A Comparison of Function of the First and Second Somatosensory Areas of the Dog[1]

It was found in a previous investigation that unilateral removal of the cerebral somatosensory receiving areas in the posterior sigmoid (SI) and anterior ectosylvian (SII) gyri of the dog caused transient impairement of a preoperatively established tactile conditioned reflex[2]. The impairment consisted in a reduction of the ability to elicit the reflex from the peripheral fields corresponding to the areas removed. The finding was taken to indicate that elements located in these areas participate in the conditioned reflex under normal conditions. It is, on the other hand, not known whether one area or both participate. Thus, it has now been examined whether a similar postoperative impairment of a comparable tactile conditioned reflex can be caused by removing SI or SII alone.

Dogs have been trained to react to a light tactile stimulus or a visual stimulus by pressing a button (33 mm diam eter) with the nose. The tactile stimulus consisted of puffs of air (100 msec duration, 3/sec) delivered through 1 of 4 nozzles, 2 of which were attached to each hindlimb; tibia and paw. The visual stimulus, used for control purposes, consisted of flashes of white light of the same duration and frequency as the tactile stimuli. The stimuli (14 each session, 3 tactile through each nozzle and 2 visual) were presented in pseudo-random order and at pseudo-random intervals. Correct responses (button-pressing performed during a stimulation not exceeding 10 sec) were reinforced with food; the dogs not having been fed for the last 24 h preceding a session. A 'blind', tactile stimulus, representing all parameters of the ordinary stimulus except for its tactile component, was used to check that the conditioned response was an effect caused by the activation of peripheral cutaneous receptors.

Lesions were made when a dog was performing accurately at a stable level; i.e. over 90% correct responses for the last 8 preoperative sessions. The lesions were restricted to the hindlimb area of SI or SII which was removed by subpial suction under aseptic conditions. The somatosensory areas were mapped with electrophysiological technique in each animal at the beginning of the operation.

In 6 dogs the following lesions were made initially: SI unilaterally, SI bilaterally, SII unilaterally, SII bilaterally in 1 animal and SI and SII together unilaterally in 2 animals. Of these animals only the 2 where both SI and SII had been removed showed any postoperative impairment (i.e. incidence of postoperative responses less than 50% of preoperative). It thus appeared as if SI and SII could replace one another functionally and that removal of both was necessary to obtain impairment[3]. However, when further lesions were made in these animals a different picture emerged.

For example, removal of the remaining SII in the dog where SII had already been removed unilaterally, caused transient impairment of the reflexes from the limb contralateral to the second operation. Similarly, contralateral impairment appeared after removal to the remaining SII of 1 dog which had recovered from a previous removal of SI and SII together on the other side. On the other hand, removal of the remaining SI in dogs with previous unilateral lesions in SI alone, or both SI and SII, caused no impairment (i.e. incidence of postoperative responses higher than 90% of preoperative). Likewise, unilateral removal of SII after bilateral removal of SI caused impairment, whereas unilateral removal of SI after bilateral removal of SII did not.

Thus postoperative impairment of the type observed previously after removal of both somatosensory areas[2] can be caused by removing SII but not by removing SI alone. It should, however, be pointed out that although this finding indicates a special significance for SII a role for SI is not excluded. For example, whereas unilateral removal of both SI and SII in the previous[2] and present material has always caused postoperative impairment, unilateral removal of SII in the present material, in one instance did not. The absence of impairment after bilateral removal of SII also remains to be explained. The present results agree with previous reports that the ability of dogs[4] and cats[5] to differentiate passively received tactile stimuli is impaired by lesions of SII but not SI.

Zusammenfassung. Ausgehend von der Annahme, dass beim Hund die somatosensiblen Gebiete im Gyrus sigmoideus posterior (SI) und Gyrus ectosylvius anterior (SII) an einem taktil bedingten Reflex beteiligt sind (Defekte am Reflex nach Abtragung des Gebietes), wurde die relative Bedeutung beider Gebiete durch Teilabtragungen studiert: Auftreten der Defekte nach Abtragung von nur SII, nicht aber von SI.

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Dehydration of the Brain by Intra-Peritoneal Injections of Hyper-Osmotic Solutions of γ-Aminobutyric Acid and DL-α-Alanine

Results of previous investigations have indicated that i.p. injections of large volumes of hyper-osmotic solutions of γ-aminobutyric acid (GABA), or other substances, can offer protection against convulsions produced by hyperbaric oxygen or by administration of chemical convulsants[1-4]. Although it was suggested originally that the effect of hyper-osmotic GABA was 'specific' to GABA and related to its entry into the brain[1], further results have indicated that this treatment causes significant dehydration of the brain[3]. Therefore, it has been postulated that the anti-convulsant action of hyper-osmotic GABA is related mainly to dehydration of the brain rather than to its penetration into the brain, and that this action is not specific for GABA[3]. Since injections of hyper-osmotic solutions of α-alanine dehydrate the brain and protect against convulsions at least as well as hyper-

osmotic GABA[3], it seemed pertinent to compare the effects ot these two substances on the water content of the brain using a sensitive radio-isotopic method.

Tritiated water (^{3}HOH, specific radioactivity, 25 mC/g, New England Nuclear Corp.) was injected i.p. (in 0.9% NaCl) in a dose of 0.1 μC/g of fasted mouse. Mice were sacrificed at various times after administration of the ^{3}HOH, and homogenates of brain (above the level of the colliculi, and not including the cerebellum) were prepared in 80% ethanol solution (v/v) and centrifuged; radioactivity was determined in aliquots of the resulting supernatants. Results shown in the Table indicate that ^{3}HOH exchanges very rapidly with brain water and that a large amount of the radioactivity remains in the brain 5 h after injection. In the Table it is shown also that i.p. injections of hyper-osmotic GABA and DL-α-alanine (1M solutions in 0.9% NaCl; 25 mmoles/kg), given 30 min before sacrificing the animals, produce a significant dehydration of the brain.

Entry of i.p. injected ^{3}HOH into the brains of mice; effects of hyper-osmotic GABA and DL-α-alanine on the entry of ^{3}HOH

Time of injection of ^{3}HOH (0.1 μC/g)	Hyper-osmotic treatment	dpm/g brain ($\times 10^{-3}$)	
1 min	none	297.7 ± 13.44	(8)
5 min	none	541.9 ± 9.44	(8)
5 h	none	482.4 ± 3.16	(8)
5 h	GABA[a]	433.8 ± 10.31	(8)[b]
5 h	DL-α-ALA[a]	461.7 ± 3.63	(8)[b]
24 h	none	287.8 ± 6.87	(16)

[a] Hyper-osmotic treatments (25 mmoles/kg) were given i.p. 30 min before sacrificing animals. These values are to be compared with the 5 h untreated control value. Means ± standard errors; numbers of mice in parentheses; [b] indicates a p-value <0.001 with respect to controls (Student's t-test, one-tailed).

These results support further the finding[3] that the mechanism of the anti-convulsant effect of hyper-osmotic treatments is related to the brain dehydration produced, and not to a specific 'inhibitory' action of GABA. Although it seems likely that the hyper-osmotic fluid injected causes a loss of water from other tissues as well as from brain, due to the increased osmolarity of the serum which occurs[3], it is thought that the anti-convulsant effect is related mainly to the loss of brain water. It is suggested that DL-α-alanine, a substance which does not exert potent inhibitory actions on CNS neurones, acts by a mechanism similar to that of GABA in protecting against convulsions when administered as an hypertonic solution[5].

Résumé. Utilisant une technique radioactive avec le ^{3}HOH, nous avons montré que les injections i.p. des solutions hyperosmotiques de l'acide γ-aminobutyrique et de DL-α-alanine, deshydratent de manière significative les cerveaux des souris.

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Apparent Activation Energy of the Nerve Impulse Conduction[1]

In this communication we calculate the apparent activation energy of the nerve impulse propagation, as expressed by the temperature dependence of the conduction velocity in the nerve fibres. We call this activation energy 'apparent', for we do not refer, as is usually done, to a chemical reaction, but to a complex physico-chemical process, the nerve impulse propagation, considered as a whole.

The spread of the excitation along the nerve fibre obviously means the transition of certain physical structures from a 'resting' to an 'active' state; it is likely that these structures are located in the axon membrane. From this point of view, the propagation of the action potential appears to be associated, at a molecular level, with transitions of certain macromolecular components of the nerve fibre. There is some evidence that, during the action potential, some vibrorotational transitions of the protein macromolecules take place in the axon membrane[2]. Even neglecting the concrete nature of the transformation and the macromolecules which undergo it, from a physico-chemical point of view, the nerve impulse propagation implies the 'transformation' of some components from a certain state 1 (resting state) to another state 2 (active state). It thus appears that the conduction velocity of the nerve impulse represents, or at least is proportional with, the transformation rate of the components from state 1 into state 2.

The activation energy (E) of this 'reaction' is given by the wellknown Arrhenius' formula[3]: $E = -R\,(\delta(ln\,k)/\delta(1/T))$, where k is the rate constant and R, T have their usual meanings.

The conduction velocity, that is the rate of the reaction $1 \rightarrow 2$, is: $v = k \cdot C_1^{\nu_1} \cdot C_2^{\nu_2} \cdots$, where c_1, $c_2 \cdots$ are the 'concentrations' of the components undergoing the transition $1 \rightarrow 2$, and ν_1, ν_2 are the stoichiometric coefficients. As: $(\delta v/\delta T) = (\delta k/\delta T)$, we can write: $E = -R\,(\delta(ln\,v)/\delta(1/T))$. Using finite differences instead of differentials, after a few simple operations we obtain: $E \approx R\,(T_1\,T_2/(T_2 - T_1))\,ln\,(v_2/v_1)$. Here v_1 and v_2 are the conduction velocities for the absolute temperatures T_1 and T_2. The Celsius temperatures are noted with t_1, t_2.

[1] This paper is based on an investigation in progress which will be submitted by D.-G. MĂRGINEANU in partial fulfilment of the requirements for a Doctoral Degree in Biophysics under the leadership of Prof. Dr. V. VASILESCU.
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