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Paresthesias as Reflection of the Lateral Asymmetry of Neural Function in Human

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1. Introduction

1.1 Neural asymmetry in human – An overview

Most biological systems demonstrate some degree of asymmetry. From lower animals to human normal variation and specialization produce asymmetries of both function and structure. The term asymmetry is often substituted for the term laterality and indicate left-right differences, especially in neurosciences and psychology (Bryden, 1982). However, researchers generally use the term asymmetry in more global context of both structural and functional side dissimilarities while the term laterality is typically used exclusively in relation to functional asymmetry (Hughdahl, 2005). In numerous species representing major vertebrate taxa asymmetries of brain and behaviour have been demonstrated and it is supposed to be an universal feature of the vertebrate nervous system (Goutiérrez-Ibañez et al., 2011; Tommasi, 2009). In a neuroscience perspective the concepts of asymmetry in humans are closely tied to the two hemispheres of the brain (Grabowska et al., 1994; Hughdahl, 2005). Despite the mirror symmetrical organization of the body along the vertical body axis, the two brain hemispheres differ in their anatomy and function; moreover, asymmetries in the brain's functional layout and cytoarchitecture have been correlated with asymmetrical behavioural traits – handedness, footedness, auditory perception, motor preferences and also sensory acuity (see Toga & Thompson, 2003 for review). Studies on anatomical asymmetries in the brain showed differences in distribution of tissue between hemispheres, although they are similar in both weight and volume (Toga & Thompson, 2003). Structural and neurochemical asymmetries in the majority of studies were reported to be linked with functional asymmetries of the brain and behaviour (especially the handedness). Some research showed cytoarchitectural asymmetry in the *planum temporale* related to handedness- marked leftward volume asymmetry. Additionally, this was also related to the degree of right-handedness of participants (Habib et al., 1995). In experiments with MRI Steinmetz observed greater asymmetry of this structure in right-handers in comparison to left-handers (Steinmetz, 1996). Structural asymmetry of central sulcus was reported to fit with the functional hemispheric asymmetry in relation to handedness (Babiloni et al., 2003), what indirectly confirms the relationship of laterality pattern in limbs and the motor cortex structure and function. Some investigators found differences between two brain hemispheres in levels of neurotransmitters (dopamine, norepinephrine), what was linked with various behavioural asymmetries (Glick, Ross & Hough 1982; Tucker &

Williamson, 1984). Generally, asymmetry in the neuromotor performance is assumed to be linked with the brain functional and laterality i.e. hemispheres specialization (Springer & Deutsch, 2004; Tommasi, 2009). Functional asymmetry of the human brain is related to different behavioural traits. One of the earliest observations of brain asymmetry was the specialization of the left hemisphere for language functions (Binder, 2000). Some research has pointed towards the right hemisphere as being specialized for spatial processing and emotional control (Springer & Deutsch, 2004) and all this came to develop standard models of hemispheric asymmetry claiming that each hemisphere has its own characteristic domain of competence - the left hemisphere is commonly regarded as the verbal and logical brain area, the right hemisphere is responsible for creativity and spatial relations. However, brain function lateralization is evident in the phenomena of right- or left-handedness and of right or left ear preference, but a person's preferred hand is not a clear indication of the location of brain function. Although 95% of right-handed people have left-hemisphere dominance for language, only 18.8% of left-handed people have right-hemisphere dominance for language function. Additionally, 19.8% of the left-handed present bilateral language functions (Springer & Deutsch, 2004). All these findings seem to link the neural asymmetry with motor and sensory traits in human. More recent studies confirmed asymmetry as the norm when the it comes to functions of he brain and nervous system, however researchers underline the fact that lateralization of the brain functions varies depending on several individual biological and environmental factors and also their interactions (Grabowska et al., 1994; Olex-Zarychta & Raczek, 2008; Tommasi, 2009). Manifestation of lateralization of the brain and nervous system can be explicitly observed in handedness as well as in footedness, which expresses in consistent preference for one arm or leg over the other in certain motor tasks. Therefore handedness and footedness in human has been linked with the asymmetry of the motor control system.

1.2 Laterality and motor control

Studies on human motor control incorporate research on different types of movements. Generally, movements can be graded along the scale from the most to the least automatic. It has been suggested that different neurophysiologic processes are involved in phylogenetically old behaviors like reflex reactions or rhythmic patterned outputs and discrete movements like grasping or reaching (Rothwell, 1996; Schaal et al., 2004). Lateral asymmetry is a prominent, but still poorly understood aspect of the human motor performance in all mentioned above types of movements. Lateralization of motor performance emphasized by handedness and footedness is characterized by the consistent preference for one extremity over the other in performing the majority of motor actions (Bagesteiro & Sainburg, 2002, 2003). Generally, it is accepted that handedness and footedness results from different (i.e. lateralized) neural control of each extremity with an assumption that motor asymmetry is a feature of neural organization of motor control (Shabbott & Sainburg, 2008; Wang & Sainburg, 2007). Although a feature of arm and leg preferences is well-documented in humans and nonhuman primates (Hopkins & Pearson 2000; Hopkins et al. 2003) there is still a lot of disagreement concerning the emergence of this phenomena. Lateral differences in motor performance have been reported in many tasks requiring speed, accuracy, and fast reaction time, typically with the better results for the dominant extremity (Annett, 1992; Elliott & Heath, 1999; Hore et. al. 1998; Olex- Zarychta & Raczek, 2008; Peters 1991). Differences in neural mechanisms of movement control among

different laterality patterns have been suggested with emphasis to the not exclusively central, but also peripheral control to be involved (Aziz-Zadeh et.al., 2006; Kato & Asami, 1998; Olex, 2004; Olex-Zarychta et.al. 2009). One of the first studies on handedness was published by Liepmann (1905) who suggested that the hemisphere which is contralateral to the dominant arm is as well dominant. As such it plans movements of both arms. Since that time considerable body of evidence has confirmed the hypothesis that cerebral hemisphere contralateral to the dominant arm plays a particular role in the performance of both arms. Several studies suggested that this hemisphere (hereafter referred to as the "dominant hemisphere") and premotor areas are more active comparing to the nondominant equivalent during ipsilateral (Kim et al. 1993; Kawashima et al., 1997), contralateral (Kim et al. 1993; Dassonville et al. 1997; Taniguchi, 1999) and bilateral arm movements (Kim et al., 1993). Additionally, brain damage subject studies with unilateral lesions have revealed movement deficits in the non-dominant arm when the dominant hemisphere was damaged, but not in the dominant arm movement after lesions to the non-dominant hemisphere (Haaland & Harrington, 1994, 1996). This suggests that the dominant hemisphere encloses special circuitry for the control of both arms. Reflection of Liepmann's model of motor lateralization can be seen in the hypothesis that dominant arm advantages in performance exist due to specialization of the dominant hemisphere for the visual-mediated correction processes (Carson et al., 1990). Several studies supported this hypothesis and indicated that dominant arm movements tend to be shorter in duration (Elliot, 1993; Mieschke et al., 2001; Todor & Cisneros 1985) and more accurate (Roy, 1983; Todor & Cisneros, 1985) than non-dominant arm movements. Additionally, based on findings made by Flowers (1975) one can hypothesize that interlimb differences in movement accuracy tend to be reduced when movements are performed at high velocity, which elicit decrease of the role of visual-based error corrections. This way, feedback correction model of the lateralization predicts that the dominant arm should show distinct advantages in the timing and efficacy of corrections to visual errors. There is alternative explanation of the dominant arm advantages during reaching introduced by Sainburg (2002, 2005). It was named by the author "the dynamic dominance hypothesis" of motor lateralization and is based on the idea that a movement is initially planned by specifying trajectory parameters in an extrapersonal space (Sarlegna & Sainburg, 2007). This plan is transformed into commands that specify the dynamic properties that reflect the forces required to initiate the movement (Sainburg, 2002). This hypothesis suggests specialization of the dominant arm control in a process of dynamic transformations. Further research lead to the hypothesis that the nondominant arm controller has become specialized for regulating limb impedance, which is needed to achieve steady-state positions (Bagesteiro & Sainburg, 2003, 2005; Duff and Sainburg, 2006; Schabowsky et al., 2007). Footedness has been previously reported as an important factor in predicting the motor preparation dependent on the behavioural context of a particular task (Carpes et al., 2007; Gabbard & Iteya, 1996; Grouios et al., 2009). It has been claimed that the footedness may be a better predictor of the cerebral lateralization than the handedness (Elias, Bryden & Bulman-Fleming, 1998; Elias & Bryden, 1998; Strauss & Wada, 1983). This seems to confirm the important role of the laterality both upper and lower extremities in detecting the asymmetry of the neural organization in human. It was suggested that motor performance of upper limbs is influenced only by the central information processing, while the effect for lower limbs is influenced by the peripheral motor control (Kato & Asami, 1998). However, some other findings strongly suggested the role of peripheral factors in rapid movements performed with hands what partly contradict models and theories based

on hands performance asymmetries as an effect of exclusively central motor control (Jaric, 2000). In neurophysiologic studies it was hypothesized that the motor laterality may reflect differentially lateralized activation in the motor control system influenced by a central information processing (hemispheric specialization) and also by other structures and processes on levels of motor control such as locomotor's centers of limbs performance (CPGs) and spinal cord (Francis & Spiriduso, 2000; Schaal, 2004; Aziz-Zadeh et al., 2006; Knikou, 2007; Olex-Zarychta & Raczek, 2008; Zehr et al., 2004, 2007). All these findings suggest the neural plasticity to be involved in the motor control system in human. The term of neural plasticity was introduced for the first time by polish neuroscientist Jerzy Konorski in middle XX century (see Zieliński, 2006 for review). According to the theory of neuroplasticity learning and training actually may change both the brains's anatomy and functional organization from top to bottom. It suggests that the pattern of a neuronal activation in CNS changes in response to experience. The concept of neuroplasticity is associated with an experience-driven alteration of synaptic structure and functions: the long-term potentation (LTP) in hippocampus and motor cortex and the long-term depression (LTD) especially in cerebellum, what must influence the process of the motor control (Rothwell, 1996; Monfils et. al., 2005; Aagard et.al., 2002; Agaard, 2003; Fazeli & Collingridge, 1996). Experience-dependent plasticity and asymmetric behaviours may therefore induce different neuronal changes in the motor cortex of the two hemispheres. In interesting experiments on animals (rats and mice) asymmetric use of paws resulted in changes in cell packing density in the motor cortex, and limb preference was related to the asymmetry of sensory input (Diaz, Pinto-Hamuy & Fernandez, 1994). Therefore, it is possible that the lateral asymmetry in motor performance may result from a lateralized sensory stimulation in human development.

1.3 Neural asymmetry studies with the use of the spinal circuit research

Although the simplicity of psychomotor tests makes them an attractive means of assessing motor laterality, a neurophysiologic examination of motor and sensory functions of peripheral nerves seems to be necessary in such investigation (Goble, 2007). In motor control research extensively used tools to study the neural control of movement and to gain detailed understanding of the nervous system plasticity are the motor evoked potential techniques, with a special emphasis to the spinal reflexes circuits. Despite the detail neural mechanisms involved in motor control are still unknown, the multidimensional and temporal regulation of limb mechanics by spinal circuits is assumed to be attached to neural proprioreceptive feedback from muscles and sensory receptors as well as to organization of descending command and motor output from the spinal cord. (Christou et al., 2002; Kimura, 2001; Rothwell, 1996; Zehr 2002, 2004; Zehr & Wolpaw, 2006; Misiaszek, 2003; Olex-Zarychta et al., 2009; Olex-Zarychta, 2010). One of the most extensively studied reflexes in the literature on human neurophysiology is a Hoffmann reflex (H-reflex). The relative ease with which this reflex can be elicited in muscles throughout the human body and few neural parameters involved in this circuit makes it a very attractive research tool in motor control research (Misiaszek, 2003; Zehr & Wolpaw, 2006). Studies incorporating the H-reflex as a neural probe showed changes in excitability of the reflex occur while movement actions and also in the absence of movement what suggests the existence of intrinsic modulating factors in motor control system, connected with the spinal circuit organization and/or with transmission parameters in motor and sensory pathways (Aymard et al, 2000; Kimura, 2001;

Misiaszek, 2003; Zehr et. al, 2004; Zehr, 2006; Zehr et.al., 2007). Previous studies with the H–reflex demonstrated clearly that adaptive plasticity could be induced in the spinal cord and that it could be examined by using the H-reflex (Agaard, 2003; Carp & Wolpaw, 1994; Wolpaw & Chen, 2006). Some researchers have investigated the effectiveness of the Ia monosynaptic pathway in leg muscles in relation to the handedness. Goode et al. (1980) observed a lateralization of the H-reflex responsiveness towards the non-dominant side, which was significant only in case of right-handed participants. Other findings showed the recovery curve lateralization of the H-reflex from the wrist flexors (Tan, 1989). The amplitude of the H-reflex was shown to depend on muscle use and exercise, what suggests the possible relation of the laterality and the plasticity of neural pathways (Mynark & Koceja, 1997; Sigh & Maini, 1980). Previous studies from our laboratory indicated significant depression of the H-reflex on dominant side in groups of both left-sided (left-handed/ left-footed) and right-sided participants (Olex-Zarychta et. al., 2008), what suggests that this effect may be associated with greater central steering influences on the dominant side in confirmation of previous findings that depression of the H-reflex is the dominant corticospinal effect on interneurones projecting the Ia afferents (Aymard et al., 2000). Previous results showed also differences in a sensory (Vs) and motor (Vm) conduction velocity between two examined laterality patterns. Higher values of the Vs in the non-dominant extremity in right-sided participants were recorded, what may contribute to a relatively better perception by the right cerebral hemisphere in this group of subjects. A lack of such effect in left-sided participants was interpreted as an effect of more symmetrical motor activity related to the right-sided social pressures in daily life or/and of a possible different pattern of the cerebral perception in this group of subjects (Olex-Zarychta et. al., 2008; Olex-Zarychta 2010). The selective hemispheric activation may thus play a role in the motor output asymmetry in human extremities. Assuming that the afferent sensory feedback is the neural basis for interlimb coordination and contributes strongly to the modulation of the spinal reflexes as well as control on supraspinal levels (Freitas et al., 2007; Pearson and Gordon, 2000; Rothwell, 1996; Zehr et al., 2004; Zehr, 2006), it was hypothesized that the functional dominance in limbs may be an important modulating factor for the motor coordination (Olex-Zarychta & Raczek, 2008; Olex-Zarychta, 2010). Earlier studies indicated asymmetries in the number of corticospinal axons (Nathan et al., 1990) as well as in cortical representations of the dominant limb muscles (Nudo, 1992) and brought evidences supporting the adaptive plasticity in muscle and cutaneous afferent reflex pathways induced by training and rehabilitative interventions. The activity-dependent plasticity of the neural system was found in both strength and endurance training (Olmo et. al., 2006). Changes of the H-reflex amplitude were found in the trained leg after couple of weeks of heavy strength training, with no such effect in untrained leg despite the comparable gains in strength due to cross – education program (Zehr, 2006) The increase of the H-reflex response was observed during maximal muscle contraction after resistance training (Aagard et al., 2003). Authors suggested the existence of chronic plastic adaptations in the Ia spinal reflex pathway leading to increased reflex excitability and co-existence of both spinal and supraspinal contributions to reflexes due to external factors. The existence of neural adaptation mechanisms has been suggested to comprise an increased central motor drive, elevated motoneuron excitability and changes in a presynaptic inhibition (Aagard, 2002). The motor laterality research brought some evidence that laterality pattern in limbs is related to the lateralization of excitability in the motor

system, connected with interhemispheric inhibition as a function of handedness (Baümer et al., 2007). All these findings enabled to suppose that laterality pattern may strongly influence the motor control process and neural asymmetry (Marchand-Pauvert et al., 1999; Olex-Zarychta & Raczek, 2008). However, in the majority of cited interesting experiments the model of laterality pattern in hand-foot combination was not provided. When the handedness of participants was taken into consideration, results of bilateral studies confirmed differences in lateral asymmetries of the H-reflex in right and left handed participants (Goode et al., 1980). Other experiments with respect of the sidedness of participants (preference of hand and foot on the same body side) indicated significant depression of the soleus H-reflex amplitude in the dominant lower extremity in those laterality patterns, what strongly suggests that inhibition of the soleus H-reflex on the dominant side what may be related to descending motor commands associated with greater cortical influences on the dominant side (Olex-Zarychta, 2010).

1.3.1 Paresthesias and neural asymmetry in human

The special attention during experiments incorporating the evoked potentials should be paid to the feedback from participants. Cooperation with patient before, during and after the laboratory session is crucial for obtaining proper results of neurophysiologic testing taking into consideration influence of patient-dependent factors as an emotional state, any voluntary movement or even a motivation or attitude towards procedures (Kimura, 2001; Misiaszek 2003; Zehr et al., 2004, 2006, 2007). Before neurophysiologic testing, especially the bilateral one and in healthy participants careful screening of handedness/footedness should be provided, in order to detect any possible factor influencing the asymmetry of future results. At least self-reported handedness/footedness should be recorded, however, sometimes participants are not conscious about their footedness and more specific laterality tests should be recommended (f.ex. footedness test by Chapman, 1987). During testing the special care should be taken to the symmetry protocol to avoid erroneous results. In neurophysiologic testing , the use of feedback monitors during laboratory sessions makes the feedback from participant/patient not decisive or crucial for eliciting the proper results of testing. However, patients always have own feelings about the situation of testing which should not be omitted or underestimated by the researcher or medical staff. Paresthesias, sensations of tingling, pricking, or numbness of skin during surface stimulation of the nerve (electrical or magnetic) are the most common feedback from patient during neurophysiologic testing which have no apparent long-term physical effect and are totally harmless for the patient (Miller, 1986; Olex- Zarychta et al., 2009). Paresthesias are common, transient symptoms of inhibiting or stimulating of the function of the nerve. Removing the pressure from the nerve (i.e. removing the stimulation electrode from the skin) typically results in gradual relief of these sensations. The incidence of paresthesias during electrical stimulation depends on many individual factors related to the body composition, neural system characteristics and also factors attached to experimental conditions (Miller, 1986). Paresthetic sensations are used by anesthesiologists to localization of nerves and target areas in regional anaesthesia procedures as standard technique of needle positioning f.ex. in nerve blocks (Miller, 1986), but transient paresthesias are often underestimated in neurophysiologic testing with the use of the evoked potentials method. Transient asymmetrical paresthesias during sensorimotor testing are common and harmless, and should be more appreciated by physicians and researchers as a valuable information on

individual level of the neural asymmetry. Taking into consideration the assumption that asymmetry of the human neural system is a normal, physiological phenomenon (see paragraph 1.1 of this chapter) it seems quite logical that the handedness/footedness should be related to the level of neural reactions on the peripheral level. Therefore, the possibility of the physiologic neural asymmetry should be taken into consideration during both symmetrical or asymmetrical testing with the method of evoked potentials. Neural feedback from the patient – among others also paresthesias – may be therefore a reflection of the neural function on both central and peripheral level of the neural system. Bilateral testing makes a good opportunity for comparison the asymmetry of the neural feedback from the patient during nerve stimulation. Observations of differences between the motor and the sensory feedback from the dominant and the non dominant extremities may bring some additional information about the neural state of the patient and may help in diagnosis. Taking into consideration previous findings on motor control mechanisms it is possible that laterality (limb dominance) is related to structural asymmetry of the neural system, what may influence a conduction process in peripheral nerves. Asymmetrical paresthesias are typical in some demyelination disorders as sclerosis multiplex (SM) and indicate hyperexcitability of demyelinated axons, however there is no specific data on relations of the handendness/footedness and a pattern of paresthesias in SM and other demyelination diseases patients. There is also no reference data of the neural asymmetry in healthy population–some authors indicate 5% as a normal asymmetry range in neurophysiologic testing, however in sport physiology and rehabilitation side differences in healthy participants exceed sometimes 40% as the effect of the asymmetrical muscle stimulation in sport training or daily life (Olmo et al., 2006; Shewmann, 2007). All this suggests that the neural asymmetry should be treated as a normal, physiological phenomenon and probably depends on learning, experience and personal activity model of the person with the special role of a physical activity history. Asymmetrical paresthesias during the neurophysiologic testing both in health and disease may be thus related (at least partially) to the physiologic neural asymmetry. It may be sometimes a helpful diagnostic hint for researchers and medical staff. In the light of all mentioned above, side asymmetries in results of any neurophysiologic testing do not necessarily indicate a pathological process in human and caution should be exercised in interpreting lateral asymmetries of results. The knowledge of the normal function of the peripheral nervous system is important to physicians. Only by understanding of normal recordings may proper diagnoses be achieved. Described below results of a simple experiment incorporating the H-reflex elicited in healthy young adults may be the contribution for detecting the role of careful handedness/footedness screening before neurophysiologic testing and the role of paresthesias as a reflection of the neural asymmetry in human.

2. Lateral differences in neurophysiologic testing: The H-reflex study on healthy adults

2.1 Aim of research

The aim of this experiment was to investigate the effect of the laterality pattern in limbs on the H-reflex asymmetry in groups of participants with four laterality patterns in hand-foot combination: two congruent and two crossed ones. Analysis of asymmetries in sensory and/or motor parameters of the spinal circuits among experimental groups are expected to

throw a new light on the effect of the laterality pattern on the motor control system in human. Taking into consideration mentioned earlier findings on the human laterality, individuals with crossed patterns in the hand–foot combination are expected to present different level of the neural asymmetry than congruent ones. Paresthesias are expected to be valuable indicators of the neural asymmetry and are also expected to be attached to the laterality pattern (footedness and/or handedness) of participants. Differences in sensory or/and motor parameters of the spinal circuit among experimental groups would throw a new light on the effect of the laterality pattern in limbs on plasticity of motor control system in human. Results are expected to contribute introduced before hypothesis (Olex-Zarychta & Raczek, 2008; Olex-Zarychta, 2010) that the functional dominance of human limbs is an important modulating factor in the motor control system in human. According to this hypothesis asymmetry of the motor performance may be an evidence for the behavior-induced plasticity of the CNS. Thus, the motor asymmetry may be an effect of the integration process of information from both ascending and descending neural pathways. Moreover, the limb dominance may be an effect of the cortical re-mapping and may influence the function of the whole motor control system, with an assumption that greater central steering influences should affect the dominant (more experienced) side. Asymmetrical paresthesias during neurophysiologic testing may be therefore a reflection of structural/ functional differences in the nervous system, what was previously supposed as a result of training and experience (Zehr, 2006). Therefore, the pattern of paresthesias during testing is expected to fit the pattern of the handedness/footedness of participants. Results of an experiment incorporating the H-reflex are expected to throw a new light on relations between the laterality and the neural asymmetry in human.

2.2 Participants

A total of 33 healthy male volunteers aged 21-23 (mean age 21.6, mean height 186±6) participated in a study. The study was accepted by the local Ethics Committee and each participant gave informed consent. Participants were carefully screened to eliminate any current or past neurological or muscle diseases or trauma. The functional dominance of upper and lower extremities of each participant was established by the use of a questionnaire (selection from Edinburgh Handedness Inventory by Oldfield, (1971). Additional items on foot preference were provided according to 11-item foot performance inventory of Chapman that has previously shown good internal consistency and test-retest reliability (Chapman et al., 1987). Self-reported handedness and footedness have also been recorded. Participants qualified for the experiment presented no signs of an ambidexterity both in upper and lower extremities and presented four main laterality patterns in hand-foot combinations. Research group consisted of four subgroups of 10 right-handed and right-footed (RH/RF), 7 right-handed and left-footed (RH/LF), 10 left-handed and left-footed (LH/LF) and 6 left-handed and right-footed (LH/RF) participants.

2.3 Experimental setup and procedures

The soleus H-reflex was elicited in the left and right lower extremity in the same laboratory session for each participant (Brinkworth et al., 2007). All experimental sessions were organized in the same lab with a stable air temperature of 22°C, always in the morning (10-12 AM) to provide the most comparative conditions of an experimental environment for all

participants. (Kimura, 2001; Waxman, 2004). During recording session participants were lying comfortably on stomach, with their head positioned centrally and arms close to the body. No moves were allowed during experiment to prevent any influence on results. The control of the level of alpha motor neuron pool excitability by maintaining bilaterally relaxed soleus muscles during recording session was provided. The position of participants was comfortable for releasing antagonist muscles (tibialis anterior). Monopolar recording Ag/AgCl self adhesive electrode (Sorimex, Poland, diameter 30 mm) was fixed on the soleus muscle distal to the belly of gastrocnemius, medial to the Achilles tendon (Zehr, 2002), symmetrically on the left and right lower extremity, with the use of anatomical landmarks to keep the symmetry. The reference electrode on each leg was localized on patella. To provide a total safety to participants the stimulator was double isolated from a patient by the use of a passive isolation unit (IST-1, Medicor, Hungary) and an additional ground electrode was placed above a recording site. Skin was prepared before by shaving and cleaning with an alcohol swab. The bipolar surface electrode and ST-3 electro stimulator (Medicor, Hungary) were used for stimulating the tibial nerve in the popliteal fossa of each extremity. The non dominant extremity was tested first in all participants, taking into consideration results of previous research indicating greater responsiveness of the H-reflex towards the non-dominant side (Goode et al.,1980). Before recordings some training pulses were provided on each extremity to find the best possible muscle response in the target area, taking into consideration the possibility of morphological differences in the tibial nerve location. The best impact to the nerve was found in each participant by slightly changing the stimulating electrode location in popliteal fossa to obtain the largest electric field in the nerve area. The single square impulses of 0.5 ms duration were triggered from a computer.
Stimuli were applied 10 seconds apart to reduce any effect of a post activation depression of the reflex (Palmieri et al., 2004). Stimulus intensity required to obtain the maximum H-reflex amplitude was determined by increasing the stimulus intensity from 0 in small increments. The stimulus intensity was fixed individually for each participant in a manner to obtain the maximum reflex amplitude in the extremity. Before recordings full H/M recruitment curves (from a stimulus intensity smaller than required to elicit a H-reflex to a stimulus intensity larger than required to reach the maximal M-wave) in both legs were performed to control the experimental setting (Hultborn et al., 1987). On the basis of the H/M ratio any differences in resistance that may occur at the electrode-skin interface and in the soft tissues, as well as differences in electrode placement were recognized and measures were repeated when necessary. Maximal H-reflex amplitudes reached up 60% of the maximal M-waves in all participants, what stayed in concordance with values referenced for healthy adults (Tucker, Tuncer & Türker, 2005). Electromyography signals (EMG) were recorded by CyberAmp 380 amplifier with AI 405 head stages (Axon Instruments, USA). Signals were amplified and filtered in the range of 10-1000 Hz. Data were collected, stored and analyzed by the Axotape-V2 computer software (Axon Instruments, USA). Ten trials for each extremity were recorded and an average of results obtained from all trials was involved in a statistical analysis (Tucker, Tuncer, & Türker, 2005). The following parameters of evoked potentials were recorded: the onset latency of the M-wave (LatMR, LatML) and of the H-reflex (LatHR, LatHL), amplitude of the H-reflex (AHR, AHL) and duration of the H-reflex (TH). Peak-to-peak amplitudes of the H-reflex were measured for each extremity. Onset latencies were measured as time intervals between stimulus artifact and onset of electrical muscle response (latency of the M-wave) in the range of 5-8 ms after the stimulus artifact

and in the range of 30-45 ms (latency of the H-reflex), with the respect of normal values for healthy young adults (Gupta, 2008; Kimura, 2001;Tucker Tuncer, & Türker, 2005) and taking into consideration subjects' height. Duration of the H response was measured from the initial take off to the final return to the baseline, taking into consideration a biphasic waveform of the H-reflex in soleus muscles (Kimura 2001; Tucker et al., 2005). To calculate the asymmetry size in the H-reflex in subjects and among groups of participants the special protocol was introduced to make measurements the most comparable in the aspects of the asymmetry evaluation. In this study relative differences in parameters for dominant and non-dominant legs were provided by the use of the calculated for each participant symmetry coefficients (SC).

2.4 Data analysis

To make a comparison of data obtained in participants with different laterality patterns reliable enough, the symmetry coefficient (SC) for response parameters was calculated for each participant on the basis of the following equation:

$$SC = (X_D - X_N) / (X_D + X_N)$$

where: SC- the relative difference between two sides
-            X_D- value for the dominant extremity
-            X_N- value for the non dominant extremity

From the methodological point of view, the use of the SC seems to be valuable in asymmetry evaluation. It enables to compare side differences among groups taking into consideration asymmetries between the dominant and non-dominant extremity of each participant in a particular group. It makes comparisons more powerful and more informative. Statistical analyses were done by the use of Statistica software 9.0 (Statsoft, USA). The basic statistics included arithmetic mean (M) and standard deviation (SD) calculated for each parameter and SC. The pair sequence Wilcoxon's test (T) was used for analysis of differences between dominant and non-dominant extremities of participants in subgroups and the nonparametric Mann-Whitney's test (U) were used for analysis of results obtained from groups of right and left-handers with different dominance in lower extremities. The use of non-parametric measures was justified by recognized lack of symmetry in research groups (on the basis of the Kołmogorov-Smirnoff normality test and a visual inspection of the data). The normality assumption of ANOVA was not met, so the distribution-free tests were used as its equivalents.

2.5 Results

2.5.1 Latency

Tendency towards longer latency was observed in the dominant leg in all laterality patterns. In left-handers significantly longer latency was found in the right leg in left-footed participants in relation to right-footed ones U (293,5) p=0.002. However, the greatest differences between the H-reflex latency in the dominant and non-dominant lower extremity was found in the group RH/LF, where results of the T test were significant T (11) p= 0.004.

2.5.2 Duration

In the duration of the H-reflex the tendency towards prolonged response was observed in dominant leg in right-handers, but with no statistical effect. In left-handers difference in the degree of TH asymmetry varied significantly between left and right footed subjects (see table 2 for details). However, longer duration of the H-reflex was recorded in the dominant extremities of all participants (see table 1 for details).

2.5.3 Amplitude

Left-handers with crossed laterality pattern presented significant depression of the H-reflex amplitude in the non-dominant lower extremity in comparison to left-sided participants (p= 0.014). In right-handed subjects no footedness effect on the amplitude was found (see tables 1 and 2).

parameters	RIGHT-HANDED			LEFT-HANDED	
	Right footed	Left footed	U	Right footed	Left footed
Lat HR	32.75±2.63	33.11±2.69	ns	**35.68±0.95**	**31.49±7.79**
Lat HL	32.72±2.85	37.59±14.02	ns	34.11±3.93	32.67±3.51
AHR	2.23±2.48	2.69±1.85	ns	**1.02±0.13**	**2.91±1.83**
AHL	2.47±2.10	2.65±1.54	ns	1.96±1.17	3.50±1.29
THR	8.19±2.76	8.55±3.16	ns	9.36±3.92	8.42±3.44
THL	8.04±2.08	9.13±4.01	ns	8.45±3.36	9.47±3.82

Lat-latency; A-amplitude; T – duration; H-H-reflex; R – right lower extremity; L-left lower extremity; U – p value in The Mann-Whitney's non parametric test, p<0.05

Table 1. Data summary (means ± SD)

SC	RIGHT-HANDED			LEFT-HANDED	
	RF	LF	U	RF	LF
RL LatH	-0.0004±0.05	-0.0441±0.08	ns	0.0254±0.05	-0.0174±0.05
RL AH	-0.1415±0.43	0.0661±0.53	ns	-0.0907±0.35	0.1178±0.32
RL TH	0.002±0.15	-0.0176±0.23	ns	**0.0483±0.06**	**-0.0579±0.13**

SC– right-left symmetry coefficient; U – p value in The Mann-Whitney's non parametric test
The negative value of the SC indicates the asymmetry towards the non dominant lower extremity in the particular laterality pattern

Table 2. Right-left asymmetries of the H-reflex in subjects

However, it was observed that the degree of asymmetry was greater in two congruent laterality patterns in comparison to crossed ones and this tendency was opposite to the latency of the H-reflex. In right-handed and right-footed participants decrease of the amplitude of the H-reflex in the dominant lower extremity was very distinct in comparison to other laterality patterns in limbs.

However, in totally right–sided participants amplitude of the H-reflex was greater on the non-dominant side in all cases (figure1).
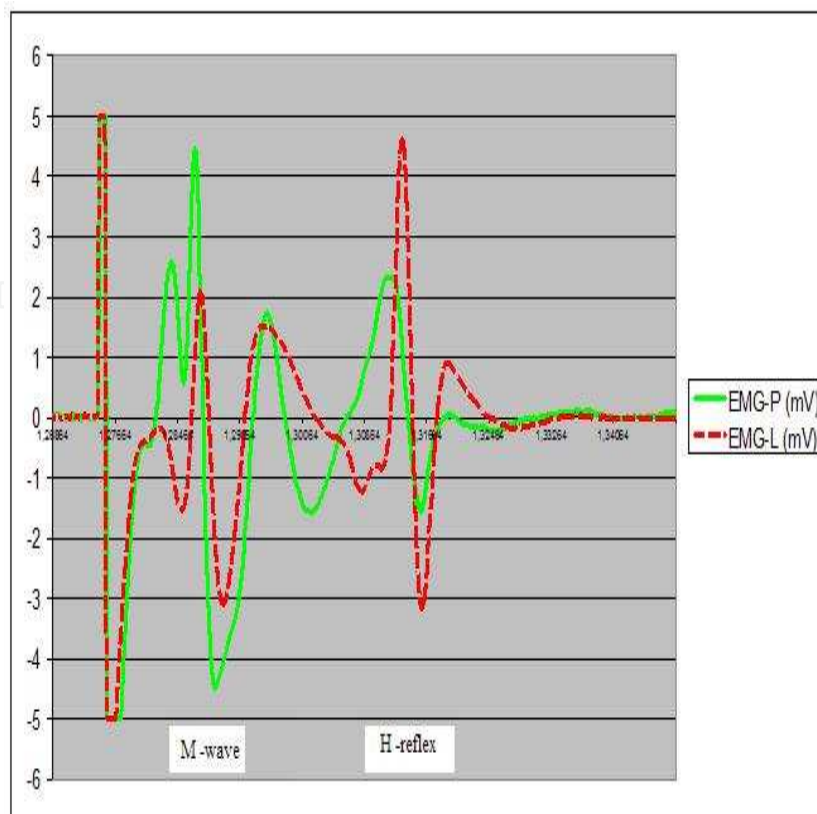
Fig. 1. The electromyographic recording (the averaged data form 10 sweeps) of the right (dominant) and the left lower extremity of participant nr 6 from the group RH/RF. Visible typical for this group depression of the soleus H- reflex in the dominant lower extremity.

Results indicated no particular differences in the side asymmetry degree among laterality patterns in hand-foot combination (see table 1 and 2 for data summaries).

2.5.4 Paresthesias

During experiment right-left differences in feedback from participants were observed. The majority of participants felt tingling in both legs during nerve stimulation and these sensations were not painful or unpleasant for them. In some participants no paresthesia occured (5 persons) or the same levels of sensations on both legs were reported (7). In 1 participant (right-handed and right-footed one) the sensivity on dominant side made recordings of dominant leg difficult (very strong sensations even in very low intensity of impulse was used, with no such problems with testing the left (non-dominant) extremity. Participants reported stronger paresthesias in their dominant extremities in the majority of cases; in this leg minor intensity of electric impulse was needed for eliciting the maximum H-reflex. Stronger sensations during stimulation were attached to the depressed amplitude of the maximum H- reflex. This effect was the most evident in right-handed and right-footed subjects. (figure 1). In this group of participants stronger paresthesias were reported on dominant lower extremity in the majority of tested participants. Left-footed participants generally reported minor side differences in level of paresthesias in comparison to right-footed ones and rarely felt the stimulation discomfortable.

2.6 Discussion

2.6.1 Handedness, footedness and neural asymmetry

Results of this experiment partially confirmed the relationship of the neural asymmetry with the laterality pattern in hand-foot combination and generally indicated relations of asymmetrical paresthesias with results of neurophysiologic testing. Results indicated the laterality pattern in hand-foot combination as a factor influencing somehow reflex pathways probably by an afferent feedback. Footedness influenced the latency and amplitude of the H-reflex especially in left-handed participants, however neural asymmetry seems to be very individual. In previous studies incorporating the H-reflex when only handedness or sidedness of subjects was taken into consideration indicated the statistical effect of the reduced amplitude of the H-reflex in the dominant lower extremity in strongly lateralized, right-handed participants (Goode et al.,1980; Olex-Zarychta, 2010). It was interpreted as an effect of greater central influences on the dominant side, assuming that the normal opposite control is exerted by the motor cortex on primary afferent interneurones in lower and upper limbs. In this experiment the H-reflex amplitude was analyzed in relation to footedness and laterality pattern in hand-foot combination and results were not so obvious- significant effect of footedness occurred only in the left-handed group of subjects. This seems to indicate the footedness to play a greater role in the neural organization in left-handers than right-handers and that not only laterality in the tested extremity, but also laterality pattern in hand-foot combination seems to influence neural asymmetry in human. Neural coupling between upper and lower extremities was previously reported by Knikou (2007), and present results seem to confirm this findings. Recorded differences in H-reflex amplitudes among groups may be associated with laterality-dependent organization of the synaptic transmission as previously suggested (Goode et al., 1980; Olex-Zarychta, 2010). Present results indicate the tendency towards greater side asymmetry in the H-reflex amplitude in two congruent laterality patterns. Taking into consideration that depression of the H-reflex is the dominant corticospinal effect on interneurones projecting the Ia afferents (Aymard et al., 2000) in crossed laterality patterns the cortical effect should be more symmetrical, through the effect on interneurones projecting the Ia afferents from the dominant hand and foot in opposite body sides. According to the neural plasticity concept the muscle use may induce changes in cortical representations of the dominant limb muscles. This makes both left-handed subjects and persons with crossed laterality patterns more complicated in motor functions (Beling, 1998; Olex-Zarychta & Raczek, 2008). Longer duration and longer latency in dominant extremities may indicate the longer central pathway of the reflex in the spinal cord (Rothwell, 1986). Differences in motor and sensory parameters between right and left-handed persons were recorded in some previous studies (Gupta et al., 2008; Tan, 1993). Results may be influenced by strength of limbs' dominance both in upper and lower extremities of participants and they need to be verified in studies on populations selected according to the degree of lateralization in limbs and physical activity models. In this experiment participants were not particularly selected in the aspect of a model of stimulation in their motor activity. Many previous experiments with spinal reflexes suggested multitude factors influence the neural reflex mechanisms in movement and at rest (Goode et al., 1980; Kimura, 2001; Misiaszek, 2003; Sibley et al. 2007; Zehr, 2006). Muscle use is supposed to determine not only the structure of muscles but also the asymmetries in the structure and function of neural pathways (i.e. number of corticospinal axons) and in cortical representations of the dominant limb muscles (Carpes et al., 2007; Fomin & Fomina,

2007; Mynark & Koceja, 1997; Nathan, 1990; Nudo, 1992, Tanaka 2009). In some previous studies asymmetry of the motor units responsiveness did not depend on the biomechanical properties of the muscle tested (Aimonetti et al., 1999). Motor asymmetries thus may contribute to functional differences in rather sensory than motor functions on various levels of the neural system. Present results seem to confirm this suggestion. It was previously suggested that a compound nerve conduction velocity may be a reflection of proprioceptive afferents in human, what corresponds to the neural plasticity concept (Metso et. al., 2008). According to the neural plasticity idea the greater feedback from the dominant side could alter the pattern of neuronal activation in response to experience (Monfils et al., 2005). Previous research brought some evidence for an interhemispheric inhibition as a function of handedness (Baümer et al., 2007). Recorded in this experiment asymmetry of the H-reflex parameters may be thus an effect of different models of motor behaviors that alter the pattern of neuronal activation in human. In this study crossed laterality patterns presented greater side asymmetries than congruent ones in the H–reflex parameters.

2.6.2 Paresthesias as indicators of the neural asymmetry

The pattern of paresthesias observed during testing is similar to previous experiments in our laboratory conducted with the use of the magnetic stimulation (Olex-Zarychta et al., 2009). It suggests the asymmetry of paresthesias to be an effect of the neural system functioning not related to the specific method of testing. Results indicated side differences in paresthesias to be common phenomenon in healthy adults. Stronger sensations on the dominant side observed in participants regardless their handedness (but more evident in right-sided persons) indicate possibility of the existence some structural/functional differences in peripheral nerves related to the laterality and therefore should be taken into consideration in neurophysiologic testing as a valuable information on the nervous system of the patient. Asymmetry of the neural system should be treated as a norm in human and this physiologic asymmetry may influence the result of each neurographic test- presented experiment on healthy young adults indicated a degree of side asymmetries very individual and multidimensional. So, asymmetry of neurography results not always must indicate the pathology or disease, but may be a reflection of the neural asymmetry resulting from experience. Careful screening of the handedness/footedness and a lifestyle model of each patient/participant before any neurophysiologic testing may help achieve the proper diagnosis. The explanation of the mechanism of stronger paresthesias on the dominant side observed during own experiments exceeds the frames of this article and it needs further research. It would be interesting, for example to find out if paresthesias in demyelinating diseases as SM are attached to the handedness/footedness of patients; it would throw a new light to the problem of both origin and treatment of such diseases.

2.7 Conclusion

Results confirmed the concept of neural asymmetry in human as a physiological process, as suggested previously (Tucker & Williamson, 1984). Neural side asymmetry in the H-reflex parameters is probably related to many factors and the laterality pattern in limbs seems to be one of them. Results suggested the laterality pattern in hand-foot combination as a factor influencing the neural plasticity by an afferent feedback. If the hand/foot functional dominance would be an effect of greater amount of experience (motor activity), it may be

assumed that this is the factor inducing the changes in neural networks on different stages of motor control by afferent feedback from all extremities. According to the neural plasticity concept the greater feedback from the dominant side could alter behavior by altering the pattern of neuronal activation in response to experience (Monfils et al. 2005). The main conclusion is that the laterality pattern may be a part of a very complicated feedback loop where the motor activity pattern in limbs induces the process of the neural adaptation in response to experience. In the effect both structural and functional changes occur in the motor cortex, what influence the functional organization of the motor control on all levels. This concept may be named the adaptation theory of the motor laterality. Asymmetrical paresthesias during electrophysiologic recordings may be treated as helpful indicators of neural asymmetry in human assuming that the laterality pattern in limbs (handendess and footedness) is a part of a very complicated afferent feedback system where the motor activity is involved in the process of the neural adaptation in response to experience. Asymmetry of motor and sensory reactions of the nervous system, including paresthesias in health and disease may be related to the asymmetry of neural functions in human and these physiologic asymmetries should be taken into consideration in neurophysiologic testing with the use of evoked potentials. If the concept of the neural plasticity related to learning and experience is the proper one, analysis of asymmetry of paresthesias during neurophysiologic testing and other medical procedures might be useful in diagnoses and treatment. They can be a reflection of the complex link between neural and behavioural lateralization in human. This concept needs to be verified on neurophysiologic and behavioral studies on populations with different laterality patterns in hand-foot combinations presenting various models of motor activity; in health and disease.

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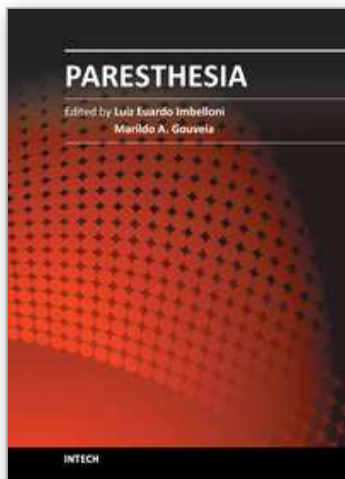
Paresthesia

Edited by Dr. Luiz Eduardo Imbelloni

Paresthesias are spontaneous or evoked abnormal sensations of tingling, burning, pricking, or numbness of a person's skin with no apparent long-term physical effect. Patients generally describe a lancinating or burning pain, often associated with allodynia and hyperalgesia. The manifestation of paresthesia can be transient or chronic. Transient paresthesia can be a symptom of hyperventilation syndrome or a panic attack, and chronic paresthesia can be a result of poor circulation, nerve irritation, neuropathy, or many other conditions and causes. This book is written by authors that are respected in their countries as well as worldwide. Each chapter is written so that everyone can understand, treat and improve the lives of each patient.

How to reference

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