

Giuseppe Moruzzi's midpontine pretrigeminal preparation and its continuing importance for neuroscience

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ABSTRACT

More than 50 years ago Giuseppe Moruzzi and his collaborators reported that cats with a complete transection of the pons in front of the origin of the trigeminal nerve were almost continuously awake, suggesting that the brain had been separated by sleep-inducing structures in the brainstem behind the section. Several pieces of experimental evidence were subsequently obtained to show that the isolated brain of midpontine pretrigeminal cats was capable of conscious awareness, learning and sensitivity to rewarding brain stimulation. The current interest of those data for clinical neurology is that there are striking resemblances between the midpontine pretrigeminal preparation and the human locked-in syndrome, in which the patients are fully conscious but unable to move except for palpebral or ocular movements. Here I present the basic evidence for assuming that the midpontine pretrigeminal cat may serve as an at least partial model for the locked-in syndrome and suggest that it may provide useful insights into the neural mechanisms of consciousness in absence of behavior.

Key words

Giuseppe Moruzzi • Midpontine pretrigeminal preparation • Locked-in syndrome • Body-brain interactions • Communication by eye movements

The midpontine pretrigeminal preparation

The description of the midpontine pretrigeminal preparation in the cat by Giuseppe Moruzzi and his associates Cesira Batini, Mario Palestini, Gianfranco Rossi and Alberto Zanchetti goes back to more than fifty years ago (Batini et al., 1959). I have always thought that their work proved no less important for neuroscience than Moruzzi and Magoun's celebrated discovery of the arousing function of the brainstem reticular formation (Moruzzi and Magoun, 1949). It is important for neurophysiology because it has pointed unambiguously to an active induction of sleep by caudal brainstem structures, thus suggesting a possible

mechanism of insomnia, but it is especially important for clinical neurology because it showed that an almost completely de-afferented and de-efferented brain could sustain a state of conscious awareness, as occurs in the so-called locked-in syndrome in humans. And yet, unlike the Moruzzi-Magoun paper (1949) which continues to be amply cited in the neurological literature, the article by Batini et al. (1959) has largely disappeared from the references of the latest editions of popular textbooks of basic neuroscience (e.g. Kandel et al., 2000), as well as of clinical treatises dealing with the neurology of consciousness and its disorders (e.g. Posner et al., 2007; Laureys and Tononi, 2009). As of December 2010, Google Scholar shows 2142 total citations for Moruzzi and Magoun (1949), with 51 citations in

2010, and 213 total citations for Batini et al. (1959), with only 1 citation in 2010.

Batini et al. (1959) reported that cats with an electrolytic transection of the pons at pretrigeminal level showed on average an activated (desynchronized) electroencephalogram (EEG) 78% of the recording time (range 65-90%), as opposed to 37% (range 20-50%) of cats with an intact brain. Since a sleep phase with rapid eye movements and a desynchronized EEG had just been described by Dement (1958), they were aware that the EEG alone cannot be indicative of wakefulness, let alone consciousness. However they noticed that the eyegaze of midpontine pretrigeminal cats could follow stimuli moving across their visual field, and that their pupil would dilate, though not systematically, upon the presentation of supposedly emotional visual stimuli like a dog or a mouse. Tracking eye movements were limited to the vertical plane because ocular motility could be controlled by the isolated brain only through the oculomotor and trochlear nerves, but not through the abducens nerve which originates from the pons behind the section and is required for horizontal eye movements. All ocular reactions were absent during the short periods of EEG synchronization, but the authors prudently refused to offer this finding as a definite proof that *conscious perception* was present during EEG activation. The phrase “conscious perception” is in italics in the Batini et al. (1959) paper, presumably because in those times neurophysiologists were wary even to mention the word consciousness and its derivatives.

When a few years later Moruzzi gave the Harvey Lecture at Rockefeller University in New York (Moruzzi, 1963), he had considerably more data to support the claim that the midpontine pretrigeminal preparation was in a state of true alertness. Pier Lorenzo Marchiafava, a young post-doctoral student working in Pisa in the early 1960s, had been involved in most of the studies providing those data, in addition to being responsible for simplifying the midpontine transection through the use of a stereotactically guided spatula instead of electrolysis (King and Marchiafava, 1963). In collaboration with Jorge Affanni from Argentina and Boguslaw Zernicki from Poland, Marchiafava showed that the ocular reactions of the midpontine pretrigeminal preparation underwent habituation upon repeated presentation of visual stimuli, and that dilatation

of the pupil could be conditioned according to a pavlovian paradigm using electric stimulation of the hypothalamus as an unconditioned stimulus (Affanni, Marchiafava and Zernicki, 1962a,b,c). Further, in collaboration with Frederick King from the U.S. he showed that the vertical eye movements of the midpontine pretrigeminal preparation were true tracking or pursuit movements rather than mere optokinetic nystagmus (King and Marchiafava, 1963). Finally, in collaboration with Rafael Elul from Israel he showed that the eyes of midpontine pretrigeminal cats accommodate in response to near visual targets during EEG desynchronization but not during EEG synchronization (Elul and Marchiafava, 1964). Other contributions to the understanding of presumably conscious visual processes in the midpontine pretrigeminal cat came from experiments carried out in Moruzzi's Institute in Pisa for studying the transfer of visual information along the retino-geniculo-cortical pathway (Maffei et al., 1965) and by the corpus callosum (Berlucchi et al., 1967; Berlucchi and Rizzolatti, 1968).

The midpontine pretrigeminal preparation is exported from Pisa

Zernicki's experience with pavlovian conditioning had been crucial for establishing the learning ability of the midpontine pretrigeminal cat. In 1958, Moruzzi had visited the Warsaw Nencki Institute of Experimental Biology headed by Jerzy Konorski along with Horace Magoun and Mary Brazier (Fig. 1; see Zernicki, 1986a). Moruzzi thought highly of Konorski and of his attempts to reconcile the neurophysiological thinking of Pavlov with that of Sherrington (Konorski, 1948). He asked Konorski about the possibility of obtaining a behavioral proof of awareness in the midpontine pretrigeminal cat, and Konorski arranged for his pupil Zernicki to go to work in Pisa. After his successful work in Pisa with Affanni and Marchiafava, Zernicki exported the midpontine pretrigeminal preparation to Warsaw and in the course of a few years became the world authority on the subject. Much of his work, which includes analyses of the sleep-waking cycle, the arousal response, the targeting ocular reflexes and their conditioning and differentiation, and the influence of age at the time of the section on the



Fig. 1. - Giuseppe Moruzzi, Horace Magoun and Liliana Lubinska in the Nencki Institute of Experimental Biology in Warsaw in 1958 (see Zernicki, 1986a).

characteristics of the preparation is reported in an extensive review published in 1986 in the *Archives Italiennes de Biologie* (Zernicki, 1986b). After that, Zernicki, who died in 2002, continued to work with midpontine pretrigeminal preparations, producing significant results on the visual fixation reflex and visual neglect from cortical lesions (Zernicki, 1988; Zernicki and Stasiak, 1996) and on the lack of inter-hemispheric transfer of habituation after callosal section (Zernicki et al., 1997).

Zernicki's conditioning and differentiation studies on midpontine pretrigeminal cats were mostly performed according to pavlovian paradigms, in the tradition of his teacher Jerzy Konorski.

Operant conditioning of eye movements in midpontine pretrigeminal cats was developed especially by Hiroshi Kawamura, who in the mid 1960s had become familiar with the preparation by working with Marchiafava in Pisa (Kawamura and Marchiafava, 1966, 1968). It was known that cats with intact brains learn to press a bar in order to deliver electrical stimuli to their own lateral hypothalamus, proving that such stimulation is rewarding and can

therefore act as an operant reinforcer (Wilkinson and Peele, 1963). There also was some preliminary evidence for the possibility to induce lateral hypothalamic self-stimulation by ocular movements in midpontine pretrigeminal cats (Shlaer and Myers, 1972). After his return to Japan, Kawamura and his associates were able to show that midpontine pretrigeminal cats can indeed be trained by operant conditioning to use their ocular movements for obtaining rewarding lateral hypothalamic stimulations. They found that the rate of ocular motility strongly increased when the hypothalamic stimulation was made contingent on spontaneous eye movements, whereas no significant enhancement occurred when the association between the hypothalamic reinforcement and spontaneous eye movements was random. In addition, midpontine pretrigeminal cats could successfully learn by the same operant procedure a light-dark discrimination and its reversal. These findings provided strong evidence for the presence not only of general awareness, but also of sensitivity to reward and of capabilities for operant learning and intentional motor control in the isolated brain of

midpontine pretrigeminal cats, independent of any feedback from the sensory periphery and from the caudal brainstem (Ikegami et al., 1977, 1979).

Ikegami and Kawamura (1981) also tested midpontine pretrigeminal cats with presumably aversive brain stimulations, that is with stimulations which are actively avoided by cats with intact brains. Surprisingly, when midpontine pretrigeminal cats were given the opportunity to turn off such stimulations by inhibiting eye movements, they failed to do so, possibly because they did not experience aversive effects. Aversive effects of brain stimulation may indeed depend on feedback from the sensory periphery, unlike the above reward effects from lateral hypothalamic stimulation. This hypothesis was supported by the finding that in *encéphale isolé* cats, supposedly aversive brain stimulations associated with contraction of the facial muscles had a marked passive avoidance effect on eye movements, and that such effect disappeared after blocking both the trigeminal and facial nerves or either one of them. Ikegami and Kawamura (1981) specifically proposed that the midpontine pretrigeminal cat could represent an animal model of the human 'locked-in' syndrome which had long been known in principle, but had been named and neurologically defined only a few years earlier (Plum and Posner, 1966; Nordgren et al., 1971). The syndrome, usually caused by bilateral basal pontine infarction, is characterized by a total inability to move or by an extremely scant repertoire of motor behaviors, usually restricted to vertical eye movement or blinking, as opposed to fully preserved conscious awareness and near-normal sensory and cognitive functions. Patients with this syndrome can communicate intelligently using a code based on blinking, or, as in the midpontine pretrigeminal cat, on up and down ocular movements.

The locked-in syndrome

There is now extensive information on the locked-in syndrome in the neurological (e.g. Bauer et al., 1979; Patterson and Grabois, 1986; Smith and Delargy, 2005; Gosseries et al., 2009) and even the belletristic literature, given that some patients have written sophisticated books or poetry on their condition as seen from the inside (e.g. Dudzinski, 2001; Sledz et al., 2007; Gosseries et al., 2009). The

Italian neurologists Cappa and Vignolo (1982) were the first to perform a series of formal neuropsychological tests on a 31-year old male patient with a chronic locked-in syndrome precipitated 12 years beforehand by an acute ventral pontine infarction. The patient was unable to speak but could respond yes or no to oral and written questions by downward and upward eye movements respectively. There were no deficits on verbal and visuospatial tasks and only a mild impairment on a test of nonverbal intelligence, in spite of the prolonged, almost total de-efferentation. Further communication established via a typewriter controllable by small residual head movements confirmed the general absence of cognitive deficits. Formal neuropsychological testing in two other cases of locked-in syndrome from acute pontine damage supported the existence of normal cognition (Allain et al., 1998), while mild to moderate deficits in attention, speed of processing, perceptual organization and executive skills, and verbal learning were reported in a further single case (New and Thomas, 2005). A more recent evaluation has confirmed the possibility of fully normal cognitive functioning in chronic locked-in subjects, provided that there is no supratentorial damage in addition to the causative pontine lesion (Schnakers et al., 2008). Cappa et al. (1985) investigated subjective quality of his life in the patient found to be neuropsychologically normal by Cappa and Vignolo (1982). While agreeing on the objective hardness of his condition, the patient expressed a general sense of acceptance of it and even a contentedness with his daily occurrences and interactions with the family, and explicitly denied that his situation made death desirable. There are now extensive statistical investigations (reviews in Smith and Delargy, 2005; Gosseries et al., 2009) to confirm that on an intellectual level patients with locked-in syndrome, despite being fully aware of their huge behavioural limitations, do not differ from an age-matched healthy controls in expressing psychological distress and concern about their personal general health. Countering the popular belief that death would be preferable to imprisonment in one's own body, suicidal thoughts and requests of euthanasia are rare and their frequency is correlated with the presence of physical pain. Poems written by a locked-in patient have been found to indicate that his emotional and spiritual existence is similar to that of any able-bodied person, and his

goals and his self-confidence are realistic and level-headed (Sedz et al., 2007).

Damasio (1999) has attempted to provide a neurophysiological explanation of the surprisingly serene attitude toward life of locked-in patients. He believes that what is lacking in these patients is the neural component of the “body loop”, that is the neural feedback from the bodily changes which in an intact organism are at the same time partly effects and partly causes of emotional reactions. Because of the general de-efferentation of the locked-in state, “any mental process which would normally induce an emotion fails to do so through the body loop mechanism: the brain is deprived of the body as a theatre for emotional realization” (Damasio, 1999). This explanation is quite similar to that advanced by Ikegami and Kawamura (1981) for accounting for the apparent lack of aversive effects from brain stimulation in midpontine pretrigeminal cats. In turn, the presence of rewarding effects from brain stimulation after pretrigeminal section may fit Damasio’s (1999) concept of the “as if body loop”, that is the enacting of bodily changes entirely within the brain, in absence of such changes in the body proper. Damasio (1999) believes that the brain structures in front of a midpontine pretrigeminal section are sufficient to implement the protoself, that is the coherent collection of neural patterns which map, moment by moment, the state of the many dimensions of the organism. He acknowledges the presence of wakefulness and even attention in the midpontine pretrigeminal preparation, but denies the possibility to decide whether there is consciousness as well, thereby also implicitly denying that the preparation can serve as an animal model of the human locked-in syndrome. Damasio is right when he points to the lack of evidence about the effects of complete pontine transections in humans, which probably never occur in nature, and it is true that there is a substantial difference between locked-in patients, who can experience somatic sensations, and midpontine pretrigeminal cats, which cannot. Nevertheless the impressive similarities in the communication of perceptions and internal states through vertical eye movements, and particularly the Kawamura results on rewarding and aversive brain stimulations, which Damasio seems to be unaware of, suggest that findings in midpontine pretrigeminal cats can be quite relevant for the neurology of consciousness in the locked-in syndrome.

EEG and the sleep-wake cycle in midpontine pretrigeminal cats

The potential implications of the findings from midpontine pretrigeminal cats for understanding neuropathological conditions in humans had already been suggested by the Italian neurologist Carlo Loeb (Loeb, 1958), who was one of the first to report a “normal” waking EEG in an apparently comatose patient with acute damage to the pons (Loeb and Poggio, 1953). Several years later, in a review of a large number of locked-in cases mostly with pontine damage, Patterson and Grabois (1986) commented that “the striking feature of the EEG in the locked-in state is the discrepancy between the extreme involvement in the clinical state and the normal or minimally abnormal EEG”. There are however considerable abnormalities in the sleep-wake cycle of these patients, as revealed by the EEG. Feldman (1971) carried out the first all-night polygraphic study of sleep in a patient with a locked-in syndrome due to an embolic occlusion of the basilar artery subsequent to trauma. Total duration of sleep was relatively short (four to six hours each night), and there was a considerable reduction of the deepest stages of sleep, both during sleep with synchronized EEG and without rapid eye movements (Non-REM sleep) and especially during sleep with desynchronized EEG and rapid eye movements (REM sleep). REM sleep only occupied 3 to 4% of the total sleep tracing instead of the normal 15-20%. According to several subsequent studies, reviewed in Patterson and Grabois (1986), there is an overall reduction of sleep in most locked-in patients (1.25-6.5 hours per day) mostly affecting REM sleep which may be totally absent. A more recent review (Cologan et al., 2010) underlines the heterogeneity of sleep patterns in the locked-in state, ranging from near normality to severe disorganization of sleep stages to suppression of REM sleep. Such heterogeneity most probably depends on the different involvement in the lesion of the various brainstem neuronal populations which are known to influence and even determine the sleep-wake cycle. Discussion of this subject falls outside the scope of this paper.

Pertinent to the present purposes is instead the consideration that the general reduction of sleep duration in the locked-in syndrome is in line with similar changes in midpontine pretrigeminal cats originally observed by Batini et al. (1959) and confirmed by

Zernicki (1986). The latter author has described in chronic midpontine pretrigeminal cats an organized sleep-wake cycle with an orderly succession of sleep phases distinguished by the EEG, but with a total absence of REM sleep which normally occupies 20-25% of total sleep time in intact cats (Zernicki, 1986). Reduction and alteration of sleep in locked-in humans and midpontine pretrigeminal cats raises some interesting questions about the old problem of the functions of sleep. Sleep is supposed to be necessary because sleep deprivation impairs many metabolic and cognitive functions, while functional recovery from deprivation is achieved with a rebound of intense sleep (e.g. Tononi and Cirelli, 2006; Reynolds and Banks, 2010). There are a few experimental questions that could be addressed to advantage in the midpontine pretrigeminal preparation. Is reduction of total sleep duration and absence of REM sleep in midpontine pretrigeminal cats and locked-in humans an effect of a mere dysregulation of the sleep-wake cycle, or does it indicate a changed need for sleep contingent on the peculiar homeostatic, metabolic and cognitive situation? Given that midpontine pretrigeminal cats can learn visual discriminations, does the daily amount of learning affect the subsequent sleep? And, in turn, does efficiency of learning benefit from previous sleep? The possibility to address these and many related questions with a variety of traditional and advanced neurophysiological techniques in absence of anesthesia in midpontine pretrigeminal cats is likely to afford significant insights into the neural mechanisms of the functional benefits of sleep and the costs of sleep deprivation. In spite of the presently rare experimental use of the preparation, its potential for advancing the understanding of the brain appears far from exhausted.

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References

- Affanni J., Marchiafava P.L., Zernicki B. Higher nervous activity in cats with midpontine pretrigeminal transections. *Science*, **137**: 126-127, 1962a.
- Affanni J., Marchiafava P.L., Zernicki B. Orientation reactions in the midpontine pretrigeminal cat. *Arch. Ital. Biol.*, **100**: 297-304, 1962b.
- Affanni J., Marchiafava P.L., Zernicki B. Conditioning in the midpontine pretrigeminal cat. *Arch. Ital. Biol.*, **100**: 305-310, 1962c.
- Allain P., Joseph P.A., Isambert J.L., Le Gall D., Emile J. Cognitive functions in chronic locked-in syndrome: a report of two cases. *Cortex*, **34**: 629-634, 1998.
- Batini C., Moruzzi G., Palestini M., Rossi G.F., Zanchetti A. Effects of complete pontine transections on the sleep-wakefulness rhythm: The midpontine pretrigeminal preparation. *Arch. Ital. Biol.*, **97**: 1-12, 1959.
- Berlucchi G., Gazzaniga M.S., Rizzolatti G. Microelectrode analysis of transfer of visual information by the corpus callosum. *Arch. Ital. Biol.*, **105**: 583-596, 1967.
- Berlucchi G. and Rizzolatti G. Binocularly driven neurons in visual cortex of split-chiasm cats. *Science*, **159**: 308-310, 1968.
- Cappa S.F., Pirovano C., Vignolo L.A. Chronic 'locked-in' syndrome: psychological study of a case. *Eur. Neurol.*, **24**: 107-111, 1985.
- Cappa S.F. and Vignolo L.A. Locked-in syndrome for 12 years with preserved intelligence. *Ann. Neurol.*, **11**: 545, 1982.
- Cologan V., Schabus M., Ledoux D., Moonen G., Maquet P., Laureys S. Sleep in disorders of consciousness. *Sleep Med. Rev.*, **14**: 97-105, 2010.
- Damasio A. *The Feeling of What Happens*. New York, Harcourt Brace, 1999.
- Dement W. The occurrence of low voltage, fast, electroencephalogram patterns during behavioral sleep in the cat. *Electroencephalogr. Clin. Neurophysiol.*, **10**: 291-296, 1958.
- Dudzinski D. The diving bell meets the butterfly: identity lost and re-membered. *Theor. Med. Bioeth.*, **22**: 33-46, 2001.
- Elul R. and Marchiafava P.L. Accommodation of the eye as related to behavior in the cat. *Arch. Ital. Biol.*, **102**: 616-644, 1964.
- Feldman M.H. Physiological observations in a chronic case of "locked-in" syndrome. *Neurology*, **21**: 459-478, 1971.
- Gosseries O., Bruno M.A., Vanhaudenhuyse A., Laureys S., Schnakers C. Consciousness in the locked-in syndrome. In: Laureys S., Tononi G. (Eds.) *The Neurology of Consciousness*, pp. 191-203. Amsterdam, Elsevier, 2009.

- Kandel E.R., Schwartz J.H., Jessell T.M. *Principles of Neural Science*. 4th ed. New York, McGraw-Hill, 2000.
- Kawamura H. and Marchiafava P.L. Modulation of transmission of optic nerve impulses in the alert cat: evidence of presynaptic inhibition of primary optic afferents during ocular movements. *Brain Res.*, **1**: 213-215, 1966.
- Kawamura H. and Marchiafava P.L. Excitability changes along visual pathways during eye tracking movements. *Arch. Ital. Biol.*, **106**: 141-156, 1968.
- King F.A. and Marchiafava P.L. Ocular movements in the midpontine pretrigeminal preparation. *Arch. Ital. Biol.*, **101**: 149-160, 1963.
- Konorski J. *Conditioned Reflexes and Neuron Organization*. Cambridge, Cambridge University Press, 1948.
- Ikegami S., Nishioka S., Kawamura H. Operant discriminative conditioning of vertical eye movements in the midpontine pretrigeminal cat. *Brain Res.*, **124**: 99-108, 1977.
- Ikegami S., Nishioka S., Kawamura H. Operant conditioning of vertical eye movements without visual feedback in the midpontine pretrigeminal cat. *Brain Res.*, **169**: 421-431, 1979.
- Ikegami S. and Kawamura H. Inhibition of intracranial self-stimulation in brain stem-transected cats - a proposed mechanism of aversive effects produced by brain stimulation. *Brain Res.*, **229**: 471-485, 1981.
- Laureys S. and Tononi G. (Eds.). *The Neurology of Consciousness*. Amsterdam, Elsevier, 2009.
- Loeb C. and Poggio G.F. Electroencephalograms in a case with pontomesencephalic hemorrhage. *Electroencephalogr. Clin. Neurophysiol.*, **5**: 295-296, 1953.
- Loeb C. Electroencephalographic changes during the state of coma. *Electroencephalogr. Clin. Neurophysiol.*, **10**: 589-605, 1958.
- Maffei L., Moruzzi G., Rizzolatti G. Influence of sleep and wakefulness on the response of lateral geniculate units to sinewave photic stimulation. *Arch. Ital. Biol.*, **103**: 596-608, 1965.
- Moruzzi G. and Magoun H.W. Brain stem reticular formation and activation of the EEG. *Electroencephalogr. Clin. Neurophysiol.*, **1**: 455-473, 1949.
- Moruzzi G. Active processes in the brain stem during sleep. *Harvey Lectures*, **58**: 233-297, 1963.
- New P.W. and Thomas S.J. Cognitive impairments in the locked-in syndrome: A case report. *Arch. Phys. Med. Rehabil.*, **86**: 338-343, 2005.
- Nordgren R.E., Markesbery W.R., Fukuda K., Reeves A.G. Seven cases of cerebromedullospinal disconnection: the "locked-in" syndrome. *Neurology*, **21**: 1140-1148, 1971.
- Patterson J.R. and Grabois M. Locked-in syndrome: a review of 139 cases. *Stroke*, **17**: 758-764, 1986.
- Plum F. and Posner J.B. *The diagnosis of stupor and coma*. Philadelphia, FA Davis, 1966.
- Posner J.B., Saper C.B., Schiff N., Plum F. *Plum and Posner's Diagnosis of Stupor and Coma*. New York, Oxford University Press, 2007.
- Reynolds A.C. and Banks S. Total sleep deprivation, chronic sleep restriction and sleep disruption. *Prog. Brain Res.*, **185**: 91-103, 2010.
- Schnakers C., Majerus S., Goldman S., Boly M., Van Eeckhout P., Gay S., Pellas F., Bartsch V., Peigneux P., Moonen G., Laureys S. Cognitive function in the locked-in syndrome. *J. Neurol.*, **255**: 323-330, 2008.
- Shlaer R. and Myers M.L. Operant conditioning of the pretrigeminal cat. *Brain Res.*, **38**: 222-225, 1972.
- Sledz M., Oddy M., Beaumont J.G. Psychological adjustment to locked-in syndrome. *J. Neurol. Neurosurg. Psychiatry*, **78**: 1407-1408, 2007.
- Smith E. and Delargy M. Locked-in syndrome. *BMJ*, **330**: 406-409, 2005.
- Tononi G. and Cirelli C. Sleep function and synaptic homeostasis. *Sleep Med. Rev.*, **10**: 49-62, 2006.
- Wilkinson H.A. and Peele T.L. Intracranial self-stimulation in cats. *J. Comp. Neurol.*, **121**: 425-440, 1963.
- Zernicki B. Giuseppe Moruzzi - My Teacher. *Acta Neurobiol. Exp.*, **46**: 223-228, 1986a.
- Zernicki B. Pretrigeminal preparation. *Arch. Ital. Biol.*, **124**: 133-196, 1986b.
- Zernicki B. The orienting ocular-following reflex in pretrigeminal cats with lesions of visual and oculomotor systems. *Acta Neurobiol. Exp.*, **48**: 223-238, 1988.
- Zernicki B. and Stasiak M. Visual neglect in pretrigeminal cats with lateral suprasylvian lesions. *Arch. Ital. Biol.*, **134**: 227-234, 1996.
- Zernicki B., Stasiak M., Doty R.W. Habituation of ocular following reflex requires corpus callosum for interhemispheric transfer. *Behav. Brain Res.*, **84**: 269-274, 1997.

