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SHORT COMMUNICATION

Tele-methylhistamine[1] distribution in rat brain

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EVIDENCE accumulated from a variety of biochemical and physiological observations makes it likely that histamine serves as a transmitter in mammalian brain (GREEN *et al.*, 1977; SCHWARTZ, 1977). The metabolic fate of brain histamine is methylation, yielding *tele*-methylhistamine [1-methyl-4-(β-aminoethyl)-imidazole, *t*-MH]. For the structure or a nomenclatural discussion see BLACK & GANELLIN (1974). The role of *t*-MH in brain is likely to be nothing more than that of a transmitter metabolite. On the other hand, it has been suggested that *t*-MH might have an independent brain function (GREEN, 1970). This would be reminiscent of the relationship between dopamine and norepinephrine or serotonin and melatonin. In fact, *t*-MH has been shown to be as potent as histamine when applied iontophoretically to cortical neurons (PHILLIS *et al.*, 1968). It lacks activity on classical H_1 or H_2 receptors, however, (BLACK *et al.*, 1972).

Recently, we have developed a sensitive and specific gas chromatographic–mass spectrometric (GC–MS) method for measuring subnanogram amounts of *t*-MH in tissue (HOUGH *et al.*, in press) and shown *t*-MH to be an endogenous substrate for type B monoamine oxidase (HOUGH & DOMINO, in press). Presently, we have examined the content of *t*-MH in eight regions of the rat brain and compared the results with identical studies of histamine content. We have attempted to discover an independent distribution for *t*-MH, or confirm its similarity to that of histamine.

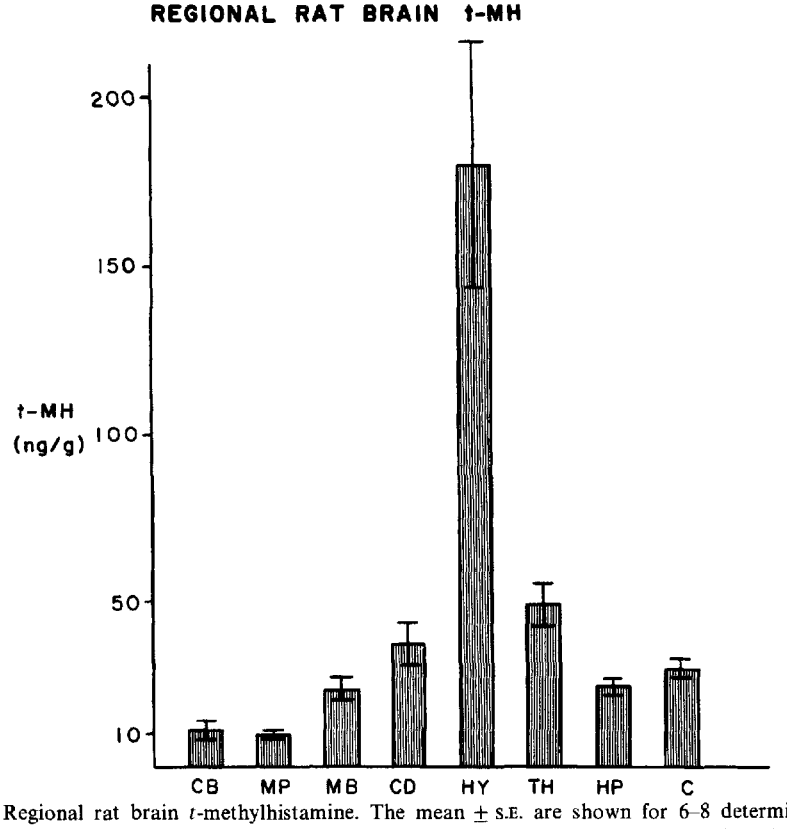

FIG. 1. Regional rat brain *t*-methylhistamine. The mean ± S.E. are shown for 6–8 determinations of the eight regions, abbreviated CB (cerebellum), MP (medulla-pons), MB (midbrain), CD (caudate nucleus), HY (hypothalamus), TH (thalamus), HP (hippocampus), and C (neocortex).

[1] *Tele*-methylhistamine (*t*-MH) is 1-methyl-4-(β-aminoethyl)-imidazole, in contrast to *pros*-methylhistamine (1-methyl-5-(β-aminoethyl)-imidazole, as per BLACK & GANELLIN (1974).

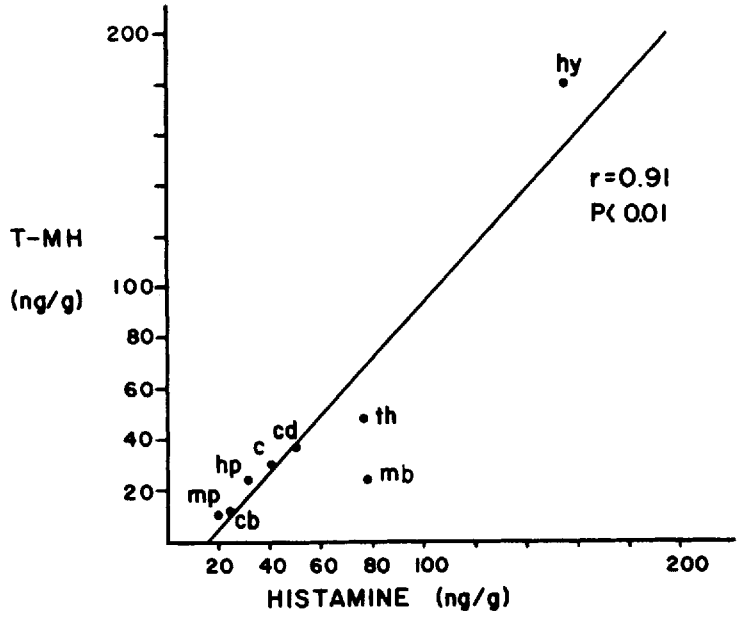

FIG. 2. Regional correlation of histamine and *t*-methylhistamine content. The *t*-MH values plotted are from Fig. 1. The histamine data were each from a mean of 4 determinations. A highly significant correlation is evident.

Male albino rats (Holtzman), weighing 200–400 g, were maintained in 12 h light–dark cycles and used for all studies. Following room temperature decapitation 2–4 h into the light cycle, the brains were rapidly removed, chilled with ice cold saline, and dissected into eight regions by a previously described modification (VASKO & DOMINO, 1978) of the method of GLOWINSKI & IVERSEN (1966). *t*-MH was measured by organic extraction, derivatization and analysis by GC–MS, as described by HOUGH *et al.* (in press). Histamine was measured following decapitation using a previously described modification (HOUGH & DOMINO, 1977) of the radioenzymatic assay. The results are expressed as ng amine (free base) per g wet wt. tissue. The results were the same when expressed per mg protein.

Figure 1 shows the striking assymmetry in the rat brain content of *t*-MH. The regions vary in their content by more than 15-fold, from 9.5 (medulla-pons) to 177 ng/g (hypothalamus). This distribution is quite similar to that found for histamine, as shown in Fig. 2. A highly significant correlation is evident for the histamine and *t*-MH content of each region.

These results support the earlier suggestion (WHITE, 1966) that the regional *t*-MH content resembles that of histamine. They also make it likely that brain *t*-MH is related to the histaminergic system, although an independent function cannot be completely ruled out. Recently, it has been suggested (BISCHOFF & KORF, 1978) that brain *t*-MH levels may be the best index to histaminergic function, much like other transmitter metabolites. While the present results do not prove the suggestion, they are definitely consistent with it.

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