# CHANGES IN TOTAL PHOSPHOLIPID PHOSPHORUS CONTENT OF WHOLE BLOOD ENTERING AND LEAVING THE BRAIN AFTER INTRACISTERNAL INJECTION OF γ-AMINOBUTYRIC ACID

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Intracisternal injection of γ-aminobutyric acid (GABA) into dogs causes a marked increase in the arteriovenous difference in the total phospholipid phosphorus concentration. This is due to lowering the phospholipid level in the arterial blood and to its elevation in blood leaving the brain. Since the same result follows intraarterial injection of GABA, it can be concluded that when this compound is injected intraarterially it passes through the blood-brain barrier and exerts a central action.

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Our earlier investigations [3] showed that γ-aminobutyric acid (GABA), if injected into the carotid artery, produces a marked increase in the total phospholipid phosphorus concentration in whole blood leaving the brain. By distributive chromatography on paper soaked with silicic acid [4], it was found that this change takes place on account of neutral phospholipids, while the content of acid phospholipids decreases.

When injected intraperitoneally and into the carotid artery, GABA is known to accumulate in nerve tissue [1, 7, 10], and this is attributed to its passage through the blood-brain barrier. Consequently, changes described above in the concentration of total and individual phospholipids may be interpreted as the result of the central action of GABA.

In the present investigation we studied changes in the concentration of total phospholipid phosphorus in whole blood entering and leaving the brain after intracisternal injections of GABA. This could provide a means in the future of assessing effects of GABA when administered to the animal by various routes on quantitative changes in individual phospholipids in blood entering and leaving the brain.

## EXPERIMENTAL METHOD

Experiments were carried out on three male dogs in which in a preliminary operation the common carotid artery was exteriorized in a skin tube and all branches of the external jugular vein were ligated with the exception of the posterior facial vein, which has direct communication with the transverse sinuses of the brain.

GABA was injected suboccipitally in a dose of 2.5 mg/kg body weight. Phospholipids were fractionated by distributive chromatography on paper soaked in silicic acid by the method of Marinetti and co-workers [8], modified by A. A. Smirnov and co-workers [6], and subsequently by ourselves [5].

Blood from the external jugular vein was taken 14-17 sec after the arterial sample; this corresponds to the time of complete circulation of blood in the brain [2]. The first two blood samples, which acted as controls for that particular day of the experiments, were taken a few minutes after the animal had been placed in the experimental room.

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TABLE 1. Arteriovenous Difference in Concentration of Total Phospholipid Phosphorus in Whole Blood in Dogs after Intracisternal Injection of GABA in Dose of 2.5 mg/kg Body Weight

| Experimental conditions | Lipid phosphorus (in μg/ml blood) | | |
|---|---|---|---|
| | common carotid artery | external jugular vein | P |
| Control | 91.80±0.90 | 96.9±1.08 | <0.05, >0.025 |
| After injection of GABA | | | |
| 5 min | 88.07±2.67 | 106.3±3.03 | <0.01 |
| 20 min | 83.50±3.46 | 109.4±2.00 | <0.001 |

## EXPERIMENTAL RESULTS

According to our data (Table 1), under normal circumstances the difference between the mean total phospholipid phosphorus concentration in whole blood entering the brain and in venous blood is not significant. The second and third blood samples were taken 5 and 20 min respectively after intracisternal injection of GABA, which was accompanied by the development of a series of external signs of excitation of the animal (restlessness, dyspnea, salivation, increased heart rate, frequent micturition, etc.). As Table 1 shows, 5 min after injection of GABA the arteriovenous difference in total phospholipid phosphorus concentration in the blood entering and leaving the brain was considerably increased. This was caused by a decrease in the lipid phosphorus concentration in the blood entering the brain and a marked increase in its concentration in the blood leaving the brain. A similar pattern was observed 20 min after injection of GABA, when the level of phospholipid phosphorus in the blood entering the brain was appreciably reduced while that in the venous blood was increased. These results show good agreement with those of our previous investigations [3, 4], when a marked increase in this arteriovenous difference in lipid phosphorus concentration was found after intracarotid injections of GABA in doses of 2.5, 3.75, and 5 mg/kg body weight. It is striking that GABA, when injected intracisternally in a dose of 2.5 mg/kg, causes more marked changes in the concentration of these substances than when injected into the carotid artery.

The results of these experiments show that the effect of GABA on the arteriovenous differences in total lipid phosphorus concentration takes place in the same manner regardless of the mode of injection of this compound into the body, and takes the form of a considerable increase in its level in the blood leaving the brain. These findings are indirect evidence that GABA can pass through the blood-brain barrier, so that in the future its role in brain metabolism can be more easily studied.

Electrometric measurement of the volume velocity of the cerebral circulation [3] revealed no significant fluctuations during these time intervals after administration of GABA. It can therefore be assumed that the observed changes in arteriovenous difference of total lipid phosphorus developing at these times after intracisternal injection of GABA are the results of corresponding changes in the metabolism of nerve tissue itself and are independent of the slight fluctuations in rate of the cerebral blood flow.

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