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ORIGINAL ARTICLE

Evidence for a neuroimmunomodulatory and a hematopoietic role of the Luschka's coccygeal body

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Abstract

OBJECTIVES: In humans the *glomus coccygeus* was described in 1860 by Luschka. It is present at the coccyx tip and corresponds to a complex anastomosis between the median sacral artery and vein, and it is innervated by sympathetic fibers. In rats and mice it has been located in the tail ventral face. Its function is not known. According to our previous work, which demonstrated that hematopoiesis is under a noradrenergic control and based on the presence of epithelioid cells and sympathetic innervation, we assumed that the coccygeal gland might influence hematopoiesis via neuroendocrine or neural mechanisms. Therefore, the present study was undertaken to analyze the effect of *glomus coccygeus* on hematopoiesis. MATERIAL & METHODS: Peripheral blood leukocyte and platelet concentrations as well as body temperature (BT) and body weight (BW), and norepinephrine (NE), adrenaline (A) and dopamine (DA) content in bone marrow of Luschkaectomized (LCGx), Sham LCGx operated (ShLCGx) and normal mice (Co) were investigated. RESULTS: We found that in LCGx *vs.* ShLCGx and Co, platelets and neutrophils increased while lymphocytes decreased. The effect of LCGx was significant from day 0 until day 65. Total leukocytes, monocytes, granulocytes, eosinophils and BT did not show any variation. Moreover, 22 days after the operation the amount of NE, A and DA seemed to be decreased in LCGx *vs.* ShLCGx while the difference was less evident between ShLCGx *vs.* Co. CONCLUSIONS: This study suggests for the first time a possible hematopoietic function and an immunomodulatory activity of the "Luschka's body" or *Coccygeal body* by a modulation of the sympathetic nervous system.

Introduction

Luschka's coccygeal gland (LCG) or *glomus coccygeum*, which normally measures several millimeters in diameter and is located in the soft tissue at the tip of the coccyx, was described for the first time by Hubert von Luschka in 1859 [1, 2]. Until 1953 the definition of this entity has been modified many times. In fact the term *glomus coccygicum (or coccygeum),* largely used before 1953, has been suggested to be incorrect: terms as *glomerula coccygica* or *glomerula arteriosa coccygica* appeared to be more appropriate to describe these multiple organs. Staubesand examined 192 humans as well as a variety of mammalian specimens. Its three-dimensional reconstruction emphasized the complexity of the structure. Moreover, on this basis, Staubesand cleary defined for the first time the position of the corpuscle: *glomerula coccygica* are arranged on the ventral side of the coccyx according to the ramifications of the medial caudal artery. Almost every ramus of this artery supplies one or more *glomerula*. The *glomerula coccygica* may show a more or less complicated arrangement of blood vessels in the form of arteries, the Soquet-Hoyer canals, and veins, joining each other without a capillary network between them. Also the precapillary parts of their artery may show some epithelial modifications [3–6].

In the different species of mammals, man included, both *glomerula coccygica* and *glomerula caudalia* may show some vessels with epithelioid cells, which form a link between arteries and veins. The *glomerula caudalia* often consist of convoluted vessels with epithelioid cells and the vessels do not join a vein. Concerning the size, *glomerula caudalia* does not increase in large species. In fact, short-tailed species such as rabbits, guinea pigs and golden hamster *glomerula caudalia* are not fused. The media of modified vessels in *glomerula coccygea* and *caudalia* shows both epithelioid cells and, in most cases, smooth muscle cells. The width of the *lumina* of the glomus vessels is not related to the size of the epitheliod cells with a clear nucleus and nucleus at their walls [3, 4]. Another interesting paper describing the anatomical structure and size of human Luschka's body has been published by Di Marino et al. [7, 8], who have considered more than 100 human coccygeal bodies (Fig. 1). Authors look for position (25% precoccygeal position on the anterior face of the coccygeal body at few mm of the tip of the bone; 48% anterior part, 20% posterior part, 7% retrococcygeal position), consistence (similar to a lymphatic ganglion), shape (85% compact form, 17% plurinodular form), outward appearance (Luschka's body presents a clear contour line and a capsule exists, the body appears shiny), dimensions (no differences between sexes, compact form with a medial dimension of 3.5 x 2 x 1.5 mm), weight (compact forms: 5 to 50 mg; plurinodular forms about 80 mg), color (on fresh corpse: color pink-yellow; on formalin fixed corpse: grey-brown).

The double innervation of the coccygeal body is performed by nerve fibers belonging to the precoccygeal sympathetic anastomose (*Ganglia trunci sympathici*) and of the parasympathetic system (*Plexus iliacus*). This double innervation has been confirmed

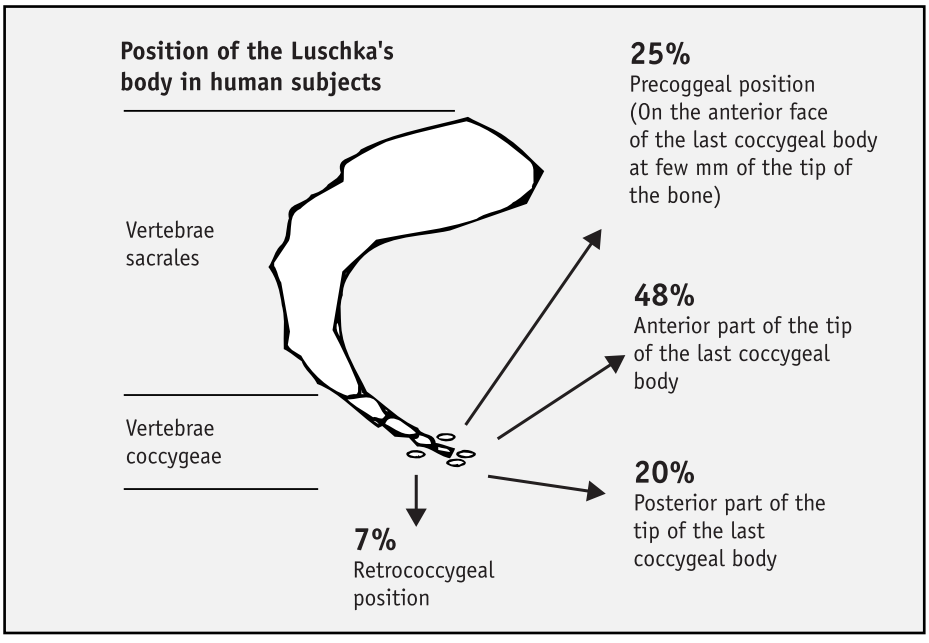


Fig. 1. Anatomical localization of LCG in humans expressed as percentage over 100 individuals [7].

by Henningsen [9]. Coccygeal bodies are innervated not only by the cholinergic system but also by the adrenergic: moreover, it seems that such innervation is more intense when epitheliod cells are present [9]. Concerning the content an extremely high concentration of acetylcholine in the human *glomerula coccygea* has been reported and a similar substance seems to exist in the glomus organ of other species [10, 11]. The content of acetylcholine was investigated in other species than humans: in particular, a report exists in which acetylcholine was measured in monkey's glomus organ (*Cercopithecus pygerythrus*) [12]. No acetylcholine was detected. Nevertheless the organ contained 3–4 times the concentration of catecholamines (mainly noradrenaline) found in nearby vessels [12–15].

Moreover, Di Marino *et al*. have performed a histological study of the human coccygeal body which confirms the connection with the nervous and vascular systems. In particular, the corpuscle presents a capsule which includes many glomi and these latter are formed by groups of perivascular epithelioid cells surrounded or penetrated by nervous fibers and mastocytes [7].

Two recent papers confirm anatomical results published by the French group [16, 17].

The physiological function and role of the Luschka's body remain unknown [18] and they have received little attention in the pathology literature [19–21]. Nevertheless, Di Marino et al. report some interesting considerations [7]. For example, on the size of *glomerula caudalia* there is no correlation between size of *glomerula caudalia* and size of animals. Rabbit, cobaye and hamster, which are animals with a shortened tail, have a similar *glomerula caudalia* than rats and mice, animals with longer tails [4] (Fig. 2). It has been suggested that this organ, in spite of its particular localization, shape, histological structure and innervation, might have a role in the local regulation of the terminal vascularization via istaminic products which could be released by mastocytes founded in the epithelioid area. On the other hand, a controversial activity related to the catecholaminergic, adrenergic and cholinergic innervation has been demonstrated [9, 22, 23] and the presence of acid mucopolysaccharides on epithelioid cells and on blood vessel sinuses [22].

The absence of previous documentation on the *Glomus coccygeum* and/or *Glomus caudalia* function and the absence of appropriate experimental models prompted us to perform this experimental study. Based on our experience in the field of neuroimmuno-modulation, we first determined a physiological role of the mouse coccygeal body by focusing its action on hematopoiesis in normal and stress conditions and on bone marrow catecholamine modulation. In previous studies, some of us obtained circumstantial evidence that in the mouse bone marrow a sympathoadrenergic neurogenic input exists, which may be implicated in the modulation of hematopoiesis and of the immune response [24, 25]. Sympathetic fibers reach the bone marrow via the paravertebral and the prevertebral ganglia [26]. Since both sympathetic and parasympathetic nerve fibers exist anatomically linking the LCG to the paravertebral and prevertebral ganglia [7, 9, 22, 23], and neuroendocrine mediators are present in LCG [10–15], we hypothesized that this gland might play

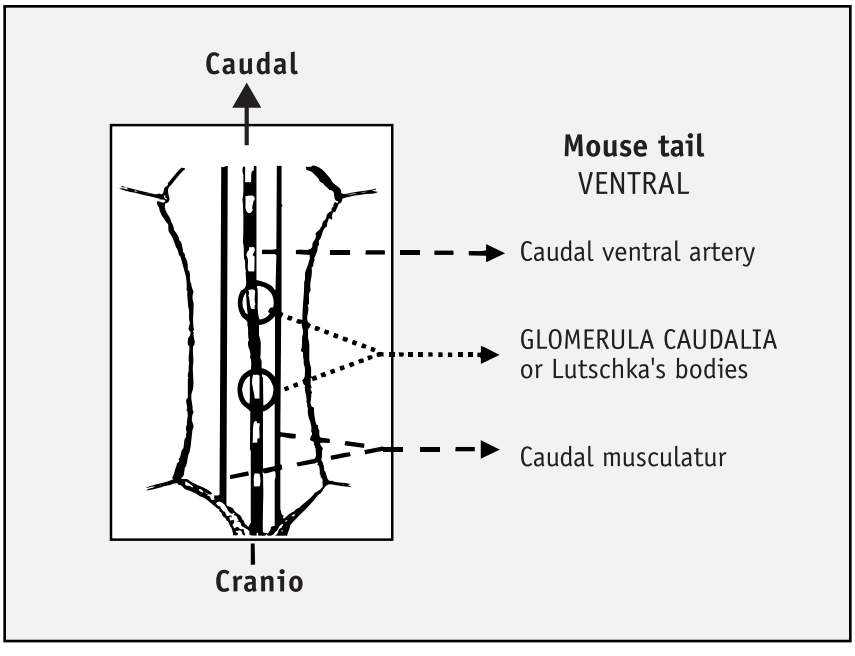


Fig. 2. Localization of LCG in animal tail, mouse and rat.

some role in the modulation of the hematopoietic and immune functions. We therefore developed an appropriate experimental model of surgical luschectomy in the mouse to investigate possible physiological consequences of the ablation of LCG.

Materials and methods

Mice

Experiments were performed on female C57Bl/6 mice 11–12 weeks old purchased from Charles River Italia (Calco, Como, Italy) and kept at 21±1°C, under a 12-hour light:dark cycle with free access to food and water. Animals were sacrificed by cervical dislocation at the end of experiment (see protocols).

Luschkaectomies, Sham luschkaectomies and controls

Female C57Bl/6 mice were luschkaectomized (LCGx) and Sham LCGx operated (ShLCGx) on week 11–12 of age. The surgical intervention was performed using a stereotactic apparatus.

Mice were anesthetized by injecting intramuscularly 100 μl of a 1:10 dilution of 50% Rompun (2% of 2-(2-6-xilidino-)5-6dihydro-4H-1,3thyamine hydrochloride) and 50% Ketalar (ketamine HCl, 100 mg/ml, Park-Davis Co., Morris Plains, USA). Following this procedure, muscle relaxation and loss of any reflex of the pupilla appeared after 1 to 3 minutes.

Animals were then fixed on the stereotactic device on their back. The skin over the median and the ventral plan of the tail was cut with the scalpel (Beaver Mini Blades (#11), Becton and Dickinson, Franklin Lakes, NJ, USA) with a median incision along 3/4 of the length of the tail. The ventral vein and artery, included the *glomi caudalia,* were cut and cicatrized with a surgical electric blade type Bipolar 1 (IHC, Institut für Hochfrequenz Chirurgie, GmBH, Freiburg i.B., Germany). The surgical intervention was done under a dissection microscope (Microscope SZH equipped with Highlight 3000, Olympus, Aigle, Switzerland).

Restraint stress

The mice were restrained in 50 ml plastic tubes aerated with a ventilation hole, for 2 hours per day (10 a.m. to 12 a.m.) on days 19, 20, 21 [27]. On day 22, mice venous blood was collected as previously described [28]. The restraint stress produced anxiety and fear but not complete immobilization. The immunologic effect of restraint stress was quantitated on hematological parameters.

Bone marrow collection and preparation

Bone marrow was flushed out from the long bones with 2 ml of 0.4 N $HClO_4$ solution containing 0.84 mg/ml disodium EDTA, 1 drop of 4% sodium pyrosulfite solution. Recovered tissue was weighted, samples were centrifuged (14'000 rpm, 4°C, 10 min.); supernatant was collected and stored at –80°C until assayed [25].

Catecholamine assay

Catecholamines in the samples were assayed by HPLC with electrochemical detection. The HPLC system consisted of a dual-piston pump (model LC9A, Shimadzu, Kyoto, Japan), a Beckman C18 ultrasphere-XL ODS 3 μm (70 x 4.6 mm) analytical column equipped with a XL ODS 3 μm (5 x 4.6 mm) guard cartridge (Beckman Instruments, Bioindustrial Business Unit, Fullerton, CA), an autosampler (model SIL9A, Shimadzu), an ESA Coulochem II electrochemical detector with a 5011 analytical cell (ESA, Bedford, MA). The first detector potential was set to +300 mV and the second detector to -300 mV. Chromatograms were collected, stored and processed with a computerized integrator (Model 1022 Personal Integrator, Perkin Elmer). Mobile phase was composed of ultra pure water/acetonitrile (82.0: 18.0, v/v), 20 mM K_2HPO_4, 0.69 mM EDTA, 0.27 mM SDS, pH was adjusted to 3.0 with H_3HPO_4 and the solution was filtered (Milllipore, 0.22 μm). The flow rate was set to 0.9 ml min^{-1} sample were added with $HClO_4$ 0.4 N and alumina extracted. Catecholamines were quantitated by using the peak area and referred to a standard curve, generated by injecting catecholamine standards (0.6–200 pg). The values were then normalized for tissue weight [25].

Experimental groups of animals

a) Surgically luschkaectomized mice (LCGx).
b) Sham luschkaectomized mice (ShLCGx).
c) Control mice (Co).

Experimental plan

To determine the hematological role of Luschka's body or *coccygeal body* on mice, in each experimental group different parameters have been measured.

In particular, body weight (g), rectal temperature (°C), hematological profile on venous blood cell population (platelets/mm^3 and leukocytes/mm^3) and hematological cell differentiation (% of lymphocytes, neutrophilic granulocytes, eosinophilic granulocytes, basophilic granulocytes and monocytes) have been considered. Animals, under a light ether anesthesia, were bled from the retroorbital sinus at

day –3 before the surgical intervention. At day 0 mice were operated and they were monitored at days 10, 22, 37, 50 and 65 after the operation. ShLCGx operated mice and normal control mice were controlled at the same timing points.

For catecholamine assays, i.e. noradrenaline, adrenaline and dopamine, another series of experiment has been organized. At day 22 bone marrow cells were collected from the long bone as described in bone marrow collection and preparation.

Clinical examination and hematological profile

Day –3 before the operation, days 10, 22, 37 and 50 post operation all animals, ShLCGx and Co included, were tested for hematological profile on venous blood, while for body weight and rectal temperature mice were examined at days 20, 31, 41 and 74 post operation.

Results

Effects of LCGx on hematological profile

To get a preliminary indication whether Luschka's body is involved in the hematopoiesis, we evaluated the effect of surgical Luschkaectomy on blood cell counts based on the concept that peripheral blood cells are the mirror of the body homeostasis and the bone marrow.

A) Effect on platelets

Female C57Bl/6 mice were luschkaectomized as described in material and methods. Three days before the surgery venous blood was collected from the *plexus retroorbitalis*. Fig. 3 shows that surgical removal of *Glomerula caudalia* increased the number of platelets expressed as platelets $x10^3/mm^3$. At day –3 before any surgical intervention LCGx group has 425'000 ± 85'000 venous blood platelets/mm^3, ShLCGx group shows 400'000 ± 76'000 blood platelets/mm^3 while Co group displays 410'000 ± 81'500 blood platelets/mm^3.

10 days after surgical intervention the number of platelets in LCGx mice is 705'000 ± 119'000 blood platelets/mm^3 and is highly significant ($p< 0.001$) when compared with ShLCGx operated mice where platelets are 396'000 ± 137'082 blood platelets/mm^3 and Co mice, 420'050 ± 82'560 blood platelets/mm^3.

The effect of LCGx is higher and statistically significant also at days 22 (453'000 ± 81549), 37 (646'000 ± 13'656), 50 (784'000 ± 127'121) and 65

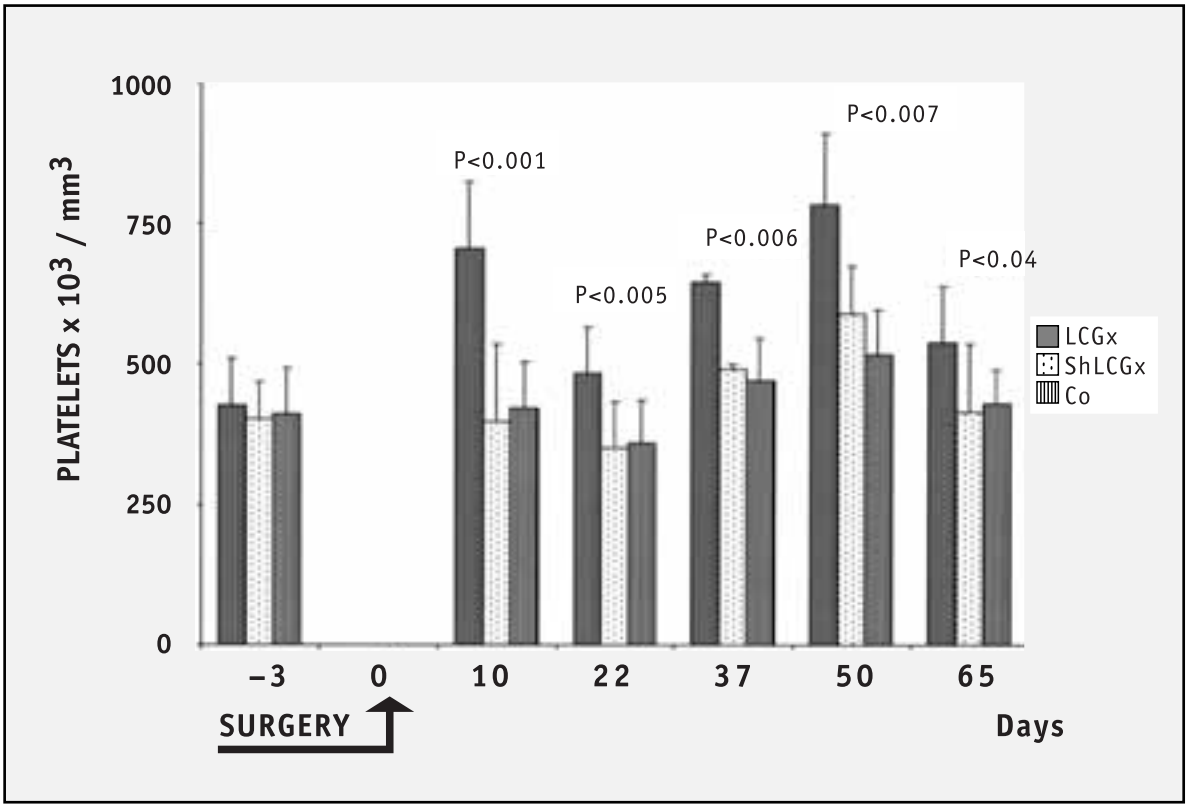


Fig. 3. Effect of LCGx on platelets expressed as platelets x $10^3/mm^3$. The values are the mean ± SD of n=20 C57BI/6 female mice per group at day –3 before the surgical intervention and at various days (10, 22, 37, 50, 65) after the operation.

(538'400 ± 101'844) after the surgical intervention. ShLCGx mice and Co mice did not show any variability in platelet values.

B) Effect on lymphocytes and neutrophils

Fig. 4 A shows that LCGx mice had the % lymphocyte counts lower than those of ShLCGx treated and Co mice. The effect of the surgical intervention is statistically significative on days 10, 22 and 37. In fact, the difference between LCGx and ShLCGx, respectively Co mice, is significative on day 10 ($p<0.03$), on day 22 ($p<0.02$) and on day 37 ($p< 0.05$).

The effect of removal of *Coccygeal body* shows an opposite effect on neutrophile counts which were significantly higher in operated mice when compared with ShLCGx and Co mice: day 10 $p< 0.03$, day 22 $p< 0.02$ and day 37 $p<0.004$ (Fig. 4 B).

LCGx did not show any effect on other hematological parameters such as eosinophilic granulocytes, basophilic granulocytes and monocytes.

Effect of LCGx on Body weight

It was surprising to observe that 20 days after the operation, LCGx mice gained body weight. In fact, as reported in Fig. 5, on day 20 after operation the weight of LCGx mice was (25.71 ± 0.528)g, while ShLCGx (21.26 ± 0.518)g and Co (20.56 ± 0.572)g were lower ($p<0.03$). This difference persists throughout more than 41 days: day 31 $p< 0.03$, day 41 $p<0.05$.

Effect of restraint stress on LCGx mice on hematological parameters

Tabel 1 reports the effect of 2 hours of restraint stress per three days [19–21], 22 days after the surgery. The LCGx stressed group showed a significant decrease in the number of platelets ($10^3/mm^3$) ($p< 0.05$), lymphocytes ($p< 0.001$) and granulocytes ($p< 0.03$) when compared with ShLCGx stressed and control stressed mice. No significative difference has been observed between ShLCGx stressed, control stressed and normal non-stressed mice.

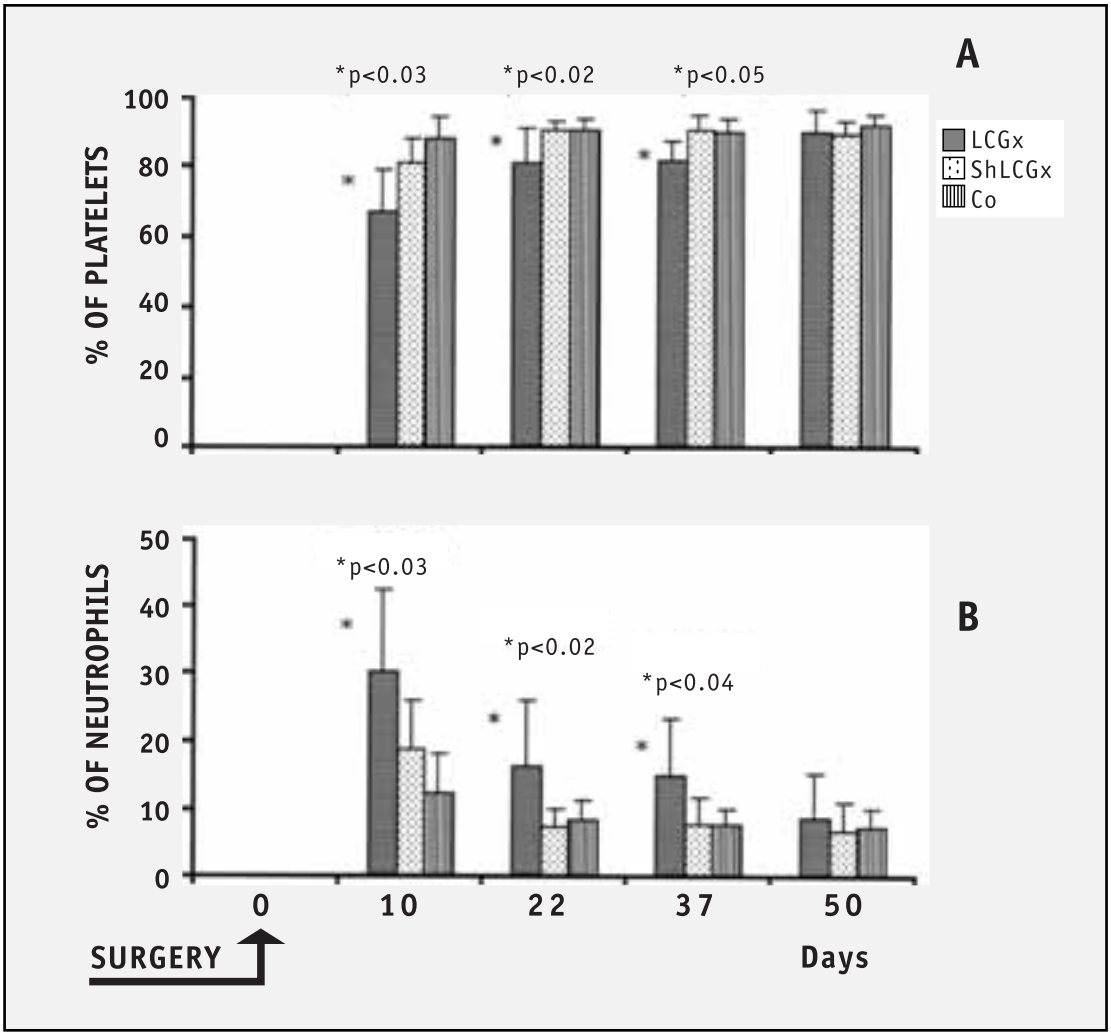


Fig. 4. Effect of LCGx on lymphocytes (A) and neutrophils (B) expressed as % of peripheral blood. The values are the mean ± SD of n=20 C57BI/6 female mice per group, 10, 22, 37 and 50 days after the operation.

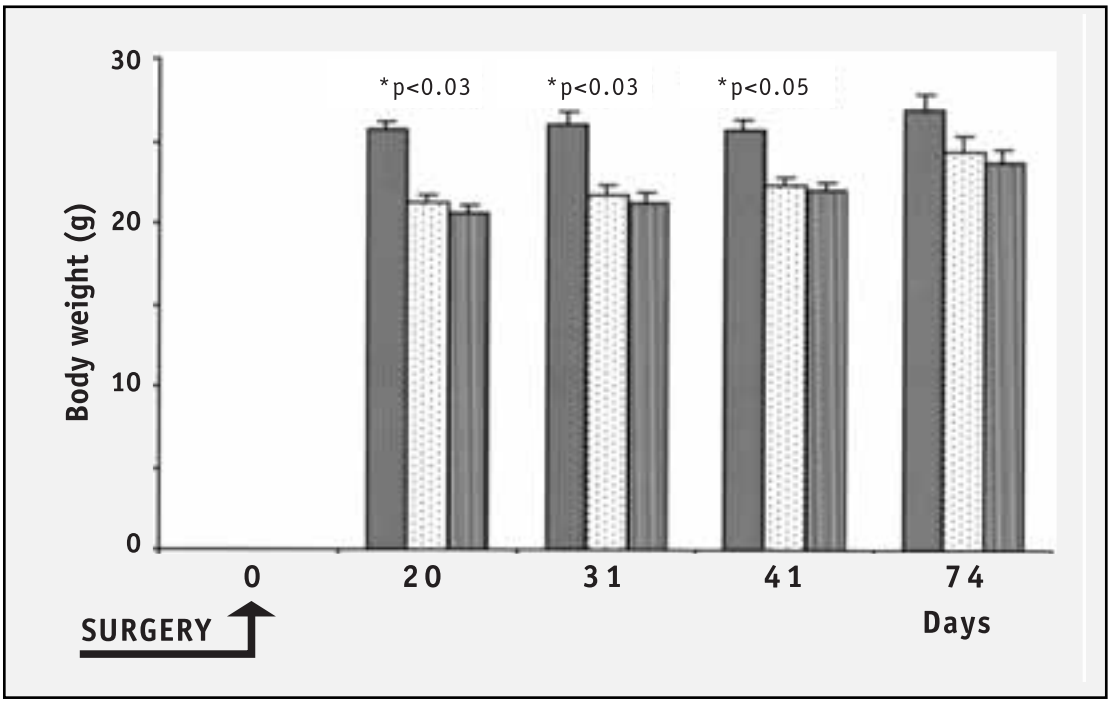


Fig. 5. Effect of LCGx on body weight expressed as g. The values are the mean ± SD of n=20 C57BI/6 female mice per group, 20, 31, 41 and 74 days after the operation.

Table 1. Effect of 3 days, 2hrs/day restraint stress on surgically luschkaectomized, sham luschkaectomized and control C57BI/6 mice 22 days after the operation on platelets, lymphocytes and granulocytes. Statistical significance of the differences was assessed by ANOVA.

Group	(n)	Restraint stress	Platelets (10^3/mm^3)	% of Lymphocytes	% of Granulocytes
A) CGx	10	X	579 ± 91*	79.40 ± 6.85**	19.83 ± 6.87*
B) ShLCGx	10	X	686 ± 58	89.90 ± 2.68	9.63 ± 2.64
C) Co	10	X	702 ±90	87.45 ± 5.17	10.15 ± 6.01
D) Co	10		740 ± 57	92.20 ± 3.13	7.45 ± 2.47

* $p < 0.05$ A vs. B, C and D
**$p < 0.001$ A vs. B, C and D

Table 2. Catecholamine levels in the bone marrow of surgically luschkaectomized, sham luschkaectomized and normal control C57BI/6 mice 22 days after the operation. Values are mean ± S.D. of 10 animals per group and are expressed as pg/g of tissue (wet weight). Statistical significance of the differences was assessed by one-way analysis of variance followed by Boferroni's post test.

Group	(n)	LCGx	ShLCGx	Co	Trend of LCGx on bone marrow catecholamines
NA	10	700 ± 212*	2311 ± 1443	2487 ± 1221	↙
A	10	1401 ± 528*	2296 ± 1713	2665 ± 1989	↙
DA	10	254 ± 140*	2846 ± 2732	3760 ± 2878	↙

* $p < 0.01$ LCGx vs. ShLCGx and vs. Co

Catecholamines: noradrenaline, adrenaline, dopamine

Table 2 shows the effect of LCGx on bone marrow noradrenaline, adrenaline and dopamine 22 days after the operation. Our data indicate that LCGx lowered the concentration of catecholamines in bone marrow where all three catecholamines were always detected in the sample. In LCGx mice noradrenaline value is (700 ± 212) pg/g of tissue, adrenaline (1401 ± 528) pg/g of tissue and dopamine (254 ± 140) pg/g. In ShLCGx operated mice and Co mice, values are clearly higher and with the same order of magnitude found in other reports [25].

Discussion

This study, which discussion is illustrated on Fig. 6, shows that surgical removal of Luschka's coccygeal gland (LCG) seems to produce an increase in neutrophil and platelet numbers and a decrease in lymphocyte count. This functional result suggests that LCG may influence hematopoiesis.

On the other hand, this conclusion, which represents the first functional demonstration connected with a possible role of the LCG, is not surprising and is in accordance with the fact that LCG represents the point of connection between the sacral artery and median sacral vein and, together with the sympathetic nervous system, forms a complex arteriovenous anastomosis [7, 8, 17, 29]. On this basis it can be assumed that LCG, whose structure has been described by different groups of morphologists and anatomists, may strongly influence the biochemical characteristics of the blood and the lymphohematopoietic system, by linking information coming from arterial, venous and nervous systems.

According to these preliminary data, in addition to a possible direct regulatory activity by the release of eventual unknown substances, the coccygeal gland could influence hematopoiesis at least in part through the modulation of the sympathetic nervous system, which has been proven to play a fundamental regulatory role on the hematopoietic system [25], since the catecholaminergic content of bone marrow has appeared to decrease after the surgical removal of LCG. Moreover, this study would suggest that, within hematopoietic processes, lymphocyte differentiation might be particularly regulated by LCG. In fact, the surgical excision of the coccygeal gland appears to induce lymphocytopenia, suggesting a possible stimulatory role of the coccygeal body on lymphocyte differentiation and proliferation, or, alternatively, on the migration of lymphocytes into interstitial space. Therefore, coccygeal gland exeresis-induced lymphocytopenia seems to indicate that the coccygeal gland may be involved in the neuroimmunomodulation (NIM), namely by promoting the differentiation of lymphocytes, which are the main cells responsible for the generation of an effective modulation of immunity and hematopoiesis.

In addition, results show that the modulatory effect of LCG on the hematopoiesis and on the immune system may change in relation to the different conditions of life, and in particular, it seems to be different in basal and stressed conditions. In fact, surgical removal of LCG may allow a multiple hematologic modulation in response to acute stress, involving a decrease of lymphoids and megakaryocytes and an increase of granulocyte cells, whereas in basal conditions only lymphocytes are negatively influenced by exeresis. In particular, the most relevant influence of LCG is observed on platelet generation where surgical ablation of LCG correlates with a platelet increase in basal conditions while thrombocytopenia occurs after restraint stress.

From an anatomotopographic point of view, LCG represents the inferior termination of the sympathetic nervous system, while the pineal gland would constitute the superior one, since it is directly innervated by the postganglionar fibers arising from the superior cervical ganglion [30, 31]. The pineal gland has also been proven to stimulate lymphocyte differentiation and activation [32, 33], whereas other hematologic cells, including red cells and neutrophils, are less influenced by the pineal gland.

The rationale and results of the present investigation suggest a functional connection between the pineal complex and the coccygeal body in regulating lymphocyte production. The bilateral collaboration between these two entities might be hypothesized to be, at least in part, regulated through a modulation of the activity of the peripheral nervous system. On the other hand, the functional influence of LCG on other hematologic parameters such as platelet production seems to be different if compared with the role played by the pineal complex on lymphocyte production.

In fact, the surgical exeresis of LCG increases platelet number in basal conditions, as shown by this study, by suggesting an inhibitory role of LCG on platelet differentiation and generation, whereas the pineal complex has appeared to play an important thrombopoietic activity by determining an increase in platelet numbers through a stimulation of megakaryocyte differentiations [34]. In any case, despite their opposite effects at least in basal conditions, this evidence might suggest a functional link between the pineal-coccygeal glands complexs involved in the reg-

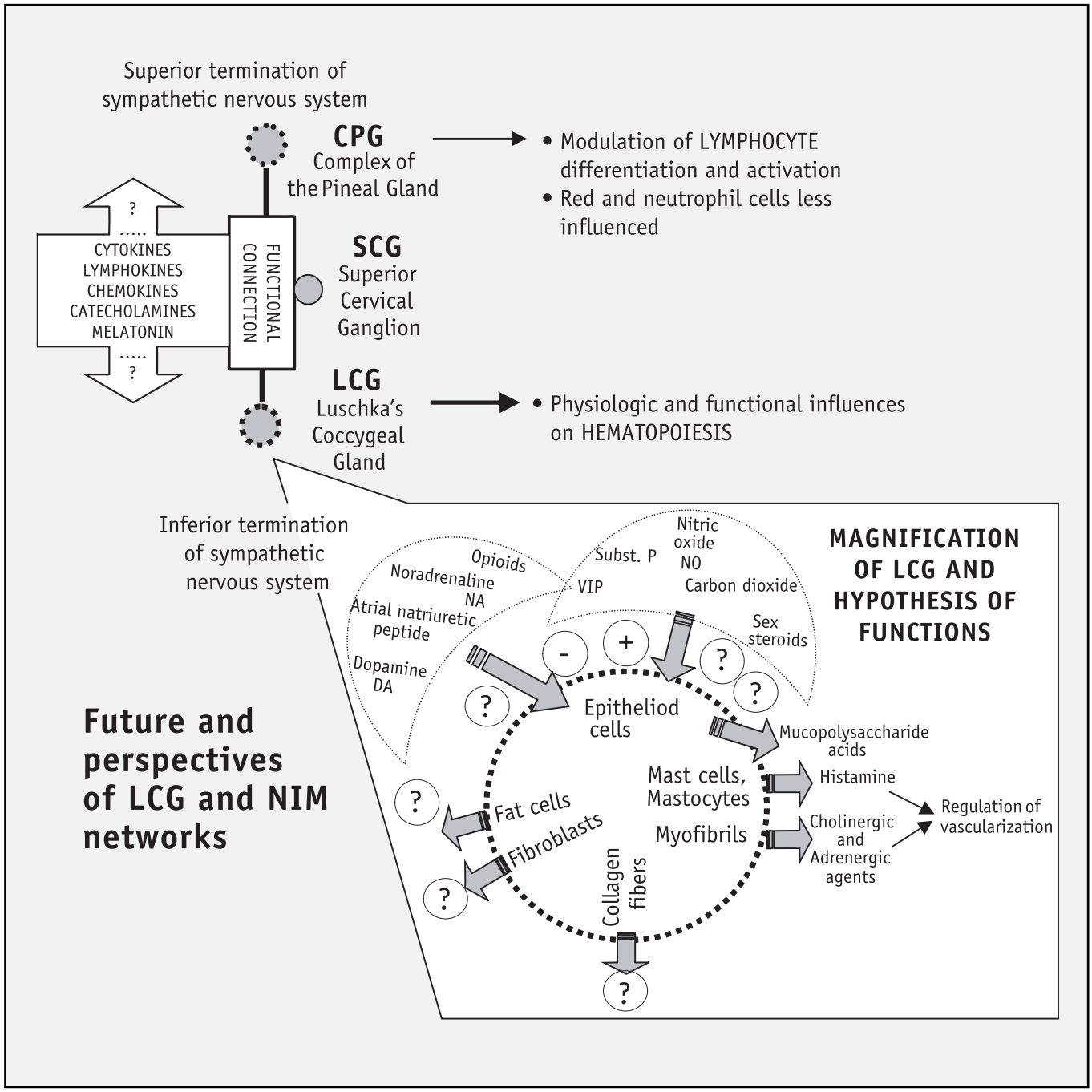


Fig. 6. The interactions between the LCG, CPG, SCG, the endocrine, the immune and hematopoietic systems.

ulation of platelet metabolism and physiology.

Therefore, on these bases, the pineal and coccygeal bodies would not only be anatomically connected and be defined as the superior and inferior termination of the sympathetic system, respectively, but also functionally linked in the regulatory control of hematopoiesis and immunity. Obviously, further studies are needed to establish whether LCG may influence the hematopoiesis by inducing changes in cytokines, chemokines and/or lymphokines blood and bone marrow concentrations. In particular, the surgical removal of LCG, as previously reported for the pinealectomy [35], might determine lymphocytopenia by suppressing the secretion of the major growth factor for lymphocytes, IL-2, whereas the increase in neutrophil number might suggest the stimulation of the production of inflammatory cytokines, such as GM-CSF, IL-8 and IL-6 [36].

The neurochemical regulation of LCG is still obscure, and in particular it will be important to establish whether it may be similar to that of other more defined glomic vascular structures, such as the carotid body [37–42], which eipthelial cells type I have been proven to be stimulated by VIP, P Substance, sexual steroids and nitric oxide (NO), whereas their activity is inhibited by dopamine (D2-

receptor), opioids (β-receptors), alpha-1 adrenergic agents (i.e. Noradrenaline) and atrial natriuretic peptide. In addition, acetylcholine may either stimulate or inhibit the activation of the carotid body, depending on its action on the nicotinic or muscarinic receptor, respectively.

As far as the anatomic definition of the coccygeal body is concerned, our previous histological studies of the human coccygeal gland documented a simultaneous presence of nervous fibers, vessels and neuroendocrine cells. These unpublished data, which have been at least in part confirmed by otherwise controversial studies [8, 16], in analogy with other forms of *glomi*, suggest that LCG may be considered as a chemoreceptor gland, rather than simply arterio-venous anastomosis, as proposed by other authors [8, 43]. Concerning the histology of human LCG there is only limited data on the microscopic structure, and frequently data are rather conflicting especially when comparing glomus tumors, which should not be confused with the normal non pathologic counterpart [44–49] and normal coccygeal bodies [16–17]. Recently an interesting paper has been published describing in detail the light microscopic and ultrastructural examination of the human coccygeal body [17]. Fig. 7 shows a section through a human coccygeal body: more generally the light microscopic examination shows structures embedded in fat tissue, fibroblasts, glomus cells, mast cells, fat cells and collagen fibers which are observed in interstices between the blood vessels. The main characteristic of this glomus remains the presence of small arteries with a highy torturous course. As previously described the arterial end of the coccygeal body is also easily determined, as composed of a single arteriole. The venous end vessels seem to be more difficult to follow [7, 8, 17].

Ultrastructural examination has shown that the epitheliod glomus cells have myofibrils and appear to be modified smooth-muscle cells that may control blood flow between the arterial and venous side of the anastomosis [46] via adrenergic and cholinergic modulation [12, 23].

If the chemoreceptor structure of LCG will be confirmed by further studies, the *Glomus coccygeum* might be considered as a neuroimmunomodulatory organ capable of directly influencing the nervous system via chemical messages arising from the blood. It is known that oxygen and carbon dioxide concentrations represent the main stimulus for the carotid body [50–53], whereas at present it is still obscure which may be the blood chemical message and physio-

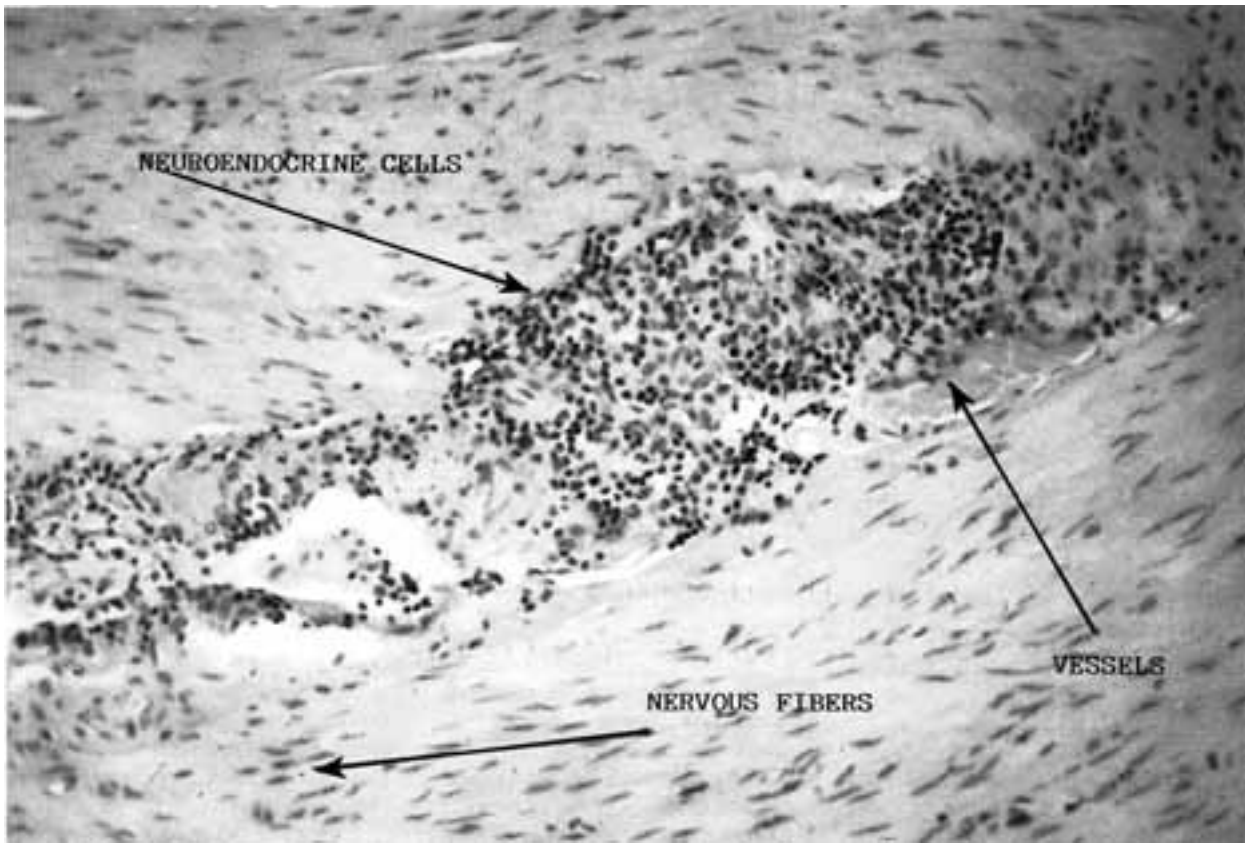
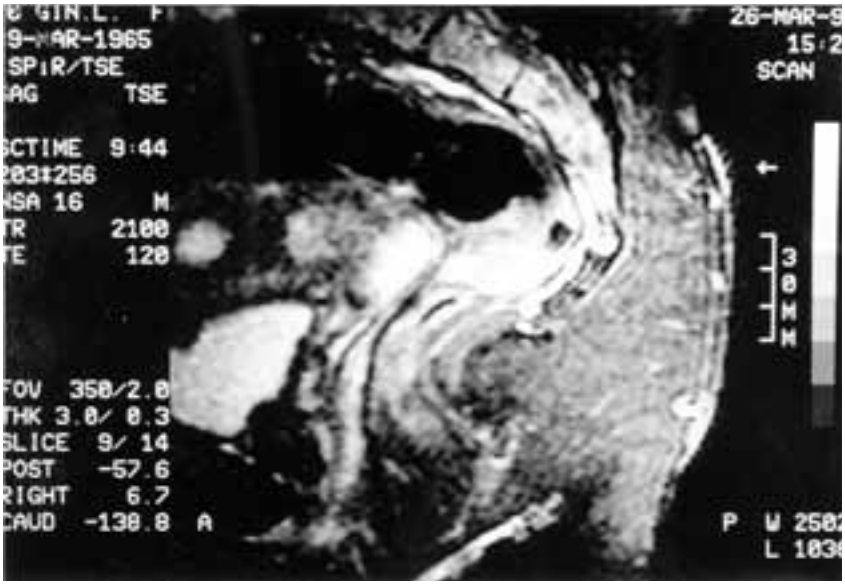


Fig. 7. Histology of human LCG.

logic road capable of activating or inhibiting the function of the coccygeal body. In particular, at present, it is unknown whether there are some comparisons between neuroimmuno- and chemical physiologic mechansims of the carotid and coccygeal bodies. The only anatomic evidence is that LCG may realize a direct connection between arterial and venous systems, being located at the end of the median sacral artery and the beginning of the medial sacral vein, which may be considered as the origin of the aorta and the inferior cava vein, respectively. This location of the LCG might deserve an important biochemical regulatory role, which, however, has still to be defined.

Finally, from a clinical point of view, as demonstrated by our previous studies (unpublished data), the coccygeal body may be easily recognized by the nuclear magnetic resonance (NMR), as illustrated in Fig. 8 A and confirm previous important anatomical studies [7]. Moreover, it has been demonstrated (see Fig. 8 B) that in patients surgically treated for pericoccygeal recurrence due to abdominal tumor, with a following accidental ablation of LCG, no coccygeal



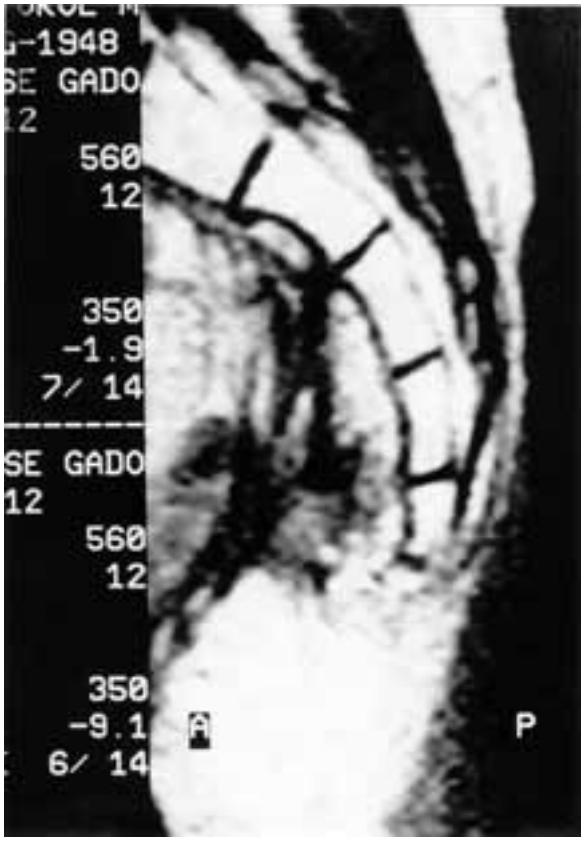


Fig. 8. Nuclear Magnetic Resonance (NMR) of normal subject (A) where LCG is easily recognized and after pericoccygeal recurrence due to abdominal tumor (B) where, following accidental ablation of LCG, no coccygeal gland may be observed.

gland may be observed at the NMR.

Dysfunctions of LCG could be involved in the coccygodynia, as previously suggested by other authors [43–49], as well as in erectile disorders, as proposed by ourselves [54] on the basis of the fact that the abdominal amputation for rectum carcinoma, which may induce surgical damage of the coccygeal body, is more frequently followed by impotence with respect to the anterior resection, which does not determine coccygeal damage even though the major importance of the innervation cannot be forgotten.

If further studies will confirm the possible involvement of the coccygeal body in the regulation of sexuality, the clinical investigation of the LCG function constitutes an important key to explain the immunosuppressive status related to the sexual repression, previously suggested and shown by Wilhelm Reitch [29].

In conclusion, a great amount of evidence would suggest that the coccygeal body may deserve promising advances in the knowledge of the link between the nervous system, hematopoiesis and immunity. This study, by showing the influence of LCG on circulating hematologic cells, would justify further experimental studies and clinical research in an attempt to better define the role of the coccygeal gland in the pathophysiology of humans, namely in the NIM in relation to one's sexual life.

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