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Visual Event-Related Potentials to Moving Stimuli: Normative Data

Z. KUBOVÁ, J. KREMLÁČEK[1], J. SZANYI[1], J. CHLUBNOVÁ[1], M. KUBA[1]

Department of Physiology and [1]Department of Pathophysiology, Faculty of Medicine, Charles University, Hradec Králové, Czech Republic

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Summary

Visual cognitive responses (P300) to moving stimuli were tested in 36 subjects with the aim to find the normal range of P300 parameters. Concomitantly, the circadian intra-individual variability of the P300 was studied in a subgroup of 6 subjects. Visual stimuli consisted of either coherent (frequent stimulus) or non-coherent motion (random stimulus). The oddball paradigm was applied for recording cognitive responses. P300 to rare stimuli had an average latency of 447.3±46.6 ms and amplitude of 12.9±6.0 μV. The average reaction time was in the range from 322 to 611 ms and there was no correlation between the reaction time and P300 latency. We did not find any significant circadian changes of the P300 parameters in the 6 subjects tested four times during the same day. Cognitive (event-related) responses (P300) displayed distinctly greater inter-individual variability (S.D. of 50 ms) when compared with pattern-reversal and motion-onset VEPs (S.D. of 6.0 ms and 14 ms, respectively). For this reason, the clinical use of P300 elicited by this kind of visual stimuli seems to be rather restricted and the evaluation of its intra-individual changes is preferable.

Key words
Visual potentials • Evoked potentials • Random stimuli • Coherent stimuli

Introduction

Detection of event-related brain potentials (ERPs) is an important step to obtain an insight into higher order mental functions. To elicit ERPs, two types of stimuli are usually presented in a random series ("oddball" paradigm) with one of two occurring relatively "infrequently", representing the event (also termed as "rare" or "target" stimulus). Stimuli can be presented in a visual, auditory or somatosensory modality and the subject is asked to react (mentally or by pressing a button) to the rare ones. Any ERP includes "early" (primary) sensory evoked potentials (dependent on the type of sensory stimulus) and "late" – "cognitive" response (with the main P300 component) similar for all types of sensory stimuli.

So far, a large variety of visual stimuli has been used for the eliciting ERPs - e.g. pattern flash (Taghavy and Kügler 1988a), pattern onset/offset (Giger-Mateeva *et al.* 1999), 3-D "structured coherent"/"unstructured incoherent" motion (Arakawa *et al.* 1999) or onset of pattern movement in the visual field (Kuba *et al.* 1998). Besides the primary complex (specific for each kind of the visual stimulus used), there is always a late wave complex consisting of a negative peak (designated in literature as N200 (or N250, N2) and a large prominent

Fax+420 2 249 20 590
E-mail physres@biomed.cas.cz http://www.biomed.cas.cz/physiolres

positive peak (P300). N200 reflects modality specific sensory qualities, is related to the irregularity and unexpectedness of the stimulus and since it does not depend on the conscious attention of the subject, it can be found both in random and in frequent conditions (Giger-Mateeva 1999). P300 has been reported to consist of two sub-components – P3a and P3b (Halgren *et al.* 1995, Comerchero and Polich 1999, Giger-Mateeva *et al.* 1999). Originally, the P3a was described as the component elicited by an unpredictable change of stimulus in a train of stimuli irrespective of the fact whether the subject ignores or notices them (Squires *et al.* 1975). Giger-Mateeva *et al.* (1999) reported this component to be present in responses to both frequent and infrequent sensory stimuli independent of their modality so that it seems to accompany the automatic cognitive process. P3b occurs only when the subject pays active attention to the stimuli, i.e. it is generated in response to those stimuli to which the subject has to perform an event-related task (Squires *et al.* 1975, Giger-Mateeva *et al.* 1999, Suwazono *et al.* 2000).

From the clinical point of view, it is highly advantageous to use various kinds of visual stimuli for the ERP acquisition. This enables simultaneous testing of one of the two basic parallel pathways in the visual system (parvo- or magnocellular) that have been reported to be affected differently in various neuro-opthalmological diseases, e.g. multiple sclerosis and amblyopia (Kubová and Kuba 1992, Kubová *et al* 1996) and cognitive functions when (changes of P300 parameters were found in dementing illnesses, migraine, alcoholism, depression and schizophrenia (for review see Polich and Herbst 2000). In addition, it is possible to estimate the "central reaction time" (latency difference between primary and cognitive EP), which can indicate the brain level where the information processing is impaired (Antal *et al.* 1996).

In our laboratory we developed a method using the onset of movement of a pattern for eliciting ERPs. In our previous study (Kuba *et al.* 1998), we described ERPs to three types of visual stimulation – a "direction" change, "velocity " change and a "coherence" change. The last one was chosen for more detailed testing in normal subjects (see the Results) as well as in various groups of neurological and psychiatric patients (Szanyi *et al.* 2001, Gayer *et al.* 2001). In general, P300 has been reported to display rather a high intra- and inter-individual variability (detailed review of various biological conditions that can influence the P300 parameters can be found e.g. in Polich and Herbst 2000). Circadian variability of ERPs to moving stimuli is presented in the following text.

Subjects and Methods

Thirty-six healthy drug-free subjects (28 women and 8 men, mean age 37±11.3 years, all right-handed) with normal visual acuity (corrected if necessary) participated in the experiments. Non-invasive examinations of patients and control subjects were approved in advance by the Ethical Committee of our Faculty of Medicine and they were performed with the full consent of the subjects.

The visual stimuli consisted of two horizontal rows each containing two low contrast (10 %) 40' checks which moved at a velocity of 10 °/s for 200 ms and remained stationary for an inter-stimulus interval of 1-3 s. In a pseudo-random order the rows moved either both in the same direction (left or right) - coherent motion or they moved in opposite directions - non-coherent motion. Oddball paradigm was applied for recording of cognitive responses. The target stimulus was the non-coherent motion. The proportion of the target (rare) and non-target (frequent) stimuli was 1:3. Subjects were asked to press a hand held button immediately when they recognized the target stimulus. This was used for off-line evaluation of the reaction time. Visual stimuli were generated using our own software (Kremlá ek *et al.* 1998) and an AutoDesk Animator (USA) on the 21" monitor ViewSonic with the vertical frequency of 70 Hz. The stimulus field subtended 45x35 deg at a viewing distance 0.5 m. The average luminance was 17 cd/m^2. Correct fixation of the center of the stimulus field was monitored with an infra-red CD camera.

Standard recordings included pseudounipolar derivations (with the right ear lobe as reference) from the midline Oz, Pz, Cz and Fz and also from Ol and Or (5 cm to the left and right from the Oz position). These lateral recording sites were used, since N170 motion-onset specific peak is mostly lateralized (irrespective of the dominant hemisphere) towards the temporo-occipital cortex (Kuba and Kubová 1992).

Forty single VEPs (440 ms epochs with sampling frequency 500 Hz) were averaged. In ERP altogether 80 sweeps were recorded (1000 ms epochs), 20 target and 20 non-target responses were averaged. In case of arteficial contamination (most frequently by electric activity related to eye blinking), the whole recording was repeated.

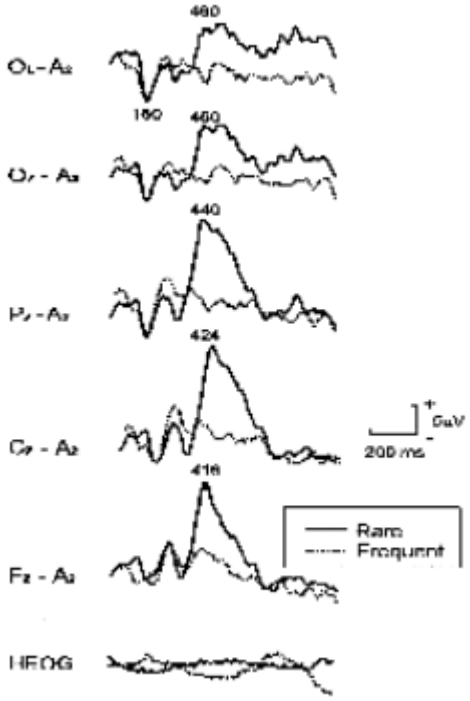

Fig. 1. *Individual ERPs to rare and frequent moving stimuli across 5 unipolar derivations (Fz, Cz, Pz, Oz and Ol – 5 cm from Oz) and simultaneously recorded horizontal electro-oculogram (HEOG). The figure shows primary motion-onset VEP (latency of 160 ms) and ERP complex and their derivation-dependent changes.*

To verify a possible contamination of motion-related VEPs by eye movements, both horizontal and vertical electro-oculograms were also recorded (electrode placement on outer canthi and above and below the right eye) in 6 subjects. No significant eye-movement related activity was found.

Results

A typical example of individual ERPs to rare and frequent stimuli from all recording sites is given in Fig. 1. In both - rare and frequent stimuli - the primary response to the onset of movement (motion-onset VEP) was represented by a distinct negative peak (N1) with the latency around 160 ms in all derivations, with a maximum amplitude dominating in the right occipital lead (in about 70 % of subjects). Cognitive response consisted of a late negative (N2) and a positive (P300) peak. Whilst the negative peak N2 does not display any substantial change across the derivations, the P300 latency shortens towards the front part of the head. Since the ERP complex was most easily to detect in the Cz lead in all tested subjects, in a further study this lead was chosen for detailed evaluation.

Table 1 shows the mean latencies of the N2 peak as well as mean latencies and amplitudes of the P300 peak to both rare and frequent stimuli in the whole group of 36 subjects. The presented amplitudes were counted as an average from inter-peak amplitudes [(P300 preceding negativity - P300)+P300 – P300 following negativity)/ 2].

Table 1. The mean latencies of the N2 peak as well as mean latencies and amplitudes of the P300 peak to both rare and frequent stimuli in the whole group of 36 subjects

	N2	**P300**	
	Latency [ms]	**Latency [ms]**	**Amplitude [μV]**
ERP to random stimuli	318±30	447±47	12.9±5.4
ERP to frequent stimuli	317±35	409±42	6.9±4.5

Table 2. The minimum, median and maximum of reaction times (RT) from the whole group of subjects

	Mean [ms]	**S.D. [ms]**
Minimum RT	322.2	59.4
Median of RT	436.0	73.2
Maximum RT	611.4	127.4

When the ERPs to rare and frequent stimuli were compared (non-paired t-test), there was no difference in the latencies of the N2 peak, but the latency of the P300 component was significantly longer ($p<0.001$) and its amplitude larger ($p<0.001$) to rare stimuli.

Table 2 shows the minimum, median and maximum of reaction times (RT) from the whole group of subjects. There was no correlation between the latencies of either N2 or P300 peaks and any of the reaction times, although the amplitude of P300 did correlate with the median of RT (correlation coefficient of – 0.39**,** $p<0.05$).

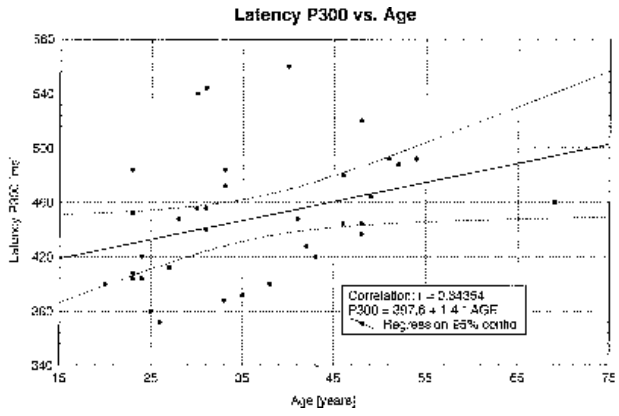

Fig. 2. *P300 latency dependence on the age of tested subjects (n=36). P300 latency significantly increases with the age (correlation coefficient r=0.34, p<0.05).*

Figure 2 shows that the P300 latency becomes prolonged significantly (correlation coefficient of 0.34) with the age of the tested subjects. However, when the whole group of subjects was divided into four subgroups: 20-30 years of age (n=11), 31-40 years of age (n=10), 41-50 years of age (n=11) and more than 51 years of age (n=4), the only significant finding was that the youngest group had shorter reaction time and also shorter latencies of both N1 and P300 peaks (Fig. 3) than any of the other subgroups (this was, however, true only for ERPs to random, not to frequent stimuli).

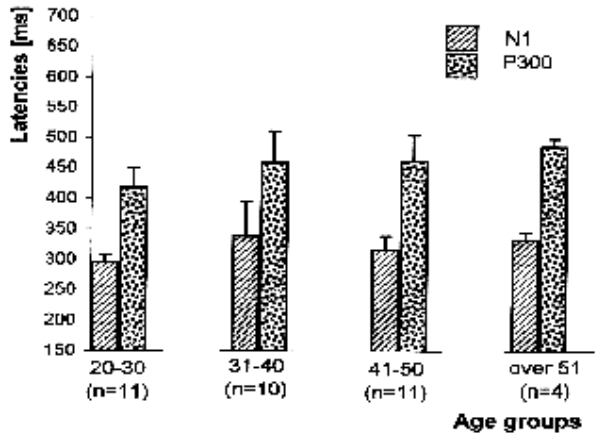

Fig. 3. *N1 and P300 latencies and their standard deviations in four age groups (results are taken from Oz –A2).*

In a subgroup of 6 subjects, the ERPs were recorded four times on the same day (in the morning, before lunch, after lunch and in the evening). The original data from all these recordings are shown in Fig. 4 together with the individual ranges of reaction time. Although the ERPs showed some intra-individual variability as to their shapes, we did not find any significant change of ERPs parameters related to the day-time in which the ERPs were recorded (paired t-test).

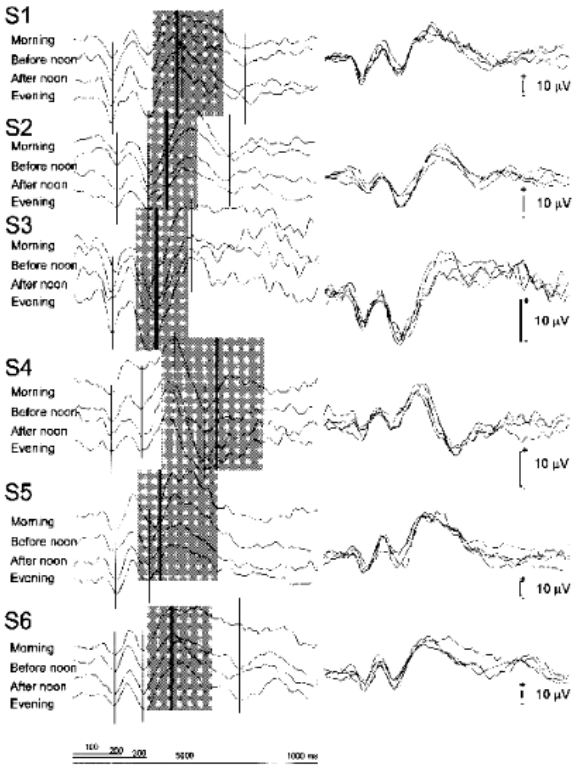

Fig. 4. *Circadian variability of ERPs in all 6 tested subjects (S1 – S6), thin lines mark all analysed peaks. The grey area represents individual range of the subjects' reaction times (RT), bold lines show RT medians.*

Discussion

To all moving stimuli – frequent as well as random - the primary motion-onset VEPs were characterized by the most prominent negative component around 160 ms. This peak is, as we believe on the basis of our previous studies (Kuba *et al.* 1992, Kubová *et al.* 1993), and as was also confirmed by other authors (e.g. by Bach and Ulrich 1994), attributable to the motion-processing magnocellular pathway.

As to the two peaks of the cognitive potential complex, it is evident that the former one (N2) had a lower variability and was even better recognisable in all subjects due to its more constant morphology in comparison to P300. However, this component was about

the same in reactions both to occasional and frequent stimuli, which confirms the data reported by Giger-Mateeva *et al.* (1999). This peak thus probably reflects a more inattentive than attentive cognitive process and its nature might be close to the so-called mismatch negativity of auditory ERPs (e.g. Sato *et al.* 2000).

On the contrary, the P300 differed significantly between the ERPs to rare and frequent stimuli. As far as the response to random stimuli is concerned, it was not only larger (suggesting that it really depends on an effort of subjects to fulfil the cognitive task) but also longer in its latency. This fact might be explained by the reported existence of two sub-components of the P300 - P3a and P3b - with only the P3b being the attention-dependent component (e.g. Giger-Mateeva *et al.* 1999). In general, the latency of the P300 component was longer to our type of visual stimuli than to the onset/offset pattern (Heinz *et al.* 1991 reported P300 of 364 ms, Giger-Mateeva *et al.* 1999 of 380 ms) or to the presentation of two different letters (Sangal and Sangal 1996 where P300 was 366 ms). This may be due to the fact that it takes a longer time to recognize whether the movement of a pattern is or is not coherent in comparison with the relatively much easier decision about the used checked size in the pattern-onset arrangement (method used in Giger-Mateeva *et al.* 1999). Antal *et al.* (1996) found P300 latency of 464 ms for ERPs to two different sinusoidal gratings and Arakawa *et al.* (1999) reported the P300 latencies of about 408 ms for both magno- and parvocellular cognitive tasks.

The P300 latency did not exhibit any correlation to the value of the reaction time. Therefore, the P300 and reaction time seem to represent results of different neural processes.

As to the relationship between P300 and age of the tested subjects, we found significant correlation between age and P300 latency, which is in agreement with the data reported e.g. by Taghavy and Kügler (1988b). We did not, however, confirm any circadian variability of the ERP parameters as well as of P300 changes dependent on meal intake (reported e.g. by Polich 1991), but the number of subjects tested in this part of our experiment was rather small.

Although there is a rather high P300 latency variability in comparison with primary evoked responses (coefficient of variation = 10.5 %), a number of standard clinical tests is routinely used despite much higher statistical limitations (Polich and Herbst 2000).

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Reprint requests

Dr. Z. Kubová, Department of Physiology, Faculty of Medicine, Šimkova 870, 500 01 Hradec Králové, Czech Republic. e-mail: kubova@lfhk.cuni.cz