Other conditions can facilitate the H reflex. A voluntary contraction of the soleus produces a recruitment curve which originates at a slightly lower threshold and attains a higher maximal amplitude (Figure 2). Some well-trained subjects have learned to maintain constant voluntary muscular activity. Under these conditions, using an auditory monitor coupled to the electromyogram of the soleus, one readily obtains reproducible recruitment curves. The curves in Figure 2 were accurately reproduced 5 times.

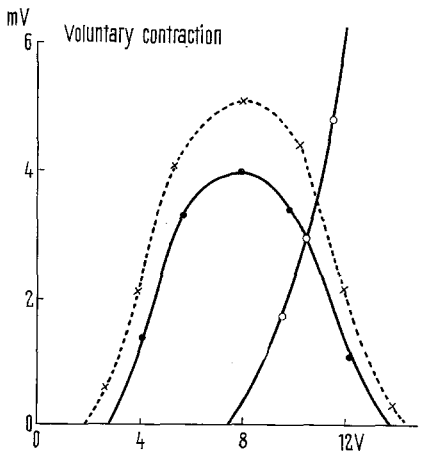

Fig. 2. As in Figure 1, the control curve is represented by black dots. The amplitudes of the H reflex recorded during a constant voluntary contraction are represented by asterisks.

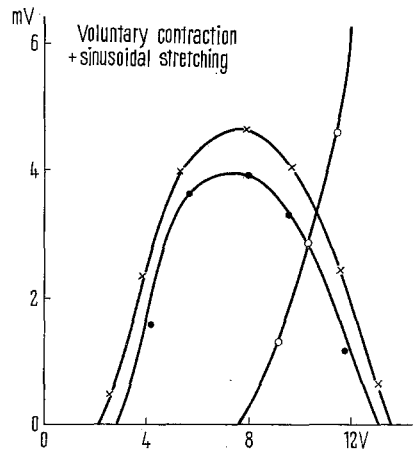

Fig. 3. As in the other graphs, black dots indicate control values. When the sinusoidal stretching and the voluntary contraction are combined, the amplitudes are higher than controls and are shown by asterisks.

It is also possible to combine passive sinusoidal stretching of the soleus with moderate voluntary contraction of the muscle. The recruitment curves obtained with this procedure are identical in every respect to those produced by a voluntary contraction of the same intensity (Figure 3). The effect of these combined manipulations on the H reflex is thus not the algebraic sum of the inhibitory and facilitatory influences. Rather, it is as if the voluntary command, at the same time as it increases motor pool activity, suppresses the inhibitory effect exerted by the proprioceptive muscle afferents.

These findings suggest a functional organization of the descending pathways which could interfere with the influence of the proprioceptive segmental afferents and in particular with the Ia afferents. This interpretation is corroborated by studies dealing with polysynaptic reflexes and voluntary contraction (HUGON[5]). It is also consistent with models of the motor system recently developed by NAVAS and STARK[6].

The competitive action of facilitatory and inhibitory influences is of great interest in investigations of spinal reflex activity in man. In this regard, the study of voluntary contraction is particularly informative.

Résumé. Les courbes de recrutement du réflexe H permettent d'exprimer de façon commode les phénomènes inhibiteurs et facilitateurs spinaux. Lorsque l'on associe la mobilisation de la cheville à une contraction volontaire de même intensité, l'effet observé est égal à celui obtenu par la contraction volontaire seule. Ces résultats suggèrent que la contraction volontaire pourrait contrôler le mécanisme inhibiteur mis en activité par les afférences musculaires.

P. J. DELWAIDE[7] and M. HUGON

Laboratoire de Neurophysiologie Comparée, Faculté des Sciences, Marseille 13e (France), 2 July 1969.

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Effect of Methyl Amphetamine on the Brain 5-Hydroxytryptamine Content of Isolated and Aggregated Rats

Drugs having central stimulatory effects increase the brain 5-hydroxytryptamine (5-HT) content. Lysergic acid diethylamide (LSD), imipramine, atropine, etc., have been shown to increase brain 5-HT content of rats[1–4]. Convulsions produced by electroshock as well as chemical agents like cardiazol have also been shown to increase the level of 5-HT in rat brain[5]. MILINE, STERN and HUKOVIC[6] observed increase of brain 5-HT in rats with experimentally induced fear. GUNN and GUARD noticed that the symptoms of excitation and stimulation caused by injection of amphetamine and related compounds were much more pronounced if the animals were kept together in one cage rather than singly, and the toxicity of amphetamine was increased nearly 10 times by keeping the injected animals in groups of 10 instead

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of one in each cage[7]. The increased toxicity of amphetamine is presumably due to a fright response and stress. Sensory stimulation including aggregation also enhances the effect of amphetamine on the brain concentration of noradrenaline[8,9].

It has also been shown by COHEN and LAL[10] that sensory stimulation increases the toxicity of amphetamine. We now report the effect of amphetamine on the concentration of brain 5-HT of rats during isolation and aggregation and in combination with chlorpromazine.

Adult male albino rats of Wistar strain, 100–150 g, were injected i.p. with methyl amphetamine sulphate, 10 mg/kg in 0.5 ml of physiological saline. Immediately after injection, the animals were isolated 1 per cage or aggregated 10 per cage[10]. The surviving rats were decapitated and 5-HT was extracted from each brain by the method of AMIN, CRAWFORD and GADDUM[11] and assayed on atropinized (10^{-6}) oestrous uterus of rat[12]. Addition of cyproheptadine, a potent antagonist of 5-HT, in the bath fluid completely abolished the responses of the extracted material thereby proving the substance to be 5-HT.

In experiments with chlorpromazine, the drug was injected at a dose of 5 mg/kg i.p., 30 min prior to the administration of methylamphetamine sulphate both for isolated and aggregated animals and 5-HT was extracted 1 h after administration of methylamphetamine sulphate.

A significant and moderate increase was found in the concentration of brain 5-HT at different time intervals in aggregated rats after administration of methylamphetamine sulphate, 10 mg/kg i.p., and this increase was maximal after 1 h of drug administration (Table I). The maximal stimulation also occurred in aggregated animals between 45–90 min.

In Table II, it is shown that chlorpromazine specifically inhibited the increase of brain 5-HT in aggregated animals treated with methyl amphetamine sulphate.

Our observations support the results of MILINE, STERN and HUKOVIC[6], who found an increase in the brain 5-HT content after chronically induced fear in hare – however, the conditions in our experiments are very different. It is interesting to note that there was only small and insignificant increase of 5-HT in the isolated animals treated with methylamphetamine, which confirms the earlier report of GARATTINI, KATO and VALZELLI[13] who found no change of 5-HT level in rat brain treated with amphetamine. In our experiments the maximal increase of brain 5-HT in aggregated rats was found after 1 h and the maximal stimulation as well as a few deaths also occurred in animals between 45–90 min suggesting the role of serotonin in amphetamine induced fright and stress. These experiments also indicate that the increase of brain serotonin in aggregated rats is not due to drug effect but to increase excitation, fear and stress caused by aggregation.

PLETSCHER and GEY[14] reported no change of brain 5-HT content in rats treated with chlorpromazine but inhibition of iproniazid induced increase of brain serotonin by chlorpromazine. In our experiments it is shown that chlorpromazine specifically inhibited the increase of brain 5-HT in methylamphetamine treated aggregated rats (Table II).

COURVOISIER, DUCROT and JULOU[15] observed that chlorpromazine antagonizes the amphetamine toxicity very effectively. The causal relationship between increased 5-HT and amphetamine-stress toxicity cannot be established at this stage, the increase may only be coincidental. It can be concluded that fright and stress causes an increase in the 5-HT content of the brain which is inhibited by chlorpromazine.

Zusammenfassung. Amphetamin bewirkt eine Vermehrung von 5-Hydroxytryptamin im Gehirn von aggregierten Ratten, während Chlorpromazin diesen Effekt hemmt.

D. K. GANGULY[16]

Division of Pharmacology,
Department of Pharmacy, Jadavpur University,
Calcutta (India), 22 April 1969

Table I. Effect of 10 mg/kg methyl amphetamine on the concentration of brain 5-HT of isolated and aggregated rats

Time after injection (h)	5-HT µg/g of tissue ± S.E. mean Control (saline) Isolated	Aggregated	Treated Isolated	Aggregated
0.5	–	–	0.53 ± 0.030 (8) n.s.	0.75 ± 0.039 (7) $P<0.05$
1.0	0.54 ± 0.029 (12)[a]	0.48 ± 0.023 (12)	0.61 ± 0.035 (11) n.s.	0.92 ± 0.042 (11) $P<0.05$
2.0	–	–	0.59 ± 0.028 (8) n.s.	0.70 ± 0.045 (8) n.s.
4.0	–	–	0.55 ± 0.035 (10) n.s.	0.78 ± 0.039 (8) $P<0.05$

[a] No. of animals in parenthesis; P calculated from student's t-test.

Table II. Combined effect of 10 mg/kg methyl amphetamine and 5 mg/kg chloroprmazine on brain 5-HT of isolated and aggregated rats

Drugs (i.p.)	No. of rats	Brain 5-HT content in µg/g ± S.E. mean Isolated	Aggregated
Control (saline)	12	0.54 ± 0.029	0.48 ± 0.023
Methyl amphetamine (10 mg/kg)	11	0.61 ± 0.035 n.s.	0.92 ± 0.042 $P<0.05$
Methyl amphetamine + chlorpromazine (5 mg/kg)	12	0.51 ± 0.025 n.s.	0.56 ± 0.031 n.s.

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