Effects of Mild Hypercapnia on Somatosensory Evoked Potentials In Experimental Cerebral Ischemia

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SUMMARY In a previous report, the authors demonstrated the effectiveness of mild hypercapnia in enhancing decreased perfusion flow in ischemic, non-infarcted brain tissues. However, the previous work lacked in verification of improvement of suppressed brain function. Therefore, this report was attempted to evaluate the effect of hypercapnia on somatosensory evoked potential (SEP), using the similar ischemic model as previously. The results showed that mild hypercapnia of 43 to 55 mm Hg range was beneficial not only for enhancing decreased perfusion flow but also for restoring suppressed SEP. This report seems to be the first publication which verifies a presence of correlation between local cortical blood flow (LCBF) and SEP under mild hypercapnia in mildly to moderately ischemic brain tissues.

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IN THE PREVIOUS REPORT,¹⁻² the authors demonstrated the effectiveness of mild hypercapnia in enhancing decreased perfusion flow in ischemic, non-infarcted brain tissues, produced by occlusion of the canine middle cerebral artery. The beneficial range of PaCO₂ for restoring the reduced flow was between 45 and 55 mm Hg. Moreover, the use of mannitol combined with hypercapnia did not produce any additional benefit in restoration of reduced blood flow. However it must be pointed out that the previous work lacked evidence of improvement of function, under mild hypercapnia which significantly improved the perfusion flow. This report was focused on evaluating restoration on somatosensory evoked potential (SEP), which seems to be one of the most reliable parameters for assessment of brain function, under the similar range of hypercapnia as the one in the previous.

Materials and Methods

General Procedure

Twenty-two mongrel dogs, unselccted as to age and sex, and weighing approximately 8 kg were initially anesthetized with intramuscular injection of ketamine hydrochloride 8 mg/kg and intravenous pentobarbital 25 mg/kg. Additional pentobarbital was given through femoral cannula as necessary. Respiration was artificially controlled by animal respirator. The femoral artery was cannulated for continuous recording of blood pressure and sampling of blood gas analysis (Blood Microsystem ABL2, Copenhagen). Mean systemic arterial pressure (MSAP) was maintained between 110 and 120 mm Hg. The hypercapnic state was maintained by regulation of respiratory rate and volume with gas containing CO₂ of 10% and O₂ of 90%.


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For production of ischemia, the left middle cerebral artery was exposed by transorbital approach and occluded with sutures and Yaşargil's clip. Autopsied brains showed that occluded site was approximately 8 mm distal to origin of the middle cerebral artery.

Monitoring of Somatosensory Evoked Potential (SEP) and EEG

A plate electrode for SEP recording was placed on the epidural space covering the left middle ecto-sylvian gyrus, which was a sensory cortex in the dog. Right ischias nerve was percutaneously stimulated at the point 5 cm proximal to the knee joint by a stimulator (NSE, Nihonkohden, Japan) with frequency of 1 Herz and intensity of 20 volts, and SEP was obtained by averaging 50 responses with an analysis time of 100 msec, which indicated that stimulus duration was 50 seconds. Reference electrodes for SEP recordings were placed on both ear-laps.

Out of components of SEP, P, to N, peak to peak amplitude, expressed as V,, was analyzed since it was rather constantly recorded under the above-mentioned condition.

EEG was also recorded in order to evaluate suppression and recovery of brain function, to regulate depths of anesthesia and to enable to exclude mixture of artefact on SEP recording.

Measurement of Local Cortical Blood Flow (LCBF)

Hydrogen clearance method was used for measurement of LCBF. Needle electrodes of 100μ in diameter were placed in the cortex of the middle ecto-sylvian gyrus of the left (occluded) side close to site of electrodes for SEP monitoring epidullary placed. 10% hydrogen was inhalated for one to two minutes, and LCBF was calculated by two minutes’ initial slope method.

Postmortem Examination

The autopsied brain was investigated macroscopically and microscopically. H-E stain was used for light microscopic examination.

Results

A) Natural Course of SEP under Normocapnia Following Occlusion of the Middle Cerebral Artery

Figure 1-a shows an actual SEP recording from one representative dog. Following occlusion of the left middle cerebral artery, SEP (V,) was obviously suppressed and gradually recovered during the period of 2.5 hours.

Figure 1-b summarizes natural course of LCBF and SEP following the arterial occlusion. At 30 minutes following occlusion of the middle cerebral artery, LCBF and SEP were reduced by 31.0 ± 3.3% (Mean ± SE) and 53.8 ± 2.8% respectively, compared to the control before the occlusion, while at 60 minutes, reduction rates of LCBF and SEP were 36.8 ± 3.2% and 56.3 ± 3.5% respectively, followed by slight restoration of two parameters. Actual LCBF before arterial occlusion was 48.4 ± 5.4 (Mean ± se) ml/100 g/min.

EEG showed significant increase in frequency of θ-wave at 15 to 60 minutes following the arterial occlusion, while α-wave tended to decrease during the same period of time.

B) Response of SEP under Mild Hypercapnia Following Occlusion of the Middle Cerebral Artery

Figure 2-a shows an actual SEP recording under mild hypercapnia obtained from one representative dog, indicating that suppressed SEP (V,) following the arterial occlusion was definitely recovered at PaCO₂ level of 48.3 mm Hg and that the activated SEP went down with CO₂ inhalation off. Figure 2-b demonstrates good correlation between LCBF and SEP under mild hypercapnia obtained from the other dog. Relationship between LCBF and SEP is summarized in Figure 3-a,b. SEP (V,) was restored by 63.1 ± 4.8%, with recovery of LCBF by 23.4 ± 4.8%, under mild hypercapnia (fig. 3-a). The activated SEP returned to the previous values following termination of CO₂ inhalation (fig. 3-b).
FIGURE 2a. Actual SEP recording under mild hypercapnia from one representative dog. Suppressed SEP (V_i) following the arterial occlusion was definitely recovered at PaCO_2 of 48.3 mm Hg and that the activated SEP went down with CO_2 inhalation off.

C) Postmortem Examination

Dogs were sacrificed with intravenous injection of pentobarbital approximately four hours following the arterial occlusion. There was no evidence of extensive infarction macroscopically and microscopically. Hemorrhagic change was not present.

Discussion

In the previous report, the authors concluded that mild hypercapnia of 45 and 55 mm Hg range is effective for enhancement of decreased cerebral blood flow in ischemic, non-infarcted brain tissues. However, the previous report lacked in verification of whether or not hypercapnia of this level would be able to improve suppressed neuronal activity. V_i, representing P_i-N_i peak to peak amplitude in somatosensory evoked potential (SEP) was selected as the reliable parameter reflecting brain function in this study.

Branston et al. beautifully demonstrated relationships between CBF and SEP in the acute stage of ischemia and in the recanalization stage following the ischemia, which contributed to inform us that SEP was one of the useful parameters reflecting brain function.

The response of cerebral arteries during hypercapnia must depend on degree and stage of ischemia. Therefore, initially authors would like to describe characteristics of the models used in the present study in relation to the one in the previous. The present study was performed within approximately four hours following
occlusion of the canine middle cerebral artery, which was the similar to the previous. LCBF measured with hydrogen clearance method was decreased by 31% and 37% at 30 and 60 minutes following the arterial occlusion respectively in this study, while in the previous study, reduction rate of CBF at 30 to 50 minutes' post-occlusion stage was 42% with intracarotid injection method using beta emitting 85Kr and 19% by using gamma emitting 133Xe. Postmortem examination showed a presence of patchy ischemic lesions in the localized areas in this study, while no infarction was observed in the previous, suggesting that the model in this study is slightly more ischemic in degree than in the previous. However, it is undoubted that both models are categorized into mildly to moderately ischemic model.

Using ischemic model of mild to moderate degree, relationship between LCBF and SEP were tested. SEP (V₁) well correlated with LCBF not only under normocapnic state (fig. 1-b) but also under mildly hypercapnic state (fig. 2-b, 3-a,b). The results suggest that mild hypercapnia of 43 to 55 mm Hg range is beneficial for restoring suppressed brain function as well as for enhancing decreased perfusion flow in mildly to moderately ischemic brain tissues. In addition this report seems to be the first publication which verified a presence of good correlation between LCBF and SEP under mild hypercapnia in mildly to moderately ischemic brain tissues.

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Effects of mild hypercapnia on somatosensory evoked potentials in experimental cerebral ischemia.
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