Sera collected from a 11 pups and mothers, taken alternately from experimentals and controls, 3–24 h after tracer, showed a progressive decrease with time of whole serum I^{125} with time ($P = 0.005$). Control pup data was not significantly greater than experimental. Protein: inorganic serum I^{125} ratios were lower in experimental (0.54) than in control (0.083) mothers. Pups' sample volumes were insufficient for testing.

In a continuous scale rating, where all animals were assigned thyroid histology ratings of 4 if normal, 1 in extreme destruction and 7 in highest functional potential, no significant differences were seen, except in marked improvement in 'functional potential' from 1Wk to 3Wk histology for controls ($P = 0.05$) in Table III. Pooled data for 1Wk and 3Wk mothers show significantly less activity in experimental than control mothers ($P = 0.01$), although all fell with time in rating.

Table III. A) Continuous scale rating of thyroids of siblings and their mothers treated with radioactive iodide in the third trimester of gestation

	First week	Third week	First and third week
Siblings of I^{131} treated mothers	3.17 ± 0.37 ($N = 12$)	3.54 ± 0.64 ($N = 13$)	3.36 ± 0.37 ($N = 25$)
Control siblings	2.62 ± 0.49 [a] ($N = 16$)	4.56 ± 0.75 [a] ($N = 9$)	3.32 ± 0.37 ($N = 25$)

[a] Student's t-test $P = 0.01$. On the continuous scale rating, 1 = least functional, with frank destruction of follicles, fibrous and leuckocytic invasion; 4 = normal, and 7 = highest functional activity.

B) Differences in histological ratings between mothers and siblings

I^{131} treated	7.09 ± 0.71 [a] ($N = 11$)	7.77 ± 0.73 ($N = 13$)	7.46 ± 0.50 [a] ($N = 24$)
Controls	4.12 ± 0.44 [a, b] ($N = 16$)	7.44 ± 0.63 [b] ($N = 9$)	5.32 ± 0.48 [b] ($N = 25$)

[a] Student's t-test $P = 0.01$. [b] student's t-test, $P = 0.01$. On the continous rating scale rating 1 = least functional compared with mother; 6 = same as mother, and 12 = most active in relation to mother.

Differences between siblings and their mothers' histological ratings were on a 12 unit scale, where 6 equalled mother, 12 highest and 1 lowest from mother (Table III b). Experimentals rated higher than both mothers and controls ($P = 0.01$). 1Wk to 3Wk improvement in controls was significant at $P = 0.001$.

Protein bound tracer, without testing T-3 and -4 I^{125} binding cannot reflect amount released to tissues, nor can direct cellular effects of irradiation of brain from our procedure be assessed, but implied by results of NAIR and BAU[8] and SPEERT et al.[6,9].

Conclusion. Irradiation of the rat on the 14th day of gestation induces varying degrees of thyroid destruction in mother and siblings and decreased ratios of iodine labeled protein; inorganic iodine in mothers, compensatory hyperactivity in thyroids of siblings, and increased perseverance of operant behavior, which decreases with maturation. Changes observed in siblings are not fully accountable by either differences in labeled iodide thyroid uptake, serum protein binding or thyroid histology[10].

Résumé. Les petits de rates irradiées au 14e jour de leur gestation, avec 3000 μC/kg de ^{131}I i.p. ont montré une plus grande réduction de leur capacité à presser sur un levier lorsqu'ls l'ont appris avant la puberté. Cet effet fut d'autant plus manifeste chez les animaux qui avaient été conditionnés lentement et qui ont généralement tendance à améliorer leur performance avec l'âge.

L. H. BOGDANOVE, A. DOODY and X. NADACKAPADAM

Department of Pharmacology, 2020 Ogden Avenue, Chicago (Illinois 60612, USA), 24 February 1971.

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Hypoprolinemia in Parkinsonism; a Case Report

In recent years various disturbances of amino acid metabolism, including proline, have been reported. SCHÄFER et al.[1] distinguish 2 types of enzyme defects in proline metabolism, both producing hyperprolinemia. Observations on hypoprolinemia have not come to our attention. We therefore wish to report a case of Parkinsonism showing this biochemical abnormality.

This 65-year-old male patient (K.M.) showed a typical Parkinsonian disease which was first observed 1 year before admission. Besides a hypertonus no other pathology could be detected, either clinically or by routine laboratory investigation. The history disclosed that the father of the patient suffered from Parkinson's disease. The patient himself had had no major illness until manifestation of Parkinsonism.

Amino acid analyses were performed in plasma on 4 different occasions within a period of 4 months using the automatic ion exchange method of SPACKMAN et al.[2]. Plasma was deproteinized with picric acid according to STEIN and MOORE[3].

The results (Table I) show the plasma levels of proline in pat. K.M. as about 10% of normal controls. The other amino acids determined were all within normal limits (Table II).

In contrast to hyperprolinemia[4], the hypoprolinemia observed was not accompagnied by a specific pathology. Till the development of hypertonia and Parkinsonism at an advanced age, the patient was a healthy person. Obviously, there is a hereditary factor in the patient's parkinsonism. So far, however, no evidence exists that hypoprolinemia plays a role in Parkinson's disease. As

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will be reported elsewhere[5], amino acid analyses in additional 12 Parkinsonian patients did not show this abnormality of amino acid metabolism. Nevertheless, the possibility that hypoprolinemia represents a biochemical factor in the Parkinsonism of this particular patient cannot be excluded.

Table I. L-Proline in plasma

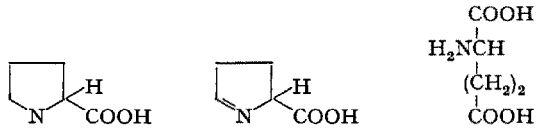
Normal adults	Patient K. M.
$160 \pm 58\ \mu M/l$	18; 11; 16; 25 $\mu M/l$

Means and standard deviations.

Table II. Amino acids in plasma ($\mu M/l$)

Normal adults[a]		Patient K. M.
Glu	69 ± 26	94
Gly	153 ± 43	120
Ala	249 ± 66	296
Val	157 ± 31	177
I Leu	42 ± 11	52
Leu	97 ± 24	85
Tyr	38 ± 8	34
Phe	36 ± 7	37
Lys	105–207[b]	104
His	32– 97[b]	39
Arg	40–140[b]	41
Orn	30– 64[b]	42

[a] Mean from 4 analyses with exception of arginine (3 determinations), runs were done at 4 different occasions within a period of 4 month. [b] The normal values for the basic amino acids are taken from SOUPART[6].



Proline $\rightleftarrows \Delta^1$-pyrroline-5-carboxylate $\rightleftarrows$ glutamic acid.

The biochemical mechanisms responsible for the hypoprolinemia observed are as yet obscure. A defect in the amino acid carrier system appears less probable, because glycine, which is transported by the same carrier system, is not affected. The observations described rather suggest an enzymatic block in the pathway from glutamic acid to proline (Figure), involving either the cyclization step to Δ^1-pyrroline-5-carboxylate or the hydrogenation by the enzyme Δ^1-pyrroline-5-carboxylate reductase[7].

Zusammenfassung. Im Vergleich zu einer Kontrollgruppe zeigten Aminosäurenanalysen im Plasma eines Patienten mit Parkinsonismus eine starke und isolierte Reduktion von L-Prolin.

K. W. PFLUGHAUPT and G. G. BRUNE

Neurologische Universitätsklinik und Poliklinik Würzburg, Luitpoldkrankenhaus, D-8700 Würzburg (Germany), 31 March 1971.

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Effect of Serotonin Depletion on HC-3-Induced Slow Wave Sleep of Cat

It has been shown in cats, with chronically implanted intraventricular cannulae as well as EEG and EMG recording electrodes, that the 4th ventricular injection of hemicholinium-3 (HC-3) dose dependently increases slow wave sleep (SWS) time[1]. Since HC-3 is a choline transport inhibitor[2,3] and the effect is frequency dependent[4,5], it was rationalized that HC-3 by blocking reuptake of choline prevents resynthesis of acetylcholine (ACh) and lowers the ACh containing neuronal activity which in turn increases SWS, and this is interpreted that brain ACh actively maintains the states of vigilance[1]. This finding, that brain ACh depletion leads to sleep, refutes the concept of a cholinergic hypnogenic system[6].

There is, however, a considerable amount of work which suggests that brain serotonin (5-HT) plays a significant role in SWS. The strongest support of this concept comes from those studies which demonstrates that in cats 5-HT depletion with *para*-chlorophenylalanine (PCPA) leads to insomnia[7–9]. The present study has, therefore, been extended to investigate whether or not brain ACh depletion with HC-3 leads to 5-HT release in the brain which in turn induces SWS. Thus, HC-3 induced SWS time was measured in cats before and after PCPA treatment. If HC-3 ultimately induces SWS by causing 5-HT release then PCPA treatment should block or alter SWS time due to HC-3, since PCPA is a relatively selective 5-HT depletor[10].

Results presented here were collected from cats reported in a previous publication[1] which also reported the methods of surgical preparations and recording arrangements. In brief, each cat was stereotaxically implanted with deep and surface brain electrodes as well as a neck muscle electrode for recording chronically both EEG and EMG in freely moving conditions, and a 4th ventricular cannula

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