

common stress range, the aortic elastic modulus was not significantly different before and after drug. One possible interpretation is that the 'operating level' of the aortic elastic modulus tends to be maintained constant by adaptive changes in the aorta which override the concurrent geometrical changes to maintain a level of elasticity consistent with the value of aortic stress, probably associated with the development of an optimal load for the left ventricle.

On the other hand, cardiac receptors signalling in unmyelinated vagal afferents are of interest. Their activation can cause an increase of vagal tone on the heart and an inhibition of sympathetic activity<sup>10</sup>. The possibility of an action of clonidine upon cardiac receptors was pointed out in a recent work of Lisander and Wennergren<sup>11</sup>. The authors concluded that clonidine could activate vago-vagal reflexes, probably emanating from the heart and secondary to peripheral hemodynamic changes.

In rabbits with cervical spinal cord transection, Petty et al.<sup>12</sup> observed that clonidine caused a significantly greater pressor effect but the hypotensive phase was completely abolished. The authors suggested that the potentiation and prolongation of the initial pressor effect may represent the direct effect of the drug on peripheral  $\alpha$ -adrenoceptors unopposed by a central hypotensive action. The present data lend further support to this hypothesis since we observed that the increases in aortic diameter, aortic stress and elastic modulus were less important when the hypertensive phase was absent.

In conclusion, the principal site of the hypotensive action of clonidine seems to be in the CNS but an additional direct

effect of the drug upon vascular smooth muscle cannot be discarded. Our results show that aortic diameter, aortic stress and elastic modulus were increased after clonidine. This direct peripheral action of the drug could play, in addition to a central effect, an important role in modifying the activity of vascular and/or cardiac receptors and thus influencing a) the central components of the baroreceptor reflex arc, b) the preganglionic and postganglionic sympathetic nerve activities, c) the parallel changes in stiffness and elastic modulus of the aortic wall.

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### Monoamine oxidase activities in human brain microvessels<sup>1</sup>

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**Summary.** Microvessels can be easily isolated from human brain samples obtained at autopsy. Human frontal cortex MAO type A and B activities are similar in microvessel and microvessel-free preparations. In microvessels, enzyme activities and the ratio of MAO type A to type B vary among the areas studied and could selectively regulate the passage of certain amines through the blood vessel wall.

Recently, methods have been developed allowing for the isolation of microvessels from various animal brains<sup>3-5</sup>. These preparations have been used to study a variety of metabolic processes and enzymes<sup>6-8</sup>, including monoamine oxidase (MAO)<sup>9-11</sup>. It was observed that rat brain microvessels exhibit a 3 times greater activity of MAO than microvessel-free brain homogenates<sup>11</sup> and that they contain type A and B activities although the final ratio of A:B is still uncertain<sup>10</sup>.

The purpose of this study was to determine if microvessels can be prepared from human brain samples obtained at autopsy, if human microvessels show MAO activities similar to those found in rat brain microvessels and if differences in MAO activities can be detected among brain regions. It was decided that human autopsy material could be used for the study since MAO in rat brain was shown to be rather stable post mortem<sup>12,13</sup>. The substrates used to obtain preliminary information on MAO activities were phenylethylamine (PEA), a general type B substrate in rat brain<sup>14</sup>, and serotonin (5-HT), a general type A substrate<sup>15</sup>. Male Wistar rats (250-300 g) were obtained from Perfection Breeders, Douglasville, PA. Human brain samples were obtained between 10-15 h post mortem from individ-

uals free of brain or major vascular disease. <sup>14</sup>C-PEA and <sup>14</sup>C-5-HT were purchased from the New England Nuclear Corporation. Microvessels were prepared according to the method of Mrsulja et al.<sup>5</sup>. Microvessel-free homogenates were obtained by using the method of Lai et al.<sup>11</sup>. MAO activity was measured basically as described by Wurtman and Axelrod<sup>16</sup>.

$V_{max}$  was calculated by linear regression analysis using Eadie-Hofstee parameters<sup>17</sup>.

Phase contrast photomicrographs showed that human microvessels can be isolated relatively pure and seem to be similar in appearance to microvessels obtained from whole rat brain<sup>3,11</sup>.

MAO type A (5-HT) and type B (PEA) activities of rat and human brain homogenates and microvessels are shown in the table. In contrast to Lai et al.<sup>9,10</sup>, who found most of the MAO activity in microvessels, we find similar MAO activities in whole brain homogenate, microvessel-free homogenate and microvessels. This indicates that MAO activities might be more equally distributed between microvessels and microvessel-free fractions. The difference between our data and those of Lai et al.<sup>9,10</sup> could be due to the procedure used to isolate microvessels; we use the 'fractionation'

MAO activities in rat and human whole brain homogenates (H) and microvessels (M) assayed with serotonin (5-HT) and phenylethylamine (PEA)

	V <sub>max</sub> (nmoles/mg/h) 5-HT	PEA	5-HT: PEA
Rat brain, whole H (N = 4)	76.9 ± 14.5	37.0 ± 5.1	2.1
Rat brain, M-free H (N = 4)	60.1 ± 11.3	30.4 ± 8.8	2.0
Rat brain, M (N = 4)	63.8 ± 17.4	25.3 ± 8.1	2.5
Human frontal cortex, whole H (N = 3)	17.8 ± 2.3	14.6 ± 3.9	1.2
Human frontal cortex, M (N = 3)	21.7 ± 1.6	14.6 ± 4.0	1.5
Human frontal cortex, M <sup>a</sup>	16.3; 14.1	14.2; 11.3	1.2; 1.3
Human sensorimotor cortex, M <sup>a</sup>	62.0; 51.0; 17.1	14.0; 10.0; 4.7	4.4; 5.1; 3.6
Human thalamus, M <sup>b</sup>	11.8; 3.7; 35.7	5.6; 1.9; 20.4	2.0; 1.9; 1.8
Human hypothalamus, M <sup>b</sup>	12.2; 17.6; 21.0	30.1; 23.3; 25.0	0.4; 0.8; 0.8
Human cerebellum, M <sup>a</sup>	37.0; 56.8; 48.0; 28.0	4.6; 6.8; 5.0; 3.7	8.0; 8.4; 9.6; 7.5
Human frontal cortex, stillborn infant, M <sup>a</sup>	24.1	12.0	2.0

<sup>a</sup>Data represent individual values. <sup>b</sup>Data represent 3 sets; each set consists of tissues from 3 individuals.

procedure which microscopically gives us better separation and recovery than the 'sieving' procedure used by Lai et al.<sup>9,10</sup>. Similar results in enzyme activities were obtained for human cortex; no major difference in MAO type A and B activities was observed between whole brain homogenate and microvessels. Processing of some human brain areas necessitated pooling of samples due to the small amounts available from different individuals. MAO activities and ratios from the same regions in these separate sets were found to be remarkably similar. This allows for a comparison of these sets among brain regions. In general, human MAO activities in microvessels are somewhat lower than those found for whole rat brain. Marked differences in MAO activities and ratios were found among the areas studied. The differences range from a 5-HT: PEA ratio of about 0.7 for hypothalamus to a ratio of about 8.0 for cerebellum. Thus, the distribution of both MAO activities in microvessels is not uniform throughout the brain but seems to be characteristic for a particular brain region. This is in contrast to the finding that MAO type A and B activities do not differ significantly in crude homogenates of different human brain regions<sup>18</sup>. Since microvessels constitute only a small fraction of the homogenates, it can be assumed that neuronal and glial MAO is more evenly distributed throughout the human brain whereas MAO activities in microvessels show a more uneven distribution. The latter finding is interesting since MAO is part of the 'enzymatic' blood-brain-barrier<sup>8,19</sup> and differences in blood vessel MAO activities could selectively regulate which amine would or would not cross the vessel wall and penetrate into a particular brain region.

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Bombesin, calcitonin and leu-enkephalin immunoreactivity in endocrine cells of human lung

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**Summary.** By immunohistochemistry, bombesin, calcitonin and leu-enkephalin was localized in endocrine cells of human lungs from various age groups. It is suggested that at least 3 different peptide containing endocrine cells may be present in human lung.

Over 40 years ago Feyrter described argyrophilic, clear cells (Helle Zellen) in bronchial epithelium and suggested that they may have an endocrine or paracrine function<sup>3</sup>. Subsequent studies confirmed the presence of these cells in fetal, newborn and adult lungs of human and various animal species<sup>4-8</sup>. These cells were found to be distributed singly,

and in distinctive innervated corpuscles referred to as neuro-epithelial bodies (NEB)<sup>9</sup>. Histochemical and ultrastructural studies have shown that these cells possess the capacity to take up amine precursors and contain neurosecretory granules - features characteristic of the system of polypeptide hormone producing APUD (amine precursor uptake and