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Asymmetric vestibular stimulation and unilateral neck muscle vibration or contraction induce long-term effects on self-motion perception—M. Schieppati [a,*], V.E. Pettorossi [b] ([a] Department of Public Health, Experimental & Forensic Medicine, University of Pavia, Italy, [b] Department of Experimental Medicine, University of Perugia, Italy)

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Background: The effect of neck proprioception was tested on self-motion perception elicited by asymmetric whole-body yaw oscillations in the dark, in the hypothesis that intense and repetitive activation of neck proprioceptive system induces immediate and sustained effects on vestibular-dependent motion perception.

Methods: Oscillation consisted of two half-sinusoidal cycles of equal amplitude (40°) but different duration, featuring a fast (FHC) and slow half-cycle (SHC). Motion perception was estimated by subjects tracking with a pointer the remembered position of an earth-fixed visual target.

Results: Asymmetric vestibular stimulation induced a progressive bias in motion perception, whereby the gain of the tracking response gradually increased during FHC and decreased during SHC. In few cycles, body position was perceived displaced toward the fast rotation side. This error was influenced by static head position relative to trunk and neck muscle vibration. Active head deviation superimposed to the asymmetric oscillation enhanced movement perception for head turned toward the side of fast rotation and decreased it for opposite direction. Vibration of the neck muscles splenius capitis or sternocleidomastoideus differentially influenced the perceived rotation during asymmetric oscillation. The error in target representation was modified not only during on-going vibratory stimulation, but also after it. After-effects endured minutes and hours depending on vibration frequency and duration. Larger and longer-lasting effects were associated with high-frequency vibration and isometric-contraction of vibrated muscle. The effect on perception was consolidated or cancelled by added vibration trains of 100 and 5 Hz, respectively.

Conclusions: The intense vibratory post-effect suggests that activation of neck proprioceptors induces plastic changes along proprioceptive and vestibular networks responsible for motion perception, and enhance motion perception in the direction of the head deviation.

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Paired neurophysiological and clinical approach to brainstem assessment in Parkinson's Disease—E.R. de Natale [a,*], F. Ginatempo [a], A. Manca [a], K.S. Paulus [b], V. Agnetti [b], E. Tolu [a], F. Deriu [a] ([a] University of Sassari, Biomedical Sciences Department, Sassari, Italy, [b] University of Sassari, Clinical and Experimental Medicine Department, Sassari, Italy)

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Background: Recent research has highlighted the role of brainstem (BS) structures in the early spread of Parkinson's Disease (PD) pathological process. Vestibular Evoked Myogenic Potentials (VEMPs) corresponding to the Vestibulo-Ocular (VOR), Vestibulo-Masseteric (VMR) and Vestibulo-Collic (VCR) reflexes can provide information on BS function. Aims: to test the aforesaid set of VEMPs in a cohort of PD patients and healthy controls and to correlate it with presence of symptoms ascribable to BS dysfunction.

Methods: 19 PD patients (age 66.9 ± 5.4 years; 12 males; mean disease duration 6.16 ± 3.54 years) and 15 age and sex matched controls underwent bilateral recording of VOR, VMR and VCR from inferior oblique, masseter and sternocleidomastoid active muscles, respectively. PD patients were additionally administered a series of clinical scales used for evaluation of brainstem-integrated activities, namely sleep disorders (Epworth Sleepiness Scale, Parkinson's Disease Sleep Scale and REM Sleep Behavior Disorder-Screening Questionnaire or RBD-SQ), postural instability (MiniBESTest) and depression (Geriatric Depression Scale). Groups' comparisons were performed with $\chi 2$ test and Mann–Whitney U-test; Sperman's *rho* test was used for correlation analysis.

Results: VEMPs were significantly impaired in patients compared to controls, absence being the main pattern of alteration. When the set of the 3-VEMP battery was analyzed, both number of altered reflexes ($p = 0.017$) and severity of alteration ($p = 0.001$) were significantly higher in patients than controls. As for each single VEMP, only the VOR and the VMR were significantly altered (VOR: $p = 0.022$; VMR: $p = 0.005$; VCR: $p = 0.056$). Clinical scales revealed the presence of some degree of depression in 36.8% of patients, sleep disturbances in 68.4%, REM sleep disorder in 26.3% and postural instability in 36.8% of PD patients. A significant correlation with VEMP alterations was found only for high scores on RBD-SQ ($\rho = 0.554$; $p = 0.014$).

Conclusions: Combined assessment of VOR, VMR and VCR was able to detect BS dysfunction in a rostro-caudal extension in PD. This may prove interesting in the perspective of identifying neurophysiological markers of BS dysfunction in early stages of the disease.

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Correlation of tau pathology in eye movement related brainstem nuclei in cases of progressive supranuclear palsy (PSP) and a proposed role of perineuronal nets—A. Horn [a,b,*], A. Fröschl [a], J. Feige [a], S. Röber [c], H. Kretzschmar [c,b] ([a] Ludwig-Maximilians University, Institute of Anatomy, Department I, Munich, Germany, [b] Ludwig-Maximilians University, German Center for Vertigo and Balance Disorders, Munich, Germany, [c] Ludwig-Maximilians University, Institute of Neuropathology, Munich, Germany)

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Background: Progressive supranuclear palsy (PSP) is characterized by hyperphosphorylated tau protein (HTP) accumulations in different brain regions. A hallmark of clinical symptoms is a vertical gaze palsy, which may be accompanied by horizontal gaze palsy, whereas the VOR is rather preserved until late in the disease. Based on monkey studies functional cell groups of the oculomotor system including transmitters have been identified in the human brainstem (Büttner-Ennever & Horn, 2010).

Methods: To study the spread of the disease through the oculomotor premotor network sections of 8 archival PSP cases with different eye movement deficits were immunostained for HTP. The analysis involved the glutaminergic rostral interstitial nucleus of the medial longitudinal fascicle (RIMLF) and paramedian pontine reticular formation (PPRF), the glycinergic saccadic omnipause neurons (OPN), the cholinergic oculomotor nucleus (nIII) and the vestibular nuclei (VN). Since the RIMLF and nIII contain well-developed perineuronal nets (PN) (Horn et al., 2003), we further stained sections of the PSP cases for the presence of aggrecan (ACAN) and HTP to prove a possible protective role of PNs as suggested from Alzheimer's disease cases (Morawski et al., 2010).

Results: All PSP-cases showed HTP-staining in neurons and glia of RIMLF, PPRF and OPNs, in late cases in motonuclei as well. Thereby a correlation between eye movement deficits and degeneration of premotor gaze centers and the complete pathways to motoneurons was found, whereas the VN are less affected. The analysis of PNs revealed that ACAN-based PNs were mainly found around HTP-negative neurons, and only few HTP-positive neurons showed weak ACAN staining.

Conclusions: The early and more severe degeneration of premotor centers compared to nIII support a hypothesis that in PSP the pathology progresses along neuronal chains in an anterograde fashion, and it is not confined to specific transmitters. The severe tau pathology in RIMLF and nIII in late PSP cases implies that the presence of PNs may not protect them from degeneration, but on a cellular basis the integrity of PNs is affected by tau-pathology.

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Modulation of force and velocity for accurate tasks by a startle—J.M. Castellote [a,b,*], J. Valls-Solé [c] ([a] Institute of Health Carlos III, Madrid, Spain, [b] Complutense University of Madrid, Physical Medicine and Rehabilitation Department, Madrid, Spain, [c] Hospital Clínic, University of Barcelona, Department of Neurology, Barcelona, Spain)

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Background: Some skilfulfast activities require control of trajectory and force to fulfill the task. It is known that voluntary reactions can be speeded up by a startling auditory stimulus (SAS) delivered at the same time as the imperative signal (IS), a phenomenon termed Start-React (Valls-Solé et al., 1999). The aim of the present study was to examine how the performance of a task that demands accuracy, mainly in terms of velocity during the trajectory or force control when holding an object, is changed by a SAS timed to occur either at the time of IS or at a pre-determined time interval when movement has already begun and motor control of accurate reaching is expected.

Methods: Nine subjects performed an accurate elbow extension between two spots placed at an angular distance of 30° when holding with their right hand a pen that monitored, through two strain gauge systems, the force of the subject's fingers during the hold, and the force at which pen-tip was exposed with table contact. According to block of trials, this end spot had three possible diameters: 5, 10, and 20 mm. Kinematic and force parameters were measured for three conditions, control, with SAS at IS or SAS delivered when movement has already started.

Results: In SAS trials, there were no evident differences with respect to control trials in the general outline but there were differences in the timing of the events. In SAS-IS trials time to peak velocity was 166 ms (SD = 41 ms), time to peak force was 95 ms (SD = 43 ms) both shorter than in control or SAS delivered when movement began. Peak velocity (315 ± 56 o/s) and peak force (8 ± 2 arbitr. units) were larger for SAS-IS trials than for control or SAS delivered when movement started.

Conclusions: Startle can advance a task that requires accuracy with velocity and force modulations, but when task onset is already launched there are not evident changes in velocity or force parameters, that seem already prepared.

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Is a multi array-contact lead able to improve STN-DBS in Parkinson's Disease?—L. Bour [a,*], F. Contarino [a], R. Verhagen [a], M. Lourens [a], R. de Bie [b], P. Van den Munckhof [c], R. Schuurman [c] ([a] Academic Medical Center, Neurology/Clinical Neurophysiology, Amsterdam, Netherlands, [b] Academic Medical Center, Neurology, Amsterdam, Netherlands, [c] Academic Medical Center, Neurosurgery, Amsterdam, Netherlands)

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Background: Multi-directional electrodes in STN-DBS give the possibility to steer the high frequency current into the direction for clinical improvement and moreover recording of multi-array local field potential recordings (LFPs) give the possibility to determine the spatiotemporal distribution of oscillatory power across the STN that is related to the symptomatology in PD patients. Ultimately this information can be used as a feedback to optimize the stimulation parameters.

Methods: Eight PD patients were included in the study. After microelectrode recording (MER), to determine the boundaries of the STN, temporarily a prototype of a new 32-contact DBS lead was inserted during the DBS procedure. Different modes of current steering were employed to improve motor symptoms and patients were scored on beneficial and adverse effects. Prior to and immediately after stimulation the distribution of spectral power was recorded by LFPs and spatiotemporal changes were evaluated with Fourier analysis.

Results: Thresholds of the effects of spherical stimulation were comparable to thresholds of stimulation through the conventional electrode at the same location in 89% of the cases. In eight of fourteen side effects, steering stimulation current increased the

threshold for side effects by $\geqslant$1 mA compared to spherical stimulation. The size of the therapeutic window could be widened in patient 6, 7 and 8 by steering stimulation in the posterior, posterior and anterior direction, respectively. LFP recordings prior to stimulation yielded the boundaries of the STN by showing increased spectral power particularly in the 13–40 Hz range. Recordings across all directions showed distinct spatiotemporal patterns of neuronal activity, which were related to the pattern of stimulation and the PD symptoms of the patient.

Conclusions: With a new DBS lead it is possible to steer stimulation current in STN-DBS such that it leads to a larger therapeutic window than with conventional spherical stimulation. Simultaneous LFP recordings across the entire STN provide spatial information about the location of the STN and its disease-related electrical activity. This may potentially be of benefit in predicting how to steer the current towards the sensorimotor part, while avoiding adverse effects.

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Functional magnetic resonance imaging of pain-related brainstem nuclei in single subjects at 7 Tesla—F. Beissner [a,b,*], J. Polimeni [b], J. Kim [b], M. Bianciardi [b], V. Renvall [b], C. Eichner [b], L. Wald [b], V. Napadow [b] ([a] Hannover Medical School, Neuroradiology, Hannover, Germany, [b] Martinos Center for Biomedical Imaging, Radiology, Charlestown, MA, United States)

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Background: The function or dysfunction of pain-related nuclei in the brainstem has only been scarcely studied in humans due to the lack of non-invasive measurement methods. The performance of functional magnetic resonance imaging (fMRI), a standard non-invasive technique, is hampered by the close vicinity of the brainstem to large arteries and ventricles as well as its propensity to spatial distortions caused by the oral cavity. Furthermore, the small average size of brainstem nuclei necessitates higher spatial resolution and accuracy than in studies of the cortex. Here, we present a new approach based on ultra-high field fMRI acquisition at 7 Tesla and a brainstem-optimized analysis method (mICA), which we apply to study pain-related activity and connectivity of brainstem nuclei in single subjects.

Methods: Following a multi-modal imaging approach based entirely on echo-planar imaging, we acquired distortion matched functional, T1-weighted structural as well as diffusion-weighted images at a resolution of 1.2 mm isotropic. Five 6 min runs of resting-state fMRI were acquired, during two of which subjects received a continuous pressure pain stimulus applied to their lower leg by an inflatable cuff.

Results: Pain intensity was percept matched at 50/100 points on a visual analogue scale. Applying our recently developed mICA approach (masked independent component analysis), we were able to detect reproducible resting-state activity for specific brainstem nuclei, like the cuneiform nuclei, periaqueductal grey and as well as brainstem-cortex functional connectivity at the single-subject level. We identified a number of pain-related nuclei that showed distinctive activity changes during pain stimulation.

Conclusions: Identification of nuclei was greatly aided by fractional anisotropy (FA) maps created from the diffusion data. Finally, assessing activity and functional connectivity of brainstem nuclei on the single-subject level may soon give us a deeper understanding of disease subtypes, individual differences in pain processing, as well as other functions localized in the brainstem.

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Investigation of the brainstem blink reflex circuitry in patients with juvenile myoclonic epilepsy—N. Uzun [a,*], M. Kandemir [b], M.E. Kiziltan [a], A. Gunduz [a], S.N. Yeni [a] ([a] Istanbul University, Cerrahpasa School of Medicine, Department of Neurology, Istanbul, Turkey, [b] Bayındır Hospital, Department of Neurology, Istanbul, Turkey)

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Background: Juvenile myoclonic epilepsy (JME) which is among idiopathic generalized epilepsies presents with myoclonus and/or generalized tonic–clonic seizures during puberty. Electrophysiological studies showed findings at several levels including cortex, thalamus and spinal cord in JME. Given these information, we aimed to analyze electrophysiological findings at the level of brainstem using blink reflex (BR) and blink reflex recovery cycle (BR-RC).

Methods: Eighteen JME patients and age and sex matched 18 healthy volunteers are included in the study. BR and BR-RC with interstimulus intervals of 200 ms and 400 ms were recorded over orbicularis oculi on the nondominant side under the same conditions.

Results: JME patients had longer onset latencies ($p = 0.046$) and higher amplitudes ($p = 0.022$) of R2 component of BR. Recovery of responses after double stimulation with interstimulus interval of 400 ms was higher in JME patients ($p = 0.040$). Use of valproate did not have an impact on reflex responses.

Conclusion: Our results support increased excitability of BR pathway in JME without relevant pathological findings regarding BR.

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Somatosensory and auditory startle reaction in patients with movement disorders—A. Gunduz [*], M.E. Kiziltan, G. Kiziltan, D. Yavuz, D. Karadeniz (Istanbul University, Cerrahpasa School of Medicine, Department of Neurology, Istanbul, Turkey)

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Background: Startle reflex (SR) is a generalized defense reaction which is elicited by unexpected stimuli. To elicit SR, auditory and electrical stimulations are used in electrophysiological investigations. Somatosensory startle reflex (SS-SR) is recently described in healthy volunteers after median and tibial stimulation. Studies in patients with brainstem lesions showed importance of upper brainstem in development of SS-SR. Here, we aim to investigate SS-SR systematically in various movement disorders to address its characteristics in comparison to ASR.

Methods: We have examined ASR and SS-SR in patients with dystonia ($n = 12$), multiple system atrophy ($n = 8$), corticobasal degeneration ($n = 5$), restless legs syndrome ($n = 14$), progressive supranuclear palsy ($n = 11$), essential tremor ($n = 18$) and idiopathic PD (n = 16) and healthy volunteers ($n = 35$) under the same conditions. ASR and SS-SR were recorded over orbicularis oculi (o.oc), sternocleidomastoid (SCM), and biceps brachii (BB) after bilateral auditory and median nerve electrical stimulations, respectively.

Results: The pattern and probability rates over each three muscle of ASR were similar in MSA, RLS, ET, PD and healthy individuals. Probability rates of responses over each muscle and total ASR probability were the highest in dystonia group whereas they were the lowest in CBD and PSP ($p_{o.oc} = 0.016$, $p_{scm} = 0.036$, $p_{bb} = 0.000$, $p_{total} = 0.009$). Onset latencies of O.oc responses were also longer in CBD and PSP groups ($p = 0.001$). Presence of SSR was also the highest in dystonia and lowest in PSP group similar to ASR. Latency of O.oc response was longest in CBD group. Pattern of SS-SR was similar to healthy individuals in all disease groups except dystonia and MSA in which BB responses were more common than SCM responses.

Conclusions: The findings of ASR parallel the previous findings. Dystonia patients are known to have exaggerated ASRs. The decreased response in PSP was previously suggested as a support to show extent of pathology. Findings regarding SS-SR also parallel ASR. SS-SR is also exaggerated in dystonia. Different pattern of response appears to be a reflection of overflow phenomenon. However, development of withdrawal reaction is a possibility. Shorter onset latencies in dystonia group probably also reflect increased excitability. Absence of SS-SR or longer latencies in PSP reflects impairment of its pathway which supports the opinion that it may share pathway with ASR and its generator is possibly in the upper brainstem.

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Effect of high frequency repetitive transcranial magnetic stimulation on brainstem excitability in SCI—H. Kumru*, C. Flores, N. Murillo, J. Benito, J. Vidal (Institut Guttmann, Research-Neurology, Badalona, Spain)

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Background: We studied the effect of one session of high-frequency repetitive transcranial magnetic stimulation (rTMS) on brainstem stem excitability in patients with incomplete SCI.

Methods: The study was a randomized, double-blind, sham-controlled trial. We recruited 27 patients with SCI to be randomly distributed in two study groups: active or sham rTMS. We recorded the blink reflex (BR) induced with electrical stimulation at 15 times sensory threshold (ST) to the supraorbital nerve (SON). A prepulse electrical stimulus on BR (PP-BR), was delivered with ring electrodes to the right index finger at 2 times ST and applied 100 ms before the SON stimulus. We also examined the excitability recovery curve of the blink reflex (RC-BR), with pairs of stimuli at interstimuli intervals (ISI) of 160, 300, 500, and 1000 ms. Patients were examined at baseline, and after high-frequency vertex rTMS (20 Hz; 40 pulses/burst, 1800 pulses total over 20 min).

Results: Fifteen patients received active rTMS and 12 sham rTMS. The age between groups was not significant. At baseline, R2 area of BR and percentage changes (%) in RC-BR at all intervals were similar in both groups. Active but not sham rTMS significantly reduced the area of R2 in BR and decreased the % inhibition with respect to baseline ($p \leqslant 0.05$), RC-BR did not change with any rTMS stimulation at any time.

Conclusions: High frequency-rTMS over motor cortex induces a decrease in brainstem reflex excitability and reduces inhibitory brainstem activity in patients with SCI.

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Startle reflex in neurocritical brainstem patients—M. Veciana de las Heras[a,*], J. Pedro Perez[a], H. Kumru[b], C. Flores[b], S. Yagüe Jimeno[a], J. Montero Homs[a], J. Valls-Solé[c] ([a]Hospital de Bellvitge, Neurology/Neurophysiology, Hospitalet de Llobregat, Spain, [b]Instituto Guttmann, Badalona, Spain, [c]Hospital Clínic, Neurology, Barcelona, Spain)

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Background: Patients in a neurocritical condition with lesions involving the brainstem cannot cooperate with electrophysiological examination and, therefore, it may be difficult to determine what are the main functions affected. We have used two tests to characterize the deficit in the motor domain, transcranial magnetic stimulation (TMS) to induce motor evoked potentials (MEPs) and loud auditory stimulation (LAS) to induce the startle reflex (SR).

Methods: The study was done in 5 patients who were in their acute/subacute phase after brainstem involvement because of neoplastic tumors (1 cavernoma and 1 meningioma), vascular lesions (1 ictus and 1 haemorrhage) and meningitis with cranial nerve involvement (1 patient). TMS was applied with a round coil or a double-cone coil over the vertex. LAS was applied by discharging the coil flat on top of a metallic platform.

Results: MEPs were obtained in three patients at normal latency while they were absent in the remaining two patients. Attempts of voluntary contraction to facilitate responses did not change the results. The SR was present in two patients (one of them with normal MEPs). Three patients had no startle response. Normal MEPs and SRs were observed only in the patient with meningitis.

Conclusion: There was no clear association between presence or absence of SRs and the standard neurological examination in our patients. Apart from direct lesions in nuclei or tracts, we should also consider alterations in excitability as one of the explanations for absence of SR or MEPs.

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Somatosensory and auditory startle reflex in patients with stroke and spinal cord injury—M.E. Kiziltan, M. Sohtaoglu, A. Gunduz*, M. Bozluolçay, N. Uzun (Istanbul University, Cerrahpasa School of Medicine, Department of Neurology, Istanbul, Turkey)

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Background: Somatosensory startle reflex (SSSR) was recently studied in healthy subjects. Following corticospinal tract lesions caused by stroke or spinal cord injury (SCI), auditory startle reflex (ASR) has been reported to enhance due to reorganization of circuits rostral and caudal to the lesion. To further understand changes in SSSR and ASR, we investigated both responses in patients with spinal cord injury (SCI) and stroke.

Methods: We examined characteristics of ASR and SSSR in 14 SCI and 40 stroke patients (16 brainstem and 24 cerebral hemispheric infarctions) and 39 age and gender matched healthy subjects. ASR was obtained after eight auditory stimuli and SSSR was elicited after median nerve stimulation at the wrist. Surface electromyographic recordings were obtained from orbicularis oculi (O.oc), sternocleidomastoid (SCM), biceps brachii (BB) and abductor pollicis brevis (APB) muscles.

Results: Total ASR probabilities at distal muscles were significantly higher in patients with SCI and in stroke patients especially with brainstem infarctions. Similarly SSSR rates were increased in both patient groups compared to controls (for APB $p < 0.05$). SSR latency of O.oc in SCI patients were similar to controls whereas it was markedly prolonged in stroke patients ($p < 0.05$).

Conclusions: In conclusion, we have found that SSR and ASR were enhanced in stroke and SCI and this enhancement was more prominent in distal muscles. Secondly, the properties of ASr and SSSR differed according to the lesion site.

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An excitatory reflex between R1 and R2 responses of the blink reflex to supraorbital nerve stimuli—L. Leon[a,*], C. Cabib[b], M. Cordoso[b], I. Motta[b], J. Valls-Solé[b] ([a]Hospital BLMB SJD, Barcelona, Neurologia, Barcelona, Spain, [b]Hospital Clinic, Neurology, Barcelona, Spain)

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Background: The typical pattern of the blink reflex to ipsilateral electrical stimuli to the supraorbital nerve (SN) is composed by an early, short duration, well synchronized, R1 response and a late, long duration, polyphasic R2 response. We examined whether the period between R1 and R2 results from lack of excitatory inputs or active inhibition.

Methods: Tests were performed in 5 healthy subjects and 10 patients of various disorders affecting blink reflex excitability, including postparalytic facial syndrome and hemifacial spasm. All subjects wore surface electrodes attached to the orbicularis oculi and stimuli were applied to the SN. After obtaining the conventional blink reflex, healthy subjects were requested to close their eyes at various levels of force while applying again the same stimulus.

Results: In healthy subjects closing the eyes with force, SN stimulation induced a response of smaller amplitude and shorter latency than the R2 (25.2 ± 1.3 ms). A short and incomplete silent period emerged after R1 and after R2. Patients with postparalytic facial syndrome and essential hemifacial spasm showed activity interfering with the silence between R1 and R2, with often expanding between the two responses, repeating in successive trials.

Conclusions: Our results show that there can be reflex responses between R1 and R2 in healthy subjects during contraction and in patients with abnormal reflex excitability. This suggests that the absence of activity between the two responses in normal conditions is the consequence of an active inhibition that reaches the facial motoneurons at that point.

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Brainstem reflexes in patients with sleep bruxism: Masseter inhibitory reflex responses and auditory startle reaction—R. Inan [a,*], G. Benbir [b], D. Karadeniz [b], F. Yavlal [c], M.E. Kiziltan [b] ([a] Dr Lutfi Kırdar Kartal Training and Searching Hospital, Neurology, Istanbul, Turkey, [b] Istanbul University Cerrahpasa Medical Faculty, Neurology, Istanbul, Turkey, [c] Bahcesehir University Medical Faculty, Neurology, Istanbul, Turkey)

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Background: Sleep bruxism (SB) is a stereotyped movement disorder characterized by grinding or clenching of the teeth during sleep. Neurophysiologic methods offer approaches to study the excitability in SB by recording the motor potentials evoked by masseter muscles and masseter inhibitory reflex (MIR). Auditory startle reaction (ASR) has been found to be increased in restless leg syndrome but it has not been studied in SB. We aimed to show the hyperexcitability in the central jaw motor pathways in patients with SB by studying MIR and ASR responses.

Methods: 10 patients (mean age 48,4 ± 10,2 years; 8 male and 2 female) and 20 healthy subjects (mean age 34,4 ± 11,2 years; 6 male and 14 female) were enrolled in the study. The EMG activity was recorded from two masseter muscles by surface electrodes. The duration and latency of early and late silent periods and suppression ratios obtained from patient and control groups were compared. ASR was recorded from o. oculi, masseter, sternocleidomastoid, biceps brachii and tibialis anterior muscles and probability and latencies were evaluated. SPSS for Windows 11.5 package was employed.

Results: The differences in silent period onset latencies between patients and normal subjects were not significant but durations of early and late silent periods were shorter in SB group.

Conclusions: These results may indicate a reduced capacity for inhibition by the circuits responsible for the late period in SB and this increased excitability in central motor pathways could derive from an impaired modulation of subcortical structures especially brainstem inhibitory circuits and not from altered cortical mechanisms. Since ASR did not differ between the control and patient groups, it can be possible to say that there's no abnormality in brainstem and reticulospinal circuits in SB patients.

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Comparison of brainstem reflex abnormalities in patients with multiple sclerosis, Behçet and stroke and its topodiagnostic value—R. Inan [a,*], F. Yavlal [b], M.E. Kiziltan [c], G. Kiziltas [d], S. Saip [c], U. Uygunoglu [c] ([a] Dr Lutfi Kırdar Kartal Training and Searching Hospital, Neurology, Istanbul, Turkey, [b] Bahcesehir University Medical Faculty, Neurology, Istanbul, Turkey, [c] Istanbul University Cerrahpasa Medical Faculty, Neurology, Istanbul, Turkey, [d] Hisar Intercontinental Hospital, Neurology, Istanbul, Turkey)

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Background: Our current understanding of brainstem reflex physiology comes chiefly from the classic anatomical–functional correlation studies that traced the central circuits underlying brainstem reflexes and establishing reflex abnormalities as markers for specific areas of lesion. Our aim is to investigate the correlation between the brainstem reflex abnormalities and lesion localization in three different diseases with brainstem lesions.

Methods: Masseter inhibitory and blink reflexes were studied in 21 multiple sclerosis, 15 stroke and 17 Behçet's disease patients with brainstem lesions on brain magnetic resonance imagings. The reflex responses were compared with those of 20 healthy subjects of comparable age. SPSS for Windows 11.5 package was employed for statistical processing.

Results: Latency abnormalities of the blink and the masseter inhibitory reflexes were the most prominent in MS group. No significant differences were found in duration and degree of suppression among the groups in MIR responses. The highest abnormality percentages in MS group were in R1component of blink reflex (% 71, 4) and S2 component of masseter inhibitory reflex (% 90, 5). And also R1 of BR and S2 of MRI were the most abnormal responses in the all groups compared to other parameters.

Conclusions: Distinct reflex abnormalities indicate lesions at specific sites. A number of lesions suspected on clinical data may be confirmed by reflex findings only and not by imaging studies. Reflex testing can be utilized to demonstrate multiple lesions and evaluate dissemination of central nervous involvement in patients with brainstem lesions. İncreased abnormality percentage in MS group may be explained by the fact that supratentoriel lesions affect brainstem reflex responses. Since lesions in Behçet's disease are localised in mesencephalon commonly, superior to MIR and BR circuits, the abnormality in this group is much less relatively.

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Startle reaction evoked by kinematic stimuli—J.M. Castellote [a,*], M. Kofler [b], A. Mayr [b], L. Saltuari [b] ([a] Institute of Health Carlos III, Madrid, Spain, [b] Department of Neurology, Hochzirl Hospital, Zirl, Austria)

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Background: Kinematic stimuli are used for both assessment and treatment in neurorehabilitation. A patient's voluntary or reflex response may be affected by a startle reaction. We therefore

explored whether certain kinematic stimuli are able to elicit a startle reaction.

Methods: Eleven healthy subjects were suspended in a Lokomat system and were exposed to unexpected passive left knee flexion at 3 velocities (6, 60, 240°/s). Subjects were asked to perform a right wrist extension as soon as they felt their leg move (conditions: 6-React, 60-React, 240-React, respectively). In some 240°/s trials movement onset was preceded by a low-intensity electrical pre-pulse to the left index finger (240-Prep-React). We recorded EMG activity from right orbicularis oculi and sternocleidomastoid muscles to assess startle responses, from left quadriceps muscle to obtain stretch reflexes, and from right wrist extensors to assess reaction time.

Results: Startle responses were present in most 240-Reacttrials, as evidenced by (1) EMG activity in orbicularis oculi and/or sternocleidomastoid, (2) significant reaction time shortening in wrist extensors, and (3) stretch reflex latency shortening in quadriceps, as compared to responses without startle reaction. Only few trials at lower angular velocities resulted in startle responses. In 240-Prep-React trials no startle responses occurred.

Conclusions: Kinematic stimuli of high angular velocity, used to assess muscle stiffness, may elicit a generalized startle reaction, which in turn may modulate stretch reflex latencies of the muscle tested in a passive movement paradigm.

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Preparation for reaction time tasks in multiple sclerosis—C. Cabib [a,*], S. Llufriu [b], A. Saiz [b], J. Valls-Solé [c] ([a] Clinic Hospital of Barcelona, EMG Unit, Barcelona, Spain, [b] Clinic Hospital of Barcelona and Centre d'Investigacions Biomediques August Pi i Sunyer (IDIBAPS), Center for Neuroinmunology, Neurology Service, Barcelona, Spain, [c] Clinic Hospital of Barcelona, EMG Unit, Department of Neurology, Barcelona, Spain)

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Background: Sensorimotor integration can be assessed using simple reaction time tasks to somatosensory stimuli (ssRT). Tasks performed to stimuli applied to the contralateral hemibody would reveal interhemispheric transfer of information (IHT) across corpus callosum, while tasks performed when a startling-auditory stimulus (SAS) is presented together with the somatosensory cue would reveal the level of subcortical motor preparation. We studied both preparation and IHT in MS patients in whom callosal pathways and subcortical structures may be particularly involved.

Methods: In 13 controls and 20 mildly disabled relapsing-remitting MS patients, we studied ssRT for voluntary wrist-extension to ipsilateral and contralateral low intensity electrical stimuli, applied to the index finger. Percentage delay (PD) of contralateral vs ipsilateral responses was calculated as a measure of IHT. StartReact trials were performed applying randomly a SAS in ssRT trials (20%). Percentage shortening (SAS-Short) with respect to ssRT was calculated as a measure of the effectiveness of preparation. Motor conduction time (MCT) was assessed by recording the motor-evoked potentials to TMS.

Results: In controls, mean PD of contralateral responses was 105.7% longer than for ipsilateral responses. In StartReact trials, the mean SAS-Short was 29.7% for ipsilateral and 23.3% for contralateral responses. With respect to controls, patients had no differences in PD (105.4%) but showed significantly lower SAS-Short for ipsilateral (23.4%; $p = 0.02$) and contralateral trials (10.9%; $p = 0.005$). Contralateral SAS-Short was inversely correlated with MCT ($r = -0.294$). Two patients had abnormally delayed orbiculari-oculi responses to SAS.

Conclusions: Patients with MS have defective subcortical motor preparation that is worse when IHT sensorimotor integration is required.

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Essential tremor, the olivocerebellar system and motor timing – An fMRI study—A. Buijink [a,b,*], M. Broersma [c,d], M. van der Stouwe [c,d], N. Maurits [c,d], A.-F. van Rootselaar [a,b] ([a] Academic Medical Center, Neurology and Clinical Neurophysiology, Amsterdam, Netherlands, [b] Academic Medical Center, Brain Imaging Center, Amsterdam, Netherlands, [c] University Medical Center Groningen, Neurology, Groningen, Netherlands, [d] University Medical Center Groningen, Neuroimaging Center, Groningen, Netherlands)

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Background: Essential tremor (ET) is the most common tremor disorder. It has been repeatedly shown that the olivocerebellar system is involved in ET, consisting of the inferior olive nucleus (ION), dentate nucleus (DN) and cerebellar cortex. Impairment of the central timing mechanism in ET has been suggested. The olivocerebellar system plays an important role in motor timing. In order to study the functional involvement of this system in ET, we employed a task involving motor timing during functional MRI (fMRI).

Methods: Thirty propranolol sensitive ET patients with familial upper limb tremor and 30 healthy controls were included. T2*-weighted EPI sequences were acquired (180 volumes, TR: 2s, voxel size: $3.5 \times 3.5 \times 3.5$ mm, 3TMRI). The task consisted of alternating rest and finger tapping (rate of 2 Hz) blocks. Task performance was measured by electromyography. Analysis was performed in SPM8 (standard preprocessing, normalization according to the spatially unbiased infra-tentorial template, 4 mm smoothing kernel). The left ION was localized with a conjunction analysis of patients and controls. For this abstract, quantified tapping performance is not yet incorporated.

Results: Within-group random-effects analysis restricted to the brainstem and cerebellum showed activations throughout the cerebellum (bilateral lobules V, VI, VIIIA) and in both left and right ION. Preliminary between-group analysis of the ION and CB right lobule VI showed significantly higher activations in controls compared to ET patients.

Conclusions: Exploratory analysis suggests altered activity in the olivocerebellar system in ET patients compared to controls during a motor timing task. Inclusion of task performance and effective connectivity analysis will be carried out to aid us in discriminating between altered activity due to task performance and pathological motor timing related to ET. Understanding the role of the olivocerebellar system in ET is of great importance for unraveling the mechanism of tremor genesis.

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Oscillatory activity in primate reticular formation—B. Zaaimi [*], M. Cunningham, G. Collins, S. Baker (Newcastle University, Institute of Neuroscience, Newcastle Upon Tyne, United Kingdom)

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Background: Piper rhythmicity (35–60 Hz) has been reported in EMGs since 1907. These oscillations are often assumed to originate in the cortex, as they are coherent with sensorimotor EEG (Brown et al., 1998). However, we have recently seen similar oscillations in a slice preparation of primate brainstem reticular formation.

These oscillations were decreased by the GABA-A antagonist bicuculline, and completely suppressed by the GAP junction blocker carbenoxolone, suggesting generation by a complex intrinsic network. Given our recent work showing the importance of the reticular formation for recovery after corticospinal tract lesion (Zaaimi et al., 2012); we were interested in whether such oscillations might become more visible during functional recovery.

Methods: Macaque monkeys were trained to pull a lever, which opened a door allowing them to retrieve a food reward. In two animals, after training we made a unilateral lesion of the pyramidal tract by thermocoagulation, and allowed recovery, which reached plateau after ~4 months.

Results: The recovery differed between the two lesioned monkeys: one was moderately impaired and could still take the food with the paretic hand, whilst the second lost the ability to perform precision grip but was still able to pull a lever. Recordings were then made of local field potential (LFP) from the reticular formation and EMG. Recordings from one unlesioned animal served as a control.

Conclusions: In the control and in the less impaired monkeys reticulomuscular coherence was observed in the beta band (20–30 Hz); this was not seen in the more impaired monkey. By contrast, the more impaired animal showed ~70 Hz oscillations in reticular formation LFP around the time of movement. These preliminary results suggest that intrinsic rhythmicity around 40–60 Hz is present in the reticular formation and could be unmasked after lesion of pyramidal tract.

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Visualization of human brainstem substructures using gray matter nulling 3D-MPRAGE at 7 Tesla—B. Daeubler [a,*], M. Wyss [b], M. Bruegger [b,c], L. Vionnet [b], D. Brunner [b], K. Pruessmann [b] ([a] University Hospital Zurich, Neuroradiology, Zurich, Switzerland, [b] University of Zurich and ETH Zurich – Swiss Federal Institute of Technology, Institute for Biomedical Engineering, Zurich, Switzerland, [c] University of Zurich, Center of Dental Medicine, Zurich, Switzerland)

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Background: The human brainstem is one of the most complex neural entities, in both, structural and functional domains. Its plurality of small and densely packed substructures results in demanding settings for in vivo MR visualization. We addressed this issue applying ultra-high field MRI at 7 Tesla focusing on enhanced differentiation of brainstem substructures. This approach is an essential prerequisite breaking down the complex brainstem anatomy.

Methods: A modified 3D-MPRAGE-sequence in the sagittal and transverse plane was applied in a 7T MR-system. To compensate for B1-inhomogeneities, a highly adiabatic inversion prepulse was implemented. Five healthy volunteers were examined. The resulting images were visually correlated to histological plates and post-mortem MRI images from Duvernoy's Atlas.

Results: We identified 22 structures (sagittal), clearly assignable to histology data. In the brainstem 12 substructures were manually outlined for all five subjects, also based on histology. Adopting histology nomenclature clearly identifiable structures were labeled.

Conclusions: Optimized 3D-MPRAGE-imaging in the gray matter nulling regime at 7 Tesla provides enhanced image contrast between substructures in the human brainstem, giving rise to better understanding anatomy and potentially related pathology.

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Assessment of brainstem reflexes improves the diagnostic sensitivity of multimodal evoked potentials, MRI and clinical testing in the investigation of brainstem function in multiple sclerosis—I. Magnano [a,*], G.M. Pes [a], F. Ginatempo [b], M.P. Cabboi [a], G. Pilurzi [a], M. Conti [a], J.C. Rothwell [a,c], F. Deriu [b] ([a] University of Sassari, Dept. of Clinical and Experimental Medicine, Sassari, Italy, [b] University of Sassari, Dept. of Biomedical Sciences, Sassari, Italy, [c] UCL Institute of Neurology, Queen Square, London, United Kingdom)

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Background: Brainstem (BS) functions are conventionally studied by multimodal evoked potential (EP) recordings, MRI and clinical examination (CLIN). In Multiple Sclerosis (MS), increasing evidence accounts for a BS involvement, often undetected by standard testing. Recently, brainstem reflexes (BSRs) have drawn attention in evaluating BS dysfunction in MS especially the vestibulocollic (VCR) and vestibuloocular reflexes. In contrast, the vestibulomasseteric (VMR), acousticmasseteric (AMR) and trigeminocollic (TCR) reflexes have never been studied systematically in MS. Aims: to investigate whether the diagnostic sensitivity of CLIN, EPs and MRI can be improved adding the assessment of VMR, AMR, TCR and VCR either as single reflexes or in a 4-BSR battery.

Methods: The 4-BSR battery was recorded in 60 patients (33.3 ± 8.3 yrs) with relapsing-remitting MS (illness duration 8.2 ± 6.4 yrs). EP set included standard BAEPs, median and tibial SEPs Conventional MRI scans were focused on the BS lesion load. Group differences and correlations between variables were analysed with Mann–Whitney U test and Mc Nemar test.

Results: Distribution of BSR and EP abnormality frequencies in MS was: VMR 62.1%, AMR 55.1%, TCR 58.6%, VCR 25.9%; BAEPs 37.3%, median SEPs 60.3% and tibial SEPs 58.6%. Overall, BS dysfunction was detected as follows: BSRs 86.9%, EPs 82.7%, MRI 71.7%, CLIN 37.7%. While the performance of BSRs and EPs, taken separately, was not significantly higher than that of combined MRI/CLIN testing (70%), the paired use of BSRs/EPs had a sensitivity of 93.3%, which was significantly superior ($p = 0.007$), in a subset of patients with a disease duration $\leqslant$6.4 yrs.

Conclusions: BSRs revealed brainstem lesions otherwise undetected by CLIN and MRI, thus providing additional evidence of BS dysfunction in MS. Noteworthy, BSRs could effectively complement the usual EP testing in early detection of clinically and radiologically silent lesions. This may encourage EPs/BSRs paired use in newly diagnosed.

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Longitudinal assessment of brainstem reflexes in Multiple Sclerosis compared to multimodal evoked potentials, MRI and clinical evaluations—I. Magnano [a,*], G.M. Pes [a], F. Ginatempo [b], M.P. Cabboi [a], G. Pilurzi [a], E. Tolu [b], M. Conti [a], F. Deriu [b] ([a] University of Sassari, Dept. of Clinical and Experimental Medicine, Sassari, Italy, [b] University of Sassari, Dept. of Biomedical Sciences, Sassari, Italy)

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Background: We have previously shown in patients with relapsing-remitting Multiple Sclerosis (MS) that: *(i)* the vestibulomasseteric (VMR), acousticmasseteric (AMR), trigeminocollic (TCR) and vestibulocollic (VCR) reflexes are able to spot brainstem (BS) dysfunctions undetected by clinical and MRI examinations; *(ii)* the combined use of these Brainstem Reflexes (BSRs) with multimodal

Evoked Potentials (EPs) is more valuable than each single test in the early years after onset. Our aim was to document BS changes over time by BSRs, EPs, MRI and BS signs/symptoms (CLIN) before and after at least one year follow up, in MS.

Methods: Forty-five MS patients (34.8 ± 8.6 yrs old; disease duration 8.9±6.6 yrs) underwent BSRs, EPs (namely Brainstem Auditory Evoked Potentials – BAEPs, median and tibial Somatosensory Evoked Potentials-mSEPs and tSEPs), MRI and CLIN examination. BSR and EP data were ranked and summed up to obtain a cumulative score expressing severity of neurophysiological impairment. Before-after changes were tested with Wilcoxon test.

Results: After 15.1 ± 4.2 months from initial evaluation, no relapses had been reported by any patient. This was in line with the stability of the frequency of CLIN and MRI abnormalities (37.3% and 71.1%, respectively) at the follow up. Despite this, BSRs and EPs revealed a worsening of BS function. In particular, although the proportion of altered BSRs did not change significantly (80.6% *vs* 90.3%; $p = 0.180$), a significant worsening of scores was observed for VMR ($p = 0.001$), AMR (0.018) and TCR ($p = 0.013$). Similarly to BSRs, the incidence rate of EP abnormalities did not increased significantly (84.4% *vs* 86.7%, $p = 0.564$), but the analysis of cumulative score showed a significant worsening for the whole EP set ($p = 0.03$) as well as for median SEP (68.9% *vs* 75.6%, $p = 0.03$), P14 mSEP (33.3% *vs* 51.1%, $p = 0.005$), tibial SEP (60% *vs* 66.7%, $p = 0.03$).

Conclusions: BSRs and EPs were able to reveal a significant worsening of BS functions in spite of any variation of both BS signs/symptoms and of MRI BS lesion load. This is in agreement with previous reports on BSR/EP ability to detect clinically and radiologically silent BS lesions. Further studies are needed in a larger cohort of patient to assess BSR clinical usefulness in a longitudinal perspective.

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The spectrum of ocular motor abnormalities as the only clinical sign of brainstem lesions—F. Thömke (Klinikum Worms, Neurological Department, Worms, Germany)

Background: The widespread use of magnetic resonance imaging (MRI) revealed an increasing variety of ocular motor abnormalities as the only clinical sign of (mainly ischemic) brainstem lesions.

Methods: This paper reviews the variety of such abnormalities.

Results: Ocular motor abnormalities as the only clinical sign of MRI-documented brainstem lesions include complete and partial 3rd, 4th and 6th nerve palsies, vertical gaze palsies, crossed vertical gaze palsy, monocular elevation paresis, internuclear ophthalmoplegia, horizontal gaze palsy, horizontal gaze palsy with facial palsy, $1\frac{1}{2}$-syndrome, $1\frac{1}{2}$-syndrome with facial palsy ("$8\frac{1}{2}$-syndrome"), upbeat nystagmus, horizontal-rotatory nystagmus, horizontal nystagmus, skew deviation, and ocular tilt reaction.

Conclusions: Brainstem lesions causing isolated ocular motor abnormalities may be divided into 4 main groups. (A) Lesions involving infranuclear ocular motor nerve segments cause complete and partial 3rd, 4th and 6th nerve palsies. (B) Lesions affecting nuclei related to eye movements such as 3rd and 6th nerve nucleus, rostral interstitial nucleus of the medial longitudinal fasciculus, interstitial nucleus of Cajal, nucleus intercalatus Staderini are followed by horizontal and vertical gaze palsies, upbeat nystagmus, horizontal-rotatory nystagmus. (C) Lesions interrupting internuclear connections lead to internuclear ophthalmoplegia, monocular elevation paresis, skew deviation and ocular tilt reaction. (D) Combined lesions of nuclear and internuclear or infranuclear structures are the anatomical basis of $1\frac{1}{2}$-syndrome, $8\frac{1}{2}$-syndrome, or horizontal gaze palsy with facial palsy. The clinical significance of these disorders is not known.

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Optokinetic nystagmus of Chiari Malfromation. The aim of our study is to determine the special characteristics of disorders of the Optokinetic nystagmus in the early stages of Chiari Malformation—D. Demidenko *, V. Viktor (North-West State Medical University named after I.I.Mechnikov, Otorhinolaryngology, Saint-Petersburg, Russian Federation)

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Background: Diagnosis and treatment of cochleovestibular dysfunction becomes complicated in case of genetically based combination of pathology. The Chiari Malformation (CM) is a congenital development defect and associated with the caudal displacement of cerebellum and brain stem.

The aim of this study is to determine the special characteristics of disorders of the Optokinetic nystagmus in the early stages of CM.

At the otorhinolaryngology department of North-West State Medical University named after I.I.Mechnikov (Russia, St Petersburg), 54 cases (patients aged 16–69) were studied. All patients showed the symptoms of cochleovestibular dysfunction.

Methods: The Optokinetic nystagmus was taken in a dark-room using VNGULMAR system manufactured by the German company "Heinemann Medizintechnik GmBH" running software developed by the French company Synapsys. The fixed speed horizontal and vertical Optokinetic stimulus on screen (20 o/s) was applied with distracted and focused attention of the patients.

All the studies were conducted before the calloric test (CT) and after CT. The intensity of Optokinetic nystagmus was assessed as per SSC (speed of slow component) of nystagmus. Later on the relative asymmetry in Optokinetic nystagmus was calculated for each same name pair of horizontal and vertical Optokinetic reactions.

Results: The studies showed that in order to diagnose CM in the early stages it is important not only to identify the asymmetry in horizontal and vertical Optokinetic nystagmus but to mark the value and the sign of asymmetry as well. The sign of asymmetry is especially important after CT. Patients with the low placement of cerebellar tonsil Optokinetic reactions are more susceptible to CT.

Conclusions: Therefore, in the early stages of CM and "in the risk group", i.e. the patients with low placement of cerebellar tonsil, before the neurological symptoms have taken place and we have only vestibular dysfunction, the videonystagmography with quantitative evaluation of Optokinetic reaction becomes a voluble source of important diagnostic information and an indication for MRI studies.

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Trigeminal somatosensory evoked potentials in assessment of craniofacial pain: Preliminary results—F. Karaali-Savrun, B. Ekinci, A. Gunduz *, Y. Gulen-Abanoz (Istanbul University, Cerrahpasa School of Medicine, Department of Neurology, Istanbul, Turkey)

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Background: Craniofacial pain syndromes include various kinds of primary and secondary headaches, most of which are related to trigeminal system such as trigeminal neuralgia, trigeminal neuropathy, cluster headache or other trigeminal autonomic cephalalgia. Blink reflex, masseter inhibitory reflex, jaw jerk and trigeminal laser-evoked potentials are known to be more reliable in

neurophysiological testing of trigeminal system and electrophysiologic testing of trigeminal reflexes accurately distinguishes symptomatic and classic trigeminal neuropathy.

Here, we aimed to evaluate the reliability and stability of trigeminal nerve somatosensory evoked potentials (TSEP) in less frequently encountered craniofacial pain syndromes.

Patients and method: TSEP and blink reflex (BR) were recorded in 10 patients with craniofacial pain during the active disease period and in 25 healthy individuals. The latencies of N2, P2 and N3 waves as well as amplitudes of N2/P1 and N2/P2 were measured.

Results: We could not obtain TSEP in three patients (30%) whereas it was elicited in all healthy subjects ($p = 0.01$). All of the patients without TSEP response had idiopathic etiology and only one of them also lacked BR responses. Latencies appeared to be longer in patients with craniofacial pain compared to healthy subjects. However, BR responses were symmetrical and within normal ranges.

Conclusion: Keeping in mind the low number of participants included, we think that TSEP is able to be obtained in a stable manner in healthy subjects and it may be more capable to reflect changes in pain conditions compared to BR.

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fMRI evidence for a reduction in affective processing of thermal pain in responders of transcutaneous vagal nerve stimulation (TVNS)—R. Laqua [a,*], M. Lotze [a], B. Leutzow [b], T. Usichenko [b] ([a] University Medicine, Institute for Diagnostic Radiology and Neuroradiology, Greifswald, Germany, [b] University Medicine, Department for Anesthesiology and Intensive Care, Greifswald, Germany)

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Background: Although the transcutaneous vagal nerve stimulation (TVNS) is increasingly used in treatment of chronic pain, the underlying mechanism is unclear. The goal of this study was to analyse the cerebral effects of TVNS under experimental pain in fMRI.

Methods: Twenty healthy volunteers took part in two separate fMRI sessions (3 Tesla) with experimental pain, which was applied to the right forearm with MEDOC Sensory Analyser. During TVNS session the electrical stimulation was applied bilaterally to auricular concha with rectangle impulses (8 Hz frequency; 200 μs wave length); the intensity was maximal but not painful. During placebo session the stimulation device was switched off. The order of the sessions was randomised. Individual sensory thresholds were registered before and after each fMRI session. fMRI data was afterwards processed with standard settings in SPM8 and differences in BOLD effects between verum and placebo session were calculated. We used region of interest (ROI) based analysis on ROIs, which were previously identified in association with thermal pain.

Results: Cerebral pain processing areas were activated bilaterally under thermal stimulation. The group analysis did not show the differences in sensory parameters but revealed stronger activation of right amygdala under TVNS. The group of responders (subjects with increased pain threshold after TVNS, $n = 8$), showed a reduction in BOLD signal in the right nucleus caudate, the middle frontal cortex and left hypothalamus under TVNS in comparison to placebo.

Conclusion: Thermal stimulation elicited bilateral fMRI activation in pain processing regions of the brain in healthy volunteers. Responders to TVNS showed decreased activation in cerebral areas associated with affective processing of pain.

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