Table 1 Improvement of the disability after Madopar and Madopar plus (–)-deprenil treatment in Parkinsonian patients.

Duration of disease (yrs)	*No.*	*Age (yrs)*	Percentage disability				
			Before therapy		*After Madopar*		*After Madopar + (–)-deprenil*
0–6	115 (55♂, 60♀)	68.5 ± 0.8	54.3 ± 1.5	$P < 0.001$	36.5 ± 1.4	$P < 0.001$	25.3 ± 1.3
7–15	108 (60♂, 48♀)	69.4 ± 0.7	60.1 ± 1.3	$P < 0.001$	37.2 ± 1.4	$P < 0.01$	28.4 ± 1.4

Results are stated as mean ± s.e. mean.

to Madopar therapy results in an improvement of disability independent of the duration of the illness (Table 1) and suggests that the inclusion of deprenil leads to a better utilization of synthesized dopamine from L-dopa.

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Autoradiographic evidence for the effects of specific uptake-inhibitors on the selective accumulation of [^{3}H]-5-HT by supra-ependymal nerve terminals and for the localization of binding sites for [^{3}H]-D LSD

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It can be shown, by light microscopic autoradiography, that intraventricular injection of tritium-labelled 5-hydroxytryptamine ([^{3}H]-5-HT; 70 μM) leads to its accumulation not only in the brain parenchyma in the rat but also on the ependymal surface of some regions, e.g. corpus callosum, nucleus caudatus and cranial floor of the fourth ventricle; electron microscopy of these regions reveals that the radiolabel is localized to supra-ependymal nerve terminals. The ependymal surface of regions which are known to lack these nerve terminals, e.g. hypothalamus ventralis anterior, eminentia mediana and roof (velum medullare) of the fourth ventricle, was free of label. Intraventricular administration of both [^{3}H]-dopamine (DA; 350 μM) and [^{3}H]-noradrenaline (85 μM) led to their accumulation in the parenchyma but not above the ependyma in all brain regions investigated, i.e. supra-ependymal nerve terminals were not labelled.

Chlorimipramine and reserpine, which block neuronal uptake and storage respectively in

tryptaminergic nerves, prevented the accumulation of [^{3}H]-5-HT in supra-ependymal nerve terminals. However, desipramine, a known catecholamine-uptake blocker, had no effect on this accumulation.

The demonstration of a specific uptake mechanism for 5-HT in supra-ependymal nerve terminals confirms the tryptaminergic nature of these nerves (Richards, Lorez & Tranzer, 1973; Lorez & Richards, 1973; Richards & Tranzer, 1974; Lorez & Richards, 1975). The physiological significance of this uptake mechanism is likely to be the removal of the amine from the vicinity of the effector organ (periventricular target cell) in order to terminate the possible neurotransmitter action of 5-HT. The presence of 5-HT in CSF (Holman & Vogt, 1972), probably secreted in part by supra-ependymal nerve terminals, suggests that there may be specific receptors and a physiological role for this amine in periventricular brain regions. This may also be true of the human brain since supra-ependymal nerve terminals have recently been observed in the lateral and fourth ventricles of human postmortem tissue by electron microscopy; it might be expected that these nerves also store and accumulate 5-HT although this has to be demonstrated.

Since the hallucinogenic drug DLSD is known to have a high affinity for 5-HT (Bennett & Snyder, 1975) and DA (Creese, Burt & Snyder, 1976) receptors, the localization of binding sites for [^{3}H]-DLSD was studied by autoradiography in order to identify 5-HT receptors in periventricular brain regions (presuming the absence of DA receptors in these regions). The results indicate that, 1 h after intraventricular administration of 350 μM [^{3}H]-DLSD, a significant binding of LSD could be observed in the ependymal and subependymal zone of several periventricular brain regions. However, the label did not seem to be selectively bound to any particular structure. Experiments are now in progress to test the ability of DLSD and 2-bromo-LSD, but not LLSD, to displace the [^{3}H]-DLSD visualized by autoradiography and thereby identify specifically bound label and possibly the target sites for the 5-HT.

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5-HT and LSD high affinity binding sites to brain synaptosomal membranes

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5-HT and LSD binding have been studied, using purified synaptosomal membranes isolated from different regions of bovine brain by a density gradient centrifugation technique or in some experiments a lysed P_2 fraction isolated either from bovine or from rat brains.

Membranes were incubated at various temperatures (generally 22°C or for different purposes 0°C) in Tris-HCl buffer 50 mM pH 7.4 using tritiated ligands ([^{3}H]-5-HT 17 Ci/mM, [^{3}H]-LSD 22 Ci/mM). Separation of bound and free radioactivity was performed using an ultra-filtration technique (Whatman GFB glass fibre filter) under vacuum. The filter was rinsed with 10 ml of Tris-HCl buffer 0°C and the radioactivity trapped onto the filter was counted by liquid scintillation using Triton X 100 with a Toluene PPO-POPOP mixture.

Previously we described a saturable, reversible, high affinity binding for 5-HT, specific for tryptamines and related structures (Fillion, Fillion, Spinakis, Bahers & Jacob, 1976). Here, parallel studies for 5-HT and LSD bindings show that LSD binding corresponds to a saturable reversible high affinity site with a corresponding dissociation constant similar to that of 5-