## Evidence of Recruiting Responses in the Cat's Mesencephalic Reticular Formation [1]

DEMPSEY and MORISON[2] first described the production of recruiting responses in the cerebral cortex upon stimulation of certain thalamic nuclei. Their own findings, extended and further precised, especially by JASPER *et al.*, suggested an interpretation for the mechanism of the electroencephalographic spindles usually recorded for instance during natural or barbiturate sleep. Indeed, a striking similarity exists between those spontaneous rhythms and the bursts of waves induced by a slowly repetitive stimulation of the diffusely projecting thalamic nuclei.

On the other hand, it was shown that this non-specific thalamic system is itself controlled by the mesencephalic and bulbar reticular formation, which, when activated, is able to counteract the cortical recruitment. Thus, as a clear ascending influence exists between the rostral and caudal parts of the so-called centrencephalic structures, it seemed interesting to test the reverse possibility, namely a feed-back action of the thalamus upon the brain stem reticular formation. This was done by seeking for recruiting responses in the mesencephalic region.

Cats were prepared under ether anesthesia and paralysed by Flaxedil. Although barbiturates in small doses are known to facilitate the production of recruitment, it seemed advantageous, at least for the preliminary experiments, to eliminate this additional variable. Electrical stimuli (repetitive 1 ms square pulses) were applied by bipolar electrodes inserted in a steel needle. Bipolar electrodes of the same type or glass microelectrodes (about 5 $\mu$ at the tip) were used to record the potentials in the central core of the mesencephalon at the Horsley-Clarke frontal plane 2 and lateral planes 1 to 3.

Various types of responses were elicited in the mesencephalic region upon repetitive stimulation of different subcortical and cortical structures. Among them, the typical patterns described here as 'recruiting responses' fulfilled the following criteria, adopted by JASPER and AJMONE-MARSAN for similar phenomena recorded on the cerebral cortex[3]:

(1) While the first of a series of stimuli at 8 or 10/s produced little or no visible potential, a maximum amplitude of the responses was reached after the third to the sixth repetitive shock; then the amplitude gradually decreased to a more or less constant value.

(2) The optimum frequency of stimulation was found to lie between 5 and 12·5/s. At lower frequency, the potential waves escaped the driving by the afferent impulses. At higher frequency, recruitment simply did not occur.

(3) The latency of the responses was about 20 to 50 ms.

The records of Figure *A* and *B* illustrate the given definition. Such patterns may be easily obtained from stimulating points anywhere in the diffusely projecting nuclei of the thalamus. Moreover, when cortical and mesencephalic recordings were simultaneously made, recruitment either appeared at both sites or did not appear at all, according to the location of the stimulating electrodes. On many occasions, a shock intensity of 1·5 V was sufficient for the production of good responses.

Other observations were also made, which can be summarized as follows:

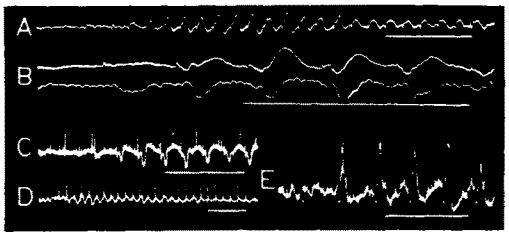
(1) Reticular units, responding to various and widespread peripheral stimulations, most often also discharged in relation with the local recruiting waves. The characteristics of their induced firing have not yet been fully analysed, but it appears that several patterns of response may be distinguished on the basis of both latency and relation with the polarity of the slow potentials. Two typical examples are presented in Figure *C* and *E*.

(2) Under favourable conditions, it was sometimes possible to elicit mesencephalic recruiting responses by stimulation of the cerebral cortex.

(3) However, recruiting responses were still elicitable from the thalamus into the mesencephalon after removal of the whole cerebral cortex of both hemispheres (Fig. *D*).

(4) Effective sites of stimulation were found exclusively in and around the area of the non-specific thalamic nuclei.

(5) Although no systematic exploration of the receptive field in the brain stem has been so far achieved, it may be stated that the recruiting responses, when occurring, seemed to extend broadly in the whole field of the medial mesencephalon.




Oscillographic records of recruiting responses in the mesencephalic reticular formation. *A* Recording point inferior and lateral to griseum centrale, 10/s stimulation of nucleus centralis lateralis with intensity 1·5 V. – *B* Upper trace from prefrontal cortex, lower trace from medioventral mesencephalon, parallel development of recruiting waves at both sites by stimulating at 6/s at the border between nucleus ventralis lateralis and nucleus paracentralis. *C* Mesencephalic reticular unit discharging in relation to the recruiting waves, 8/s stimulation of nucleus centralis lateralis. *D* Mesencephalic recruitment upon 10/s stimulation of nucleus centralis medialis after total decortication of both hemispheres. *E* Short latency unitary responses in the mesencephalic reticular formation upon 8/s stimulation of nucleus paracentralis. All time marks: 0·5 s except for trace *E* where it is 0·3 s.

(6) A high frequency stimulation (100/s and more) of the cerebral cortex and single or repetitive shocks applied to a peripheral nerve might reduce the amplitude or even suppress the production of recruiting responses.

These experiments demonstrate the back action of the diffusely projecting system of the thalamus on mesencephalic regions which are physiologically considered as belonging to the reticular system. Faced with this fact, one would naturally inquire about the significance and importance of this feed-back mechanism. The problem has been approached by studying the interaction between impulses of central and peripheral origin, elicited at various time intervals by stimulation of the thalamus and cutaneous nerves. The first attempts indicated that these two types of afferents do not activate the reticular neurones in the same way. So the resulting figure of interaction cannot be easily interpreted in simple terms of occlusion and facilitation. Further complication is brought

[1] This work has been sponsored by the Office of Air Research and Development Command, U.S. Air Force, under contract No. A.F. 61(514)-22.

[2] E. W. DEMPSEY and R. S. MORISON, Amer. J. Physiol. *135*, 293 (1942).

[3] H. H. JASPER and C. AJMONE-MARSAN, in *Patterns of organisation in the central nervous system* (Williams and Wilkins Co., Baltimore 1952), p. 493.

in by the reciprocal action of central and peripheral stimuli because of the mutual alterations induced by signals in these two channels. Nonetheless, the present interest in this field[4] is expected soon to clarify our understanding of the descending influences on the ascending activating reticular system.

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*Résumé*

La stimulation des noyaux non-spécifiques du thalamus chez le chat non anesthésié, provoque des réponses de recrutement dans le mésencéphale. Il est démontré que ces réponses sont analogues à celles qu'on enregistre classiquement sur le cortex et que les neurones réticulés participent à cette activité induite. Ces résultats impliquent l'existence de relations réciproques entre les structures diencéphaliques et mésencéphaliques qui contrôlent le niveau d'activation cérébrale.

[4] W. R. ADEY, J. P. SEGUNDO, and R. B. LIVINGSTON, J. Neurophysiol. *20*, 1 (1957).

## Inhibition of Anaphylactic Shock by Oral Lipids

In the course of a comparative study on the mechanism of action of anti-allergic substances undertaken in our laboratories, it was found that dietary lipids can produce an immediate anti-allergic effect inasmuch as guinea-pigs may be protected against lethal anaphylactic shock within 1 h after the ingestion of certain lipids. The following is a preliminary account of these experiments.

*Methods.*—Male guinea-pigs weighing from 300–350 g were sensitized by a single subcutaneous dose of 0·5 ml of a 20% (v/v) egg-white solution. Three weeks later, anaphylactic shock was elicited by an intravenous injection of 0·2–0·3 ml of a 2% (v/v) egg-white solution. This procedure resulted in the death of 39 out of a total of 47 control animals and never killed less than $^3/_4$ of the actual control group run in the same series. The egg-white used in these experiments was obtained from several fresh eggs; it was homogenized by repeated freezing and thawing and straining through gauze. Identical batches were used for sensitization and challenging. The lipids to be tested were warmed to 38–40° C and fed drop-wise with a pipette. In most cases, the amount administered was 2 ml/animal and the interval between feeding and challenging 60 min. In a few cases the interval between feeding and challenging or the amount of lipid fed were varied. Oils and fats were employed as available from various commercial sources. Cod-liver and sesame oil were of the type specified by the Swiss Pharmacopoea (Ph. H. V.). Linoleic and linolenic acid (Hoffmann-La Roche) were obtained from ampoules sealed under nitrogen and mixed with the specified amounts of arachis oil or propylene glycol *ex tempore* 5 min prior to being fed.

*Results* (see Table). – A single oral dose of certain lipids exerted a protective effect against lethal anaphylactic shock in the guinea-pig. The list of active lipids comprises three oils of vegetable origin, i.e. cotton-seed, sesame and corn oil, and one animal fat, i.e. bone oil. The effects obtained with arachis oil, linolenic acid and cod-liver oil are probably not significant in view of the restricted number of animals employed. Olive oil, soy bean lecithin mixed with arachis oil, linoleic acid, fresh cream, butter, lard and egg-yolk were ineffective in the amounts studied.

From the experiments performed with corn oil it is evident that a minimum of lipid must be fed in order to obtain protection. With the material employed here, the minimal dose would seem to lie between 1 and 2 ml.

The lacteals of animals dying from anaphylactic shock within 5 to 20 min after challenge, i.e. 65 to 80 min after feeding of the lipid were visible as white turgescent strings; in a few cases, the serum taken from such animals at death was slightly opaque. Likewise, in cases where 2 ml amounts of corn oil etc. were fed to non-sensitized guinea-pigs or to guinea-pigs sensitized but not challenged, the lacteals showed the same whitish content 90 min after receiving the lipid. Of the sensitized guinea-pigs protected against lethal anaphylactic shock by corn oil or by sesame oil, a few were killed in order to examine the lacteals after the animals had recovered, i.e. 20–30 min after challenging. In all these protected animals, the lacteals were entirely transparent. It would thus appear that during anaphylactic shock in the guinea-pig some clearing agent is released—most probably from the intestinal tract.

| Lipids | Amount fed* (ml) | Protection** |
|---|---|---|
| *Vegetable* | | |
| Arachis oil | 2 | 3/10 |
| Cotton-seed oil | 2 | 6/10 |
| Sesame oil | 2 | 7/14 |
| Olive oil | 2 | 2/10 |
| Corn oil | 2 | 7/13 |
| | 1 | 2/7 |
| | 0·5 | 1/5 |
| Soy bean lecithin | 1 | 2/10 |
| plus arachis oil | 1 | |
| Linoleic acid | 0·5 | 1/8 |
| plus arachis oil | 1·5 | |
| Linolenic acid | 0·5 | 2/5 |
| plus propylene glycol | 1·5 | |
| *Animal* | | |
| Fresh cream | 2 | 2/8 |
| Butter | 2 | 1/9 |
| Lard | 2 | 2/8 |
| Egg-yolk | 2 | 2/9 |
| Cod-liver oil | 2 | 3/8 |
| Bone oil | 2 | 4/10 |
| Controls (no feeding) | – | 8/47 |
| Controls: Peptone 10% | 2 | 1/9 |

* Oral administration of lipids etc. 1 h before challenging.
** Number of animals protected/number of animals employed.

From further experiments with corn oil in 2 ml amounts it became evident that the protective activity of this lipid sets in when absorption has reached a certain level, i.e. in this case not until 30–45 min have passed; it then lasts for about 2 to 3 h and is practically finished 5 h after feeding the lipid.

Preliminary but unequivocal experiments in which groups of sensitized guinea-pigs were fed with corn oil and simultaneously injected with anti-anaphylactic doses of *Proteus* polysaccharides[1] or antihistamines, such as tripelennamine or promazine, showed that feeding of the anti-anaphylactically effective lipid together with an injection of the anti-allergic polysaccharide resulted in no

[1] R. MEIER, H. J. BEIN, and R. JAQUES, Exper. *12*, 235 (1956); Int. Arch. Allergy *11*, 101 (1957).