SUMMARY

This article is written to commemorate the 40th year of the scientific career of Professor Maria Pąchalska, Head of the Department of Neuropsychology and Neurorehabilitation at Krakow University, President of the Polish Neuropsychological Society, and the Editor-in-chief of Acta Neuropsychologica, with whom I have been collaborating for over ten years. The subject matter of our work includes the introduction of HBI methodology to clinics and the search for neuromarkers in particular disease entities.

What is the new methodology we are talking about? In general, we think of a biomarker (or biological marker) as a characteristic that can be objectively measured and evaluated as an index of normal or pathological biological processes. For disorders of the central nervous system, biomarkers can be classified as clinical, neuroimaging, biochemical or genetic, according to the type of information they provide. Expectations for the development of biomarkers are high, since they could lead to a significant improvement in diagnosing and possibly preventing neurological and psychiatric diseases.

Neuroimaging is an array of neuroscience methods that include the techniques of magnetic resonance imaging (MRI), functional MRI (fMRI), and PET (positron emission tomography), as well as Electroencephalogram (EEG) and Magnetoencephalogram (MEG) techniques, such as quantitative EEG (QEEG), event related de/synchronization (ERD/ERS) and event-related potentials (ERPs).

Key words: neuroimaging, quantitative EEG, event related de/synchronization, event-related potentials
TYPES OF SCIENTISTS

There are two types of scientists:

1) those who are investigating the details of already established facts and are trying to reveal the truth of nature hidden behind those details;
2) those who are searching for new facts and trying to establish new approaches to nature.

If you compare science with a process of building a house, the first type are bricklayers, the second type are architects. Maria Pachalska definitely belongs to the second type of scientists. She is an architect of neuropsychology who is searching for new windows to look at brain functioning.

HISTORY

I met Professor Maria Pachalska for the first time in Wroclaw in 2007, at a conference organized by a Polish organization – Fundacja “Promyk Słońca” (see: Fig. 1). She was lecturing about affective brain functioning from the perspective of a neuropsychologist, but instead of conventional neuropsychological terminology she used many neuroscience concepts.

As a neuroscientist with a mathematical background I was fascinated by this new neuroscientific approach to neuropsychology. We had a short talk at the coffee break and immediately realized that we were speaking the same scientific language. She discovered for herself the possibility of using functional neuromarkers in neuropsychology, and our joint journey into this fascinating field had begun.

Fig. 1. Prof. Maria Pachalska, MD., Ph.D., the President of the Polish Neuropsychological Society, Editor-in-Chief of Acta Neuropsychologica
Source: Library of Prof. Juri D. Kropotov
WHAT IS A FUNCTIONAL NEUROMARKER?

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Using neuroscience methods, very many objective measures of brain anatomy and physiology can be obtained in clinical practice. These objective measures are called neuromarkers. The term comprises any neuropsychological parameter of behavior, any structural or functional index of the brain. The structural parameters include anatomical measures of brain anatomy and axonal pathways taken from postmortem brains or from in vivo by MRI and Diffuse Tensor Imaging (DTI). PET is used for in vivo imaging of neurotransmitter systems within the brain. Functional parameters include dynamic measures of brain metabolic activity in a second/deco-second time frame by means of fMRI, PET, as well as dynamic measures of brain electrical activity at millisecond time resolution by means of EEG/MEG, including event-related potentials (ERPs).

There is a consensus that an ideal biomarker must have 1) diagnostic sensitivity > 80, and 2) diagnostic specificity > 80%. In addition, the biomarker must be 3) reliable, reproducible, and inexpensive to measure, non-invasive, and simple to perform, 4) confirmed by at least two independent studies conducted by qualified investigators with the results published in peer-reviewed journals. All those requirements are fulfilled for ERPs.

WHY USE FUNCTIONAL NEUROMARKERS IN NEUROPSYCHOLOGY?

Historically neuropsychology studies the structure and function of the brain in relation to psychological processes. The goal of neuropsychology is to understand how behavior and cognition are influenced by brain functioning, and to use this knowledge for the diagnosis and treatment of the behavioral effects of neurological disorders. So basically, the term neuropsychology has been associated with lesion studies in humans and animals.

Batteries of neuropsychological tasks have been designed to associate specific performance on the task with specific neurophysiological processes. These tests
are standardized so that the normative data (means and standard deviations) for a healthy population are computed. These data are as the comparative standard against which individual performance in the tasks is compared. Examples of neuropsychological tests include the Wechsler Memory Scale, the Wechsler Adult Intelligence Scale, the Boston Naming Test, the Wisconsin Card Sorting Test etc.

In the new approach that Maria Pachalska and I are developing, functional neuromarkers as indexes of brain functioning are added to the arsenal of tools of neuropsychology. This opens a new window to brain functioning and enables the user to directly assess neuronal activity associated with different neuropsychological operations in sensory, affective, memory and cognitive domains.

**CURRENT STATUS**

In 2011, Maria Pachalska organized the Chair of Neuropsychology an Neuorehabilitation at the Andrzej Frycz Modrzewski Krakow University. Together we started a series of lectures and workshops for students, in which we taught the new methodology of neuropsychology with functional neuromarkers as the key concept.

Moreover, we applied this methodology to clinical practice and tested many patients with different psychiatric conditions. The results of the work have been published in a series of papers (see the list of papers at the end of this article). In 2014, a book entitled “Neuropsychologia kliniczna” by Professors Pachalska, Kaczmarek and Kropotov was published by the Wydawnictwo Naukowe PWN SA. This book summarized our research.

**NORMATIVE DATABASE**

In the series of our joint studies with Maria Pachalska we assessed functional neuromarkers in patients with ADHD, schizophrenia, obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), brain tumor, and traumatic brain injury (TBI). We also assessed functional neuromarkers in highly functioning healthy subjects, such as athletes. For the last studies, the author of this paper was awarded the title of Doctor Honoris Causa by the Academy of Physical Education and Sport in Gdansk (see: Fig. 2).

Functional neuromarkers in our studies have been used not only for the diagnosis of brain dysfunction, but also for constructing protocols of neuromodulation, such as neurofeedback, transcranial direct current and transcranial magnetic stimulation (tDCS and TMS). We also used pre- and post- recordings of functional neuromarkers for monitoring the results of treatment by means of neuromodulation techniques.

For comparison with healthy controls we used the normative Human Brain Index (HBI) a database obtained in joint research by Swiss, Norwegian and Russian neuroscientists. The database included behavioral parameters and ERP measures in 6 different neuropsychological tasks of 1000 healthy subjects. In the data collection, subjects were recorded by 19-channel EEG during two rest-
ing state conditions with eyes open and eyes closed and in six task conditions (three passive stimulus tasks presenting standard, deviant and novel sounds, an active auditory oddball task, two cued GO/NOGO tasks with animal/plants and happy faces/angry faces as GO/NOGO stimuli, a mathematical task with arithmetical operations on visually presented numbers, and a reading task with matching auditory and visually presented stimuli. The age of subjects was between 7 and 90 years, so that all subjects were able to complete the tasks with a relatively small numbers of errors. To improve the signal-to-noise ratio for ERPs, the number of trials in each category was selected to be 100, except the passive auditory three-stimulus task, where the number of standard trials was 2000.

**AN EXAMPLE OF THE APPROACH**

To give some sense of the methodology used in our studies I show here a recent example from a study on a patient with PTSD (see: Fig. 3). His behavioural parameters of cognitive control, such as omission error’s were quite normal, but ERP measures clearly indicated hypo-activation of the pre-supplementary motor cortex – a hallmark of dysfunction of the brain system responsible for action inhibition/overriding of prepared action in situations when this action either is not needed or must be replaced by another action.

Knowing the brain dysfunction in this patient we can suggest neuromodulation techniques for activation this cortical area by neurofeedback, tDCS or TMS. This example demonstrates the use of the new methodology for assessment brain dysfunction as well for constructing protocol of neuromodulation.

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**Fig. 2.** Prof. Maria Pachalska (reviewer) on the ceremony of awarding Prof. Kropotov the title of Doctor Honoris Causa at the Akademia Wychowania Fizycznego i Sportu in Gdańsk, Poland

Source: Library of Prof. Juri D. Kropotov
NEW VISTAS IN NEUROPSYCHOLOGY

Ivan Pavlov said that science develops in steps, with each step opening a new technology and a new window to nature. In the field of neuroscience, we are now facing a decade of translation, which focuses on applying functional neuromarkers obtained by neuroscientific methods for early detection and prevention of brain abnormalities associated with mental disorders. The research of Professor Pachalska (and her team) plays a leading role in this approach.

RECENT RESEARCH ARTICLES BY MARIA PACHALSKA (AND HER TEAM) RELATED TO THE APPLICATION OF FUNCTIONAL NEUROMARKERS IN NEUROPSYCHOLOGY


Fig. 3. Dysfunction of the pre-supplementary motor cortex in a patient with PTSD. Left and right. Two independent components of event-related potentials in GO/NOGO task for the patient (green) in comparison to the grand-average ERP of a group (N=23) of healthy subjects of corresponding age (red). Bottom – topography of the component. Right – sLORETA image of the topography. Source: Pótrola, Kaczmarek, Góral-Pótrola et al (2016)


