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Bioscience Research

Print ISSN: 1811-9506 Online ISSN: 2218-3973 Journal by Innovative Scientific Information & Services Network



RESEARCH ARTICLE BIOSC

BIOSCIENCE RESEARCH, 2019 16(4): 3747-3762.

OPEN ACCESS

Mammary gland surgical affections in correlation to other surgical skin affections among cats in Egypt.

Nasser A. Senna¹, Haithem A. Farghali¹ Marwa S. Khattab² and Reda K.I. Shalaby³

¹Department of Surgery, Anesthesiology and Radiology, Faculty of Veterinary Medicine,

Cairo University, Giza, Egypt

² Department of Pathology, Faculty of Veterinary Medicine, Cairo University, Egypt

³Tanta Pet Animals Clinic, Tanta, Egypt

*Correspondence: amr_amz_9@yahoo.com Received: 17-09-2019, Revised: 13-11-2019, Accepted: 29-11-2019 e-Published: 26-12-2019

The present study was conducted to ascertain mammary gland surgical affections in correlation to other surgical skin affections in cats. during 3-years period from October 2016 to March 2019. In addition, study the effect of age, sex and breed on the distribution of feline skin surgical affections. A total of 11334 cats (included 6434 queens and 4900 tom cats) which belonging to different ages and breeds were included in this study. Feline skin surgical affections were registered for age, sex, breed, and the main complaint from their owners. A complete history and detailed clinical examination of each case were applied to aids of radiographic, ultrasonography, laboratory database preoperative surgery, microbiology examination, and histopathological examinations according to examination sheet. A total number of 392 of cats suffered from skin surgical affections. Mammary neoplasm was the prevalent skin affections in relation to total skin surgical affection followed by skin wound. Highest incidence of bite wound among skin wound affection followed by accidental wound. Finally, mastectomy was most widely used treatment for mammary tumors in the cat. In conclusion, mammary neoplasm was the highest recorded problems among surgical skin affections in cats. The present data enable veterinarians in Egypt to ascertain their needs for diagnostic tools and surgical interference that must be present at any pet clinics.

Keywords: Feline, mammary neoplasm, skin wound, Egypt.

INTRODUCTION

The skin is the largest and most easily observed organ in the body and therefore it is not surprising that the skin is a common site for tumor. Feline mammary tumors are the most common tumors. When mammary neoplasia occurs, it is more often malignant; they account for about 17% of neoplasia in queen and 1-5% all tumors in male cats (Lana et al., 2007; Jacobs et al., 2010). Histologically, most malignant MT are adenocarcinomas, being the tubular and papillary types more common than the solid or mucoid types (Shafiee et al., 2013). Feline mammary carcinoma are highly infiltrative tumors, frequently associated with lymph node metastases at the time of the initial diagnosis and have a mean survival rate from the time of diagnosis that ranges between 6 to 12 months (Sorenmo et al., 2013).

Fibroadenomatous hyperplasia (fibroepithelial hypertrophy, feline mammary hypertrophy) is the most common histopathologic lesions in cats. It is a consequence of an exaggerated proliferative response of mammary glandular tissue to several situations, namely pregnant or pseudo-pregnant queens, cats receiving prolonged megestrol acetate or medroxyprogesterone acetate therapy, cats receiving progestational compound when endogenous levels of oestrogen are increased (Gimenez et al., 2010).

The cause of mammary tumors (MTs) remains poorly understood, however some factors have been pointed as risk factors for namely age, breed, reproductive status and exposure to oestrogen and progesterone (Sorenmo et al., 2013). In fact, MTs are more frequent in middle-aged to older cats, with the mean age of diagnosis between 10-12 years. The risk increases with age, presenting a peak between 7 to 9 years and continuing to increase until 12 to 14 years (Morris, 2013).

The Domestic Short-hair cat is the breed more frequently affected. Nevertheless, when MTs are diagnosed at younger age, Siamese cats and other Oriental breeds are the most affected (von Euler, 2011). Since genetic predisposition for a disease is often associated with a younger age of diagnosis, and young Siamese cats have an increased risk for many types of tumors, it is possible that Siamese cats present breedassociated germ line alterations that confer increase risk for many different malignancies. Oestrogen and progesterone play an important role in mammary tumorigenesis, and exposure to these hormones at an early age seems to be crucial for MTs development (Overley et al., 2005).

Queens spayed before one year of age have a decreased risk of developing MTs and that sexually intact queens have a sevenfold higher risk of feline mammary carcinoma than spayed cats (Morris, 2013). Ovariohysterectomy (OHE) may be protective against MTs development; nevertheless, the protective effect of OHE diminishes quickly over the first years and no benefit after 24 months (Overley et al., 2005). According to, (Overley et al. 2005) cats spayed after 2 years of age had a statistically significant increased risk to develop MTs compared with intact cats, and also that a gradual loss of protection occurred with increasing hormone exposure prior to OHE.

Endogenous ovarian hormonal influence, the long-term exposure to exogenous progestins or to estrogen-progestin to prevent pregnancy or control of aggressive behavior, increases the risk of both benign and malignant MTs development, while intermittent or occasional progestin administration has no effect (Sorenmo et al., 2013). These effects were associated to the fact that a prolonged steroid exposure induces proliferation of mammary epithelial cells and facilitates the accumulation of genetic errors, contributing to the development of MTs (Misdorp et al. 1991).

As already mentioned, MTs are rare in males, but in a report of 22 cases, 8 (36%) had a history of progestin administration (Skorupski et al. 2005). In other study, performed by (Jacobs et al. 2010) with repeatedly iniections cats of medroxyprogesterone acetate for inter-cat aggression and urinary house soiling, also demonstrated development of mammary adenocarcinoma.

Obesity and an unbalanced diet have been linked to increased risk of tumors of the mammary gland (Nunes et al., 2011). Other breeding-related factors such as age at first pregnancy, number of pregnancies, pseudopregnancy and changes in the estrous cycle were suggested as risk factors, but there is no consensus regarding their contribution for the development of MTs (Overley et al. 2005).

Skin wounds are common in cats. Abscesses are common after a cat fight. Cats are territorial animals, and will fight with other cats to defend their territory. If your cat is bitten during a fight, bacteria from the other cat's teeth infect the wound and cause an abscess. Bites are most common around the face and shoulders or around the rump and tail (Laurie-Chalmers, 2019).

Skin tumors is very common in cats, the skin being the second most reported site of malignancy after lymphoid tissue. Unlike dogs, skin tumors in the cat are more likely to be malignant than benign. The most common feline tumors reported in several studies in the UK and USA are fibrosarcomas, squamous cell carcinomas, and basal cell and mast cell tumors (Murphy, 2006).

Mammary hypertrophy (mammary hyperplasia) is a benign disease consisting of a proliferation of one or more mammary glands of young or adult queen, which was first reported in 1973. A common risk factor is administration of progestogens, especially in high doses (Hayden et al., 1989).

According to the previous facts, this study was carried to determine the prevalence mammary gland surgical affections in cats in correlation to skin surgical affections that were brought to veterinary hospital, Cairo University, Egypt and Tanta pet clinics.

MATERIALS AND METHODS

Ethical Approval

All procedures of the current study were approved by and in accordance with the rules of animal use and care ethical committee of Faculty of Veterinary Medicine, Cairo University, Egypt.

Study area

The queens and tom cats used for this study were those admitted to the teaching veterinary hospital, Faculty of Veterinary Medicine, Cairo University, Giza, Egypt and different pet clinics in Cairo and Tanta provinces, Egypt during three years study period from October 2016 until March 2019.

Animals in the study

A total of 11334 cats (included 6434 queens and 4900 tom cats) which belonging to different

ages and breeds were included in this study. This number included 3218 soft tissues surgical affected cats (included 1831 queens and 1387 tom cats), 7444 apparently healthy cats (included 4035 queens and 3409 tom cats) which admitted either for vaccination or for general health checkup, and 672 with orthopedic problems (included 163 queens and 509 tom cats).

Clinical investigation

All the cases were firstly recorded in the registration book for date, age, sex, breed, and complaint of their owners. Full clinical examination of each cats was carried out including complete medical, vaccination, dietary, and environmental history according to previously designed examination sheet (Fig., 1).



Visual inspection was done, and pulse, respiration rates, and rectal temperature were carefully taken. Also, examination of different organs and body systems was performed (Rijnberk and Stokhof, 2009)

Other diagnostic approaches:

Radiological examination was applied according to (Parry and Lamb, 2010) using X-machine (Fischer imaging, with X- ray tube EMERALD-125, A-045211, Chicago, U.S.A.) and (EPSILON) 50-M, made in India.

Ultrasonography was applied according to (Kealy and McAllister, 2000) using ultrasonographic devices (TOSHIBA, 2004, made in JAPAN, CHISON, 2016, made in China and MANDRY, 2010, CHINA).

Surgical techniques:

All surgeries were performed under injectable general anesthesia. The cats were generally anaesthetized by (Atropine Sulphate, 0.05mg/kg) I/M or S/C and (Xylazine HCl, 2mg/kg) I/M as premedication. Then induction by (Ketamine HCl, 25 - 30 mg/kg) I/M and maintenance by Ketamine HCl were applied (Kaiser-Klinger, 2007). Another regime of injectable anesthesia for cats was by Atropine sulphate and Xylazine HCl as premedication. Then induction by (Propofol, Lipuro 1%) 1mg/kg I/V and maintenance by it (Vanlersberghe and Camu, 2008).

Histopathological examination

Tissue samples were collected from excised tumor masses in the mammary gland of cats and were fixed in 10% neutral formalin buffer. Fixed tissue was then processed by paraffin embedding technique and sectioned using microtome (Leica 2135, Germany) into 4-micron thick sections. Tissue sections were stained by hematoxylin and eosin stain, examined using light microscope (Olympus XC30, Tokyo, Japan) and photographed by digital camera (Olympus, Tokyo, Japan).

Statistical analysis

Data that were collected about age, sex, breed, and season were collected and to Microsoft Excel 2010^{R} spreadsheet, stored separately and exported to analytical software using Chi-square test. Values of < 0.05 were considered as statistically significant

RESULTS

| | Sexes | | total | Ages | | | Breeds | | |
|------------------------|----------|--------|-------|---------|----------|---------------------|-------------|---------|---------|
| Affections | Tom cats | gueens | Total | (sw9-0) | (6-24ms) | Ages Over 2years | Mixed breed | Siamese | Persian |
| Mammary neoplasm | - | 187 | 187 | - | - | 187 | 131 | 7 | 49 |
| skin wound | 23 | 70 | 93 | 31 | 62 | - | 47 | 9 | 37 |
| Subcutaneous abscesses | 16 | 37 | 53 | 29 | 21 | 3 | 29 | 3 | 21 |
| Mastitis | - | 27 | 27 | - | 27 | - | 23 | - | 4 |
| Mammary abscesses | - | 14 | 14 | - | 11 | 3 | 8 | - | 6 |
| Skin tumors | 9 | 2 | 11 | - | - | 11 | 7 | 4 | - |
| Mammary hypertrophy | - | 7 | 7 | - | - | - | 1 | - | 6 |
| Total | 48 | 344 | 392 | 60 | 128 | 204 | 245 | 23 | 124 |

| Table 1: Number | , sex, ages and b | reed of different | surgical affections | of skin in cats |
|-----------------|-------------------|-------------------|---------------------|-----------------|
|-----------------|-------------------|-------------------|---------------------|-----------------|

Table 2 : The incidences of different surgical skin affections in cats

| | | 5 | | | |
|------------------------|-----|---|---|--|--|
| Affections | No. | % out of total skin affections in cats | % out of total soft tissue surgery in cats | | |
| Mammary neoplasm | 187 | 47.7% | 5.9% | | |
| skin wound | 93 | 23.8% | 2.9% | | |
| Subcutaneous abscesses | 53 | 13.6% | 1.6% | | |
| Mammary mastitis | 27 | 6.8% | 0.8% | | |
| Mammary abscesses | 14 | 3.5% | 0.43% | | |
| Skin tumors | 11 | 2.8% | 0.34% | | |
| Mammary hypertrophy | 7 | 1.7% | 0.2% | | |
| Total | 392 | 100% | 12.2% | | |

| Type of wound | No. | % out of total skin wound affections in cats | |
|------------------|-----|---|--|
| Bite wound | 47 | 50.5% | |
| Accidental wound | 37 | 39.8% | |
| Burn wound | 5 | 5.4% | |
| lacerated wound | 4 | 4.3% | |
| Total | 93 | 100% | |

Table 3: Incidence of different skin wound affections in cats

Table 4: The incidences of different surgical skin interventions in cats

| | Operations | Operated cases | | | | |
|--------|-------------------|----------------|--|--|--|--|
| System | | No. | % out of systemic surgical operated cases | % out of total feline surgical operated cases | | |
| | Abscess treatment | 19 | 38.7% | 0.7% | | |
| Skin | Mastectomy | 17 | 34.7% | 0.6% | | |
| | Bandage | 9 | 18.3% | 0.3% | | |
| | Skin suturing | 3 | 6.1% | 0.11% | | |
| | Skin flap | 1 | 2.04% | 0.03% | | |
| total | | 49 | 100% | 2.04% | | |



Figure 1: A case of 13 years old mixed breed queen suffered from mammary gland tumor of the left cranial thoracic mammary gland and the axillary lymph node was involved, A) before and B) after mastectomy. (C)- B-mode ultrasound sagittal scan of 15-years old mixed breed queen suffered from mammary neoplasm. Notice mixed echo pattern of mammary tissue (anechoic and hyperechoic within the hypoechoic mammary parenchyma. (D) B) lateral views of abdominal radiograph showed mammary enlargement without evidence of chest metastasis.





Figure 2: A case of 11 years old Persian queen suffered from mammary gland tumor of the right cranial and caudal abdominal mammary gland, A) lateral view of chest radiograph of the case revealed evidence of pulmonary metastasis, B) before, C) during and D) after mastectomy.



Figure 3: A case of 9 years old Persian queen suffered from mammary gland tumor of the left caudal abdominal and inguinal mammary gland, A) during radical mastectomy of the affected glands, B) tumor mass after mastectomy, C) and D) the case after mastectomy.



C

D

Figure 4: A) A case of 12 years old mixed breed cat suffered from old wounds at the ventral aspect of the chine associated with maxillary fracture due to accident. B) A case of 2 years old mixed breed tomcat suffered from lacerated wounds at the neck due to cat fighting. C) A cases of 9 months old Persian tom cat suffered from lacerated wounds at the inner aspect of the thigh. D) A case of 10 years old Persian queen suffered from mammary gland tumor of the right inguinal mammary gland.



С

D

Figure 5: A case of 10 years old mixed breed cat suffered tumor at the right tarsal region, A) cranio-caudal view of right hind limb revealed soft tissue swelling which did not involve the bony structures. B) Clinical presentation of the tumor at the caudal aspect of the right tarsal region, C) the tumor and D) the limb after surgical excision.



Figure 6: A) and B) A case of 3 years old mixed breed cat suffered from lacerated wound at the level of neck region before and two weeks post treatment. D) and C) A case of 2 years old Persian tom cat suffered from old septic wound at the ventral aspect of the tail before and three weeks post treatment. E) and F) two cases affected with abscess at the anal gland and at the side of the chest region



Figure 7: A) A case of 3 years old Persian queen suffered from mammary gland hypertrophy, B) lateral and C) ventro-dorsal views of abdominal radiograph showed mammary enlargement and filled with fluid.



Figure 8: (A) Mammary gland of queen showing tubular carcinoma (T) with necrosis (N) and inflammatory cells infiltration (H and E stain X 200).

- (B): Mammary gland of queen showing fibroadenoma (F) (H and E stain X 200).
- (C): Mammary gland of queen showing fibroadenoma (F) (H and E stain X 100).
- (D): Mammary gland of queen showing solid carcinoma (H and E stain X 100).



Figure 9: (A) Mammary gland of queen showing tubulopapillary carcinoma (H and E stain X 100). (B): Mammary gland of queen showing tubulopapillary carcinoma (T) with necrosis (N) and inflammatory cells infiltration (H and E stain X 40).

(C): Mammary gland of queen showing papillary carcinoma (H and E stain X 100).

(D): Mammary gland of queen showing tubulopapillary carcinoma (H and E stain X 100).

(E): Mammary gland of queen showing invasive tubular carcinoma (T) with hemorrhage (H) (H and E stain X 100).

Fig (9F): Mammary gland showing fibroadenoma with hyperplastic proliferation ductal lining epithelium (arrows) (H&E×200).



Figure 10: (A&B): Bundles of fibroblastic cells proliferation running in different directions with few collagens and surrounded by connective tissue capsule. No signs of malignancy.

Mammary gland tumors observed in the queen was tubular carcinoma (two cases) in which there were tubular formations with slit like lumen. The cells showed atypia, hyperchromasia and mitosis. Areas of necrosis, hemorrhages and inflammatory cells infiltration were seen in the tumor (Fig. 8a, 9e).

Two cases of fibroadenoma were observed in which there were tubules lined by single layered epithelium surrounded by stromal elements (Fig. 8b, 8c and 9 F). One case of solid carcinoma was recorded in which the epithelial cells were arranged in a solid pattern with minimal stroma and exhibited criteria of malignancy (Fig.8d).

Tubulopapillary carcinoma was recorded in two cases in which there were tubular formation with papillary projections (Fig.9a, 9b, and 9d). Massive area of liquefactive necrosis and neutrophils infiltration was observed in first case figure 8d. There was one case of papillary carcinoma in which pedunculated epithelium with a core of delicate fibrovascular stroma is found (9c).

Mammary neoplasms are described as the third most common type of feline tumor, after haematopoietic and skin tumors, and present a challenge for clinicians because the prognosis for feline mammary tumors ranges from guarded to poor (Cassali et al. 2018). However, in a survey conducted in Brazil, mammary neoplasms represented the second most common type of tumor in the species (Togni et al., 2013).

Mammary tumors are among the most common neoplasms in both cats and dogs, but the prevalence of malignant histological types is far higher in cats (ratio of malignant: benign is at least 4:1). Mammary tumors usually affect older female cats, mainly entire females. Siamese and Oriental breeds may be predisposed. Male cats can develop mammary neoplasia, but this is rare. (Morris, 2013).

Mammary tumors present as a single subcutaneous nodule or mass within the mammary glands, which may be discrete and mobile, or attached to underlying tissues and possibly ulcerated in appearance (Fig1-3).

In the present study, the most affected cat with mammary neoplasm over age 2 years. In addition, (Loretti et al. 2010) reported that the majority of the affected cats are young queens of reproductive age, queens during their first oestrous cycle, queens during pregnancy or pseudopregnancy, or males or females after treatment with progesterone.

Highest incidence of mammary tumor was observed between 10 and 11 years of age (Misdorp, 2002) and in intact females (Lana et al. 2007). Intact cats have a seven-fold higher risk of developing mammary tumors when compared to spayed cats (Waldrow, 2001).

The mammary tumors represent 17% of tumors affecting female cats, being less frequent in males (1 to 5%) (Simeonov and Simeonova, 2009; Morris, 2013) and at least 85% to 95% of feline mammary tumors are malignant (Misdorp et al., 1991).

In one study, entire cats were seven times more likely to develop a mammary tumor than cats neutered at six months (Rutteman and Kirpensteijn, 2003). This mean that Hormonal status is thought to influence disease development. These results supported by a case control study reporting that cats spayed before 1 year of age had a decreased risk of developing mammary cancer (Overley et al., 2005). Exogenous progesterone administration to prevent pregnancy, or for behavioural aggression, causes tumor development (benign and malignant) in both male (Jacobs et al., 2010) and female cats (Keskin et al. 2009).

In the present study, mammary neoplasm was frequent in mixed breed this results agree with (Cunha et al. 2016) who reported that mammary carcinoma were frequent in mixed breed. Mammary neoplasm was frequent in Persian cats than Siamese cats. In contrary to, (Sorenmo et al., 2013) who found that, Siamese cats to be more predisposed to mammary tumors than other breeds but in Brazil, a breed predisposition was not observed (Cunha et al., 2016).

Tumors of the mammary gland of felines are histologically divided according to the diagnostic criteria proposed by the World Health Organization (WHO) into four main groups: mammary hyperplasia/dysplasia; benign tumors, malignant tumors, and unclassified tumors (Zappulli et al. 2005).

Approximately 80% of feline mammary masses are neoplastic. The remaining 20% are benign and are predominantly mammary fibroadenomatous hyperplasia (MFH) (Little, 2011). MFH can affect all or most of the mammary glands, without involving the adjacent lymph nodes, and is not usually accompanied by milk secretion (Marti and Fernandez, 2013). The hyperplasia can be severe, leading to tissue necrosis, ulceration and infection (Little, 2013).

Fibroadenoma relatively common benign neoplasia in cats. It is characterized by a proliferation of epithelial cells in a tubular array enveloped abundantly by fibroblast stromal elements Fig (8). These findings supported by (Morris, 2013) reported that benign tumors are uncommon in cats but, of these, fibroadenoma is most frequently reported, with simple adenoma or duct papilloma rarely seen.

In cats, carcinomas may be tubulopapillary Fig (8), solid, cribriform or mucinous, although carcinoma squamous cell and mixed carcinosarcoma are also reported (Misdorp et al. 1999). Inflammatory mammary carcinoma, which has a particularly poor prognosis owing to an additional inflammatory component blocking the lymphatics and affecting lymph drainage and causing swollen, painful glands, has been reported in three cats with underlying highly malignant, papillary mammary carcinomas(Perez-Alenza et al. 2004).

Mammary ultrasonography may also be helpful on the diagnosis of feline mammary

fibroepithelial hyperplasia. Furthermore, it is a rapid and easily performed method for assessment of the mammary gland structure (Payan-Carreira, 2013).

Feline mammary hypertrophy the lowest incidence among surgical skin affections at incidence 1.7%. Feline mammary hypertrophy can treated by surgery (ovariectomy be or ovariohysterectomy), mastectomy or both, and by immediate withdrawal of synthetic progestin therapy. However, performing surgery when the condition is full-blown may lead to potentially fatal complications (Carpenter et al. 1987). In general, mammary swelling regresses completely within 3-4 weeks following spaying (Wehrend et al. 2001). Recently, it was shown that the condition is responsive to targeted endocrine therapy with progesterone antagonists i.e. progesterone receptor blockers such as aglepristone (Meisl et al. 2003).

Wounds typically develop signs of infection within 12 to 24 hours. Owners may notice the cat is lethargic, not eating well, and painful when handled. Swelling from tissue infection (cellulitis) in one or more locations is often present. A fully developed abscess may be seen in 3 to 5 days. As further painful swelling develops, the hair over the swelling falls out, the skin discolors, and eventually the skin ruptures and drains. The discharge (pus) is usually yellowish, blood-tinged, and foul-smelling. This discharge is made up of red blood cells and degenerating white blood cells that contain engulfed bacteria (Thayer, 2014).

The most prevalent wound type was bite wound followed by accidental wound in relation to total skin affections especially in tomcat due to cats have outdoor access and interact with other cats during breeding season. Common sites for bite wounds are the legs, base of the tail, face, neck, and along the back as in (Fig 4&6).

Mastectomy considered the second most prevalent operations after abscess treatment in relation to systemic surgical operations, while only one case of skin flap amongst systemic surgical operation was reported.

The mainstay of treatment for mammary tumors is still surgical resection. The extent of surgery is influenced by the lymphatic drainage in the feline mammary gland, as tumor cells spread readily beyond the primary site and complete excision should encompass all known drainage pathways (Morris, 2013).

Surgery is the most widely used treatment for mammary tumors in the cat; it is used alone or in combination with chemotherapy. Radical mastectomy is the surgical method of choice because it significantly reduces the chance of local tumor recurrence. The inguinal lymph node is virtually always removed with the mammary gland, while the axillary lymph nodes are removed only if enlarged and cytological positive for neoplastic cells (Antunes, 2014). Santana et al. (2014) reported a case of a cat with a highly malignant MT treated with radical mastectomy.

CONCLUSION

It is concluded that, the most prevalent surgical skin affections were mammary neoplasm followed by skin wound and subcutaneous abscesses. Mammary tumors more common affecting female cats, being less frequent in males. Several risk factors affecting mammary tumors namely age, breed and hormonal status. Bite wound was the highest incidence among skin wound affections followed by accidental wound.

CONFLICT OF INTEREST

The authors declared that present study was performed in absence of any conflict of interest.

ACKNOWLEGEMENT

All grateful thanks for the stuff members of department of Surgery, Anesthesiology and Radiology, Faculty of Veterinary Medicine, Cairo University, Giza, Egypt for their assistance in collection of the scientific data.

AUTHOR CONTRIBUTIONS

Reda Shalaby carried out surgical preparation, the surgical procedures, postoperative care, follow up, clinical and radiological evaluations and wrote the paper, other authors participated in the interpretation of the results and revision of the present paper.

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