LOCALIZATION OF MONOAmine OXIDASES A AND B IN PRIMATE BRAINS RELATIVE TO NEURON-SPECIFIC AND NON-NEURONAL ENOLASES

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Using serotonin and phenylethylamine deamination as measures of MAO A and MAO B activity respectively, positive correlations were observed between the activities of MAO A and MAO B in different areas of rhesus monkey and human brains. When the activities of MAO A and MAO B were compared with those of neuron-specific enolase and nonneuronal enolase (isozymes which are markers for neurons and glia), a slight but non-significant correlation was observed, suggesting that a simple distribution of MAO A in neurons and MAO B in glia is unlikely. This conclusion is supported by studies using synaptosomes, but contrasts with that from investigations of MAO from peripheral tissues, where experiments indicate that MAO A is predominantly localized in neurones.

INTRODUCTION

Monoamine oxidase (monoamine:oxygen oxidoreductase deaminating: EC 1.4.3.4., MAO) exists in two forms designated A and B on the basis of a bimodal inhibition of tyramine deamination by increasing concentrations of clorgyline (1). Their cellular localization in the CNS is controversial, although in peripheral tissues, MAO A is preferentially located in sympathetic neurones both within and outside adrenergic neurones (2–4). This is supported by the finding that in rodents at least, the neurotransmitters, norepinephrine, 5-hydroxytryptamine (5HT) and dopamine are deaminated primarily by MAO A (5), while MAO B deaminates...
compounds such as phenylethylamine (PEA), phenylethanolamine, t-lelemethylhistamine and benzylamine (6-9). In addition, mouse neuroblastoma cells in tissue culture possess solely MAO A and no MAO B activity (10).

The cellular localization of MAO A and MAO B in the CNS is unclear due to difficulties in separating cell types. Most studies of different regions have shown 1- to 3-fold differences in MAO A versus MAO B activity but the norepinephrine-rich locus ceruleus is reported to have 5-fold higher MAO A than MAO B activity (11). In the pineal gland, MAO A has been shown to be predominantly neuronal on the basis of its disappearance after sympathectomy (12).

Enolase (EC 4.2.1.11) exists in brain as cell specific isozymes (13-16). Structural, functional and immunological studies have defined a neuron-specific (NSE) (17, 18) and a non-neuronal enolase (NNE) which is localized in glia (19). Antisera against the purified isozymes do not cross react with each other (19, 20) and this has allowed the development of specific radioimmunoassays (RIA). The NNE/NSE ratio in defined areas of rat and monkey brain correlates in most instances with the ratio of white/grey matter (20, 22) and it has been proposed that NSE and NNE are specific markers for neuronal and glial cells, respectively (16).

Human and other primate brains contain largely MAO B (70-85%) (21). This raises the possibility that, at least in primates, MAO B may be partially localized in neurons. We have compared the distribution of MAO A and MAO B with that of NSE and NNE in the CNS of human, rhesus and vervet primate brains.

EXPERIMENTAL PROCEDURE

Human brains from four postmortem subjects were dissected and frozen within hours of death. Following pentobarbitol anaesthesia, removal of the calarium and severing of the medulla (21) brains of four adult vervets (Cercopithecus aethiops sabeus) and one adult rhesus monkey (Macaca Mulatta) were rapidly dissected and frozen at -70°C until assayed. The limited number of areas studied in the human and vervet samples was related to availability of tissues. Both MAO (22) and enolase isozymes (Marangos, unpublished information) are stable at 4°C for several hours and at -70°C for at least six months (27).

MAO activity was determined as previously described (23, 24) using 5-[3H]HT (55 mCi/mM, final concentration 1 mM, NEN, Boston, MA) as substrate for MAO A and [14C] PEA (50.9 mCi/mmol, final concentration 20 μM, NEN) as substrate for MAO B. Assays were done at 37°C for 20 min in 80 mM phosphate buffer (pH 7.2) using crude sonicated homogenates containing 0.2-0.8 mg protein/sample for 5-HT and 0.01-0.02 mg for PEA. Reactions were stopped by immersion in an ice bath. Products were isolated using an Amberlite CG 50 type II ion exchange resin and counted by scintillation spectrometry.

NSE and NNE were measured in cytosol (obtained by ultracentrifugation of the homogenates used for MAO) using a double antibody solid phase RIA procedure (20). Samples