intensified the pentagastrin effect progressively ($p < 0.05$) and inhibited the action of histamine ($p < 0.05$; figure 3).

Discussion. Activities of AC of human fundic gastric mucosa were log-normally distributed and this should be considered to avoid misinterpretations. In our experiments with human gastric mucosa, pentagastrin activated AC in vitro. A stimulating action of histamine has been reported previously by us[10]. Cimetidine antagonized the histamine effect on AC, whereas the pentagastrin activation was even enhanced. These results support the view that pentagastrin and histamine act upon distinct receptors in stimulating AC and confirm recent findings in the rat and dog gastric mucosa.

Náfrády and Wollemann[7] showed in vitro stimulation of rat gastric mucosal AC by pentagastrin, an activation which could not be inhibited by histamine H_2-receptor blockade with cimetidine. Soumarmon et al.[5] showed 'high affinity gastrin receptor sites' in isolated parietal cells; and they detected furthermore a gastrin-sensitive AC in purified plasma membranes[6]. Brown and Gallagher[11] reported a specific and concentration-dependent binding of gastrin to rat gastric mucosal particles. Again, H_2-receptor blockade with cimetidine did not interfere with the binding. Soll[12,13], using isolated parietal cells of the dog gastric mucosa, presented findings indicating that the gastrin effect on oxygen consumption, uptake of ^{14}C-aminopyrine and cAMP production was not influenced by cimetidine. Although our results with human gastric mucosa fit well the data of these animal experiments, they offer no plausible explanation to the effect of pentagastrin increased through the presence of cimetidine in the incubation medium. A methodical origin of that phenomenon can be excluded, because cimetidine did not influence basal AC. However, one could assume a reciprocal inhibiting interaction between gastrin and histamine receptors, as already reported for adrenergic alpha and beta receptors and cAMP and cGMP production in rat gastric mucosa[14].

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Brain stem projections to the cerebral cortex in the rat

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Summary. By means of the HRP method it was shown that the entire cerebral cortex, but in greater proportion the frontal and posterior temporo-parietal regions, receive fibres from the dorsal and medial raphe nuclei and from the locus coeruleus. In contrast, the pars compacta substantiae nigrae and the tegmental area send projections to the motor and cingular areas respectively.

In the past few years, great importance has been given to the projections from the brain stem to the cerebral cortex, since the cortical activity is largely influenced by these afferences. In this preliminary study, several facts stressing the influence of some mesencephalic nuclei on the telencephalon are reported.

Material and methods. 50% horseradish peroxidase solution (HRP) was injected (0.02–0.05 µl) into different areas of the cerebral cortex of rats (51 animals). The injection was performed under nembutal anesthesia and under the control of a stereoscopic microscope by means of a 1-µl Hamilton syringe provided with a glass capillary.

After a survival of 24–36 h the rats were perfused and processed according to the Llamas and Martínez-Moreno's[1] technique, modification of the La Vail's one[2] for demonstration of the HRP labelled neurons.

Results. The HRP deposited in the cerebral cortex did not reach the white matter, except in 2 cases. The animals were divided according to the location of the HRP injections, in 5 groups: 1. frontal (areas 8 and 10 of Brodman); 2. motor (6 and 8); 3. parietal (1, 2, 3 and 7); 4. posterior temporo-parietal (20, 39, 40); 5. occipital and cingular (17, 18 and 29).

In all cases, labelled neurons were found in the medial and dorsal raphe nuclei, mainly in ipsilateral side. A significant number of marked neurons were also present, bilaterally, in the locus coeruleus (figure 2). The number of marked neurons in these nuclei was different depending on the area where HRP was deposited, the labelled neurons were more abundant when the HRP injection was performed in the frontal and in the posterior temporo-occipital cortex (figure 1, A and B). The rats of both groups (1 and 4) showed also labelled neurons in the nucleus linearis (pars caudalis et intermedia) and in the periaqueductal grey matter, although in sporadic form. No somatotopic order of the marked neurons was found in any of these nuclei.

The animals of group 2 (HRP injection in motor areas) showed labelled neurons in addition to the nuclei, mentioned above, in the pars compacta of the homolateral substantia nigra (figure 1, C). When the HRP was deposited in the medial surface of the motor cortex, the labelled neurons were located in the medial portion of the pars compacta. In contrast, when the HRP was injected in the convexity of the motor cortex, the labelled neurons could be seen in the lateral portion of the pars compacta substantiae nigrae.

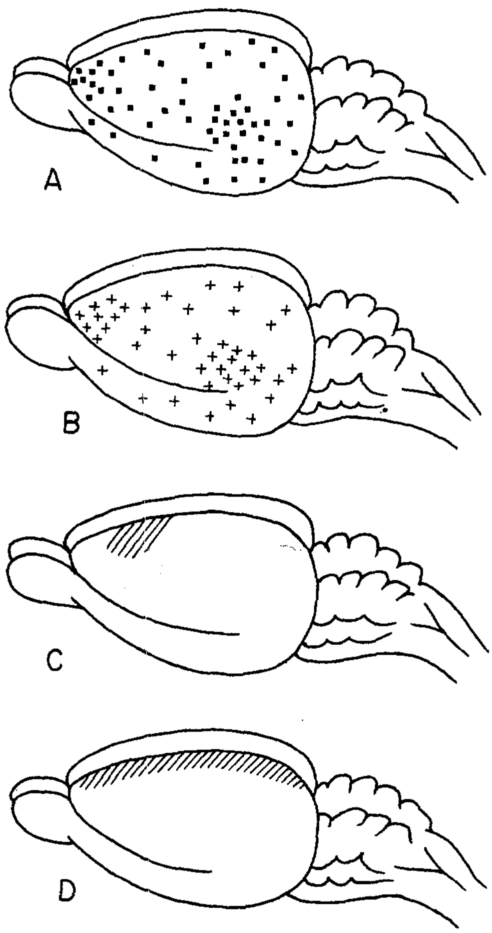

Fig. 1. Cortical areas to which the brain stem nuclei are projecting. *A* N. dorsalis and medialis raphes, *B* locus coeruleus, *C* substantia nigra, pars compacta, *D* ventral tegmental mesencephalic area.

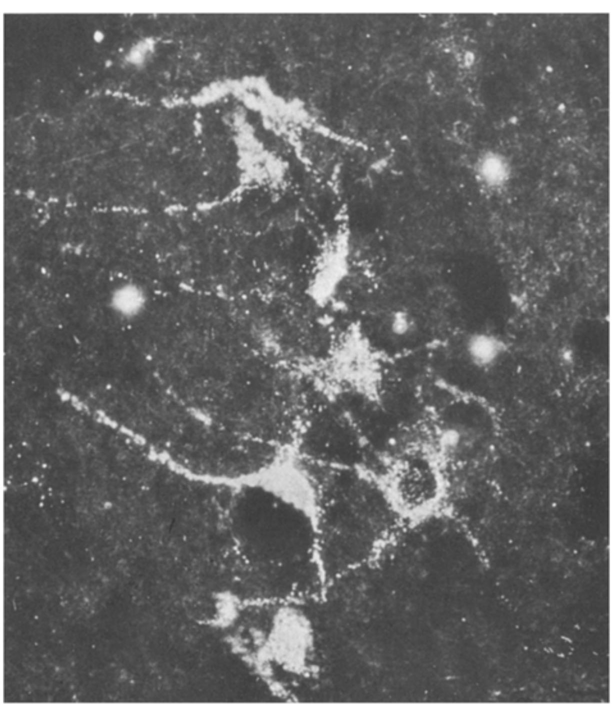

Fig. 2. A group of labelled neurons in the locus coeruleus. × 384.

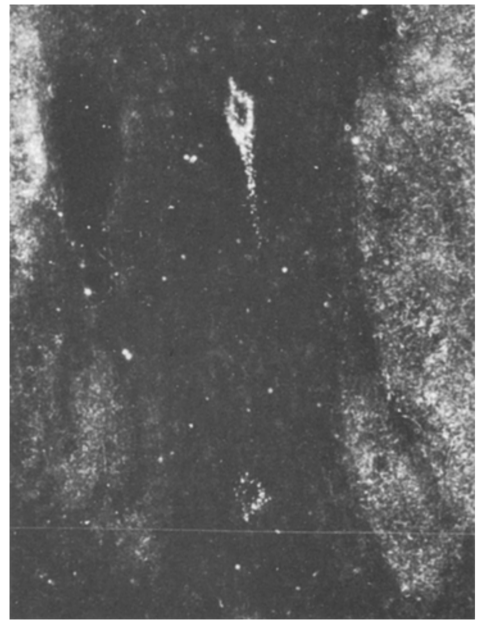

Fig. 3. 2 labelled neurons of the nucleus dorsalis raphes. × 384.

Positive HRP pericarya were also found in the ipsilateral tegmental area (pars basalis) of the rats injected in the cingular areas (figure 1, D).

Discussion. The results described above show that all cortical areas studied receive afferences from the locus coeruleus and from the dorsal and medial raphe nuclei. Those connections were already, although only partially, described[3-6,10], but not accepted by McBride[7]. Although in a certain sense it would be possible to speak of a diffuse projection, it is also evident that both the raphe nuclei and the locus coeruleus have a closer relation with the frontal and posterior temporo-parietal areas that with the remaining cortex.

This similarity of cortical projections between the raphe nuclei and the locus coeruleus, its reciprocal connections and the fact that the raphe nuclei are serotonergic while the locus coeruleus is noradrenergic, favour the hypothesis that both carry out a complementary action in the regulation of the cortical activity.

It should also be stressed the somatotopy of the projections from the substantia nigra to the motor cortex; the medial portion of the pars compacta substantiae nigrae projects to the medial surface of the motor cortex while the lateral to the convexity, as Molina-Negro[11] pointed out following a different experimental method.

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