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Hyperventilation as a Model for Acute Ischaemic Hypoxia of the Brain: Effects on Cortical Auditory Evoked Potentials

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Summary. Controlled hyperventilation (HV) may be used as an experimental procedure to produce transient ischaemic hypoxia of the brain. The effect of HV on the cortical auditory evoked potential (AEP) components N1 and P2 was studied in ten healthy adult subjects. AEP were recorded before HV, during 3 min of controlled HV, and 1 min and 5 min after the end of HV. The P2 amplitude was significantly reduced by HV and regained its initial value 1 min after the end of HV. The P2 amplitude decrease probably reflects an impairment of synaptic function produced by cerebral hypoxia. Thus, the investigation of cortical AEP components may provide a useful parameter in the study of anti-ischaemic or anti-hypoxic therapies.

Key words: Hyperventilation – Ischaemia – Hypoxia – Brain – Auditory evoked potentials

Introduction

Acute hypocapnia produced by hyperventilation (HV) may reduce the cerebral blood flow (CBF) to half of the normal values [15, 25, 29]. Blood flow in the internal carotid, vertebral and middle cerebral arteries is reduced [12, 19]. The reduction of the CBF equally affects grey and white substance, thalamus and brain stem [27]. HV-induced alkalosis increases the affinity of haemoglobin for oxygen [6]. By these mechanisms HV produces cerebral tissue hypoxia [1, 7, 13, 20] and a decrease of the cerebral metabolic rate of oxygen [27]. Tissue hypoxia is ameliorated by inspiration of hyperbaric oxygen [13, 14]. Metabolic changes subsequent to HV have been demonstrated as a reduction of the utilization rates of glucose, glycogen and adenosine triphosphate (ATP) [16] and an increase of cerebral lactate [16, 23]. The increase of lactate during HV is ameliorated by the administration of hyperbaric oxygen [24]. Thus, HV has been shown to produce a decrease of CBF, cerebral tissue hypoxia, reduction of cerebral energy metabolism and lactacidosis. The difference of these changes from those observed in cerebral infarction may be only quantitative.

In the spontaneous EEG, HV produces a decrease in alpha and beta activity and an increase in slow activity [5, 18]. These changes can be interpreted as the result of cerebral hypoxia [9, 20], especially as they are reversed or ameliorated by the administration of hyperbaric oxygen [9, 14, 26]. The effects of HV on the evoked electrical activity of the brain have so far only been the subject of a few investigations [4, 8]. In this study, we determined the effects of controlled HV under capnographic monitoring on the cortical auditory evoked potential (AEP) components N1 and P2 [22].

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Subjects and Methods

The study was performed in ten healthy students (6 female, 4 male), between 18 and 22 years of age. Physical and laboratory examination, audiometry, ECG and EEG recording was normal in all subjects.

Capnography. Capnographic monitoring was performed by means of an infra-red gas analyser. Gas was continuously sampled from a mouthpiece at a flow rate of 500 ml/min through a side tube, while the nose was closed with a noseclip.

AEP Recording. Tones of 1 kHz with a duration of 50 ms, including each 10 ms of linear increment and decrement, were applied binaurally through headphones at a stimulus intensity of 70 dB SL and a stimulation frequency of 1 Hz. AEPs were recorded from Cz using linked mastoids as reference. Filter settings were 1–100 Hz; 100 sweeps of 250 ms duration including a 25-ms pre-stimulus baseline were averaged.

Study Design. To achieve the baseline, the subjects breathed at normal speed and depth through the mouthpiece. Instructions for appropriate ventilation were given by visual feedback of the end-expiratory PCO_2 values by means of a computer display. At a PCO_2 of 40 mm Hg the first AEP recording was performed. Then the subjects were instructed to increase the frequency of ventila-

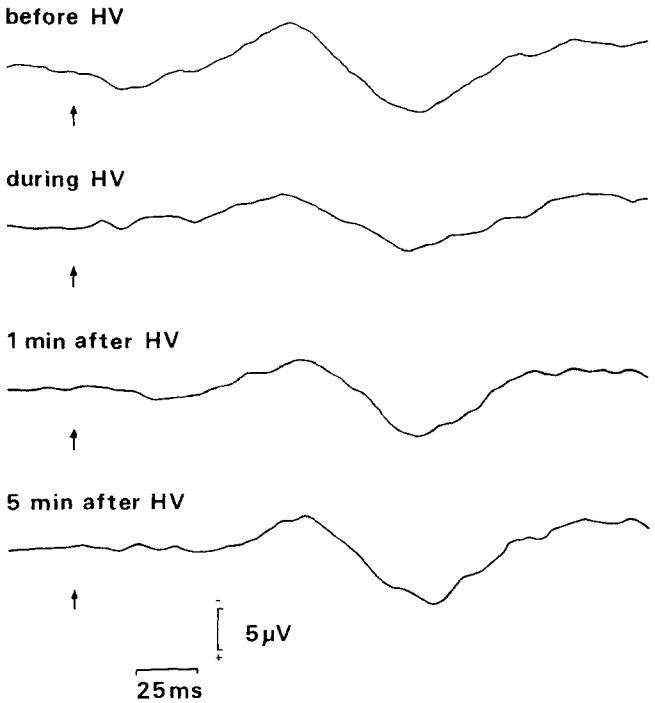

Fig. 1. Auditory evoked potential grand averages.
Grand averages were calculated from the recordings of the ten subjects investigated. Above each trace the recording condition is given. Negativity is plotted upwards. *Arrows* indicate stimulus onset. *HV*, Hyperventilation

tion to achieve a PCO_2 of 18 mm Hg for 3 min. Under these conditions AEPs were recorded again. After this, the subjects were asked to breath normally to obtain a PCO_2 of 40 mm Hg for 10 min. The third and fourth AEP recordings were started 1 min and 5 min after the end of HV at a PCO_2 of 40 mm Hg.

Data Analysis. In the AEP recordings the N1 and P2 peak latencies were measured to stimulus onset, the N1 and P2 amplitudes to the pre-stimulus baseline. Measurements were performed on the computer-displayed waveforms using a digital cursor.

Results

HV was easily performed by all subjects and all reached the PCO_2 values aimed at with a maximal deviation of 2 mm Hg. Visual inspection of the EEG recorded from Cz revealed an increase in slow activity during HV, which rapidly disappeared after the end of HV. The N1 and P2 AEP components could be identified in all recordings. AEPs were markedly altered during HV as shown by the grand averages of the ten subjects investigated (Fig. 1). The mean amplitude and latency values of N1 and P2 for each recording condition are given in Table 1. During HV the amplitudes of N1 and P2 decreased. In the AEP recording started 1 min after the end of HV, the amplitude of P2 had regained nearly the same size as before HV, whereas N1 amplitude had only slightly recovered. In the AEP recording started 5 min after the end of HV, the amplitudes had further increased, the P2 amplitude even exceeded its initial value. During and after HV the latencies of N1 and P2 remained unchanged. A statistically significant effect of HV could only be ascertained for the P2 amplitude ($P < 0.01$, analysis of variances).

Discussion

In this study, the effects of HV on the cortical AEP components N1 and P2 were determined under continuous capnographic control. Both AEP components can be recorded from fronto-central scalp regions [11] and represent the activation of widespread cortical areas [21, 22]. Stimulus intensity was adjusted to achieve stable large amplitudes of N1 and P2 [2]. HV reduced the amplitudes of N1 and P2, but only the decrease of P2 amplitude was found to be statistically significant. This effect probably results from a depression of synaptic function under hypoxic conditions [3]. Such a depression of synaptic function can be supposed to lead to an impairment of spatial and temporal summation processes. Evoked potential components with longer latencies, such as N1 and P2, may be assumed to be especially susceptible to such alterations because of their polysynaptic generation. The decrease of the amplitudes of cortical AEP components during HV parallels the well-known increase in slow activity and a decrease in alpha and beta activity in the spontaneous EEG [5, 9, 14, 17, 18, 20, 26]. Simultaneous changes of the EEG and the N1 and P2 AEP components have also been observed in states of physiologically decreased vigilance before falling asleep [10, 28]. At the present stage, the causal relationship between EEG and AEP changes must remain a matter of speculation. Taking the state of vigilance into account, the decrease of the P2 amplitude provides an easily quantifiable parameter that may allow conclusions on the depression of synaptic function produced by ischaemic hypoxia. Thus, the AEP investigation may be incorporated in studies on the efficacy of therapeutic measures in ischaemia and hypoxia of the brain.

Table 1. Auditory evoked potential latencies and amplitudes

	Before HV	During HV	1 min after HV	5 min after HV	*P*
N1 latency	86.1 ± 7.7	87.4 ± 11.6	90.8 ± 13.8	89.2 ± 16.5	NS
P2 latency	137.6 ± 5.8	138.3 ± 11.9	140.1 ± 7.3	140.7 ± 13.3	NS
N1 amplitude	6.30 ± 3.36	4.88 ± 2.75	5.19 ± 3.05	5.69 ± 2.34	NS
P2 amplitude	7.02 ± 2.14	4.27 ± 0.92	6.60 ± 1.73	7.63 ± 2.54	< 0.01

Values are given as means ± SD, latencies in milliseconds, amplitudes in microvolts. Significances were calculated by analysis of variances. HV, Hyperventilation; NS, not significant

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