1999). The observation that, in animals, a second symmetric lesion on the opposite side greatly decreases these symptoms in spite of doubling the extension of brain damage (Lomber and Payne, 1996) indicates that the symptoms of the former lesion depend upon the unbalance created in hemispheric brain activity. In humans, these symptoms are greatly attenuated when the tonic activity arising from vestibular receptors or muscle proprioceptors is enhanced on the ipsilateral or contralateral side, respectively (Vallar et al., 1990; Karnath et al., 1993; Rorsman et al., 1999). This indicates that asymmetric sensory stimulation promotes the brain activity rebalancing. In conclusion, our findings indicate the existence of a tonic control exerted by sensorimotor trigeminal signals on autonomic structures modulating pupil size and disclose the possibility that these signals may also modulate sensorimotor functions not involving the orofacial region.

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