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THE IMPORTANCE OF STIMULI AND PARADIGMS IN AUDITORY EVOKED POTENTIALS

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Auditory evoked potentials are generated by the response of the ear, the brainstem and the auditory cortex on the sound stimulus. Their application is great: from hearing screening in newborns, hearing tests, psychological research, research of the speech and language impairments, to the applications in cognitive tests of various neurological disorders.

Recording auditory evoked potentials is the similar as in the other evoked potentials. Participant sits comfortably in a chair, EEG data are collected by electrode cap on his head and he listens to stimuli presented binaurally through the in-ear headphones and distributed in the specific intervals, i.e. paradigm (Figure 1.). During stimulation, subject actively listens to stimuli or ignores them by watching the visual content. Young children, who sleep, and people in a state of coma also respond to stimulation, although they don't participate conscious in a study. EEG epochs are averaged after recording to obtain the required potentials.

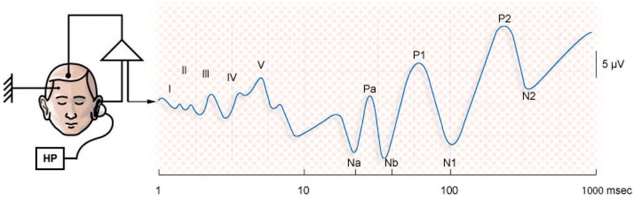

Fig. 1: The system for recording auditory evoked potentials [1]

Depending on the location of the electrical activity generation, evoked potentials are divided into the early (1 to 10 ms), middle (10 to 50 ms) and long (after 50 ms) latency evoked potentials (Figure 2.).

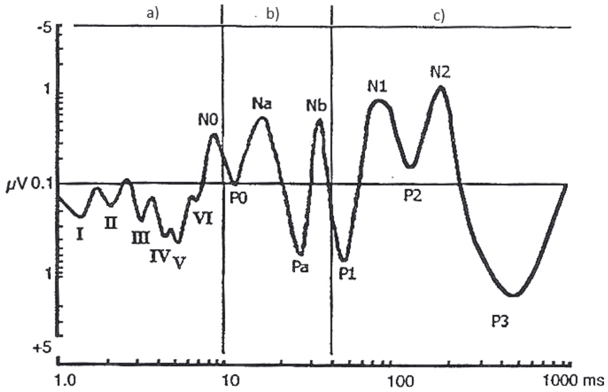

Fig. 2: Auditory evoked potentials: a) brainstem evoked potentials; b) middle latency evoked potentials; c) cognitive evoked potentials [2]

Early latency auditory evoked potentials are generated by the transmission of electrical signal on the auditory pathway to the thalamus, while middle latency evoked potentials represent thalamus electrical activity and arrival of auditory information in primary auditory cortex [2]. Long latency evoked potentials are function of cognitive factors such as attention, memory, language, etc.

EARLY LATENCY AUDITORY EVOKED POTENTIALS

Within 10 ms after stimulus occur responses of the cochlea, auditory nerves and brainstem (Figure 3.). Each of six waves (I-VI) is anatomically connected with neural structures of the auditory pathway. Diagnostic significant are latencies of the waves and latencies between the first, third and fifth wave, because these waves are most evident during the measuring. Brainstem potentials provide important information about the sound content processing at a very low level, especially in infants and young children, because early intensive rehabilitation begins with early detection of the hearing impairment.

The most used are click and sinusoidal stimuli of different frequencies and envelopes. Click stimuli are generated by the activation of a sound transducer with monophasic rectangular electric pulse of shot time (e.g. 100 µs) and presents a series of sound waves lasting a few milliseconds in frequency range 50-3000 Hz. Polarity of evoked activity depends on the polarity of rectangular pulse that affects the initial direction of the membrane acoustic transducer movement. Applying alternating stimuli eliminates this dependency.

Pure sinusoidal tones are used in finding hearing thresholds, as well as recording cognitive evoked potentials. The shape of the stimulus is determined by the maximum intensity, rise time, duration and fall time of trapezoidal envelope of the sine signal, and times are in the order of tens of milliseconds [4].

In each research, it is strived to better recording the brain activity. Due to specific structure of the cochlea and the distribution of receptors in frequency bands, we can adjust the sound stimulus in order to obtain a higher amplitude response. During the click stimulation there are no all receptors activate at the same time, different receptors, depending of the frequency, react in different time (Figure 4.).

Replies to click stimuli for higher frequencies are delayed and therefore the sum of these amplitudes is less.

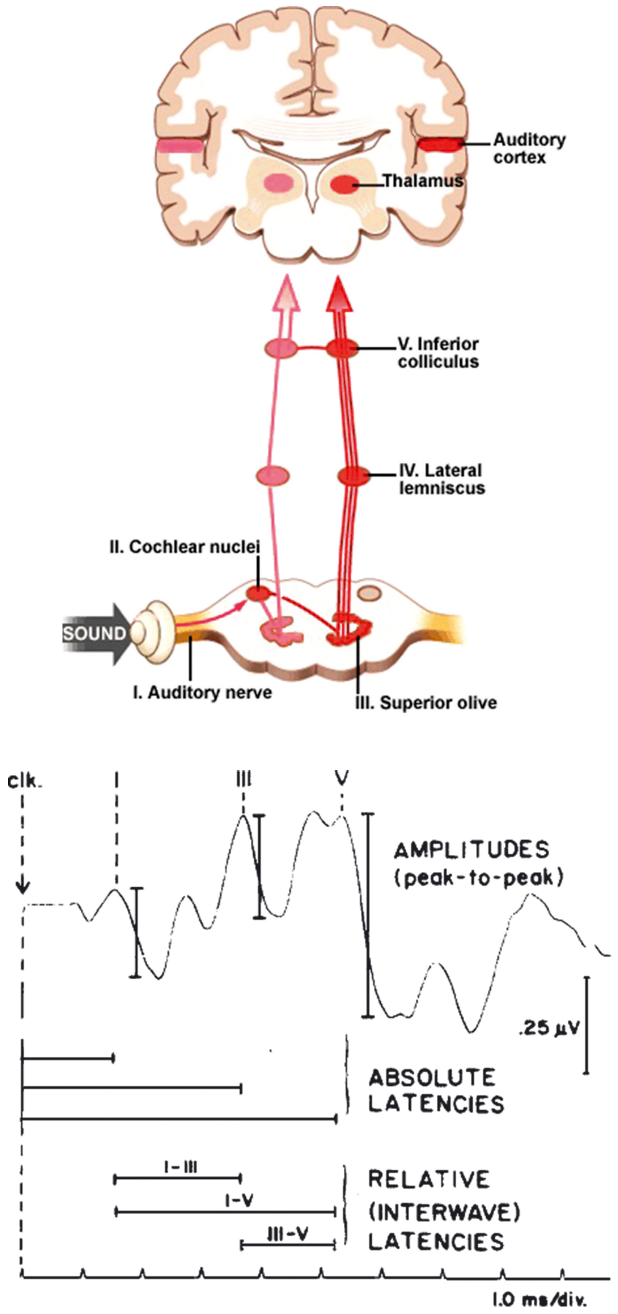

Fig. 3: Auditory pathway [1] and early latency auditory evoked potentials [3]

If the sound signal is adjusted so that its high frequency components are delayed, and all the stimuli are received at the same time to corresponding receptors, the sum of responses will be greater and we get a better signal (Figure 4.), and therefore we can get the accurate diagnoses. Such a stimulus is called a chirp stimulus [5].

Auditory brainstem response (ABR) is commonly used in paediatric diagnosis, especially in neurology and audiometry tests with the purpose to detect the hearing disorders.

ABR represents the objective audiogram (Figure 5.), and therefore provides better diagnostic information in patients whose subjective responses are unreliable. In addition to the time domain, as shown in ABR, functional testing of hearing times can be analysed in the frequency domain.

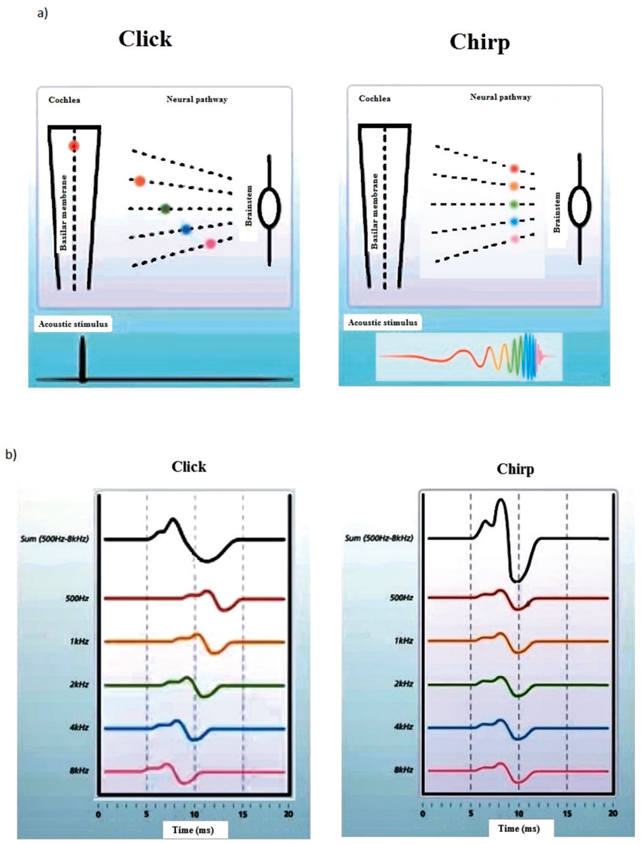

Fig. 4: a) the impact of the cochlea sound stimulation in the time; b) brainstem responses depending on the frequency components of the sound stimulus (adapted from [5])

Search based on different analysis calls Auditory Steady State Response, ASSR. The stimulus is the frequency and/or amplitude-modulated tone of 500 Hz, 1 kHz, 2 kHz and 4 kHz or broadband signals (click noise, AM noise and chirp). If there is a response, EEG activity will be synchronized with the frequency content of stimulation [6]. Due to the rapid response and to get a short time of measurement, ASSR are used in the hearing screening of new-borns.

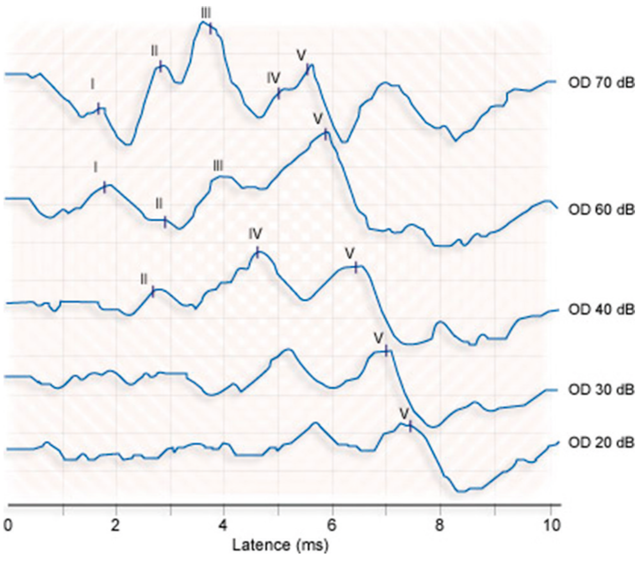

Fig. 5: ABR dependent of the auditory stimulus intensity [1]

Early latency auditory evoked potentials are unambiguous in most subjects and are thus applicable for clinical purposes. In contrast, long latency auditory evoked potentials are not represented in the diagnostic practice. There are many paradigms and stimuli used by researchers, but clinical applications are less successful for the following reasons: paradigms are complicated to use and time-demanding, relationship of the evoked components and cognitive difficulties is poorly defined, differences between the control group and the population with cognitive disabilities are not significant, and it all reduces the diagnostic value of cognitive potential [7].

LONG LATENCY AUDITORY POTENTIALS

The first responses in the auditory cortex, between 60 and 250 ms after stimulus, represent P1 and N1 waves (Figure 2.). They reflect the analysis of the physical characteristics of stimuli, e.g. intensity, frequency, pitch and timbre, and are specially influenced by attention [2]. Repeated stimuli evoke a basic N2 wave. Small probability of these stimuli contributes to increasing the amplitude of this wave, and it is considered that a component N2 corresponds to the process of categorizing stimuli [8].

When the current excitation content of the memory model is preserved, because stimuli did not cause a change in the perception, we will record only the sensory evoked potentials (N1, P2, and N2). In the process of stimulation are involved different auditory stimuli, we want to participant pays attention to some of them and therefore they are called the target, others are standard stimuli. When we insert an unknown stimulus i.e. the target stimulus, observation processes manage a changing or upgrading representations of stimuli followed the appearance of the wave P3 or P300.

A paradigm in which only the target stimulus occurs randomly in time provides a basic P3 component, as well as oddball paradigm in which between the standard stimuli are inserted target stimuli. Paradigm with three different stimuli evokes P3 wave subcomponents (Figure 6.). Subcomponents P3b, parietal maximum, occurs when between the standard stimuli is insert the target with an aim to check the subject's ability to compare and discrimination two stimuli. While the subcomponent P3a, frontal maximum, is got with one more inserted stimulus used for distraction [9]. It is considered that P3b reflects cognitive processing of stimuli [10].

When creating a paradigm, determined parameters are very important because they affect the response. Small target stimulus probability contributes to greater P3 wave amplitude and the weight of the task changes the amplitude of the wave. If the task is heavy, subject invests more effort and the amplitude is higher, which leads to the conclusion that the P3 wave generation is in relation to the amount of the effort. But if the task is too heavy and the participant is not sure whether the default stimulus is target or non-target, the amplitude decreases. It is therefore very important to work out the details of the test.

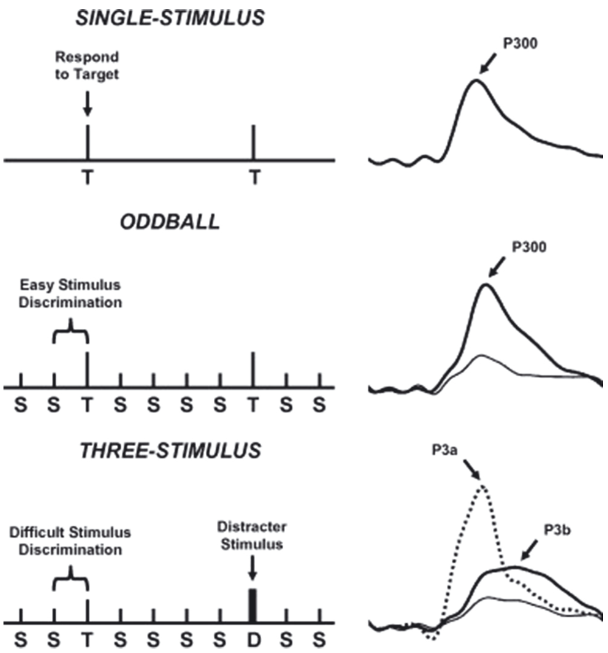

Fig. 6: Paradigms for eliciting P3 wave and subcomponents P3a and P3b [9]

Peak of the P3 wave is largest in the time range from 250 to 500 ms. For simplicity, the widely used is the oddball paradigm. Auditory oddball paradigm requires a set of standard (around 80%) tones (e.g. 65 dBHL, 1000 Hz, 50 ms duration, 10 ms fall/rise time) with randomly presented rare tones (around 20%, e.g. 65 dBHL, 2000 Hz, 50 ms duration, 10 ms fall/rise time). The interstimulus interval is about 1500 ms and it is minimum necessary 50 target stimuli. Participant counts standard tones or presses the button in the dominant hand for each target tone, thus provides the subject's attention. Very important variable is the age (latencies increase with age) and the results should be compared with the corresponding control group [11].

If the oddball paradigm is applied with the same stimuli, but the participant have to ignore the auditory stimulation and pay attention to the visual content (e.g. a silent movie or read the book), it will appear evoked potential mismatch negativity, MMN (Figure 7.).

Negative falling wave MMN, the largest on the central electrodes with the peak between 160 and 220 ms, is generated through the process of a mismatch between rare stimuli sensory inputs and sensory-memory trace that represents the physical property of the standard stimulus [8]. This process, as well as the sensory analysis of the auditory input and their coding into the memory trace, happens automatically, because MMN is elicited by changing auditory stimuli without participant's attention. MMN is especially interesting, because it is possible to access to the discrimination abilities of individuals whose sound capacities difficult to determine, including infants, young children and people with stronger cognitive impairments [7].

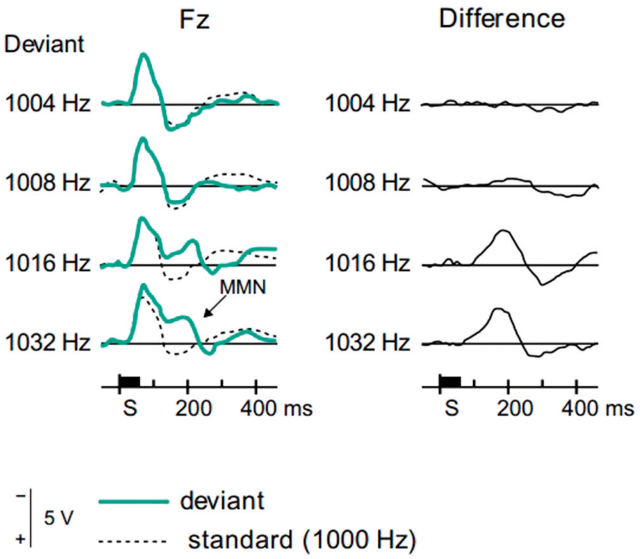

Fig. 7: MMN as a function of frequency change [11]

Only the stimulus alone does not always serve as the standard comparison for the characteristics of the stimulus. In the simplest auditory oddball paradigm the process also include factors of the larger context of the sound sequence. The basis of the appearance of MMN is extraction of the irregularity. Also, only the ratio of deviant and standard stimuli evokes no MMN, and probability alone is not sufficient for eliciting MMN (Figure 8.). The key influence on the occurrence of MMN has a repeated standard pattern. MMN is a result of a series of processes that precede the detection of differences and are sensitive to a larger auditory context [12].

MMN is counted by subtracting the averaged ERP response to the standard stimuli from the averaged response to the deviant stimuli. The interstimulus interval is about 500 ms to 1s [13], and it should be present at least 150 deviant stimuli. MMN is elicited by the different paradigms: standard oddball paradigm, the multiple deviant paradigm, paradigm without standard stimuli, uninterrupted sound paradigm.

Stimuli can also be words or sentences, and a language processing occurs after 400 ms. N400 is a negative wave maximal at the central and parietal electrodes and modulated with an expectation or anticipation words from the sentence context, a violation of semantic form is achieved by changing the last word in a sentence, a pair of words (which are more or less semantically dependent), only one word (which participant has not heard or has rarely heard) or the images that represent an object or action [14]. It should be present at least 50 rare stimuli, also each target stimulus should be different because repetition reduces the amplitude of the wave N400, also distractor stimulus should be in the category of the same semantic field, the same frequency of occurrence in speech and the same length [7]. Late component which is correlated with a syntax process is represented by the central parietal positivity with latency 600-1000 ms. This is the wave P600 [14].

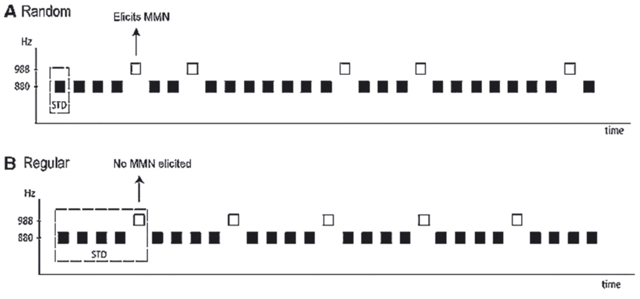

Fig. 8: A) MMN is elicited by paradigm - probability of deviant stimuli is variable; B) The regular sequence of stimuli elicit no MMN [12]

In view of the above, the cognitive evoked potentials research requires a good knowledge of paradigm development and influence of its parameters in the desired response. The same paradigm with the subject's attention or inattention can cause a variety of responses. There are many other parameters that may change the response like characteristics of the stimulus, interstimulus interval length, deviant stimulus probability, and the analysis, which can provide a clearer result if e.g. instead of in the time domain, responses are analysed in the time-frequency domain. For this reason, the auditory late latency evoked potentials still apply in the research purposes, in order to get future diagnostic value.

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