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"Petit mal" or "grand mal" epileptiform manifestations in rabbits

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Epileptiform manifestations result from dysfunctions of neuronal activity in the brain. In rabbits, they are rarely primary, but rather secondary to trauma, infectious diseases or parasitosis

In a healthy individual, chemical or electrical signals strictly regulate cerebral activity. When this system is deregulated or

maladjusted, sudden and simultaneous electrical discharges can occur, leading to a neuronal hyperactivity in a specific region of

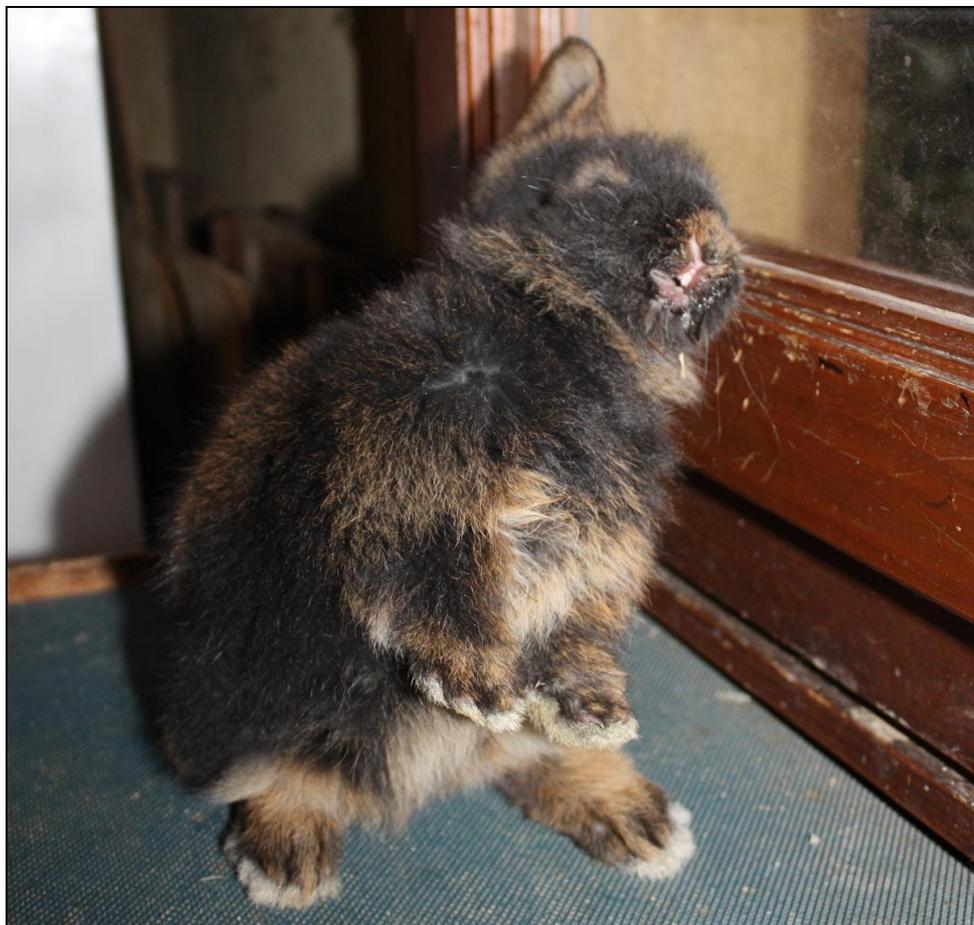


Figure 1: Young Belgian bearded rabbit during an absence epileptiform crisis or "petit mal" with disorders of consciousness, eye movements, swinging of the body and excessive salivation.

the brain, or in the entire brain.

When a region of the brain is affected, the affected individual suffers from local seizures characterized by disorders of consciousness or perception and/or convulsions. When the whole brain is affected, the seizures are said to be generalized. The character of the epileptiform manifestations thus varies greatly according to the type of neurons involved and the region of the brain.

- **Absence seizure or “petit mal” seizure**, which lasts only a few seconds. Disorders of consciousness are accompanied by an empty gaze, salivation and sometimes convulsions. In humans this type mainly affects children (Figures 1, 2 and 3).
- **Atonic seizure** with loss of muscle tone, falling and tilting of the head.
- **Tonic seizure** characterized by the stiffening of spine and limbs muscles (Figure 4).
- **Myotonic seizure** with muscle contractions or sudden and strong involuntary shaking of muscle groups, more rarely of all muscles. A rhythmic, intense, bilateral or unilateral, and synchronous movement of limbs is observed. The severity of myotonic seizures varies from one individual to another.



Figure 2: Continued from Figure 1, young rabbit during an absence epileptiform seizure. The bluish color of the eye is the result of a late opening of the eyelid accompanied by an eye infection. This Belgian Bearded rabbit is about 30 days old and does not suffer from inbreeding and consanguinity problems. Its female mother was a pure breed and its father is 25% Fauve de Bourgogne, French breed from Burgundy.



Figure 3: Pancake, a male mini-lop rabbit has suffered from hydrocephalus and epileptic seizures since its birth. Here during a crisis "petit mal" (top) and immediately after the end of this seizure. Photos taken from videos that can be viewed here: <http://www.medirabbit.com/EN/Neurology/seizure.htm>

- **Tonic-clonic or "grand mal" seizure** with loss of consciousness. The tonic phase is characterized by the stiffening of the body and limbs, and a deformation of the face. The next phase, known as clonic, is characterized by convulsions of

the limbs and hyper-salivation. These tonic-clonic seizures can last up to a few minutes (Figure 5).

- **Status epilepticus seizure** is a succession of seizures, without complete remission between two seizures. *Status epilepticus* is a medical emergency because lack of oxygen in the brain tissue can lead to permanent and irreversible damages. The rabbit may not recover from it, or even die.

The most common seizures observed in rabbits are absences, also known as "petit mal"; more rarely seizures are of the tonic-clonic or "grand mal" type.

Some rabbit breeds have a hereditary predisposition to idiopathic epileptic seizures (Figure 7).

Isolated or chronic

An epileptic manifestation may be an isolated phenomenon appearing suddenly and lasting from a few seconds to a few minutes. It is often a secondary reaction to a drug, hyperthermia linked to fever or heat stroke, a lack of oxygen due to respiratory distress, or an excessive itching caused by skin parasites or severe pain. Some rabbits are sensitive to stroking their fur contrary to the growth direction and start to seizure.

An epileptiform/epileptic seizure may become chronic when it is associated to changes in the brain due to a disease, an injury or a head trauma, a parasitosis or a tumor.

Numerous causes

An epileptiform manifestation is a heterogeneous phenomenon. There are many triggers (Table 1).

Viral causes: Some viruses have a tropism for tissues of the nervous system and cause epileptic seizures once they invade the

central nervous system. These include the virus causing viral hemorrhagic disease (VHD) as well as the *Herpes simplex* virus. They cause epileptic-like seizures in the rabbit, and lead to its death. The rabies virus also can lead to seizures. Rabies must thus be part of the diagnostic differential in areas where this virus is endemic.

Bacterial Causes: some bacteria living in the nasal cavity can migrate to the middle and inner ear via the Eustachian tube, e.g. *Pasteurella multocida* or *Listeria* sp. If the infection is poorly treated, bacteria can migrate along the auditory nerve path and invade the brain, causing meningitis or encephalitis, or cerebral abscesses secondary to otitis of the inner ear.

Parasitic causes: the best known parasite is *Encephalitozoon cuniculi*, which lives in the nervous system of rabbits. Precursor symptoms of the parasitosis are incontinence, weight loss despite a strong appetite and paralysis of the hind limbs. Epileptic attacks appear during the later stages of the disease. More rarely, the rabbit can be infected by *Toxoplasma gondii*, another parasite of the nervous system. Clinical manifestations are similar to those of encephalitozoonosis. The presence of cerebral nematodes is rare in rabbits.

Metabolic causes: few diseases can cause metabolic alterations, e.g. ketosis as a result of liver lipidosis, azotemia or imbalance of blood electrolytes as a result of renal failure, or pregnancy toxemia. Hormonal disorders of the thyroid can cause tonic-clonic attacks.

Respiratory causes: Respiratory distress as a result of pneumonia, empyema.

Cardiovascular causes: arteriosclerosis or spontaneous mineralization of blood vessels of the brain.



Figure 4: Posture of a rabbit during a seemingly tonic-type seizure. This type is characterized by muscle contraction and stiffening in the spine and limbs and eyes wide open.

Traumatic causes: a cranial trauma caused by an accident or a sudden panic can cause irreversible brain damage. A stroke can also lead to an epileptic seizure with paralysis of the limbs, although strokes usually cause the immediate death of rabbits.

Nutritional causes: vitamin A deficiency.

Toxic causes: ingestion of toxic products or lead poisoning is responsible of convulsive seizures.

Environmental causes: high temperature caused by an elevation of the body temperature, e.g. fever or heat stroke.

Non-epileptic causes: seizures may be linked to congenital vascular or structural cerebral malformations, e.g., an encephalocele (Figure 6). Some breeds of rabbits are also susceptible to idiopathic seizures. These include dwarf rabbits and lion-head rabbits, as well as white-furred and blue-eyed rabbits, e.g. the Vienna White rabbit or the Beveren rabbit (Figure 7).

Clinical characteristics

Clinical manifestations of epileptiform seizures vary widely, ranging from very short moments of partial loss of consciousness (absences) to major crises with loss of consciousness, bilateral spasmodic, symmetrical, and uncontrolled movements (tonic-clonic crisis). In most cases, there are no clinical signs that are indicative of the onset of such seizures.

Some manifestations are nonetheless regularly observed during seizures, such as:

- A sudden muscular weakness or brusque rolling on its side before the onset of a "grand mal" crisis.
- Insensitivity to the immediate environment, not responding when touched or called.
- Rotary movement of the body.
- Limbs showing a rowing movement.
- Actions such as licking, swallowing, even biting.



Figure 5: Clonic phase followed by the tonic phase in Flora, a 7.5-year-old Rex rabbit, during a "grand mal" epileptic seizure caused by the parasite *Encephalitozoon cuniculi*.



Figure 6: Detail of the head of a rabbit newborn with an encephalocele.

- Mental confusion and loss of consciousness.
- Loss of muscle tone or spasms.
- Loss of vision.
- Nodding of the head or torticollis.
- Hyper-salivation and saliva around the nostril.

Fainting is rare.

The tonic-clonic seizures are the most difficult and spectacular to observe.

Phase 1, excitement during which the animal is unconscious, falls to the side and begins to roll.

Phase 2, tonic with generalized muscle contraction and nystagmus. The body is rigid and the muscles stiffen. Breathing is hardly visible and respiratory distress is possible. Jaws are tense and involuntary contractions of the jaw muscles can lead to biting the person holding the animal. Pupils are dilated. Cyanosis of the mucous membranes of the oral cavity is possible as blood is centralized in the core of the body in order to protect the internal organs. This

phase is very fast and lasts only a few seconds.

Phase 3, clonic or "relaxation" phase with a decrease in body stiffness, opening of eyes and chewing movements. Limbs have rapid spastic movements. Breathing becomes visible again. Pupils contract and dilate. Excessive salivation or urinary or fecal incontinence is possible at this stage.

Recovery Phase 4, the rabbit stands up and appears groggy. After several minutes, the rabbit is normal.

After a crisis, the rabbit regains consciousness and relaxes. It may appear tired, confused, or resume the course of its activities as if nothing has happened.

Anamneses and diagnostic tests

When a rabbit is examined clinically, it usually has suffered several epileptiform seizures from which it recovered more or less well. Indeed, epileptiform/epileptic seizures usually occur at the living place of the rabbit and only rarely during a consultation at the veterinary clinic. Collaboration of the owner and medical history of the rabbit are therefore very important. The owner should observe his/her rabbit and note as much details as possible about each seizure, take photos or videos of his/her suffering rabbit and show them to the veterinarian during the consultation. These details include:

- Circumstances of the appearance of seizures;
- Movements observed on a part of the body, on the whole body;
- Absence or loss of consciousness;
- Drug treatment given to the rabbit, even if there seem to be no connection with

the seizures;

- Ingestion of toxic substances.

Depending on the disorders of consciousness and the phases observed, the veterinarian will be able to determine the form of epilepsy.

Diagnostic tests include a physical and neurological examination of the rabbit, an analysis of cerebrospinal fluid and/or urine. A complete blood test will enable to rule out an imbalance of electrolytes in the blood or deficiencies in vitamins and/or minerals.

The electrical recording of cerebral activity (electroencephalogram) allows to measure the variations of the electrical activity of the brain. It may help conclude if there is a predisposition to epileptiform or epileptic seizures.

Diagnostic imaging techniques include X-rays, CT scan or MRI. They help visualize the different cerebral structures and locate possible brain damage, mineralized regions or a hydrocephalus.

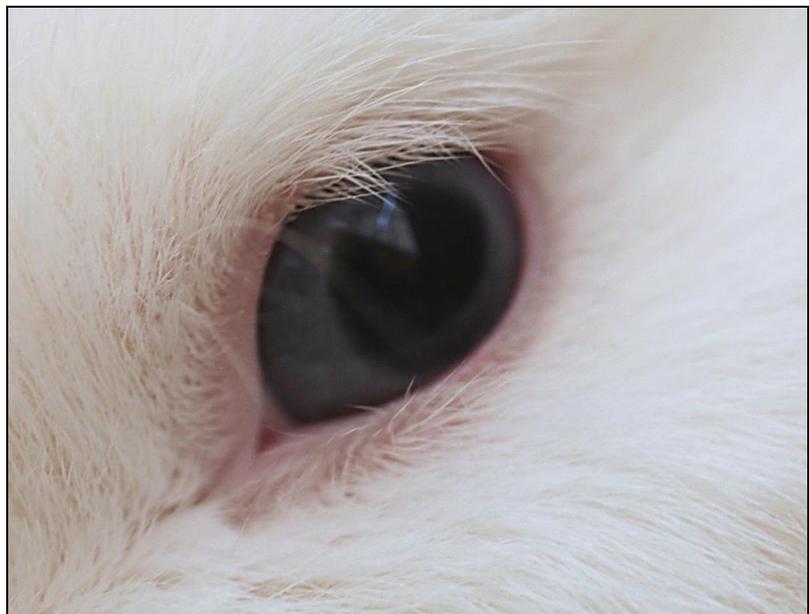


Figure 7: White fur and blue-eyed rabbits are more likely to suffer from idiopathic epileptic seizures.

Treatment

The treatment of epileptiform or epileptic manifestations in rabbits varies according to the type of seizure and their frequency.

A single crisis with non-significant encephalographic and radiographic findings usually requires a short and targeted treatment only, depending on the cause.

When seizures become chronic, medication can be started. Many drugs are

available, that treat defined types of epilepsy. Only a few are administered to rabbits:

- Diazepam, IV, IM or SC;
- Midazolam, IV, IM, SC;
- Phenobarbitone, OP, 1-2 mg / kg. It is used when diagnostic tests cannot determine the cause of seizures. It can control seizures.

Table 1: Recapitulative table for epileptiform seizures in rabbits

Viral infection	<i>Herpes simplex virus (HSV)</i> related encephalitis
	Viral Hemorrhagic Disease (VHD), terminal stage
Parasitic infection	Presence of burrowing (rodent) mites
	<i>Encephalitozoon cuniculi</i> in the brain, accompanied by an inflammatory response of brain cells
	Presence of the parasite <i>Baylisascaris procyonis</i>
	Toxoplasmosis
Central nervous system	Trauma or disease of the CNS or head
	Cerebrovascular disorder, after e.g. head trauma
	<i>Pasteurella multocida</i> related encephalitis or <i>otitis interna</i>
Metabolic anomalies	Gastro-intestinal stasis, accompanied by severe pain
	Terminal hepatic lipidosis and ketosis
	Azotemia (excess of nitrogen in the blood), eventually accompanied by renal failure
	Hyper- or hypoglycemia
	Hyper- or hypocalcemia
	Magnesium deficiency
	Cardiovascular diseases
	Gestation toxemia
"Mechanical" causes	Arteriosclerosis and mineralization of brain blood vessels/arteriosclerosis
	Tumor, neoplasia, abscess, or lesion that invades a sensitive part of brain tissue, or the nervous system
	Surface irritation, e.g. rubbing fur, piece of hay trapped in anal gland
	Agonal phenomenon
Medical treatment	High dosages of antibiotics, like quinolones or penicillin's
Toxicity	Toxic plants or heavy metals, e.g. lead
	Insecticides
	Fertilizer



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The treatment best suited to the rabbit's condition and the least toxic should be favored, while a monotherapy is preferable to the combination of two drugs. Treatment should be started gradually with slow increases of the doses to avoid the effects of sudden sedation. It is usually continued during the life of the rabbit and should never be interrupted abruptly. A rabbit may respond poorly to antiepileptic therapy. The long-term prognosis is poor.

A phenomenon of habituation to antiepileptic drugs exists in rabbits; the body gets used to the drug and its doses must be increased, increasing the risk of side effects, and sometimes the death of the animal.

If general anesthesia is required, it is essential to use the anesthetic Propofol. Complications can occur such as damage during a seizure.

It is important to take into account drugs taken by the rabbit for other health problems in order to avoid interferences with anti-epileptic drugs. Rabbits that have suffered from epileptic seizures should not be administered certain drugs such as the neuroleptic acepromazine – used during the premedication phase to calm an animal, metoclopramide – used in veterinary medicine to stimulate gut motility in case of gastroparesis, and xylazine – used as an α -agonist in veterinary anesthesiology.

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