

SHORT COMMUNICATIONS

Evolution of Diabetes after early Testosterone Treatment in Rats*

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Summary. Evolution of diabetes caused by subtotal pancreatectomy was altered when the animals were sterilized by subcutaneous injection of testosterone propionate (1 mg/rat) on the third day of life. Androgenized, subtotally pancreatectomized female rats had a mean blood sugar level higher than the controls, at the first and second month after pancreatectomy. — The percentage of these rats with blood sugar level above 120 mg% was also higher than that of the controls at the same period of time. In the same experimental conditions androgenization of male rats had no effect on the evolution of diabetes.

Evolution du diabète après traitement précoce à la testostérone chez les rats

Résumé. L'évolution du diabète causé par la pancréatectomie subtotale était modifiée quand les animaux étaient stérilisés le troisième jour de leur vie par une injection souscutanée de propionate de testostérone (1 mg/rat). Les rats femelles androgénisés, ayant subi une pancréatectomie subtotale avaient un taux moyen de glycémie plus élevé que les témoins, le premier et le deuxième mois après la pancréatectomie. — Le pourcen-

tage de ces rats ayant un taux de glycémie supérieur à 120 mg% était aussi plus élevé que celui des témoins à la même période. Dans les mêmes conditions expérimentales, l'androgénisation de rats mâles, n'avait pas d'effet sur l'évolution du diabète.

Diabetesentwicklung bei Ratten nach Frühbehandlung mit Testosteron

Zusammenfassung. Die Entwicklung eines durch subtotale Pankreatektomie ausgelösten Diabetes ließ sich bei Ratten durch s.c. Injektion von 1 mg/Ratte Testosteron am 3. Lebenstage, die zur Sterilität führt, modifizieren. Mit Androgenen behandelte weibliche Ratten zeigten 1 und 2 Monate nach subtotaler Pankreatektomie einen höheren Blutzuckerspiegel als Kontrolltiere. Gleichzeitig fand sich unter diesen Tieren zum gleichen Zeitpunkt ein höherer Prozentsatz mit Blutzuckerspiegeln über 120 mg% als bei Vergleichstieren. Androgengaben an männliche Ratten beeinflussten unter den gleichen Versuchsbedingungen die Diabetes-Entwicklung nicht.

Key-words: Testosterone treatment, evolution of diabetes.

It has long been established that removal of 95% the pancreas in the white rat, is followed by the development of diabetes some months later. The period of time between subtotal pancreatectomy and the onset of diabetes is characterized by normal fasting blood sugar level, normal glucose tolerance test, aglycosuria and normal growth of the rats, and is called prediabetes [6].

Several factors may change the evolution of diabetes in subtotally pancreatectomized rats; for example, treatment with hormones may shorten or lengthen the period before the diabetic syndrome is established. Female sex hormones have a protective action and male hormones have a deleterious effect on the development of diabetes [8].

A single injection of testosterone propionate given to female rats early in life has been found to provoke continuous oestrus and definitive sterility [1]. It has been proposed that the injection of testosterone changes the pattern of gonadotrophic secretion, making the female hypothalamus secrete the releasing factor in a tonic way similar to that of the male [2].

The present investigation was undertaken to ascertain whether androgenization of rats can change the

evolution of diabetes in partially pancreatectomized rats.

Material and Methods

Testosterone propionate was injected subcutaneously into three-day-old rats in doses of 1 mg per rat. Those testosterone-treated rats that were found to be in permanent oestrus at the second month of life, were partially pancreatectomized following the technique previously described by one of us [6]. The blood sugar level was determined after a fast of seven hours at the first and second month after pancreatectomy, by the method of Somogyi-Nelson on blood obtained by cutting the tip of the tail.

The following groups of animals were studied: 1: androgenized, partially pancreatectomized male and female rats; 2: olive-oil-injected, partially pancreatectomized male and female rats (controls).

Results

The blood sugar levels obtained in the different groups of animals are shown in table 1. Female rats injected with testosterone showed a mean glycaemia higher than the corresponding control group, at the first and second months after pancreatectomy. This difference is highly significant ($p < 0.001$, t test). On the other hand, there was no statistically significant

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difference between blood sugar levels of testosterone-treated male rats and the controls, although both groups of animals were hyperglycaemic at the same period of time.

In order to have a better appreciation of the phenomenon, we used a different statistical approach. The percentages of rats with a fasting blood sugar levels higher than 120 mg% were compared within groups, and the results are shown in table 2. At the first and second month after pancreatectomy the percentage of androgenized female rats with hyperglycaemia was higher than that of the control. This difference is significant ($p < 0.02$, *t* test). No difference was observed in the male treated group.

Table 1. Fasting blood sugar level^b in androgenized^c subtotally pancreatectomized rats^d

Month after pancreatectomy		First	Second
Female	Androgen	171 ^a ± 12.6 (23)	198 ^a ± 10.5 (16)
	Control	110 ± 4.0 (25)	114 ± 5.2 (20)
Male	Androgen	196 ± 12.2 (22)	232 ± 41.8 (19)
	Control	218 ± 22.7 (16)	285 ± 21.8 (12)

^a Higher than corresponding control group ($P < 0.001$).

^b Mean ± standard error.

^c 1 mg of testosterone propionate was injected on the 3rd day of life.

^d Pancreatectomy was performed the 2nd month of life.

() Number of animals.

Table 2. Number and percentage of rats with fasting blood sugar levels higher than 120 mg%

Month after pancreatectomy	Females		Controls		Males		Controls	
	No.	%	No.	%	No.	%	No.	%
First	21/23 ^a	91 ^b	4/19	21	18/22	82	15/16	94
Second	16/16	100 ^c	10/20	50	19/19	100	12/12	100

^a Number of diabetic animals above total number of pancreatectomized rats.

^b $p < 0.02$.

^c $p < 0.005$.

Discussion

The present experiment shows that the injection of testosterone propionate in female rats early in life enhanced the evolution of the diabetes caused by subtotal pancreatectomy. In female rats treated with testosterone on the third day of life, hyperglycaemia was established sooner than in subtotally pancreatectomized control rats injected with olive oil. This pattern closely approximates to that which is seen in male rats, with or without exogenous androgen treatment.

We cannot be sure of the mechanism involved which might explain these results. It may be that an alteration of hypothalamic function is responsible, but we do not know the role played by changes in the F.S.H. and L.H. pattern of secretion. The mechanism by which the hypothalamus acts on carbohydrate metabolism is not clear. Electrolytic lesions of the anterior hypothalamus and preoptic region in rats increase the sensitivity to insulin [9], and rats with elec-

trolytic lesions of the ventromedial region have improved glucose tolerance test and increased sensitivity to insulin [10]. The amelioration of the diabetic glucose tolerance of the sand rat after hypothalamic injury has also been described [4]. In guinea pigs, electrolytic lesions of the anterior and middle hypothalamus were followed by insulin hypersensitivity and lower fasting blood sugar levels [3].

It should also be kept in mind that androgen injection may change the secretion of other releasing factors, and also that testosterone may act directly on the pancreas. The direct action of the sex hormones on the pancreas has been previously reported [5, 7]. Further studies are in progress, aimed at clarifying the deleterious action that early androgen injection into female rats has on the evolution of diabetes.

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