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Review

COGNITIVE EVOKED POTENTIALS: A METHOD FOR INVESTIGATION OF LANGUAGE PROCESSING IN BRAIN

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Abstract

Electroencephalography is a method for the record of brain's spontaneous electrical activity. During electroencephalography recording an additional signal not related to brain activity can also be captured. This signal, so-called artifact, is considered as a noise and it should be avoided or removed from the recorded signal afterwards. Furthermore, during the exception of the signal contaminated with artifact from further analysis, there are number of methods for the removal of artifact with the preservation of signal recorded from brain. Among those methods independent component analysis, second-order blind identification and others can be singled out.

Cognitive evoked potentials present the electrical activity of brain in response to external stimulus and reflect its cognitive activity. Unlike electroencephalography, which is widely used in clinic, the technique of cognitive evoked potentials is currently used only for research purposes. Despite this, its potential is already proved in the early detection, confirmation of diagnosis and prognosis of a number of neurological (aphasia, mild cognitive decline, dementia) and psychiatric (schizophrenia, depression) disorders.

Due to its optimal temporal resolution, the technique of cognitive evoked potentials is widely used in investigation of language comprehension's separate aspects, since those processes evolve within milliseconds. The most studied cognitive evoked potentials that are elicited in response to linguistic stimuli are early left anterior negativity, left anterior negativity, P600 and N400. First three is believed to reflect the syntactic processing and the last one – the processing of semantics by brain. Early left anterior negativity peaks around 150-200 ms after the presentation of interest stimulus (post - onset) and reflects the parsing of word-category and its prediction in the sentence context. Left anterior negativity can be elicited in response to subject – verb disagreement and gender of nouns. It peaks about 400 ms post – onset and has more left and anterior location on the scalp. P600 reaches its highest amplitude about 600 ms post – onset and represents syntactic re-analysis of sentence. It can be elicited in response to both syntax violation and so called "garden path phenomenon".

Unlike previous cognitive evoked potentials, N400 reflects the processing of semantics (potentially meaningful stimulus). It is elicited in response to both linguistic and non-linguistic specific (pictures, natural sounds, videos) stimulus.

Keywords: *electroencephalography, cognitive evoked potentials, artifacts, speech processing.*

Electroencephalography, physiological origin, cognitive evoked potentials: Electroencephalography (EEG) and its components, so-called cognitive evoked potentials (CEP), are one of the effective methods for investigation of cognitive processes along with psychological tests and MRI.

Electroencephalography is a method for the recording of spontaneous electrical activity of cerebral cortex [*Ropper A et al., 2009*]. For each synapse, whenever a neurotransmitter binds to the receptors of the postsynaptic membrane, ionic membrane channels are opened or closed leading to a change in membrane potential. This in turn changes the potential of the apical (negative) dendrite as well as that of the basal dendrite and the cell of body (positive) leading to the formation of a small dipole. In case of a simultaneous generation of such inhibitory and excitatory potentials, dipoles can cancel each other out if they have opposite directions. As pyramidal cells in cerebral cortex are pCEPendicular to cortical surface, than the dipoles formed in these cells are orthogonal to the skin of brain, as a result of which it is possible to measure the effect of post-synaptic potentials on

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the scalp's surface. These recording scalp potentials are called electroencephalography. CEPs are stereotypical EEG potentials that are formed in response to external stimulus [*Luck S, 2005*]. As the electrical currents associated with these dipoles can be propagated throughout the whole cerebral cortex, the potential generated in one brain area can be detected on another brain area. This makes spatial resolution of CEP technique quite poor. However the main advantage of this method is its excellent temporal resolution. It is also non-invasive, inexpensive and highly portable technique, which can be used outside the hospital or laboratory. Unlike the existing available psychological tests with the recording of response speed, the CEP method can detect changes that occur in cerebral cortex long before the behavioral response is recorded. CEPs can even be recorded without the need of behavioral reaction or an additional task, which facilitates the examination of patients with motor or verbal disorders. Furthermore, when an additional task is involved, as the subject could apply a strategy for solving this task, the recordings could not reflect the cognitive activity one is interested in.

Electroencephalography in clinical practice: Electroencephalography is widely used in clinical practice. Present medical technique almost daily is used for the diagnosis of several neurological disorders including different types of epilepsy [*Panayiotopoulos C, 2005*], cognitive decline of an unusual genesis (for example, Creutzfeldt-Jakob disease, etc.) [*Wieser H et al., 2006*], prognosis of global hypoxic-ischemic encephalopathy [*Murray D et al., 2009*] and etc. But unlike the clinical use of electroencephalography, the CEP technique is of great importance while its use for diagnosis confirmation purpose, early detection and prognosis of several neurological disorders as mild cognitive impairment and dementia, schizophrenia, aphasia and other speech disorders [*Papaliagkas V et al., 2008; 2011; Saavedra C et al., 2012; Gozke E et al., 2013*; *Thurm F et al., 2013; Jiang S et al., 2015*]. However unlike the present dividends, CEP method is still the subject of separate investigation, observation and improvement.

Electroencephalography recording: Electroencephalography is usually recorded by placing on the subject's scalp a cap in which electrodes are mounted. Additionally, electrodes for reference and ground are used. The latter is usually placed as far from the brain and other sources of electrical activity (mostly muscles and heart), as possible. It is usually placed on one of the mastoid bones, the tip of the nose or the earlobe. The reference electrode is usually placed on the other mastoid bone or the other earlobe (E_1, E_2) (Fig. 1). There are mostly two types of electrodes – active and passive. Active electrodes are immediately connected to amplifiers to provide a better signal. A drop of gel is applied between each electrode and the skin to lower the impedance between the electrode and skin.

Artifacts and cognitive evoked potentials*:* During electroencephalography recording process, signals coming from other sources can become convolved with the signal of interest and are regarded as noise. There are two main types of noise: 1) physiological noise, coming from the body (heartbeat, ocular movements, eye blinking and other muscle activity like chewing, swallowing, and so on) and 2) non-physiological noise due to external sources such as electrical devices. Often the signals of non-cerebral origin are referred as artifact [*Fisch B, 1999*]. There are several ways to obtain as clean electroencephalography signal as possible. One way is to avoid such noise sources; the other one is to clean the recorded signal afterwards. Among the options to avoid the contamination by noise is to restrict the number of electrical devices in the room, to dim the lights in the room, to shield the amplifier from environment and to use active electrodes. Though this might help to partially cope with artifacts, there are some types of noise that are unavoidable. Among these are artifacts connected to eye movements, eye blinking, heartbeat, and so on, especially while working with vulnerable subject groups, such as patients or children. The rejection of signal parts contaminated with artifact is the generally accepted method for the minimization of artifacts' data. This procedure can lead to the loss of a significant amount of valuable data depending on the task, type and duration of the experiment. That is why different methods for artifact rejection (e.g. – independent component analysis or second-order blind identification) are widely adopted [*Makeig S et al., 1996; Jung T et al., 1998; Jung T et al., 2000*].

Among a number of methods for the rejection of eye-movements and blinking artifacts, electroencephalography is offered to be used by electroocu-

logram method, placing electrodes among th eyes, one electrode is on the external canthi of the right and left eye for the record of their horizontal movements (E_3, E_4) and the other one below and above the right or left eye for the record of vertical movements (Fig. 1) [*Croft R, Barry R, 2000*]. Sometimes, in order to reject artifacts due to heartbeat, in parallel, the heartbeat is also monitored. In order to clean the data from power-line noise (50 or 60*Hz*), which comes from the other electrical devices in the room (computers, wall-sockets, monitors etc.), one uses notch filter for the signal. Furthermore, depending on the signal of interest, filtering may be in the different range, like: 0.1-30*Hz*, 0.5-70*Hz*, and so on.

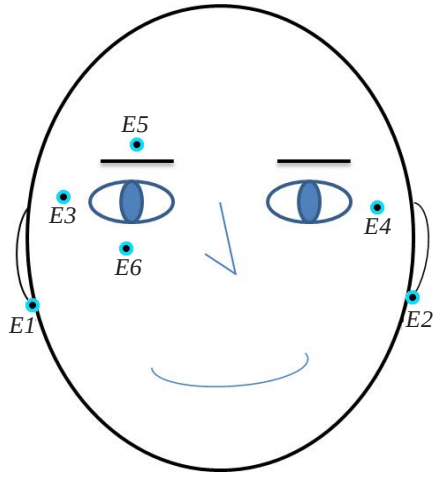

FIGURE 1. *Distribution of reference and ground electrodes for electrooculogram recording.*

Paradigms for cognitive evoked potentials: One of the important features of CEP technique is the use of paradigm: stimuli elicited by the participants of study (verbal, textual, visual) in response to which CEPs are evoked by brain. In order to correctly design a CEP experiment, one should manipulate single stimulus parameters with the assessment of its effect on CEPs.

Types of cognitive evoked potentials in speech processing: Taking into account its optimal temporal resolution, the technique of CEPs is often used for investigating the time-course of speech processing in brain. The most investigated CEPs that are related to speech processing are the early left anterior negativity (ELAN), left anterior negativity (LAN), P600 and N400. The first three are believed to reflect the syntactic parsing of written and conversational speech (words, sentences, paragraph) whereas the last one reflects semantic processing.

ELAN refers to early left anterior negativity and occurs in the range from 150 to 200 *ms* after the presentation of verbal stimulus of interest and is more biased to the left hemisphere. It is believed to be related to the parsing of word-category and the prediction of the latter in the context of a sentence [*Friederici A et al., 1993; Lau E et al., 2006*]. So, in order to evoke an ELAN, sentences with a violation in word category should be presented as a stimulus (e.g. the baby was in the fed vs. the baby was fed) (Fig. 2). In case of an auditory presentation of the sentence, the word category can be changed by switching the suffix and prefix, by adding or removing the suffix, and so on (e.g. refine vs. refinement, illegal vs. legalization).

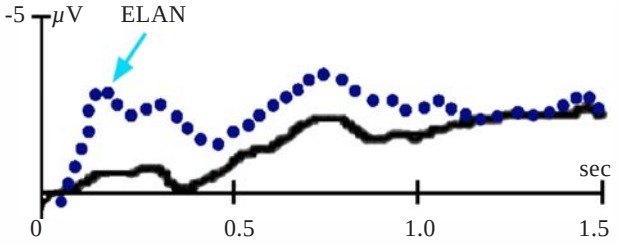

FIGURE 2. *Early left anterior negativity elicited in response to word-category violation* [*Friederici A, Kotz S, 2003*].

LAN stands for left anterior negativity. It is located on the frontal region of the left hemisphere in the range from 300 to 500 *ms* post-onset with a peak around 400 *ms*. It represents the morpho-syntactic integration of words in a sentence and is elicited in response to a subject-verb disagreement (The girl play with the dog. vs. the girl plays with the dog) [*Osterhout L, Mobley L, 1995*] and in response to gender violation [*Gunter T et al., 2000*], e.g., "He apologize" vs. "He apologizes". The manipulation or violation of prepositions in the sentence context may elicit a LAN (e.g. they eat restaurant vs. they eat in the restaurant). In addition, the LAN is believed to reflect working memory span for speech processing [*King J, Kutas M, 1995*]. That is why complex sentences, such as "The reporter (who harshly attacked the senator) admitted the error" evoke smaller LANs compared to compound sentences such as "The reporter (who the senator harshly attacked) admitted the error".

P600 is a widely investigated positive potential that peaks around 600 *ms* post-onset (Fig. 3). P600 is believed to be responsible for syntactic re-anal-

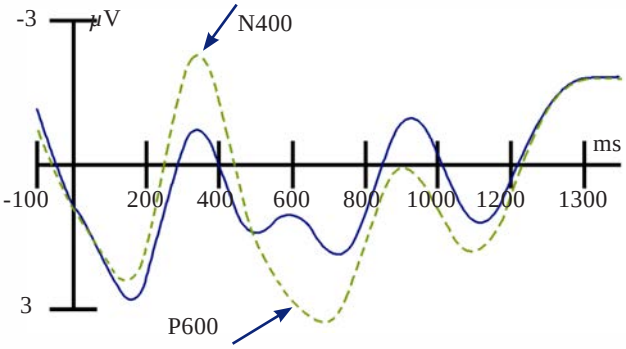

Figure 3. *CEPs elicited in response to semantic (N400) and syntactic violation (P600) in the sentence* [*Gouvea A et al., 2010*].

ysis of a sentence or paragraph. It can be elicited in response to both syntactic violations in the sentence and to the so called "garden path phenomenon" [*Gouvea A et al., 2010*]. In this "garden path phenomenon" the sentence as a whole is meaningful, but the reader must reconsider the sentence after getting the punch line point. For instance, in the sentence "The broker persuaded…" the reader would rather expect to have a direct object like "the man" such as in the following sentence "The broker persuaded the man to sell the stock", compared to an indirect object like "to sell" in the sentence like "The broker persuaded to sell the stoke was sent to jail". Both sentences are congruent (correct), but for the second sentence the reader must consider rereading the sentence because the context was changed from the "broker doing his job" to the "broker being sent to jail".

N400 is a negative going potential that starts at around 300 *ms* post-onset and lasts till about 500 *ms* (Fig. 3). It peaks around 400 *ms* post-onset and has mostly a central parietal scalp distribution. N400 is responsible for semantic (meaning) processing of a word in the context of speech processing. It is worth noting that N400 is not a language specific potential. Although it was discovered while performing linguistic manipulations [*Kutas M, Hillyard S, 1980*], it can be generated in response to any kind of potentially meaningful stimuli, such as a sequence of pictures, video, sign language, mathematical equations and calculations, and so on. Though the N400 potential is being studied for more than 30 years, it is still an open question whether it reflects the sentence-level (semantic) or word-level (lexical) processing. The semantic processing of the sentence is a controlled process [*Daltrozzo J et al., 2012*], involving conscious perception. Lexical processing is believed to be subconscious and can be performed even without attendance of the subject. As a proof of this, lexical processing was observed in conditions of stimulus masking [*Deacon D et al., 2000*], as well as in a condition of disturbed consciousness [*Balconi M et al., 2013*]. It is shown that for the elicitation of N400, semantic violation is neither necessary, nor a sufficient factor. This potential can be elicited in response to single words without any context, as well as in response to a word within a context such as another single word (lexical priming). In case of unrelated word pairs, the amplitude of N400 increases – becomes more negative and vice-versa. N400 is also generated if the context of a processed word is a sentence [*Kutas M, Federmeier K, 2009*]: the higher the expectation of this particular word as a continuation of the presented part of the sentence, the smaller the N400 amplitude [*Kutas M, Hillyard S, 1984*].

So, as long as N400 can be generated in response to both normal sentences/related word-pairs and anomalous sentences/unrelated word-pairs, it is preferred to use the term N400 effect rather than N400 potential. The N400 effect is a difference between N400 potentials in response to normal (pending) and anomalous words in a particular context (word, sentence or paragraph). Besides context, several factors influence on the N400 amplitude, among which the length, frequency and orthographic features of the presented word. Orthographic size is the number of existing words that can be composed by changing one letter in the presented word [*Kutas M, Federmeier K, 2009*].

Precautionary measures while recording cognitive evoked potentials: Before conducting any experiments on speech processing using the CEP technique, a number of particulars of the experiment need to be taken into account. Some of those are common to all studies of CEP while the others are unique for speech studies. These are some common factors:

- The subject should have no history of epileptic seizures even though there is a very low risk for generating seizures due to the rapid flashing of stimuli (photosensitive epilepsy);
- Whenever possible (mostly in case of healthy participants) the subject should avoid being on psy-

chotropic medication, because that also can affect the recorded CEPs and lead to wrong conclusions;

- Subjects should have normal or corrected to normal vision (in case of visual stimuli) and hearing (in case of auditory stimuli);
- Subject age (or age range) is another important factor. It was shown that the amplitude of CEPs flattens with age: after 40 years of age the amplitude of CEPs becomes smaller with every decade. Therefore, while conducting the experiment, in order to obtain truthful results, the age factor should be considered.

These are factors specific to speech processing:

- Handedness of the subject. Although the center for speech processing is located in the left hemisphere in more than 90% of right handed subjects and more than 70% of left handed ones, it is still possible to obtain different and confusing results regarding the location of CEPs in left-handed person;
- The native language of the subject. MRI studies showed that there are some differences in speech processing between monolinguals and bilinguals [*Kovelman I et al., 2008*]. Therefore, this factor should be taken into account while analyzing of obtained data.
- In case of studying the natural processing of speech by brain, the presented stimuli should be in native language of the subject.
- The continuation of the subject's formal education. The human word-stock grows over the years of formal education. It impacts on the amplitude and latency of CEPs in speech processing studies.
- Working memory span: depending on targeted CEPs and the research question, working memory span may play a significant role in processing of certain type of information and may affect the characteristics of recorded CEPs.

CONCLUSION

The CEP technique is an easy-to-use, highly portable, non-expensive and non-invasive method for the investigation of sensorial and cognitive processes dynamics in cerebral cortex. It has an excellent temporal resolution and can detect changes in brain activity within the accuracy of milliseconds. However, it has a poor spatial resolution, that's why it is very difficult to localize the source of CEPs in brain.

Considering this we can conclude that the CEP technique can effectively shed light on particular aspects of brain activity asking right questions and using appropriate paradigms. While solving the problems for which the brain activity localization has an important significance, the CEP technique can be combined with imaging techniques that yield a better spatial resolution, such as MRI or magnetoencephalography. The latter has both good temporal and spatial resolution but the equipment is bulky, expensive and requires a magnetically shielded environment. This explains its limited availability for both theorists and clinicians. With MRI – CEP joint record the scientists can combine the advantages of the two methods – high temporal and spatial resolution. However the main defect of present method is its price and the high level of noise again the impossibility to bring it to the patient.

Nowadays CEPs are regarded as one of the informative methods of brain processes' study, which require a very high temporal resolution, for example, such as speech processing.

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