Topographic Mapping of Cognitive Event-Related Potentials in a Double-Blind, Placebo-Controlled Study with the Hemodervative Actovegin in Age-Associated Memory Impairment

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Abstract. In a double-blind placebo-controlled study, the effects of Actovegin on cognitive event-related potentials were studied in 18 age-associated memory impairment (AAMI) patients. Actovegin is a protein-free metabolically active hemodervative improving oxygen and glucose utilization. Each patient was treated, in randomized order, for 2 weeks with 250 ml 20% Actovegin and 250 ml placebo daily with an interval of 3 weeks in between. Psychophysiological tests were carried out by means of the Viennese Psychophysiological Test System (VPTS) before as well as 5 h after the administration of one single infusion on day 1 (acute effect), before (subacute effect) as well as after one additional superimposed infusion on day 15 (superimposed effect). There was no effect on earlier stages of information processing measured by N1 and P2 component of nontarget ERP nor on ERP latencies. However, P300 amplitude increased after acute, subacute as well as superimposed infusion of Actovegin as compared to placebo, confirming the hypothesis that nootropic drugs may influence the P300 amplitude in the sense of an improved availability of cognitive processing resources. This increase of P300 amplitude (up to 4.8 μV), seen specifically in central and parietal regions, proved to be significant in a confirmatory test.

Introduction

The development of various effective drugs for the treatment of different types of dementia is an important task in neuropsychopharmacological research. Nootropics and metabolically active compounds may modify central cholinergic, serotonergic, dopaminergic, GABA-ergic, and peptidergic transmission [Whalley, 1989; Nicholson, 1990]. Catecholamine function in relation to age-associated memory impairment (AAMI) was recently discussed by McEntee and Crook [1990]. AAMI is a clinical state defined by Crook et al. [1986] which describes loss of memory function in otherwise healthy persons aged 50 and over. Previous investigations with quantitative EEG analysis demonstrated that the metabolically active hemodervative Actovegin, which increases oxygen and glucose utilization, also improves vigilance in elderly subjects [Saletu et al., 1984, 1986].

Several studies demonstrate positive clinical and behavioral effects of Actovegin in patients with organic psychosyndrome [Jansen and Bruckner, 1982; Scholling and Clausen, 1974]. Recent findings with EEG brain mapping indicated that Actovegin improves vigilance in AAMI, which was seen also by psychometric investigation, regarding certain noopsychic, thymopsychic and psychophysiological measures [Saletu et al., 1991]. In addition to this EEG brain mapping study we investigated specific effects of Actovegin on P300 event-related potentials (ERP) for several reasons: (1) There is a strong relationship to cognitive aspects of controlled information processing [Johnson, 1986; McCarty and Donchin, 1983; Rössler et al., 1986, for a review]. In signal detection paradigms, latencies of the P300 complex, specifically the so-called P3b first described by Squires et al. [1975], seem to reflect stimulus evaluation time, but not response selection time. Amplitudes of these compo-
ments have been shown to be related to processing resources which are requested when a perceptual set has to be changed according to the environmental demands. (2) Age-related changes in a variety of cognitive functions are correlated with changes in ERP components evaluated by means of different experimental approaches in the auditory, visual and somatosensory modality and different recording and analysis techniques. Many studies demonstrated that latency of P300 increases with increasing age [Pfeiferbaum et al., 1984]. There is also strong evidence that P300 amplitude decreases over central and parietal regions and that the scalp distribution changes to a more frontal orientation [Friedman et al., 1989]. (3) In various neurological disorders P300 seems to be abnormal: In dementia of Alzheimer type, for instance, amplitude was reduced and latency was lengthened [Ito et al., 1990; Polich et al., 1990] and in multiple sclerosis latency was prolonged [Newton et al., 1989]. Goodin and Aminoff [1986, 1987] suggested that ERPs may be helpful in elucidating the underlying pathogenesis of different dementia syndromes, such as dementia associated with Alzheimer’s disease, Parkinson’s disease and Huntington’s disease. When interpreting abnormal ERPs in dementia and pharmacological effects on ERPs, it is important to consider the cortex as major current source of the P300, although various subcortical generators like the hippocampus and amygdala have been proposed too [Rockstroh et al., 1989]. (4) A number of drugs have been reported to affect P300 ERPs: e.g. the catecholaminergic psychostimulant methylphenidate enhanced P300 amplitude depending on the subject’s state and task demands [Klorman et al., 1988]; the anticholinergic drug scopolamine slowed P300 in young women [Callaway, 1984]; the neuroleptic flupentixol suppressed P300 amplitude, indicating an impairing effect on human information processing resources [Rösler et al., 1985]. A cholinergic nootropic (WEB 1881 FU) significantly influenced the overall amplitude of cognitive ERP components in incidental and intentional memory task in young healthy subjects, suggesting effects on cognitive processes [Münz et al., 1988]. On the other hand, there was no effect on ERP correlated to visual spatial attention, suggesting that early perceptual processes are not influenced by this cholinergic nootropic drug [Münz et al., 1989]. In our own psychophysiological study by means of the Viennese Psychophysiological Test System (VPTS) described in Semlitsch et al. [1989], the antihypoxidotic/nootropic drugs tenilestat and co-dergocrine mesylate increased P300 amplitudes as compared to placebo, which suggests an improving effect on information processing resources. P300 latencies were unchanged, which indicates no effect on stimulus evaluation time. In addition, tenilestat affects also early stages of information processing [Saletu et al., 1989].

Thus the aim of the present double-blind, placebo-controlled crossover study was to investigate psychophysiological effects of Actovegin by means of cognitive ERPs.

Methods

Subjects

Eighteen patients of both sexes (10 females and 8 males) aged 50–80 years (mean 64 years) who met the criteria of AAMI defined by Crook et al. [1986] were included in the double-blind, placebo-controlled crossover study. Inclusion criteria were at least 50 years of age with complaints of memory loss reflected in daily life problems as e.g. difficulty remembering names of individuals, following instructions, misplacing objects, difficulty remembering multiple items to be purchased or multiple tasks to be performed, problems remembering telephone numbers or zip codes, and difficulty recalling information quickly following distraction. Onset of memory loss must have been described as gradual, without sudden worsening in recent months. Memory test performance was at least one standard deviation below the mean established for young adults on the standardized Grünberger verbal memory test [Grünberger, 1977] and/or in the Benton Visual Retention Test. Intellectual functioning was adequate as measured by the WAIS vocabulary subtest. The absence of dementia was determined by a score of ≥ 34 on the Mini-Mental State Examination [Folstein et al., 1975]. Exclusion criteria were the ones established by Crook et al. [1986]. Patients were not allowed to take any psychoactive drugs 3 weeks before and/or during the period of the study.

Treatment and Time of Measurement

Each subject had 2 weeks treatment with Actovegin infusion daily (250 ml, 20% Actovegin infusion, infusion rate: 4 ml/min, length of infusion: 1 h) and another 2-week period with placebo infusion (250 ml NaCl). The application of drug or placebo was randomized with a 3-week treatment-free interval in between. 1 actovegin infusion contained 40 ml deproteinized hemodilysate (dry weight 2 g) from calf-blood.

EEG brain mapping, psychometric tests and evaluation of pulse, blood pressure and side effects were carried out on days 1 and 15 before as well as 2, 4, 6, and 8 h after the start of the infusion as described elsewhere [Saletu et al., 1991]. Psychophysiological investigations based on the VPTS were carried out on days 1 and 15, before and 5 h after the start of the infusion.

Thus, the study design allowed for investigation of drug-induced changes after one single dose of Actovegin (5HR/DAY1), after subacute administration of Actovegin over 2 weeks (PRE/DAY1) and after one superimposed infusion on top of subacute administration (SHR/DAY15) as compared to baseline (PRE/DAY1). The study was performed in accordance with the Declaration of Helsinki and informed written consent was obtained.
Procedure

Subsequent to the application of electrodes, subjects were asked to complete the adjective checklist [Janke and Debus, 1978]. Thereafter, they were instructed to sit comfortably in a reclining chair situated in a constantly lit, sound-attenuated Faraday cage. They were instructed to open their eyes and to focus a point 2.5 m straight ahead. A background noise (white noise of 45 dB SL) was presented via earphones.

The experiment started with a 1-min rest recording with eyes open. The oddball paradigm is based on a design first reported by Squires et al. [1975] and was adapted for longitudinal studies by Semlitsch et al. [1989]. Loud tone bursts (nontargets, probability 0.9, 1,000 Hz, 50 ms duration, 5 ms rise/fall time, 90 dB SL) are presented with a constant interstimulus interval of 1 s randomly interrupted by soft tone bursts (targets, probability 0.1, 1,000 Hz, 50 ms duration, 5 ms rise/fall time, 70 dB SL). The total number of tone bursts presented was 330. The subjects were asked to mentally count the soft tone bursts and report their number at the end of the experiment.

Measurement of Subjective Well-Being

The adjective checklist of Janke and Debus [1978] was used for the evaluation of subjective well-being. This self-reporting scale is a multidimensional method to quantify thymopsychic including the following subscales: activation, deactivation, fatigue, dizziness, extraversion, introversion, assertiveness, mood, arousal, sensitivity, anger, anxiety, depression and absent-mindedness. As this instrument is sensitive to changes, it was used to quantify drug-induced changes of well-being.

ERP Recording

Gold electrodes were attached to the scalp with collodion according to the international 10/20 system. In all, 19 channels were recorded. 17 leads (F7, F3, Fz, F4, F8, T3, C3, Cz, C4, T4, T5, P3, Pz, P4, T6, 01 and 02 to averaged mastoids) were recorded by means of a 17-channel Nihon Kohden 4317 F polygraph (time constant: 1.0 s; high frequency response: 70 Hz; frequency range: 0.16-70 Hz; amplification: approximately 1:20,000). Using the same type of electrodes, vertical EOG was recorded from an electrode at midforehead to the average of one electrode below the left eye and one electrode below the right eye. Horizontal EOG was recorded from the outer canthus. Both EOG channels were recorded by means of a 16-channel Beckman 711 dysgraph (time constant: 1.0 s; high frequency response: 100 Hz; frequency range: 0.16-100 Hz; amplification: approximately 1:4,000).

On-line data acquisition as well as data analysis was performed on a Hewlett Packard Vectra Computer System using our software package [Anderer et al., 1987]. The sampling frequency was 256 Hz resulting in a time resolution of approximately 4 ms. After minimizing ocular artifacts based on regression analysis in time domain [Semlitsch et al., 1986; Anderer et al., 1989] and visual artifact elimination, averaged ERP waveforms were computed for targets and nontargets (fig. 1). Waveforms were digitally filtered by means of a phase-linear low-pass filter with a cutoff frequency of 30 Hz. Target ERPs and nontarget ERPs with less than 50% of single trials free of artifacts were excluded from further analysis.

Data Reduction

Latencies of ERP components were defined as the time of the most negative or positive point of spatial average waveforms (i.e. average across all 17 leads). For nontarget ERPs N1 and P2 latencies were computed. For target ERPs P300 (P3b) latency was determined. Latencies were detected by the following procedure: In a first step ERP waveforms were computed averaged across all 8 sessions for each subject. The peak latencies of the spatial average of these waveforms were detected visually. In a next step the nearest peak in respect to these latencies was used to automatically determine individual latencies. Amplitudes of ERP components were measured at the defined latencies relative to prestimulus baseline (0-100 ms prior to stimulus onset). The amplitude maps were calculated using an interpolation algorithm based on the cubic distance from the values at the four nearest electrodes.

Statistical Evaluation

Statistical analysis was based on the concept of descriptive data analysis as proposed by Aht [1988] for controlled studies. The 3 preselected null hypotheses for confirmatory testing based on our results with tenilsetam and co-darcrinr mesylate [Saletu et al., 1989] were: There is no increase of P300 amplitude at their location of maximal occurrence after acute, subacute and/or superimposed treatment of Actovegin as compared to placebo (maximal error probability alpha = 0.05). Alpha adjustment by Bonferroni-Holm led to individual error probabilities of p (1) ≤ 0.017, p (2) ≤ 0.025, and p (3) ≤ 0.05. Normal distribution was tested by means of one sample Kolmogorov-Smirnov test. If in no cases null hypothesis of normal distribution is rejected at alpha = 0.10, paired sample t test will be used. In case of violation of assumption of normal distribution, nonparametric Wilcoxon test will be used.

All other effects were tested descriptively using paired sample t test without alpha adjustment. The null hypotheses for N1, P2, and P300 amplitudes were: There is no decrease of N1, and no increase of P2 and P300 amplitudes after acute, subacute and/or superimposed treatment of Actovegin as compared to placebo(error probability alpha = 0.05). The null hypotheses for N1, P2, and P300 latencies were: There is no change of N1, P2 and P300 latencies after acute, subacute and/or superimposed treatment of Actovegin as compared to placebo (error probability alpha = 0.05). The null hypotheses for adjective checklist scales were: There is no change after acute, subacute and/or superimposed treatment of Actovegin as compared to placebo (error probability alpha = 0.05). This pattern of descriptive p values was judged if they corresponded to numerically relevant effects and plotted, in case of amplitudes, on descriptive significance probability maps (SPM).

Results

Two subjects had to be excluded from analysis because of muscle artifacts in frontal and/or temporal regions. One subject did not perform the task (to mentally count the targets) at PRE/DAY15 and 5HR/ DAY15. The difference between reported and presented targets was less than ± 2 in 114 out of 120 recordings. Therefore no drug-induced effects on the error rates could be observed. For the remaining subjects the minimal number of averages was 17 (out of 30) targets and 141 (out of 270) nontargets. Thus, the final number of
subjects included in the statistic was 15. No missing data or outliers were found. In Table 1 means and standard deviations of the number of artifact-free single trials used to calculate averaged ERPs are shown. There were no significant changes in the number of artifact-free trials.

**Confirmatory Statement**

Table 2 shows the individual P300 amplitudes as well as means and standard deviations at Pz, the location of maximal P300 amplitude. In no cases was the assumption of normal distribution rejected and therefore the paired sample t test was used. P300 amplitude increased 5 h after acute drug administration 2.9 µV (t = 2.8; p(2) < 0.025; d.f.: 14), after 15 days of subacute drug administration 3.2 µV (t = 1.9; p(3) < 0.05; d.f.: 14), and after one superimposed infusion 4.8 µV (t = 3.1; p(1) < 0.017; d.f.: 14), as compared to placebo. Thus, the drug-induced increase of P300 amplitude was statistically significant in a confirmatory sense.

**Descriptive p Values**

Latencies of N1, P2 and P300 components: N1 latency was 90.4 ms (SD ± 12.0 ms), P2 latency was 195.8 ms (SD ± 17.9 ms) and P300 latency was 393.8 ms (SD ± 55.8 ms) at PRE/DAY1 before infusion of Actovegin. There were no significant effects on N1, P2

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Fig. 2. N1 topography. a: Topographic distribution of N1 amplitudes at peak latency of spatial average before (PRE/DAY1) as well as after acute (5HR/DAY1), subacute (PRE/DAY15) and superimposed (5HR/DAY15) infusion of Actovegin and placebo (n = 15). To allow comparison, the scale is set at −7 to +7 µV for all eight maps. b: Descriptive SPM based on t values as compared to PRE/DAY1. c: Placebo-corrected descriptive SPM based on t values as compared to PRE/DAY1. Hot colors represent an increase, cold colors a decrease (t > 1.34; p < 0.10; t > 1.76; p < 0.05; t > 2.62; p < 0.01). For the judgement of differences between drug-induced and placebo-induced changes, descriptive p values (p < 0.05) were chosen.
Fig. 3. P2 topography. a Topographic distribution of P2 amplitudes at peak latency of spatial average before (PRE/DAY1) as well as after acute (5HR/DAY1), subacute (PRE/DAY15) and superimposed (5HR/DAY15) infusion of Actovegin and placebo (n = 15). To allow comparison the scale is set at -7 to +7 μV for all eight maps. b Descriptive SPM based on t values as compared to PRE/DAY1. c Placebo-corrected descriptive SPM based on t values as compared to PRE/DAY1. Hot colors represent an increase, cold colors a decrease (t > 1.34; p < 0.10; t > 1.76; p < 0.05; t > 2.62; p < 0.01). For the judgement of differences between drug-induced and placebo-induced changes, descriptive p values (p < 0.05) were chosen.

Fig. 4. P300 topography. a Topographic distribution of P300 amplitudes at peak latency of spatial average before (PRE/DAY1) as well as after acute (5HR/DAY1), subacute (PRE/DAY15) and superimposed (5HR/DAY15) infusion of Actovegin and placebo (n = 15). To allow comparison the scale is set at -14 to +14 μV for all eight maps. b Descriptive SPM based on t values as compared to PRE/DAY1. c Placebo-corrected descriptive SPM based on t values as compared to PRE/DAY1. Hot colors represent an increase, cold colors a decrease (t > 1.34; p < 0.10; t > 1.76; p < 0.05; t > 2.62; p < 0.01). For the judgement of differences between drug-induced and placebo-induced changes, descriptive p values (p < 0.05) were chosen.
Table 1. Number of artifact-free single trials for target and nontarget ERPs (mean ± SD; n = 15)

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<tr>
<th></th>
<th>Actovegin</th>
<th>Placebo</th>
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<tr>
<td></td>
<td>DAY1</td>
<td>5HR</td>
</tr>
<tr>
<td></td>
<td>PRE</td>
<td>5HR</td>
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<tr>
<td>Target</td>
<td>27.7 ± 1.9</td>
<td>28.2 ± 1.6</td>
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<tr>
<td>Nontarget</td>
<td>240.1 ± 18.3</td>
<td>234.3 ± 26.8</td>
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The number of stimuli presented is 30 and 270 for targets and nontargets, respectively.

Table 2. P300 amplitude (in µV) at Pz versus prestimulus baseline

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<tr>
<th>Subjects</th>
<th>Actovegin</th>
<th>Placebo</th>
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<tr>
<td></td>
<td>DAY1</td>
<td>5HR</td>
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<tr>
<td></td>
<td>PRE</td>
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<tr>
<td>1</td>
<td>6.8</td>
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<td>2</td>
<td>12.3</td>
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<td>3</td>
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<td>4</td>
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<td>SD</td>
<td>6.5</td>
<td>7.6</td>
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and P300 latencies after Actovegin as compared to placebo.

Amplitudes of N1, P2 and P300 components: N1 amplitude was maximal -7.0 µV (SD ± 2.5 µV) at Cz, P2 amplitude was maximal 5.3 µV (SD ± 2.9 µV) at Cz and P300 amplitude was maximal 12.3 µV (SD ± 6.5 µV) at Pz for PRE/DAY1 before infusion of Actovegin. Figures 2–4 demonstrate the drug effects on N1, P2, and P300 amplitudes, respectively. Figures 2–4a show the topographic distribution before as well as after infusion of Actovegin and placebo. As can be seen in part of figure 2a, the N1 amplitude is greatest at central and a frontal increase of the N1 amplitude can be seen as compared to PRE/DAY1 especially after placebo infusion. There was no drug effect on N1 amplitude as compared to placebo. The spurious finding on electrode T4 at PRE/DAY1 has no relevance (fig. 2c).

As can be seen in figure 3a, the P2 amplitude is greatest at central electrodes and smallest at occipital electrodes. The topographic distribution of P2 amplitude remained stable. In figure 3b a small increase of P2 amplitude can be seen as compared to PRE/DAY1 especially at PRE/DAY1 for both Actovegin and placebo. There was no drug effect on P2 amplitude as compared
to placebo. The spurious findings on electrode T3 and T4 as well as O2 at PRE/DAY15 have no relevance as they are not associated with considerable numerical changes (fig. 3c).

As can be seen in figure 4a, the P300 amplitude is greatest at Pz and smallest at fronto-temporal electrodes. The topographic distribution of P300 amplitude remained stable. In figure 4b, a small increase of P300 amplitude can be seen as compared to PRE/DAY1 especially at Pz after Actovegin infusion. On the other hand, a decrease of P300 amplitude is seen after placebo infusion at 5HR/DAY1, which is more pronounced at PRE/DAY15 and even more at 5HR/DAY15. Drug-induced increases of P300 amplitudes as compared to placebo are seen in figure 4c. As these findings appeared concomitantly with important numerical differences (e.g. at Pz approximately 40% increase of amplitude) and at meaningful locations (where P300 amplitudes are most pronounced), they are interpretable as drug effects.

There were no significant drug-induced changes in subjective well-being evaluated by means of the adjective checklist as compared to placebo.

**Discussion**

A study design was chosen which made it possible to investigate drug effects after acute, subacute and an additional superimposed infusion of Actovegin on cognitive ERPs. In the P300 paradigm specific sensory-cognitive performance is investigated under an accurate condition. In this very commonly used paradigm, which was adapted for repeated measurements, no motor reaction is necessary. This results in a limited control over the subject’s behavior during the experiment, but avoids superimposing motor and cognitive potentials. Nevertheless subjects performed the experiment accurately as measured by the error rate, and therefore no drug effects could be observed in this regard. High quality in data collection and artifact processing, especially minimization of ocular artifacts, resulted in a 91 and 86% usage of single trials evoked by targets and nontargets, respectively.

Previous pretreatment findings with ERPs in the elderly [Semlitsch et al., 1989] recorded with a longer time constant (10 as compared to 1 s in the present study) and evaluated with different methods for defining ERP latencies and amplitudes (single lead cross correlation technique as compared to spatial analysis in the present study) showed similar N1 latencies (90.6 as compared to 90.4 ms), P2 latencies (191.6 as compared to 195.8 ms) and P300 latencies (402.8 as compared to 393.8 ms). N1-P2 amplitude at Cz reported in the previous study was 12.8 μV as compared to 12.3 μV in the present one. N2-P300 amplitude at Cz reported in the previous study was 9.7 μV. In the present study P300 amplitude versus baseline was 10.1 μV at Cz. Note that comparing N2-P300 evaluated by cross-correlation technique and P300 evaluated by spatial analysis is of limited value. Nevertheless, these findings demonstrate that ERP components are robust measures with high reliability.

In addition, the P300 component is sensitive to age-related and drug-induced changes of human information processing. As compared to findings collected in young healthy subjects (aged between 18 and 39 years, n = 14), using the same paradigm and data analysis [Anderer et al., 1991], P300 latencies are delayed in AAMI: 393.8 versus 349.0 ms for AAMI and young subjects, respectively. In addition, P300 amplitude was reduced in central and parietal leads (e.g. at Cz 12.7 vs. 13.7 μV and at Pz 14.5 vs. 16.9 μV for AAMI and young subjects, respectively) and augmented in frontal leads (e.g. at Fz 11.9 vs. 7.3 μV for AAMI and young subjects, respectively). These findings are in accordance with the reported change in the scalp distribution of P300 amplitude in the elderly to a more frontal orientation [Friedman et al., 1989].

According to the recommendations for statistical design and analysis of pharmacoencephalography studies [Abt et al., 1991; Hermann et al., 1989], hypotheses were postulated in the planning phase of the study based on previous investigations of nootropic drug effects on P300 ERPs. For the confirmatory statement target variable (P300 amplitudes) and its location (maximal occurrence) were defined. As p values are only approximate values, we selected the simplest statistical approach, paired samples t test.

The strategy of descriptive data analysis was successful both in a descriptive and confirmatory sense. Judgment of the maps of descriptive p values in association with numerical relevant effects resulted in the conclusion that Actovegin increases P300 amplitude as compared to placebo. These drug effects proved to be significant after a single infusion of Actovegin as well as after subacute and additional superimposed infusion, suggesting a positive effect on information processing resources. The augmentation of the P300 amplitude is seen specifically over central and parietal regions, where AAMI patients have smaller amplitudes as compared to young subjects.
The reduction in the P300 amplitude under placebo conditions at PRE/DAY1 compared to PRE/DAY15 may be attributed to a repeated measurement effect. As can be seen in figure 4a, the P300 amplitude was reduced under placebo conditions at 5HR/DAY1 compared to PRE/DAY1 and at 5HR/DAY15 compared to PRE/DAY15. This seems to reflect, in addition to a repeated measurement effect, a time of day effect, as premeasurements were obtained in the morning, while postmeasurements were obtained in the early afternoon. A marked time of day effect with higher P300 amplitudes in the morning compared to afternoon was reported recently [Wesensten, 1990]. This may reflect better cognitive performance in the morning than in the afternoon.

As can be seen in figure 4a, under Actovegin conditions the P300 amplitude showed no time of day effect and no repeated measurement effects.

While the P300 amplitude decreased significantly 5 h after acute placebo infusion, infusion of Actovegin compensated this decrease, leading to an amplitude increase of about 11% of the pretreatment value (fig. 4b). In a previous study [Saletu et al., 1989] N2-P300 amplitudes also decreased significantly 2 h after placebo administration, while tenilsetam compensated this decrease in a dose-dependent manner, leading to an amplitude increase after the highest dosage. Five milligrams of col-d ergocrine mesylate also increased the N2-P300 amplitude. It may be speculated that nootropics prevent a reduction in the allocation of cognitive processing resources. Although these drugs have supposedly different mechanisms of action [Saletu and Grünberger, 1985; Saletu, 1989; Whalley, 1989; Nicholson, 1990], they affect the P300 component in a similar way.

In our present study, Actovegin showed no significant effects on N1 and P2 amplitudes associated with numerical relevant differences. This suggests that the drug has no influence on the earlier stage of information processing. The same result was reported after co-d ergocrine mesylate, while after tenilsetam an augmentation of these components was seen [Saletu et al., 1989].

There were no effects on ERP latencies after Actovegin. Thus, stimulus evaluation time is not accelerated by Actovegin, which is in agreement with our results concerning tenilsetam and co-d ergocrine mesylate [Saletu et al., 1989]. Recent findings in demented patients showed that idebenone and calcium hopantenate significantly shortened P300 latencies [Hiramatsu et al., 1989].

Subjective well-being, evaluated by the adjective checklist, did not show drug effects at times of VPTS investigations and this excludes the possibility that the significant P300 augmentation after infusion of Actovegin was mediated by thymopsychic improvement.

Using statistical methodology of selecting study design and null hypotheses was successful in detecting drug effects on cognitive ERPs. Additionally signal analysis including artifact processing and objective component determination is a critical step in topographic mapping of ERPs. In conclusion this approach seems to be a valuable complementary tool in psychopharmacological research, specifically with regard to nootropic drugs.

References


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