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NEUROPHYSIOLOGICAL BASIS OF MICROGENESIS THEORY: STAGES OF VISUAL INFORMATION FLOW AS REFLECTED IN FUNCTIONALLY DEFINED COMPONENTS OF EVENT RELATED POTENTIALS IN MAN

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*"Every step forward, in life and in thought, is a return
to a beginning..."*

Jason W. Brown The self-embodying mind.

SUMMARY

This is a first study that experimentally tested the basic premise of microgenetic theory: existence of recurrent stages of information processing in the brain. The application of Independent Component Analysis (ICA) to a substantial number of individual multi-channel ERPs in two variants of the cued GO/NOGO task enabled us to decompose the sensory-related ERP waves into four functionally distinct components. In the first variant of the cued GO/NOGO task images of plants were compared with images of animals (Animal-Animal pairs corresponded to GO trials, whereas Animal-Plant pairs corresponded to NOGO trials), in the second variant faces of the same person with different emotional expressions were compared. According to sLORETA the extracted components were generated in the occipital, left and right temporal and right parietal cortical areas. Each of the components was characterized by two sequential activation patterns in the GO condition. Each activation pattern included a positive fluctuation followed by a negative fluctuation. In the NOGO condition an additional mismatch positivity followed the GO-like positive fluctuation. At the early stage (around 160 ms after stimulus) the mismatch positivity at the left temporal component was associated with the hypothetical operation of comparing the physical features of the stimuli with working memory. At the late stage (around 260 ms) the mismatch positivity at the left temporal component was associated with the operation of comparing semantic features of the stimuli with working memory.

Key words: neurometrics, electroencephalography (EEG), ERPs, sensory-related components, microgenetic theory, Russia

INSTEAD OF AN INTRODUCTION: A FLASH BACK

The first author's initial acquaintance with microgenesis theory happened in the late 1980s, just before the collapse of the Soviet Union. A psychologist from Tartu University in Estonia (the former republic of the Soviet Union), Talis Bachmann, was visiting my laboratory. In those days the lab was located at the Institute of Experimental Medicine of the Medical Academy of Sciences of the USSR. Talis had recently come from the United States, where he had learned microgenetic theory from Jason W. Brown.

On the basis of the microgenetic approach, Talis developed a perceptual retouch theory (Bachmann, 1984) in which he suggested that specific sensory information processing is modulated ("retouched") by activity of "non-specific" brain areas. Occupied by this idea, he came across my studies on reflection of cognitive functions in the basal ganglia thalamo-cortical networks. That was exactly what he was looking for. That is how we met with Talis.

Together we carried out a pilot study on neurological (Parkinson's disease, phantom pain, epilepsy) and psychiatric patients (OCD) to whom electrodes were implanted for diagnostic and therapeutic purposes (Gogolitsin & Kropotov, 1983). We recorded impulse activity of multiple neurons located near the electrodes in a psychological test in which visual stimuli (digits of the red LED matrix) were presented at near threshold expositions. Digits were presented in pairs so that at some interstimulus intervals the patients were not able to correctly identify the order in which they were presented.

In the globus pallidus of the Parkinsonian patients we found neurons that were suppressed by stimulus presentation. If the two stimuli induced clear separated responses in the pallidal neurons the patients were able to perform the task, but if the responses were overlapped they had clear difficulties. So it looked like the neurons in the basal ganglia indeed retouched the sensory input. Unfortunately, shortly after this pilot study the Soviet Union collapsed. Estonia became an independent country and the connection between the Institute of Experimental Medicine in Saint Petersburg in Russia and Tartu University in Estonia was lost.

EXTRACTING FUNCTIONALLY MEANINGFUL COMPONENTS FROM EVENT-RELATED POTENTIALS: A NEW APPROACH

After the collapse of the Soviet Union in 1991 funding for fundamental research decreased dramatically. Our laboratory was forced to start doing more practical and financially profitable activities. Together with the Institute of Television in 1992 we created a company ambitiously named "Potential". The company was intended to design EEG recording and analyzing hardware/software. We further used these devices in our laboratory for doing research on quantitative EEG (QEEG) and event related potentials (ERPs) in the ADHD population (Kropotov et al., 2005).

One of the goals of my laboratory in those days was to develop a diagnostic ERP-based procedure that would enable us to discriminate various diagnostic psychiatric conditions. It also became clear for me that the traditional way of separating functionally meaningful ERP waveforms that existed in those days was not sufficient for clinical practice. The idea was to find a method that would decompose the multi-channel ERPs into functionally meaningful components. After trying several different approaches we chose Independent Component Analysis (ICA). This method worked very well when applied to a collection of ERPs computed for a substantial number of healthy subjects performing a psychological task with varying stimulus-response associations (Kropotov & Ponomarev, 2009; Kropotov et al., 2011; Pachalska et al. 2011).

The goal of Independent Component Analysis (ICA) is to utilize the differences in scalp distribution between different generators of ERP activity to separate the corresponding activation time courses (Makeig et al., 1996). Components are constructed by optimizing the mutual independence of all activation time curves, leading to a natural and intuitive definition of an ERP component as a stable potential distribution which cannot be further decomposed into independently activated sources.

In our approach ICA was performed on the full “ERP scalp location” x “Time series” matrix. The assumptions that underlie the application of ICA to individual ERPs are as follows (Makeig et al., 1996; Onton, Makeig, 2006):

- (1) the summation of the electrical currents induced by separate generators is linear at the scalp electrodes;
- (2) the spatial distribution of the components’ generators remains fixed across time;
- (3) the weights of the components vary independently across different task conditions and across different subjects.

Briefly, the method implemented is as follows: The input data are the collection of individual ERPs arranged in a matrix P of 19 channels (rows) by T time points (columns), where T is a product of N (number of subjects) and number of time intervals in the epoch of analysis for the two task conditions. The ICA finds an “unmixing” matrix (U) that gives the matrix S of the sources (ICs) when multiplied by the original data matrix (P),

$$S=UP$$

where S and P are $19 \times T$ matrices and U is a 19×19 matrix. $S(t)$ are maximally independent. In our work matrix U is found by means of the Infomax algorithm, which is an iteration procedure that maximizes the mutual information between S .

According to linear algebra,

$$P=U^{-1}S,$$

where U^{-1} is the inverse matrix of U (also called the “mixing matrix”), and the i -th column of the mixing matrix represents the topography of the i -independent

component; S_i represents the time course of the i -independent component. The ICA method (Makeig et al., 1996) was implemented in the analysis software written by a senior researcher of my laboratory, V.A. Ponomarev. The topographies and activation time courses of the components were tested against the corresponding results obtained by means of "InforMax" software in EEGLAB, a freely available interactive Matlab toolbox for processing continuous and event-related electrophysiological data (<http://sccn.ucsd.edu/eeglab>). The topographies of the independent components are presented as topographic maps, while the time courses of the components (also called "activation time courses") are presented as graphs, with time corresponding to the X-axis.

PROCESSING DIFFERENT TYPES OF IMAGES: PLANTS, ANIMALS, FACES

In this paper we are going to focus on ERP components associated with stages of visual processing. We designed two types of the cued GO/NOGO task (Fig 1A). In the first experimental condition (Exp 1) the stimuli were images of plants and animals presented in various pairs, such as A-A, A-P, P-P trials, with the instruction to press the button as fast and as precisely as possible whenever an AA-pair appears (Fig 1B). In this task, an A-A pair is a GO condition and an

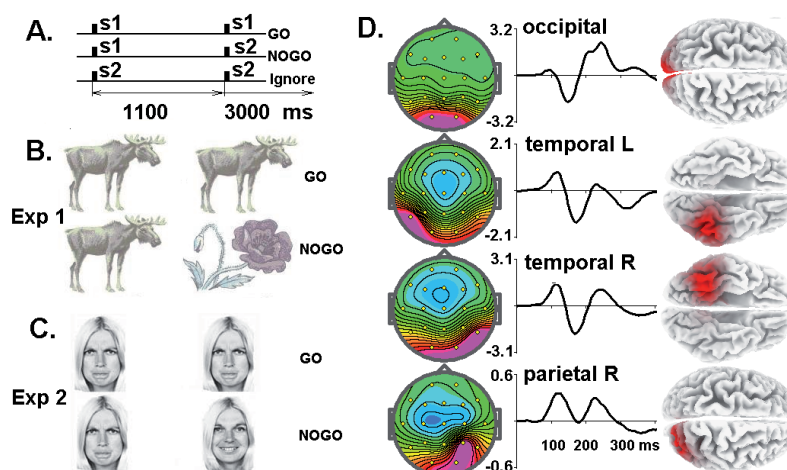


Fig. 1. Independent components of Event Related Potentials (ERPs) reflecting visual sensory processing

A: scheme of the cued GO/NOGO task. In the task s1 and s2 stimuli are presented in pairs s1-s1, s1-s2, s2-s2 with the subject task to press a button in response to s1-s2 pair as fast and as precise as possible.

B: examples of stimuli in experiment 1.

C: examples of stimuli in experiment 2.

D: from left to right, topographies, time dynamics and sLORETA images of the sensory-related independent components separated by Independent Component Analysis applied to a collection of ERPs recorded in Experiments 1 and 2. On graphs – X-axis – time in ms, Y-axis – amplitude in standard units.

A-P pair is a NOGO condition. In the second experimental condition, the stimuli were images of angry (AF) and happy (HF) faces presented in various pairs (AF-AF, AF-HF, HF-HF trials), with the instruction to press the button as fast and as precisely as possible in response to an AF-AF-pair, so that an AF-AF pair is the GO condition and an AF-HF pair is the NOGO condition (Fig 1C). The interstimulus interval within pairs was 1000 ms, the interval between trials was 3000 ms. The number of healthy subjects participating in Exp 1 was 247, the number of subjects participating in Exp 2 was 143. The age of the subjects varied from 17 to 50 years.

THEORETICAL MODEL

Previous research has developed a background for a theoretical model of operations taking place in the GO/NOGO paradigm. In 1984, the concept of preparatory set was introduced for the explanation of higher cognitive functions (Evarts et al., 1984). Briefly, two preparatory sets were defined: a state of readiness to receive a stimulus and a state of readiness to perform a movement. In terms of the GO/NOGO paradigm with equal GO and NOGO probabilities, when the task instruction is presented to a subject, a prepotent model of behavior is formed in neuronal networks of the brain (see also the review by Folstein & Van Petten, 2008). This neuronal model includes two parts: a sensory part, i.e. preparation to receive a stimulus (GO cue), and an executive part, i.e. preparation to perform an action in response to the GO cue. The ERP correlates of these two preparatory activities were found in contingent negative variations (CNVs) recorded from the scalp in the paired stimulus paradigm in response to warning cues (Rohrbaugh et al., 1986).

In the GO/NOGO design in our study, sensory and motor preparatory sets are primed by the first stimulus in pairs. When an image of an animal in Exp 1 (or an image of an angry face in Exp 2) is presented as the first position in a pair, the subject is preparing to respond to the same image in the second position, so that there is preparation to receive the same image and preparation to press a button. A mismatch in the sensory domain elicits sensory mismatch operations, while a mismatch in the motor domain elicits action suppression and conflict monitoring operations.

FUNCTIONAL MEANING OF INDEPENDENT COMPONENTS

The functional meaning of the independent components in Exp 1 was studied by changing stimulus response association in this experimental design (Kropotov et al., 2011). Three variants of the same stimulus task manipulated sensory mismatch, action inhibition and conflict monitoring operations by varying stimulus-response associations. The anterior N2 and P3 waves obtained by subtracting GO ERPs from NOGO ERPs were decomposed into components by means of

independent component analysis (ICA). Three of the independent components were selectively affected by the task manipulations, indicating the association of these components with sensory mismatch, action inhibition and conflict monitoring operations. According to sLORETA the sensory mismatch component was generated in the left and right temporal areas, the action suppression component was generated in the supplementary motor cortex, and the conflict monitoring component was generated in the anterior cingulate cortex.

SENSORY-RELATED COMPONENTS IN THE VISUAL MODALITY

The visual-related independent components extracted in the cued GO/NOGO task are presented in Fig. 1 D. The first component is generated in the primary and secondary visual cortical areas. This component appears to reflect the fastest information processing. Indeed this component reaches its first positive peak as fast as 96 ms both for Exp 1 and Exp 2. The time dynamics of this independent component resembles the conventional visual P1/N1 waves commonly found in visual recognition tasks (see, for example, Hillyard & Anllo-Vento, 1998). The localization of this component in occipital areas is almost identical in localization with the P1 component in high-density ERPs recording in the GO/NOGO paradigm (Bokura et al., 2001).

Two other components are generated in the inferior temporal cortical areas in the left and right hemispheres. Each of these components in GO condition shows a sequence of positive/negative fluctuations (as measured at T5 and T6 respectively). The positive fluctuations have peak latencies at 120 and 240 ms respectively. These positive fluctuations are followed by negative fluctuations with peak latencies at 170 ms and 300 ms respectively. The temporal independent components appear to correspond to bilateral occipitally-temporally distributed N170 waves, described in numerous studies on ERP correlates of object processing in visual recognition tasks (Itier & Taylor, 2004). The localization of the temporal components found in the present study is similar to the localization of the N170 wave in a high-density GO/NOGO ERP study by Bokura et al. (2001), who, by using LORETA imaging, localized their N170 ERP wave bilaterally in the inferior temporal cortex. Additional mismatch positivities emerged in the NOGO (sensory mismatch) condition, with latencies of 160 and 260 ms.

Finally, the fourth component is generated in the right inferior parietal cortex. This component appears to be the fastest to register the mismatch between stimuli in Exp 1.

SENSORY MISMATCH IN THE TEMPORAL COMPONENTS

In our previous study (Kropotov et al., 2011) the sensory mismatch operation was manipulated in the experimental task, in which subjects had to press a but-

ton, not to A-A trials as in the above described experiment Exp 1, but to A-P trials. In this condition no sensory template was formed, and the difference in the NOGO-GO wave at early time intervals disappeared (Kropotov et al., 2011). This fact enabled us to associate the NOGO-GO difference at the temporal component with the active sensory mismatch operation. Our data fit well with other ERP studies showing that the mismatch operation in the sensory domain is reflected in a temporal wave with frontally distributed N2 counterpart (Wang et al., 2003; Kimura et al., 2005). In contrast to auditory attention independent mismatch negativity (Näätänen et al., 1978), this wave appeared only in an actively attended mismatch between stimulus and mental template (Fu et al., 2003).

The current study enabled us further to dissociate the sensory mismatch component into two parts: the early part, with latency of about 160 ms, and the late part, with a latency of about 260-270 ms. The late parts are present in both Exp 1 and Exp 2, but the early part disappears in Exp 2.

We can speculate that the early part in the sensory mismatch of the temporally localized component is associated with comparing the physical features of the stimuli with working memory. Indeed, as one can see from Fig 1B and C, the physical features of the stimuli (animals and plants) in Exp 1 are quite different, while in Exp 2 they are almost identical. Further, we suggest that the late part of

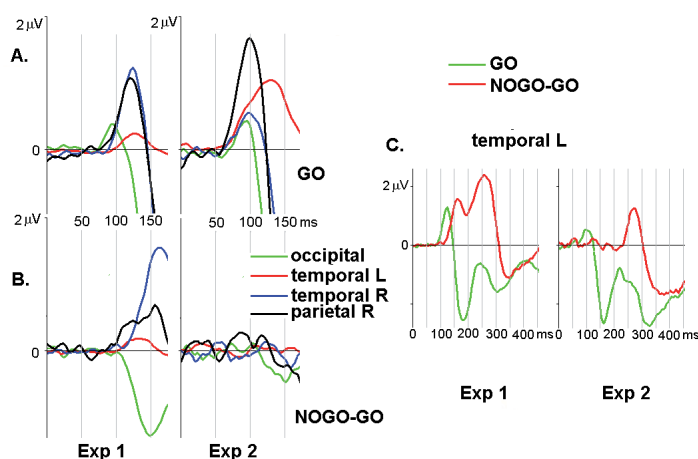


Fig. 2. Activation patterns and mismatch-related NOGO-GO differences for sensory-related independent components

A: activation patterns in GO condition for the four sensory-related independent components computed separately for Exp 1 (left) and Exp 2 (right). Independent components are named according to localization of their cortical generators (as shown by sLORETA) and their dynamics are colored differently. X-axis – time in ms. Note that only the first 200 ms are depicted. The components are projected to electrodes by means of spatial filtration of ERPs. The corresponding time courses are presented at the electrodes at which the projected components reach their maximums or minimums. Y-axis – amplitude in μV .

B: the NOGO-GO difference patterns.

C: activation patterns in GO condition (green line) and the NOGO-GO difference patterns for the independent component generated in the left temporal cortex and computed separately for Exp 1 (left) and Exp 2 (right).

the sensory mismatch component is associated with the semantic/emotional meaning of the stimuli. Indeed, the semantic/emotional meanings of stimuli in Exp 2 are quite different: angry vs. happy expressions of the same face. In this context, we can infer that processing the semantic meaning of the stimulus takes the brain an additional 100 ms in comparison with processing the physical features of stimuli. It is also important to mention that the early mismatch component follows the first positive peak at 120 ms of the activation pattern at GO condition, whereas the late mismatch component follows the second positive peak at 240 ms of the activation pattern at GO condition.

In sum, we can hypothesize that the sensory processing in temporal areas occurs in two stages. Each stage is characterized by a positive-negative pattern of activation of the left temporal cortex in the match (GO) condition. In the mismatch (NOGO) condition, additional activation positivity emerges at each stage. This mismatch positivity follows the positive activation positivity with a 20-40 ms delay. We can further suggest that the second stage represents a recurrent activation pattern, in which a more sophisticated (semantic vs physical) stimulus comparison operation takes place.

CONCLUSION

This study appears to be the first attempt to test experimentally the basic premise of microgenetic theory: the existence of recurrent stages of information processing. The application of Independent Component Analysis to a collection of a substantial number of individual multi-channel ERPs in two variants of the cued GO/NOGO task enabled us to decompose the sensory-related ERP waves into four functionally distinct components. According to sLORETA these components are generated in the occipital, left and right temporal and right parietal cortical areas. Each of the components is characterized by two sequential activation patterns in GO (sensory Match) condition. Each activation pattern includes a positive fluctuation followed by a negative fluctuation. In NOGO (sensory Mismatch) condition an additional potential fluctuation follows the positive fluctuation. At the early stage the additional positivity in the left temporal component is associated with comparing physical features of the stimuli with the memory trace. It should be noted that this additional (mismatch) processing occurs later than the one in the right parietal cortex. This observation fits the theory that information processing in the dorsal visual stream is faster than processing in the ventral visual stream. At the late stage, the additional positivity in the left temporal component is associated with the operation of comparing semantic features of the stimuli with working memory.

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