(I, V, VI and VII) where linearity of the regression lines was seen both on day 1 and day 3 a good accordance was seen between the half-lives calculated on the two days. Also in the patients with non linearity on one or both days (II, IV, and VIII) the biological half-lives are in agreement with each other. Only in one patient (III) was a big difference seen between the biological half-lives on the two days. Since III was the only patient in the group who received other drugs during the study (diazepam, nitrazepam and lithium carbonate) the difference is possibly due to a varying influence from these drugs on the elimination and/or metabolism of amitriptyline. None of the three drugs or their metabolites interfere with the determination of amitriptyline and nortriptyline. The calculated mean biological half-life of 15·1 h differs widely from that reported by Braithwaite & Widdop (1971). This may be because they used healthy volunteers, while we used patients. However, data (Jørgensen & Hansen, to be published) from an infusion study with four volunteers treated according to a two compartment open model give elimination half-lives in the range 15·5–19·5 h.

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On the direct or indirect influence of apomorphine on central serotonin neurons

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Apomorphine, regarded as a drug stimulating central dopaminergic structures (Andén, Rubenson & others, 1967; Ernst, 1967), increased the concentration of 5-hydroxytryptamine (5-HT) and its metabolite, 5-hydroxyindoleacetic acid (5-HIAA) in whole rat brain (Grabowska, Antkiewicz & others, 1973; Scheel-Krüger & Hasselager, 1974) as well as in separate brain structures (Grabowska, & others, 1973), particularly in the mesencephalon region. Histochemical fluorescence analysis demonstrated marked increase of 5-HT fluorescence in the region of nucleus raphé dorsalis of rat under the influence of apomorphine (Śmiałowska, 1975).

The experiments presented here were performed to find out if apomorphine affected the 5-HT rich area of the mesencephalon directly or through descending pathway originating from dopaminergic structures of the forebrain.

Male Wistar rats (180–200 g) were treated with atropine (0·1 mg kg^{-1}, i.p. 0·5 h before operation) and were placed in a head holder when slightly anaesthetized with diethyl ether. A dorsal-ventral cut was made through the occipital cortex and the frontal parts of the superior corpora quadrigemina and the nucleus interpeduncularis. The transection totally separated the mesencephalon and the diencephalon. The raphé region in the mesencephalon with the 5-HT containing cell bodies was left intact caudally to the lesion.

Fourteen to 16 h after transection the concentration of 5-HT and 5-HIAA in the whole mesencephalon was simultaneously determined using the methods of Maickel, Cox & others (1968) and Miller, Cox & others (1970) respectively. Apomorphine was administered subcutaneously 45 min before decapitation.

The intensity of 5-HT fluorescence in the cell bodies of the nucleus raphé dorsalis area was evaluated according to Falck, Hillarp & others (1962) 2–4 h after the mesencephalic-diencephalic transection. Apomorphine was injected 30 min earlier. This

Table 1. *Mesencephalon concentration of 5-HT and 5-HIAA under the influence of apomorphine in normal and mesencephalon-diencephalon transected rats.*

Procedure	Drug treatment mg kg^{-1}	5-HT ng g^{-1} ± s.e.m.	5-HIAA ng g^{-1} ± s.e.m.	Intensity of 5-HT fluorescence in dorsal raphé nucleus
Control	Saline	1188 ± 36	1106 ± 151	++
Control	Apomorphine 5·0[a]	1501 ± 512**	1528 ± 58	+++
Transected	Saline	1079 ± 40	1198 ± 112	++
Transected	Apomorphine 5·0[a]	1109 ± 18	1163 ± 88	++

[a] For histochemical analysis apomorphine (20 mg kg^{-1}, s.c.) was injected 30 min before decapitation. Each group consisted of 7–8 animals (biochemical analysis) or 3–6 (histofluorescence analysis).
** $P < 0.01$ (Student's *t*-test).
+++ Strong intensity.
++ Moderate intensity.

time interval is optimal for an effect by apomorphine on the 5-HT in the cell bodies (Śmiałowska, 1975).

Apomorphine increased the concentrations of 5-HT and 5-HIAA in mesencephalon of normal rats but not in those with mesencephalic-diencephalic transection (Table 1). Transection by itself did not significantly affect the concentration of 5-HT and its metabolite. Transection caused the loss of righting reflex, while the spinal reflexes were maintained.

There was no increase of histochemical 5-HT fluorescence under the influence of apomorphine in the nucleus raphé dorsalis region of rats with the above transection; this latter transection did not produce any change in the intensity of the 5-HT fluorescence in the nucleus raphé dorsalis area.

The results obtained suggest that apomorphine does not affect the 5-HT rich area of mesencephalon directly. The increase of 5-HT after apomorphine administration measured spectrofluorometrically in the mesencephalon as well as histochemically in the nucleus raphé area may derive from stimulation of dopaminergic structures in diencephalon or telencephalon, which are the primary site of action of apomorphine.

This suggestion is corroborated by the fact that spiroperidol, which is believed to block central dopaminergic structures (Janssen, Niemegeers & others, 1967), inhibited the apomorphine-induced increase of the 5-HT fluorescence in the nucleus raphé dorsalis (Śmiałowska, 1975) and at the same time counteracted the increase of both, 5-HT and 5-HIAA, under the influence of apomorphine in the whole rat brain (Grabowska & others, 1973).

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