Ultrastructural Distribution of Vasodilator and Constrictor Nerves in Cat Cerebral Arteries

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SUMMARY This study examined the ultrastructural distribution of agranular vesicle-containing nerve (AVN) and granular vesicle-containing nerve (GVN) in cat cerebral blood vessels fixed in KMnO₄. The percentages of the AVN and GVN throughout the adventitial layer in the basilar, middle cerebral, and anterior cerebral arteries were 63.4 and 36.7, 53.9 and 46.1, and 80.2 and 39.8, respectively. The AVN in the cat basilar artery is approximately 37 times denser than that in the rabbit basilar artery. This morphological result, in correlation with the previous pharmacological findings, provides indirect evidence that the AVN are the dilator nerves. The lack of neurogenic vasoconstriction in the cat basilar, middle cerebral, and anterior cerebral arteries may be attributable in part to a combination of denser dilator than constrictor nerves, a possible closer synaptic cleft distance for dilator than for constrictor nerves, and the reported insensitivity of the posteynaptic α-receptors. The small pial vessels (branches of the middle cerebral arteries), on the other hand, contain predominantly GVN (88%), suggesting that dilator nerves relative to constrictor nerves decrease as the size of the cerebral blood vessels becomes smaller. Furthermore, the synaptic cleft distance is found not parallel to the outer diameter of the artery. Thus, the results of this study indicate that the neurogenic control of brain circulation varies with brain region, lending further support to the theory that the dual cerebral vessel innervation varies among species. Circ Res 49: 971-979, 1981

Morphological examination of the adventitia of cerebral blood vessels reveals nerves which exhibit two distinct profiles. When fixed with KMnO₄, the terminal axons contain either small granular vesicles or agranular vesicles. The granular vesicle-containing nerves (GVN) are of sympathetic origin, whereas the agranular vesicle-containing nerves (AVN) are apparently not sympathetic, since they remain after sympathetic denervation of the blood vessels (Iwayama et al., 1970; Owman et al., 1974; Lee et al., 1980). Previous work has established that the GVN mediate vasoconstriction (Lee et al., 1976, 1980), and although it has been suggested that the AVN mediate vasodilation, this idea has not been rigorously examined.

Cerebral arteries of the cat are innervated by both GVN and AVN. Curiously, when studied in vitro these arteries dilate only when subjected to transmural nerve stimulation (TNS), a situation unlike that in rabbit cerebral arteries (Lee et al., 1976, 1978). The cat blood vessels therefore were utilized in the present studies in order to evaluate the relationship between vasodilation and the AVN. The results indicate a strong correlation between the degree of TNS-induced vasodilation and AVN in the cerebral vessels. In addition, the relative distribution of the AVN and GVN in cerebral arteries of different sizes was compared in quest of possible regional variation of the vasoconstrictor and dilator innervation.

Methods

Adult cats (2-3 kg) of either sex were anesthetized with pentobarbital (40 mg/kg, i.p.) and exsanguinated. The entire brain with blood vessels attached was rapidly removed and placed in ice-cold (4°C) normal saline. Basilar arteries (BA) (10 mm long, outer diameter 0.4-0.5 mm), middle cerebral arteries (MA) (5 mm long, outer diameter 0.4-0.6 mm), anterior cerebral arteries (AA) (5 mm long, outer diameter 0.2-0.4 mm) immediately adjacent to the circle of Willis, and small branches of middle cerebral arteries (SMA) (5 mm long, outer diameter 0.1-0.2 mm) from the surface area of sylvian sulcus were excised with the aid of a dissecting microscope.

Electron Microscopy

Freshly dissected arterial segments were fixed in ice-cold 2% KMnO₄ in Millonig phosphate buffer (pH 7.4, 400 mOsmol). Preparation of the fixative, fixation, dehydration, and final embedding of the specimens were carried out as previously described (Lee et al., 1980). All blocks were oriented for transverse sectioning of the arteries. Ultrathin cross-sections of the arteries were obtained with an LKB microtome fitted with a diamond knife. The sections were mounted on slot grids coated with Formvar and were stained with 0.4% uranylacetate and...
lead citrate, then examined under a JEOL 101B electron microscope. Six blocks of specimen of each strategically selected artery from four control and six sympathectomized animals were randomly obtained. One thin section from each block was cut and all thin sections were examined.

Photomicrographs were taken at 10,000 and 20,000 x of all nerve terminals and nerve terminal-like structures throughout the adventitial layer, together with the closest smooth muscle cells. Neuromuscular distance was measured from each micrograph. The nerve terminals or varicosities were defined as regions of axonal swelling containing at least six vesicles and few or no neurofilaments or neurotubules (Daniel et al., 1977). The diameters of the granular and agranular vesicles were measured only from micrographs taken at 20,000 x (final magnification, 50,000 x) with the aid of a micrometer fitted in the eye piece of a dissecting microscope. The average diameter of vesicles of each varicosity was used to determine mean values.

6-Hydroxydopamine (60HDA) (100 mg/kg) was given iv to cats 30 minutes before the animals were killed. Presumably, 60HDA is taken up by adrenergic nerve terminals to improve the granulation of the dense core vesicles (Iwayama et al., 1970; Lee et al., 1980).

**Sympathetic Denervation of Cerebral Arteries**

Cats were anesthetized with pentobarbital (40 mg/kg, ip). Both superior cervical ganglia were isolated and extirpated by cutting the sympathetic trunk at a point proximal to the ganglia, then removing the ganglia with short lengths of their other branches attached. Tissues were examined 7 days after ganglionectomy. The effectiveness of surgical denervation was confirmed by fluorescence microscopy (Lee et al., 1978) of arterial segments which were adjacent to those examined by electron microscopy.

**Assay for Catecholamine**

Catecholamines in the vascular tissue were assayed by the modified radioenzymatic thin layer chromatographic method of Da Prada and Zurcher (1976) as described in a previous report (Lee et al., 1980).

**Statistical Methods**

The data were evaluated statistically by Student's t-test for paired or unpaired samples as appropriate. The 0.05 level of probability was accepted as significant.

**Results**

**Electron Microscopy**

The control cat basilar, middle cerebral, anterior cerebral arteries, and the small branches of the middle cerebral arteries contain two types of nerve terminals as judged by their vesicle inclusion: the granular vesicle-containing nerve (GVN) and the agranular vesicle-containing nerve (AVN) (Fig. 1).

Of the GVN terminals (n = 644), 86.8% contain predominantly small dense core granular vesicles, 478.9 ± 59.5 Å (mean ± SD, n = 36 varicosities) in diameter and a few (variable from 1 to 30) large dense core granular vesicles, 985.1 ± 106.3 Å (mean ± SD, n = 22 varicosities) in diameter, and 12.3% contain only the small dense core granular vesicles (Fig. 1). Only in very few varicosities (0.9%) do they contain more large than small dense core granular vesicles. Of the AVN terminals (n = 757), 77.9% contain predominant small agranular vesicles, 455.3 ± 30.8 Å (mean ± SD, n = 51 varicosities) in diameter, and a few (variable from 1 to 30) large agranular vesicles, 967.1 ± 85.4 Å (mean ± SD, n = 32 varicosities) in diameter, and 21.4% contain only small agranular vesicles. Only 0.7% of the AVN terminals contain more large than small agranular vesicles. The diameters of the small dense core agranular vesicle in the AVN is smaller than that of the small granular vesicles in the GVN (0.005 > P > 0.001, unpaired t-test). On the other hand, there is no statistical significance between the diameters of large granular and agranular vesicles (P > 0.5). The GVN, but not the AVN, degenerated after chronic superior cervical ganglionectomy (Fig. 2).

Results of examinations of a total of 2256 terminal axons throughout the adventitial layer in the cat cerebral arteries of control animals and of superior cervical ganglionectomized animals are shown in Table 1. In four control animals, the basilar and anterior cerebral arteries contain significantly more AVN than GVN (P < 0.025). The middle cerebral artery also contains more AVN than GVN, although this difference is not statistically significant. The small branch of middle cerebral arteries, in contrast, contains significantly more GVN than AVN (P < 0.025). Following bilateral sympathectomy (three animals), the GVN examined in basilar and small branch of middle cerebral arteries completely disappeared; less than 1% remained in middle cerebral and anterior cerebral arteries. On the other hand, unilateral sympathectomy (three animals) resulted in a 14% decrease of GVN in the basilar arteries and complete disappearance of GVN from the middle cerebral arteries of the denervated side.

Figure 3 shows the GVN and AVN frequency distribution of synaptic clefts with varying widths in the cat cerebral arteries. There are consistently more AVN than GVN (P < 0.05, paired t-test) with synaptic cleft distances of less than 6 µm in basilar, middle cerebral, and anterior cerebral arteries: the respective percentage of AVN and GVN are 60.7 and 39.3, 64.9 and 35.1, and 54.4 and 45.6. The mode of distribution of the AVN and GVN with different cleft widths also varies among these three selected
FIGURE 1 Electron micrographs of dual innervation of the cat middle cerebral artery fixed in potassium permanenate. Two varicosities containing granular vesicles (G1 and G2) belong to the same nerve fiber. Different sizes of granular vesicles, small and large (small arrow head), are present. Five other varicosities (A1, A2, A3, A4, and A5) contain agranular vesicles of both small and large types (small arrow head in A2). A1 and A3 belong to the same fiber. The varicosities of both granular and agranular-containing nerves are often closer to each other (G1 and A2). Animal was pretreated with 6-hydroxydopamine (100 mg/kg, iv) 30 minutes prior to experiment. Fibroblast process (F); mitochondria (M); collagen (C); pinocytotic vesicles (PV).

arteries. In anterior cerebral arteries, which contain more AVN and GVN than do middle cerebral and basilar arteries based on the same number of sections, the AVN and GVN are most frequently located within 1 μm from smooth muscle cells, and the frequency of both nerve terminals decreases with an increase in cleft width. When the distribution of nerve terminals was focused on within 2-μm range, a large number of AVN and GVN were found to locate at a distance of less than 1 μm away from the nearest smooth muscle cell membrane (Figs. 3A and 4A). In middle cerebral arteries, the frequency of the AVN, like that of the GVN, is evenly distributed within 2 or 4 μm of the smooth muscle cells of the media (Figs. 3B and 4B), and the frequency declines when a synaptic cleft distance is greater than 4 μm. In basilar arteries, the frequency of AVN gradually increases and reaches a peak at 3 μm synaptic cleft distance, while the frequency of the GVN is evenly distributed within 5 μm of synaptic cleft distance (Fig. 3C). Contrary to the observations in the middle cerebral, basilar, and anterior cerebral arteries, the small branch of middle cerebral arteries contain more GVN (87.9%) than AVN (12.1%) with synaptic cleft distance less than 5 μm. The closest synaptic cleft distance, defined as the shortest distance between axonal and smooth muscle cell membranes, was also determined in each arterial segment from each animal. The averages of the closest synaptic cleft distances from four cats tend to be smaller for AVN than for GVN in basilar, middle cerebral, and anterior cerebral arteries except in small branch of middle cerebral arteries (Table 2). However, the difference is not statistically significant.

Catecholamine Content

In the cat basilar arteries, the content of NE (1.11 ± 0.26 μg/g tissue weight, n = 5) is much higher than either DA (0.08 ± 0.01 μg/g tissue weight, n = 5) or EPI (0.02 ± 0.00 μg/g tissue weight, n = 5) content which are 7.2% and 1.8% of that of NE, respectively. Seven days after bilateral superior cervical ganglionectomy, the NE content...
in basilar arteries decreased to 0.13 ± 0.04 µg/g tissue weight, which is less than 10% of the control. On the other hand, the contents of DA and EPI were not affected. All values represent mean ± SE, and n represents number of arteries.

Discussion

The innervation of cerebral blood vessels of many species has been intensively studied morphologically by light, fluorescence, scanning, and transmis-
Unquestionably, the cerebral blood vessels of all species studied are dually innervated. The presence of both adrenergic and nonadrenergic nerves has been demonstrated on the basis of the appearance and size of the vesicles in the terminal axons.

When fixed in KMnO₄, the adrenergic nerve terminals in a variety of preparations are characterized by the presence of many small and a few large dense core granular vesicles (Hökfelt and Jonsson, 1968). Similarly, these granular vesicle-containing nerves seen in cerebral blood vessels are sympathetic adrenergic nerves (Iwayama et al., 1970; Owman et al., 1974; Lee et al., 1980).

There is ample evidence suggesting that the adrenergic sympathetic nerves are cerebral vasoconstrictor nerves. This conclusion is based on both in

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**Figure 3** Histogram of neuromuscular distance in cat (n = 4) anterior cerebral (A), middle cerebral (B), and basilar arteries (C), and small branches of middle cerebral arteries (D). Frequencies of the granular vesicle-containing nerve terminals (solid area) and agranular vesicle-containing nerve terminals (open area) with varying nerve-muscle distances were expressed as percentage of total varicosities of both types in the adventitia. *(P < 0.05), **(P < 0.01), and ***(P < 0.005) indicate statistical significance (paired t-test) to their respective granular vesicle-containing nerve terminals within the same synaptic left range.
FIGURE 4 Frequency distribution of synaptic clefts with varying widths within 2 μm in cat (n = 4) anterior cerebral (A) and middle cerebral arteries (B). The solid area represents incidence of the granular vesicle-containing nerve terminals and the open area represents number of agranular vesicle-containing nerve terminals.

On the other hand, those KMnO₄-fixed nerves containing exclusively agranular vesicles, not affected by sympathetic denervation or 6-hydroxydopamine pretreatment, are nonadrenergic (Iwayama et al., 1970; Owman et al., 1974; Lee et al., 1980). These agranular vesicle-containing nerves (AVN) have been claimed to be dilator nerves, probably cholinergic in nature based on circumstantial evidence (Iwayama et al., 1970; Owman et al., 1974). However, there is no direct proof that the AVN are dilator nerves and acetylcholine (ACh) is the dilator transmitter.

It has been suggested that cerebral vasodilator nerves are carried through the greater superficial petrosal nerves (Chorobski and Pennfield, 1932). However, sectioning of the superficial petrosal nerves did not result in a degeneration of the AVN or a decrease in acetylcholinesterase (AchE) activity (Vasquez and Purves, 1977). Although the failure to observe degeneration of AVN or a decrease in AchE activity after sectioning of the greater superficial petrosal nerves could be due to a preganglionic rather than a postganglionic section (i.e., a decentralization), it is possible that dilator nerves arise from another origin. Furthermore, a lack of correlation between the degree of neurogenic dilator response and that of cholinergic innervation in cerebral arteries of the cat and rabbit (Lee et al., 1978; Florence and Bevan, 1979) has been reported. The role of ACh as the cerebral vasodilator transmitter is also questioned, since the TNS-induced vasodilation was neither blocked by atropine or hemicholinium, nor was it potentiated by physostigmine (Lee et al., 1978). In fact, a recent study indicates that ACh is more likely a vasoconstrictor transmitter (Lee, 1980). Obviously, not until the dilator transmitter substance is positively identified would quantitative estimation of density of regional vasodilator innervation be possible by measuring parameters of cholinergic innervation.
(GVN), based on the vesicle inclusions in their terminal axons (Fig. 1). The presence of different populations of large and small vesicles in both AVN and GVN terminals may further suggest that each type of nerve can be divided into three subtypes. The first and most frequently observed subtype contains many small and a few large granular or agranular vesicles. The second subtype contains only small granular or agranular vesicles. The third subtype, which represents only less than 1% of the respective nerve terminals, contains more large than small granular or agranular vesicles. The size of the small agranular vesicles in AVN is slightly smaller than that of the granular vesicles in GVN, further suggesting that the GVN and AVN are of different types of nerves. Since all GVN but not the AVN disappear following chronic superior cervical ganglionectomy, it is probable that all three types of GVN are of sympathetic origin. The different ratio of small and large granular vesicles observed in the GVN varicosities may therefore be due to sectioning at different levels of the varicosities. Although the origin of the AVN is not completely known and that effect of sectioning of the superficial petrosal nerve on AVN terminals has not been examined, it is possible that all three types of AVN terminals represent the same type of nerve fibers.

The basilar artery has been shown to receive sympathetic innervation from bilateral superior cervical ganglia (Nielsen and Owman, 1967). Indeed, the unilateral ganglionectomy caused partial degeneration of the GVN (Table 1). These results confirm that the GVN are of sympathetic, and the AVN nonsympathetic, origin. It should be pointed out that less than 1% GVN containing many small dense core granular and a few large dense core granular vesicles is noted in the sympathetically denervated middle cerebral and anterior cerebral arteries from one animal (Table 1). These results suggest that only a very small portion (less than 1%) of adrenergic innervation in extraparenchymal blood vessels may originate from sites other than superior cervical ganglion.

A previous report indicates that the rabbit basilar artery contains a large number of GVN (98%) and a small number of AVN (2%) (Lee et al., 1980). In contrast, results of the present study indicate that a greater number of AVN than GVN are observed in the major arteries around the base of the cat brain (Table 1; Fig. 3).

It has been shown that the endogenous NE content (per tissue wet weight) in the rabbit basilar artery is about 2 μg/g (Lee et al., 1980), twice that in the cat basilar artery. This is in keeping with the apparent denser catecholamine fluorescence in the rabbit basilar artery than in the cat basilar artery (Lee et al., 1976; Lee, unpublished observations). Since the NE content drastically decreases and the catecholamine fluorescence disappears after sympathetic denervation (Lee et al., 1976, 1978, 1980, present results), it can be assumed that the content of endogenous NE is a useful indicator of the degree of sympathetic innervation. Accordingly, the sympathetic innervation apparently is twice as dense in the rabbit basilar artery as in the cat basilar artery. We further assume that NE is stored primarily in the vesicles of varicosities (Smith, 1979) and that all varicosities of sympathetic nerves contain equal concentrations of NE transmitter (Dahlstrom et al., 1966). According to the relative ratio of GVN and AVN varicosities in basilar artery of both species, the incidence of AVN varicosity is about 37 times greater in the cat basilar artery than in the rabbit basilar artery. This result indicates that the cat basilar artery indeed receives much denser AVN than the rabbit basilar artery.

The minimal synaptic cleft distance of varicosity from the smooth muscle cells is another determinant for functional significance of a given innervation (Devan and Su, 1974). Presumably, the more intimate the synaptic cleft, the higher the concentration of the transmitter at the postsynaptic receptor would be and, therefore, the larger the response for a given amount of transmitter release. The present results demonstrate that the cat basilar, middle, and anterior cerebral arteries contain consistently more AVN than GVN with synaptic cleft distance less than 6 μm (Fig. 3). Furthermore, it might be argued that only those nerves which are fairly close to smooth muscle cells are functionally important. This was indicated from the previous observation that the majority of sympathetic adrenergic nerve terminals in the rabbit basilar artery was located at a distance greater than 2 μm from the smooth muscle cells whereas, in the rabbit ear artery, the sympathetic nerve terminals were located most frequently at 2 μm or less from the smooth muscle cells (Lee et al., 1980). The wide synaptic cleft distance in the rabbit basilar artery corresponds to the small neurogenic vasocostriction in this artery. In the present study there are often more AVN than GVN terminals within the two-micrometer range, as in anterior cerebral and middle cerebral arteries (Fig. 4), for example.

Our previous report indicates that upon TNS the cat cerebral blood vessels (basilar, middle cerebral, and anterior cerebral arteries) exclusively relax (Lee et al., 1979), whereas the rabbit basilar arteries predominantly constrict and only half of them show an additional small dilator component of response in the presence of adrenergic neuronal blocker (Lee et al., 1976). It is clear that there is a strong correlation between the degree of vasodilatation and the AVN in cerebral blood vessels. The cat basilar artery, which exclusively dilates upon TNS, contains a large number of AVN; the rabbit basilar artery, with only a token neurogenic relaxation, contains very few AVN. In fact, in the cat basilar artery, all the 24 thin sections examined contained more AVN than GVN. This morphopharmacologi-
cal correlation provides evidence that the AVN are the dilator nerves.

The lack of constriction of the cat basilar, middle cerebral, and anterior cerebral arteries upon TNS (Lee et al., 1978) is intriguing, since these arteries, while containing a large number of AVN, are also richly innervated by the GVN, a finding which correlates with the high endogenous NE content and the catecholamine fluorescence. It could be that the constrictor component is masked by the dominant dilator response. This seems probably in view of the presence of significantly more AVN than GVN, especially with synaptic clefts less than 6 μm in these arteries (see above). Although not statistically significant, probably due to small samples, the mean closest synaptic cleft distance for the AVN also tends to be smaller than for the GVN terminals (Table 2). However, several findings from in vivo studies indicate that the sympathetic constrictor nerve in normal cat cerebral blood vessels is not important in controlling brain circulation (Aim and Bill, 1973; Heisted et al., 1978). This is compatible with the in vitro findings that the postsynaptic α-receptors in the cat basilar and middle cerebral arteries are very insensitive to NE (Owman et al., 1974; Lee, unpublished observations) and that the TNS frequency-response relationship and the characteristic of the TNS-induced dilator response in normal cat cerebral artery were by no means affected by the interruption of the sympathetic transmission (Lee et al., 1978).

It has been suggested, without quantification, that the cerebral blood vessels of several species receive approximately equal amounts of constrictor and dilator innervation (Edvinsson and MacKenzie, 1977). However, the present results indicate that the degree of innervation of these two different types of nerves varies not only with different species, but also in different brain regions. In the rabbit, for example, the basilar arteries receive dominant GVN constrictor nerves (Lee et al., 1980). On the other hand, in the cat, the density of the dilator nerves, AVN, is higher than that of the constrictor nerves, GVN, in the major intracranial arteries around the base of the brain, but in the small branch of middle cerebral artery a predominance of vasoconstrictor nerves, GVN, was observed. These results point out that the density of the dilator nerve relative to that of the constrictor nerve decreases as the size of the cat cerebral blood vessels becomes smaller. This difference may imply that the small pial vessels are influenced less by the dilator nerves. Furthermore, the greater number of AVN and GVN terminals close to the smooth muscle cell in the anterior cerebral artery (Fig. 3) suggest that the anterior cerebral artery is influenced by innervation to a greater extent than the middle cerebral and basal arteries.

According to Bevan and Su (1974), the transmitter concentration achieved at the postsynaptic α-receptor during sympathetic neuronal activity vary inversely with the width of the synaptic cleft; the concentration of the synaptic transmitter would be expected to fall off inversely with the cube of the radius. It is apparent that those AVN and GVN varicosities with synaptic cleft distance wider than 4 μm, for example, those in the middle cerebral artery would not exert influence on the smooth muscle cells to the same extent as those with synaptic cleft distance less than 4 μm. Therefore, the mean synaptic cleft distance estimated by averaging the synaptic cleft distance of the varicosities throughout the adventitial layer (Verity, 1971) could not represent the true functional synaptic cleft distance. The validity of the hypothesis that the synaptic cleft distance is parallel to the outer diameter of the vessel (Verity, 1971) is therefore not applicable, at least in cerebral vasculature. In fact, results of the present study based on the mode of distribution indicate that the majority of both the AVN and GVN varicosities in the anterior cerebral artery (Fig. 3A) are closer to the smooth muscle cells than those in the smaller small branch of middle cerebral artery (Fig. 3D).

In summary, the present results indicate that the major cerebral arteries at the base of the cat brain contain a high density of AVN. Pharmacological and morphological correlations strongly indicate that the AVN are the dilator nerves. Although the present ultrastructural approach could not determine the nature of dilator transmitter, it provides a possible way at the present time to estimate the

### Table 2 Mean Closest Synaptic Distance (μm) in Cat Cerebral Arteries

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The mean closest synaptic cleft distance (μm) of AVN and GVN in the cat cerebral artery. n = number of animals. The closest synaptic cleft distance is defined as the shortest synaptic distance between axonal and smooth muscle cell membranes observed for each artery. The difference between AVN and GVN closest synaptic cleft distance in each artery is not statistically significant (P < 0.2, paired t-test).
density of dilator innervation relative to constrictor innervation. Furthermore, it indicates that the dual innervation in cerebral blood vessels varies among different regions. The small branches of the middle cerebral arteries unlike their main artery, receive more GVN than AVN. This transition in the ratio of constrictor and dilator nerves in the vessels of varying sizes could be an important factor in neurogenic control of regional brain circulation. Results of this study also confirm species-related variation of the cerebral vessel innervation (Lee et al., 1976, 1978; Duckles et al., 1977).

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**References**


Da Prada M, Zurcher G (1976) Simultaneous radioenzymatic determination of plasma and tissue adrenaline, noradrenaline, and dopamine within the femtomole range. Life Sci 19: 1161-1174


Hokfelt T, Jonason G (1968) Studies on reaction and binding of monoamines after fixation and processive for electron microscopy with special reference to fixation with potassium permanganate. Histochemistry 16: 45-67


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