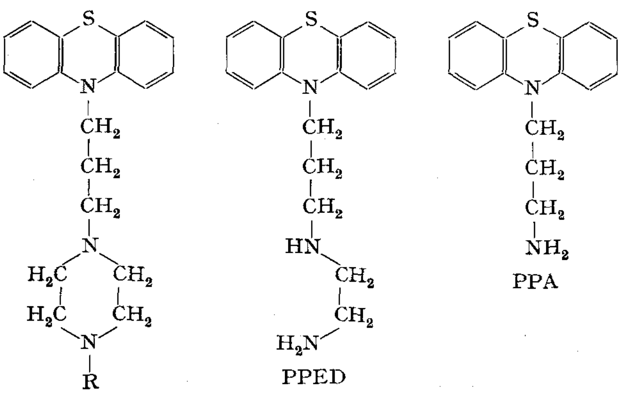
($C_{12}H_9NS$, phenothiazonium ion). Therefore, N-[γ-phenothiazinyl-(10)-propyl]-ethylenediamine (PPED) was proposed as structure of the metabolite. In accordance with this, the 100 MHz-NMR-spectrum (TMS as internal reference) showed absorptions at 6.8–7.4 (8 aromatic H), 3.92 (N^{10}-CH_2-, t, 2 H, J $\approx$ 7 Hz), 1.81 (C-CH_2-C, s, 2 H) and 2.61 ppm (N-CH_2-, m, 6 H). The UV-spectrum which closely resembled that of perazine[1] and the IR-spectrum also agreed with the proposed structure. UV-, IR- and mass-spectra of the metabolite and of synthetically prepared PPED were identical, as were the Rf values of the two compounds and of their sulfoxides in TLC (Table).

In acute experiments with 50 mg/kg perazine per os, PPED proves to be a minor metabolite in rat liver. Repeated dosage leads to a progressive increase in its tissue concentration. After termination of perazine administration, tissue levels of PPED decline much slower than those of other metabolites, and PPED is still detectable in various organs 2 weeks after the last dosage.



R = CH_3 Perazine
R = H DMP

Discussion. Though the piperazine ring forms part of a large number of pharmaceutical compounds, apparently nothing was known on its metabolic degradation in mammals. An oxidative attack on the carbon skeleton could be demonstrated by us[2] through the identification of a diketopiperazine derivative which is excreted in humans ingesting perazine. The occurrence of PPA in rat liver shows that the piperazine ring can be completely degraded, leaving only 1 amino group. PPA constitutes a common metabolite of perazine and promazine[4].

Zusammenfassung. Wiederholte orale Gabe des Neuroleptikums Perazin (Taxilan®) führt bei der Ratte zur Kumulation eines Metaboliten mit teilweise abgebautem Piperazinring, N-[γ-Phenothiazinyl-(10)-propyl]-äthylendiamin. Seine Konstitution wurde durch NMR- und Massenspektroskopie sowie durch Synthese geklärt. Als weiteres Abbauprodukt wurde γ-[Phenothiazinyl-(10)]-propylamin identifiziert.

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Neuron Populations in the Cerebellum of the Cat

Recent comparisons of the cerebellum to a neuronal machine[1] would gain in validity if consideration were given to the numerical parameters. In cerebellum research, findings made on non-primates are frequently considered applicable to man, to the extent of influencing clinical neurology[2]. The enumeration of the cerebellar nuclear cells, so clearly isolated from other neuronal groupings, renders an exact assessment of the outflow oriented cerebellar capacity[3] in a given species. Cell frequencies in the deep cerebellar grey of man were found to be but a fraction of the formerly reported range of figures[4]. Thus, estimation methods are applicable, giving a high level of confidence. Estimates of the vast number of Purkinje cells would tend to be less precise. The widest range of uncertainty is necessarily associated with attempts to enumerate the granular cells. The available estimate[5] for man ranges from 10^{10} to 10^{11}. Basic cerebellar structure on the microscopic level is remarkably constant in all vertebrates. It is of interest whether the proportionate distribution of the constituent neuronal elements is simply a function of bodyweight or size, or relates to other factors.

Neuron nucleolar counts were carried out on 25 μm Nissl stained sections of 5 cat cerebella. Brains were fixed by perfusion and subsequent immersion in neutral buffered isotonic formalin. Counts were made by periodic samples of 10 section intervals. A 5 section period was used in 1 brain. Compared to an all section count, the expected loss of accuracy[4] is 2% only.

There is little variation among cell frequencies in the deep cerebellar nuclei of 4 animals (Table I). The 5th, a young male of low bodyweight, has significantly lower cell numbers (P 0.005) in all of the nuclei. Perinatal nalnutrition is a possible but not provable correlate for this difference. Compared to cell frequencies in the same nuclei of man[4], shifts in proportions are considerable. Homologies here, comparing primates to non-primates, are accepted now with few reservations[6,7]. Whereas the medial nucleus of the cat accounts for 35% of all deep cerebellar neurons, the homologe fastigial nucleus of man contributes only 1.65% of the total. Against an assumed

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Table I. Cell frequencies cerebellar nuclei

Cat	Medial nucleus	Right nucleus interpositus	Lateral nucleus	Total	Medial nucleus	Left nucleus interpositus	Lateral nucleus	Total
1 3.5 y, 4 kg ♂	8470	10200	5360	24030	8490	10300	5180	23970
2 1.5 y, 3.5 kg ♀	8045	10580	5260	23885	8325	10105	5225	23655
3 1.5 y, 2.4 kg ♀	8860	10840	5450	25150	8710	10770	5640	25120
4 4 y, 3,6 kg ♂	8850	10740	5480	25070	8800	10630	5440	24870
5 2.5 y, 2.2 kg ♂	7880	9540	4150	21570	8190	9770	4370	22330
mean	8421	10380	5140	22940	8403	10314	5176	22989
standard deviation ±	431	473	503	1635	249	360	433	1409
S.D. % ±	5.1	4.5	9.8	7.1	2.9	3.5	8.4	6.1

Table II. Purkinje cell count and granular cells estimate in one female cat, 1.5-year-old, 2.4 kg

Section number	Purkinje cells counted	Granular cells (mean in 1000 μm²)	Surface area granular cell layer (μm²)	Ratio of Purkinje to granular cells	Estimate of granular cells
225	460				
250	1479				
275	1899	22.85	32,047,371	1:385	732,282
300	3307				
325	2929				
350	3180				
375	3024	25.31	35,366,158	1:295	894,763
400	3062				
425	3190				
450	3923				
475	3737	22.65	44,663,084	1:270	1,011,618
500	4187				
525	3581				
550	2801				
575	2451				
600	1976				
625	1595	23.10	25,009,814	1:362	577,726
650	858				
675	440				
700	78				
Total: $48,157 \times 25 = 1,203,925$ Purkinje cells. $= 1.2 \times 10^6$.				mean: 1:328; estimate of granular cells: 3.9×10^8.	804,974

overall bodyweight ratio of 20:1, man to cat, deep cerebellar neuron sums relate 12:1, fastigial nuclear cells 1:1.5. Here cell frequencies are 50% higher in the cat, not just proportionally but in absolute terms. This finding needs to be emphasized in view of the diverse connections demonstrated for the cat fastigial nucleus. In the cat the interpositus nuclear complex accounts for 44% of the total, in man for 6% only; rendering a ratio of 2.8:1. The predominantly neocerebellar nucleus lateralis of the cat contributes 21% to the neuron total, against 92% for the dentate nucleus of man, giving a ratio of 57:1.

Purkinje neurons were counted in 20 sections of 1 animal (25 period sample). The estimate of 1.2×10^6 (Table II) for the number of Purkinje cells, when related to the most recent[8] and also highest estimate 25×10^6 for the number of Purkinje cells in the human cerebellum, the ratio is 20:1, the same as the assumed ratio of bodyweight. Ratios of convergence of Purkinje to subcortical neurons are 26:1 in the cat, 40:1 in man. On the basis of lower Purkinje cell estimates for man, however, as supplied by earlier authors[5,9], ratios differ less. The need for more precise numerical data about man is apparent.

A first approximation of the number of granular cells in the same cat cerebellum renders an estimate of 3.9×10^8 (Table II). Granular cell layer surface areas and cell densities were evaluated at four levels. Thus a ratio of 1:325 Purkinje to granular cells is suggested. Available figures for man give ratios from 400:1 to 6600:1.

The above findings counsel a cautious approach towards extrapolations from cat to man, in particular as concerns proportional distribution of outflow from the cerebellum. Further, they provide a gauge for both species, for the assessment within the cerebellum of proportions related to phylogenetic stages.

Zusammenfassung. Das Verhältnis der granulären Zellen im Cortex des Kleinhirns bei Katzen zur vorhandenen Anzahl von Purkinje-Zellen ist kleiner als beim Menschen. Die Zellzahlen stellen einen Gradmesser für die phylogenetische Entwicklung dar.

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