

Reorganization of motor function and speech

Ph.D. thesis

Zsuzsanna Kalmár M.D.

Department of Neurology, University of Pécs

Leaders of project: Prof. József Janszky M.D., Ph.D., D.Sc.,

Prof. Sámuel Komoly M.D., Ph.D., D.Sc.

Leader of program: Prof. Sámuel Komoly, M.D., Ph.D., D.Sc.

Leader of Doctoral School: Prof. Sámuel Komoly, M.D., Ph.D., D.Sc.

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Abbreviations

AI: Asymmetry index. Activated voxels in the left cortex – activated voxels in the right cortex)/all activated voxels in cortices concerning to a brain region

EPI: Echo planar imaging

FLASH: Fast Low Angle Shot

fMRI: Functional MRI

LPD: Left dominant. Group of patients with Parkinson’s disease formed according to the predominantly right-sided symptoms

MR: Magnetic resonance

MRI: Magnetic resonance imaging

MS: Multiple sclerosis

RPD: Right dominant. Group of patients with Parkinson’s disease formed according to the predominantly left-sided symptoms

T: Tesla

TE: Echo time

TI: Inversion time

TR: Repetition time

UL: Upper Limb

Neuroplasticity, introduction

Neuroplasticity is the ability of nervous system to perform short- or long-term functional and structural changes to the external or internal influences.

Plasticity depends on time, it can be experience-induced and it is influenced by environment and internal state, for example motivation and attention.

Neuroplasticity can be investigated with various methods including morphological, cell- and molecular biological, electrophysiological methods and functional neuroimaging techniques such as magnetic resonance imaging (MRI) which can be mostly applied in human. By the help of this imaging technique numerous appearance of neuroplasticity has been detected on different areas of nervous system to the various stimuli.

Not only the structure of a brain area can be investigated by MRI but its function too. This method is called „functional” magnetic resonance imaging (fMRI) which is a blood oxygen level-dependent (BOLD) neuroimaging technique.

Reorganization of speech function and motor system

The two structurally and functionally identical brain hemisphere enable that in case of unilateral injury the lost functions can be reorganized in the homologue structure. The symmetry assures the reorganization ability of the most important brain functions. The hemisphere where the language centers are located is the dominant (language dominant). This is usually the left hemisphere.

According to the literary data, injuries affecting the left hemisphere and language centers can cause contralateral language reorganization. It has not been analyzed so far, whether asymmetric hand usage can influence the language cerebral organization. Thus, in one of our study I have investigated the reorganization of language-generating structures in obstetric brachial plexus injury.

Out of frequent neurological disorders stroke and multiple sclerosis (MS) are the most frequent in which the reorganization of motor system has been investigated.

There are numerous unanswered question in Parkinson's disease compared to stroke and MS, such as: to what extent does the course of disease itself define clinical picture and to what extent the disease compensatory reorganization.

Studies

Obstetric peripheral upper limb injury and speech reorganization

Aim

Our aim was to study whether such functional factors such as asymmetric hand usage can influence brain lateralization. Thus: Can obstetric peripheral upper limb (UL) injury and asymmetric hand usage as a consequence of this injury influence language lateralization?

Subjects and Methods

In this study, 15 subjects (6 men and 9 women, mean age: 15,9±5,4 years) with obstetric brachial plexus injury were included who were, from their birth, under continuous medical care. All of them suffered from a unilateral obstetric brachial plexus palsy involving the C5-Th1 nerve roots. The injured nerve roots were identified by clinical examination at birth and later we confirmed them by electrophysiological methods. There was neither history or sign of brain injuries, speech disturbances, nor physical examination indicated these signs. All subjects had a normal range of intelligence according to clinical impression, education, or intelligence quotient (IQ test). All of them attended primary school, secondary school, or university at least with moderate-to-excellent performances. Eight subjects, who had only moderate school performance, underwent Raven IQ testing and scored in the range of 81 to 118. The patients' histories and results of physical examinations were registered before the functional MRI examination. There were five subjects with a left-sided and ten with a right-sided injury.

According to the usage of the right hand, we categorized subjects into three groups:

- (1) 5 subjects with left-sided UL injuries with complete usage of the right hand,
- (2) 5 subjects with right-sided UL injuries and preserved writing with the right hand,
- (3) 5 subjects with right-sided injury without ability to write with the right hand.

Paradigm

Internal word generation paradigm demonstrates activity in speech centers (Broca and Wenicke areas). Block design technique was used to map eloquent speech centers.

MRI

Our examinations were conducted on a 1-Tesla Siemens Magnetom Harmony type clinical MRI scanner.

To characterize language lateralization in individual subjects, we calculated an **asymmetry index** (AI) of frontal activity in the course of functional MRI: **AI** = (activated voxels in the left frontal cortex – activated voxels in the right frontal cortex)/all activated voxels in frontal cortices.

Results

Association between the Presence of Right-Sided Upper Limb Injury and Language Lateralization

Positive values of AI indicate that the activation is more pronounced on the left than on the right side (AI = 1 corresponds to a complete left-sided lateralization; AI = -1 a complete right-sided language lateralization). The mean AI in subjects with right-sided UL injury was $+0,32 \pm 0,38$ (range, -0,54 - +0,85), the mean AI in subjects with left-sided UL injury was $+0,66 \pm 0,25$ (range, +0,44 - +0,95). Subjects with right-sided UL injury showed a more right-sided language lateralization compared with subjects with left-sided UL injury.

Correlation between the Degree of Right-Sided Hand Usage and Language Lateralization

The Spearman's rank correlation showed a negative correlation between the usage of the right hand and the left-sided language lateralization (AI), $R = -0,699$, $p < 0,01$.

Correlation between the Severity of Right-Sided Upper Limb Injury and Language Lateralization

The more nerve roots are involved and weaker the functions of right UL, the more right-sided is language lateralization.

Conclusions

- (1) The right-sided UL injury was associated with a shift of language lateralization from the left to the right.
- (2) The severity of the damage and the degree of the asymmetric hand usage strongly correlated with the degree of the participation of the right hemisphere in language production.
- (3) We found only a left-to-right shift of language lateralization and not a complete switching of language lateralization. The latter occurred in one subject only.
- (4) According to our study a peripheral injury may induce changes in brain organization and may affect even those morphologically intact brain regions that do not directly control the altered function.

Reorganization of motor system in Parkinson's disease

Aim

Our aim was to map the role of ipsilateral motor system in adaptive reorganization in Parkinson's disease.

According to the asymmetric beginning of Parkinson's disease we formed two groups of patients and we contrasted the brain activity in them. We do not have to face performance differences due to using a passive movement fMRI paradigm. We can more precisely investigate the role of the structures of the less affected hemisphere in the reorganization. It is

difficult to examine when we compare the activation of the normal with the Parkinsonian brain where the functions of the less affected hemisphere are also impaired.

Subjects and Methods

10 right-handed patients with Parkinson's disease were included in this study. We also included a group of 5 healthy controls in order to demonstrate the physiological response to the passive movements. In this examination we used the same settings as used in the patient groups.

We grouped the patients according to the predominant side of symptoms; thus, a right-sided dominant (RPD) and a left-sided dominant (LPD) group was formed with 5 patients in each group. There was no difference in the severity, duration and treatment of PD between the two patient groups. There were more men in the RPD group.

Paradigm

Passive finger movement paradigm applying sensorimotor stimuli is appropriate to detect activation in precentral and postcentral gyrus. The total examination protocol consisted of a 4-finger passive movement task on both hands. The movement-rest cycle (30 s each) was repeated five times according to the block design technique.

MRI

To reduce dyskinesia, we performed the fMRI examinations in the practically 'OFF' state. Our examinations were conducted on a 3-T Siemens TIM Trio MR scanner.

Results

In both groups of patients passive movement paradigm was applied on the left and on the right hand as well.

RPD Group

Within-group analysis of *right-fingers's movement* (more affected side) showed significant activated foci in the contralateral (left-sided) primary sensorimotor cortex and thalamus, in the ipsilateral (right-sided) secondary somatosensory cortex and in the inferior frontal gyrus.

The movement of *left fingers* (less affected side) is associated with activation in the contralateral (right-sided) primary sensorimotor cortex and thalamus, in the ipsilateral (left-sided) secondary somatosensory cortex.

LPD Group

LPD patients during left-fingers' passive movement (more affected side) showed activations in the contralateral (right-sided) sensorimotor cortex, in the ipsilateral (left-sided) secondary somatosensory cortex and caudal part of inferior frontal gyrus.

LPD group during right-fingers' passive movement (less affected side) activated contralateral (left-sided) primary sensorimotor cortex, secondary somatosensory area, inferior frontal gyrus, ipsilateral (right-sided) inferior frontal gyrus and secondary somatosensory cortex.

Contrasting LPD and RPD Groups

We contrasted the two patients groups with two paradigms. During the between-group analysis the right-fingers' movement in right-sided Parkinson's disease contrasted to the left-sided PD resulted in significant differences on the fMRI in right putamen, right sensorimotor cortex and bilateral prefrontal cortex.

Conclusion

Our study suggests that in the less affected brain hemisphere motor-related areas including primary sensorimotor cortex, supplementary motor area and basal ganglia may play a role in the reorganization of motor system in Parkinson's disease. However, we could demonstrate this reorganization only in Parkinson's disease with right-sided dominant symptoms.

List of publication

Publications and poster presentation related to the thesis

Auer T, Pinter S, Kovacs N, **Kalmar Z**, Nagy F, Horvath RA, Koszo B, Kotek G, Perlaki G, Koves M, Kalman B, Komoly S, Schwarcz A, Woermann FG, Janszky J. Does obstetric brachial plexus injury influence speech dominance? Ann Neurol 2009; 65: 57-66. **IF: 9.317**

Kalmar Z, Kovacs N, Perlaki G, Nagy F, Aschermann Z, Kerekes Z, Kaszas B, Balas I, Orsi G, Komoly S, Schwarcz A, Janszky J. Reorganization of Motor System in Parkinson's Disease. Eur Neurol 2011; 66: 220-226. **IF: 1.76**

Kalmár Zs, Woermann F, Schwarz A, Janszky J. Plasticity of brain lateralization in epilepsy: FMRI studies. Ideggyogy Sz 2009; 62: 120-128. **IF: 0.236**

Poster presentation

Kalmar Z, Kovacs N, Janszky J. Reorganization of Motor System in Parkinson's Disease. 10th International Conference on Alzheimer's and Parkinson's Diseases, March 9-13, 2011, Barcelona, Spain

Presentations

Studying language lateralization in subjects with brachial plexus injury

Kalmár Zs, Janszky J, Auer T, Schwarcz A, Pintér S

Magyar Neuroradiológiai Társaság 17. kongresszusa, November 6-8, 2008, Pécs, Hungary

Functional magnetic resonance imaging and its role in studying brain lateralization

Kalmár Zs

VII. Vajdasági Magyar Tudományos Diákköri Konferencia, November 21-23, 2008, Novi Sad, Serbia

Reorganization of cortical functions in neurological disorders

Kalmár Zs

1st Pecs-Brno Neurology Symposium on Epilepsy and Parkinson's disorder, February 19, 2010, Pécs, Hungary

Plasticity of motor system in Parkinson's disease

Kalmár Zs, Janszky J

Fiatal Neurológusok Fóruma, March 12-13, 2010, Pécs, Hungary

Neuroplasticity in neurological diseases

Kalmár Zs, Plózer E, Janszky J

Magyar Epilepszia Liga Tudományos Ülése, June 17-19, 2010, Kecskemét, Hungary

Connection between hand usage and language organization in the light of our study

Kalmár Zs

XVI. Korányi Frigyes Tudományos Fórum, April 14, 2011, Budapest, Hungary

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Tóth V, Hejjel L, **Kalmár Z**, Fogarasi A, Auer T, Gyimesi C, Szucs A, Janszky J. Effect of epileptic seizures on the heart rate. *Ideggyogy Sz* 2008; 61: 155-61.

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Kalmár Z, Kovács N, Balás I, Perlaki G, Plózer E, Orsi G, Altbacker A, Schwarcz A, Hejjel L, Komoly S, Janszky J. Effects of spinal cord stimulation on heart rate variability in patients with chronic pain. *Ideggyogy Sz* 2012; közlésre elfogadva **IF: 0.488**

Poster presentation

G Orsi, G Perlaki, N Kovács, A Schwarcz, Z Pap, **Z Kalmár**, E Plózer, Á Csathó, R Gábel, S Komoly, I Janszky, J Janszky. Coffee consumption may influence the hippocampus volume in young women. *ESMRMB 2011 Congress*, October 6-8, 2011, Leipzig, Germany

D Kuperczkó, Z Clemens, G Perlaki, G Orsi, **Z Kalmár**, A Schwarcz, N Kovács, B Faludi, J Janszky. Sleeping habits and brain structure: the volume of the hippocampus is smaller in “owls” than “larks”. 16th Congress of the European Federation of Neurological Societies, September 8-11, Stockholm, Sweden

Presentations

Juvenile myoclonic epilepsy with old age beginning

Tóth V, **Kalmár Zs**, Janszky J

Magyar Epilepszia Liga Tudományos Ülése, May 22-24, 2008, Miskolc, Hungary

Obesity, body mass regulation and central nervous system: volumetric MRI studies

Orsi G, Plózer E, **Kalmár Zs**, Sellyei E, Schwarcz A, Perlaki G, Karádi K, Janszky J

Magartartástudományi Napok, X. Jubileumi Konferencia, May 25-26, 2010, Pécs, Hungary

Secondarily generalized seizures in temporal lobe epilepsy

Bóné B, Fogarasi A, Schulz R, Gyimesi C, **Kalmár Zs**, Kovács N, Ebner A, Janszky J.
Magyar Epilepszia Liga Kongresszusa, May 31, June 1-2, 2012, Kaposvár, Hungary

International presentations given since the thesis has been written:

Effects of spinal cord stimulation on heart rate variability in patients with chronic pain

Kalmár Zs, Janszky J, Kovács N, Balás I.

III. Neurostimulációs szimpózium, October 12-13, 2012, Pécs, Hungary

Reorganization of motor system in Parkinson's disease

Kalmár Zs

III. Neurostimulációs szimpózium, October 12-13, 2012, Pécs, Hungary

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