

LAFORA DISEASE

by

ASSOCIAZIONE ITALIANA LAFORA

A.I.L.A.

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CONTENTS

LAFORA DISEASE

THE DISEASE

What Lafora disease is

Symptoms

Causes

The way it transmits

Diagnosis

Possible treatment

Research

Experimental treatment by a ketogenic diet

EPILEPSY

Different crises and first aid

PRACTICAL ADVICE FOR FAMILIES

Advice for the carer

How to face the changes due to the disease

Advice to promote the development of the different activities of the daily life

WITNESSES

GLOSSARY

PICTURES/ANNEXES

THE DISEASE

English name: Lafora Disease (#254780 code OMIM). Described for the first time in 1911 by Gonzalo Rodriguez-Lafora (1886-1971) a Spanish neurologist.

WHAT LAFORA DISEASE IS

It is a progressive neurologic disease characterized by seizures, mioclonia, brain symptoms and psychic deterioration. Lafora disease is commonly widespread in the Mediterranean countries (Spain, France, Italy), in restricted areas of Central Asia, India, Pakistan, North Africa, in isolated ethnic groups of the Southern United States and Canada

SYMPTOMS

Its onset appears during adolescence, with generalized tonic-clonic or clono-tonic-clonic seizures, mioclonic at rest and during the activity, negative mioclonic and focal occipital seizures associated to transitory amaurosis. The progress is characterized by a significantly and rapid cognitive deterioration, whose first symptoms may proceed motor anomalies, and by a progressive increasement in intensity of convulsions and mioclonies. The clinic treatment and progression vary according to the different patients' needs.

CAUSES

Lafora disease is due to alterations which affect one of the two known genes both situated on the sixth chromosome called EPM2A (discovered in 1998) and EPM2B (or NHLRC1 discovered in 2003) and that cause a wrong functioning in the protein which they produce, respectively Laforin and Malina.(see B scheme). The function of these proteins is not well-known even if some researchers suggest they are involved in the glycogen metabolism for their absence provokes an increase of sugar in the various body texture. A limited group of patients does not present variations in the two genes, so probably there is at least another gene involved in the disease.

TRANSMISSION

The disease is inherited in a way defined recessive autosomic. In other words an individual presents the symptoms of the disease only if he shows an alteration in both couples of the gene (apart from sexual chromosomes everyone has two couples of each chromosome, a maternal one and paternal one, therefore two couples for each gene). The one who presents a couple of the normal gene and an altered one is a healthy carrier, and generally he does not show any symptoms. So a child is affected only if he receives a wrong couple of the gene by each parent, both healthy carrier of the genetic alteration. A couple of healthy carrier will have 25% of possibilities, in each pregnancy of

conceiving an unhealthy child, 50% of possibilities of having a healthy carrier child, 25% of having a healthy-not carrier child.

DIAGNOSIS

The diagnosis of Lafora disease may also be assumed on the basis of family history, age of onset, the characteristic mode of presentation of symptoms, the rapid deterioration of cognitive function and significant features of the electroencephalogram (EEG). We must start from the evaluation of clinical symptoms epileptology and the possible cognitive impairment. It will therefore be necessary to perform a thorough medical history, neuropsychological evaluation and neurophysiologic study involving in the first instance, the EEG recording with video recording and printing and the study of evoked potentials. Neuroradiological examinations can contribute greatly to the achievement of the diagnosis, there are also markers of the disease found in blood chemistry and metabolism. The diagnosis can be easily confirmed on skin biopsy of the axillary region, which highlights the presence of Lafora bodies (accumulations of poliglucosani) (see figure A) into the cells of the sweat ducts. Genetic testing is very useful from the diagnostic point of view, since mutations in the genes EPM2A and EPM2B are found in more than 90% of cases.

TREATMENT

At present there is not a cure able to stop or slow down the progression of the disease. Anyway it is possible to limit the epileptic symptomatology by antiepileptic drugs. Particularly valproic acid seems to be the best drug, useful in all treatments where we may add different combinations based mostly on the use of drugs, successful in myoclonic epilepsies such as **etosuccimide lamotrigina** and **levetiracetam** but other combinations are possible and sometimes, the patient reacts differently. In the last years zonisamide has proved significantly positive effects on the control of seizures and the reduction of mioclonies.

RESEARCH

At present there is an increase in the number of researchers of lafora disease. Part of the research focuses on genetic since there is at least another gene, not yet identified, which contributes to the disease. Moreover, some researchers are considering the function of “Laforina and Malina” and the relation with the metabolism of glucose and of clinic manifestations. In the end, studies of genic therapy are working with the aim of substituting in a case of “murino disease” the affected gene with the healthy one.

EXPERIMENTAL TREATMENT WITH KETOGENIC DIET

The ketogenic diet is an experimental therapeutic way to treat Lafora disease.

CLASSIC KETOGENIC DIET

It is a nutritional diet containing a high amount of fats and a reduced intake of proteins and carbohydrates. It aims at inducing a state of chronic ketosis by simulating the metabolic state of starvation. By this diet the organism is obliged to use fats instead of glucose as a source of energy, thus maintaining high the development of ketonic bodies. Every kind of diet contains a large amount of fats and low amount of proteins and carbohydrates, but in the classic type, the constituent ratio is 4 gr fats: 1 gr (proteins + carbohydrates).

The use of a ketogenic diet in Lafora disease does not only aim at achieving a potential antiepileptic effect but also a possible effect of prevention. In fact Lafora bodies are made up of thick poliglucosan aggregations which differ from normal glycogen of anomalous ramifications. The use of ketogenic diet enables the organism to have a reduced amount of carbohydrates, necessary component in the constitution of glycogen and consequently a potential reduction in the formation of Lafora bodies which are the pathological amounts of glycogen.

Considering the possible preventive effect the ketogenic diet should be followed all life by patients and for this reason the nutrients ratio is 3 to 1 (3 gr fats and 1 gr proteins and carbohydrates) which results more tolerable and tasteful.

At this point a valuation by a nutritionist is necessary.

It consists in :

- parents meeting to explain the characteristic of a Ketonic diet
- detailed information about nutritional habits of each patient
- valuation of nutritional conditions with clinic anthropometric exam and study of body frame
- writing of a nutritional diary to evaluate the caloric intake
- parents information about the preparation of ketogenic meals at home

The ketogenic diet is normally well-accepted by patients. At first a diet based on aliments will be planned, but, with the progression of the disease, it will be necessary to use special ingredients for ketogenic diet. These ingredients can also be used to integrate a diet with aliments.

During a ketogenic diet:

- at home is not necessary to control glycaemia
- it is advisable to control ketonemia weekly or during the onset of crises
- if symptoms are not clear, contact a doctor
- in the presence of other therapies, ask a doctor for advice
- make sure different items for mouth (toothpaste, lips softenings) do not contain sugar.

EPILEPSY

An epileptic seizure is defined as the paroxysmal appearance of signs and symptoms due to an abnormal neuronal activity in the brain. By the word epilepsy we refer to a great number of different epileptic syndromes with various kinds of manifestations. The localization of seizures in a special brain areas determines the different reaction to the seizure itself. As a consequence there will be partial seizures if only a limited area in the brain is affected, generalized seizures if all encephalon is affected and partial seizures with a secondary generalization if the seizure coming from a confined part takes subsequently all the brain.

During seizures, the patient does not feel pain and movements are involuntary, caused by anomalous seizure. The patient may loose or keep in touch with the environment and/or own perception. He will be able to hear sounds, see images, taste and perceive smells or touch something which is only imaginary. He will be able to perform with part or all of his body, involuntary actions such as: speaking, shouting, shaking a hand or an arm, walking, falling and shaking all body.

VARIOUS SEIZURES AND FIRST AID RULES

The first thing to do during a seizure is to keep calm: that will be easier thinking that the person affected does not feel any pain even if seizures are of different kinds and intensity and besides, these end up spontaneously.

Moreover any symptom (eye or mouth deviation, limb stiffening, incontinence, etc..) will disappear with the end of the seizure. It is very useful to note carefully what happens during a seizure, how

long each seizure lasts, and note down its sequence, to be able to give the specialist detailed information. All that is really important to assess rightly the kind of seizure. So it is useful to keep a diary of seizures with their description. (See attached form about seizures diary).

NO CONVULSIVE SEIZURES

During these seizures a help is not necessary unless the patient may cause injuries moving in dangerous way.

ABSENCES

These generalized seizures are characterized by a short loss of consciousness. The patient appears “absent minded” for a few seconds and generally he stops every motor activity. In case of close seizures or in state of very prolonged absence, the patient must be protected to avoid possible sources of danger.

FOCAL/PARTIAL SEIZURES

In case of losing touch with environment, partial or total, the patient may appear confused, he wanders and acts as he could not understand what he is doing (he lifts object, gets undressed, etc..) these behaviours are defined automatisms.

- reassure and comfort the patient who might worry about the seizures effects
- keep him away from dangerous situation (for example a crowded road, hot burners, steep stairs)
- talk to him quietly and kindly so that, after the seizure, he can move as soon as possible in the surrounding environment .
- don't try to keep him still (the confusional state witch may follow a seizure might take him instinctively to wriggle and kick out) but let him have space.

TONIC SEIZURES (STIFFNESS) AND ATONIC SEIZURES (RELAXATION)

The patient who presents this kind of generalized seizures may alternatively stiffen or relax muscles and, if standing, may fall down; he recovers rapidly, sometimes showing a confusional state. Seizures involving falls, are obviously the most dangerous ones and require special attentions by parents who have to take care of their child and create a safe environment.

CLONIC/TONIC GENERALIZED SEIZURES

This kind of generalized seizures provoke loss of consciousness with cries and, usually, it is very difficult to avoid a fall. At first a tonic phase (15-20 seconds) appears, where the body, after a series of generalized and symmetric muscular spasms, stiffens in extension; after that a clonic phase follows, where involuntary and rhythmic movements appear in the head, trunk and limbs with frequency of contractions which progressively decrease, disappearing in 30-40 seconds. The position to be assumed during a convulsive seizure is on one side. Generally a tonic-clonic seizure lasts less than one minute and disappears spontaneously; the patient who regains consciousness may be confused, and speak with difficulty or he may be lucid not realizing what happened.

It is useful to follow these hints in the presence of this kind of seizure:

- keep calm and reassure those who are present during a seizure
- do not hold the patient who is having convulsions and do not try to limit his movements
- avoid people rushing around him
- time how long the epileptic seizure lasts

- get rid of hard or sharp objects nearby
- check the patient's neck is rid of anything which may interfere with breathing
- put something smooth and soft (e.g. a jumper) under the head to avoid injuries due to the rough movements caused by seizures
- turn gently the patient on one side to keep free respiratory tracts
- don't try to open his mouth by hard objects or fingers: the affected muscles have a strong action and by trying to force them you may cause dental or mandibular articulations injuries. As a consequence you might hurt yourself.
- Don't try artificial respiration except in the case the patient cannot breath at the end of the seizure (respiratory alterations caused by seizures recover spontaneously without any intervention).
- Stay by him until the natural conclusion of the epileptic seizure
- Have a friendly and reassuring behaviour as soon as the patient regains consciousness
- Evaluate if it is the case to take the patient to a Casualty.

An epileptic seizure may last longer than 3-5 minutes, or a seizure may be followed by another one without the patient regaining consciousness. In this case you need a drug intervention:

- use endorectal drugs: diazepam microclysters, if prescribed by the doctor
- don't use drugs orally as, in a situation of unconsciousness, they may affect respiratory tracts
- ask for a doctor (or take the patient to the nearest Casualty).



PRACTICAL ADVISE FOR FAMILIES

ADVISE FOR FAMILIES

Lafora disease does not affect only the patient, but all his family. Personal emotional weight is enormous, and whose care for the patients need to develop strategies to face the progression of the disease. To know one's emotions may be helpful in the care of patient and for oneself.

FAMILY

Family must become the most important source of help. It is important to accept the help who may come from other family members, so that care does not depend only on one person.

SHARING ONE'S

It is necessary to share experiences and emotions, keeping all problems inside may result harder sharing may help to perceive as normal and natural own reactions. It is useful to accept external help, even if one may worry about creating problems or difficulties to others trying to plan to get someone to help in case of emergency.

HAVING FREE TIME

It is essential to have free time. That will give you the opportunity to have a social life, your interests and enjoy life.

CONSIDERING ONE'S LIMIT

It is necessary not to ask too much to oneself. The majority of people knows their limits only when it is too late. Therefore it is advisable to prevent difficult situations, not to feel guilty or blame the patient when problems arise. It is useful to remember their cause is due to the disease itself. Moreover interpersonal relationships are great support for carers and may be useful to patient too.

KEEPING IN MIND YOU ARE IMPORTANT

It is useful to consider how important you are, for the patient too. Without your help the patient would be lost. That is why it is essential you take care of yourself.

ACCEPTING AND LOOKING FOR HELP AND ADVISE

Learning to accept help may be something new anyway, even if relatives, friends or neighbours may give you a real help. They may not know what is really useful or welcome. A word, suggestion and indication may contribute to be or feel useful, besides that will be helpful for the patient and a support in the care. A group of self aid may be a support and represent a moment of problems and solutions sharing and an occasion of mutual help. Moreover it is important to know where in the living area it is possible to have help from a medical, personal, organizational point of view. Family doctor, nurse or social worker may identify and suggest available resources.

HOW TO FACE THE CHANGEMENTS DUE TO THE DISEASE

SOCIALIZATION

When a mental or cognitive disease appears it is necessary to realize patients with these disabilities need to keep their relationship with others. Keeping friends is really important. A lot of people tend to be isolated and confined in their houses; the risk is losing a social life and interpersonal relationships. This isolation may, in turn, worsen the situation and make care even harder. Therefore social life and friendship are a real priority. In the first phase of the disease, where personal autonomy may still be preserved but a person's critical ability might begin to alterate, it is necessary to control social relationship in order to avoid someone might take advantage of the patient's disability.

COMMUNICATION

Cognitive deterioration of patient must not take to talk him in an infantile way, a patient often understands more than one thinks

Caring for a patient affected by Lafora disease often require patience. You need constantly to repeat things. You should not ask too much, you need to proceed slowly and gradually, showing the way an action might result completely new witch should be performed. It is necessary to test the comprehension and control how an action is performed.

You should compliment as much as possible: a good word instils confidence and encourages them to progress, also love and praise help patients to feel better

Cognitive deterioration represents the result of the progression of the disease. The first noticeable symptoms are: difficulty in remembering recent events and carrying out well-know daily tasks. Patient may also show confusion, personality and behaviour changes, difficulty in judging and finding words to conclude a speech. It is important not to change our way to relate to the patient even if his conditions have changed. Care may sometimes be very hard; anyway there are various useful hints to face different situations.

FIXING A ROUTINE AND KEEPING A NORMAL STANDARD

Fixing a routine for the patient may diminish the number of decisions to take and contribute to keep order and structure in his daily life, which might otherwise be confused.

SUBSTAINING PATIENT'S AUTONOMY

It is necessary that the patient is independent as long as possible to preserve his self-esteem. Lafora disease is an invalidating disease which compromises a person's autonomy.

Our aim is to keep as long as possible personal independence by utilizing care or hints which may support or facilitate patient in carrying out daily activities

HELPING A PATIENT TO KEEP HIS DIGNITY

Do not forget a patient is a person who has emotions and feelings; thus what is said may have a disturbing effect. You should avoid discussions about his conditions if he is present.

Preserving self-esteem

At the onset of the disease with the gradual deterioration and loss of some abilities, it is important to help the patient to learn to tolerate frustrations due to his new condition. Therefore remaining abilities must be supported, encouraging the patient, maximizing positive sides, limiting comments, not underlining failures

AVOID CONFLICTS

That kind of conflict may cause useless stress to both carer and patient. You should avoid to underline failures, trying to keep calm. Indisposing may only worsen the situation:

Keep in mind what happens depends on disease, not on the patient.

FIXING SIMPLE TASKS

It is useful to propose simple tasks. Do not give the patient too many choices.

HAVING A SENSE OF HUMOUR

Laugh with the patient with cognitive deterioration but not at him. Humour may be a good way to alleviate stress.

PAYING ATTENTION TO SAFETY RULES

The loss of physical coordination increases the possibility of accidents, make sure the house where the patient lives is really safe. For example use corner protections, bumpers all around the bed, avoid carpets or anything which may represent a danger.

ENCOURAGING A GOOD PHYSICAL CONDITION

Many times this attitude may help a patient to keep his physical mental abilities longer. The type of exercise depends on personal conditions. You should ask your family doctor for more specific indications.

HELPING THE PATIENT GET THE BEST FROM HIS REMAINING ABILITIES

Carrying out planned activities may reinforce or promote dignity and self esteem, having an aim in life. Anyway, abilities may change with passing of time and you need attentions and flexibility in planning activities

THE IMPORTANCE OF A GOOD COMMUNICATION

With the progression of the disease communicating with the patient may become more difficult. Some useful hints for carers:

- * speak clearly, slowly, face to face, looking at the patient's eyes
- * show your love through physical contact if this is appreciated
- * pay attention to body language, a patient whose verbal abilities have diminished, may communicate through no verbal messages

- * be aware of your body language
- * find what key-words (simple words easy to remember which may suggest others) suggestions and explanations are useful to successfully communicate with the patient
- * make sure the patient is attentive before talking to him

PRACTICAL ADVICE TO CARRY OUT DIFFERENT DAILY LIFE ACTIVITIES

PERSONAL HYGIENE

Patient may forget to wash himself or even, he doesn't realize when he needs it or he may have forgotten what he has to do or he has difficulty in carrying out necessary actions. As a consequence it is important to respect patient's dignity when offering help.

Hints:

- * do not change if possible acquired habits in personal hygiene
- * having a "bath" should be a relaxing and pleasant moment
- * the patient should be independent as much as possible
- * if the patient is embarrassed let some his body be covered while having bath
- * pay attention to safety rules; use wheel-fixed, points of support (bars) which patient can lean to, anti-skid surface
- * for personal hygiene use sponges (with anatomic grip or glove) electric toothbrush, hair-brushes with anatomic grip
- * do not use scissors, blades or other sharp objects, choose nail-files or electric razor;
- * with the progression of the disease patient may be bed ridden and may need to complete hygiene to bed. In this case pay attention particularly to product used (soft gloves, moisture and protective cream) to prevent skin damages.

CLOTHES

A patient may forget how to get dressed and may not know feel when he needs to change his clothes. Besides wearing some clothes may be difficult.

Hints:

- * avoid clothes with difficult parts (shake, belts, buttons) use comfortable clothes
- * encourage the patient when he is independent and get dressed by himself
- * if it is necessary make the patient repeat actions many times
- * use shoes and slippers with non-slippery soles

TOILETS AND INCONTINENCE

Patient may not be able to know when he has to go to a toilet, he can't find his way or doesn't know what to do when he is there.

Hints:

- * let the toilet door open, so patient may easily get to it
- * patient should wear cloche which he can easily take off
- * limit drinks before going to bed in the evening
- * let an "incontinent-chair" by the bed

NUTRITION

Patients often forget if they have eaten or how to use cutlery. In the last phases of the disease patient may need to be fed. There may be new physical problems, for example difficulty in chewing and swallowing. Those who need to use a ketogenic diet as a therapeutic way to treat Lafora disease need to follow it for long time. It changes patient's nutritional habits and affects all family members. Moreover it is important to be able to vary, following a nutritionist's indications, all food combinations present in a diet to have the patient's best compliance.

Hints:

- * use cutlery safe for material and shape (e.g. round points)
- * encourage to use fingers when eating, this may result easy for the patient and not particularly unbecoming
- * choose beakers with handles and drip-catchers and unbreakable may produce a dangerous or simply frustrating event
- * cut food in small pieces to prevent choke episodes. In the last phase of the disease grinding food and using partially solid or liquid aliments might be necessary
- * make sure the patient eats slowly and intakes small quantities to avoid choke sensations
- * be aware the patient may not be able to react to food temperature (hot or cold) or simply he may not be able to tell you while he is fed and may get burny intaking hot food and drinks
- * always check for hot food and drinks temperature
- * serve one food portion a time
- * sitting at table choose a comfortable chair
- * if the patient has difficulty swallowing ask your doctor to find new ways to facilitate this function

In patients where the progression of the disease affect swallowing, it might be necessary to utilize SNG or PEG.

PRACTICAL ADVICE IN DRUG INTAKE

If during a therapy intake, swallowing represent a problem, it might be necessary:

- to introduce a tablet into mouth, down to the tongue to favour deglutition
- break and/or melt the drug avoiding, if possible, to melt more drugs together. So it is easier to verify the drug which has not been taken in the right way
- use jellyfield water or other aliments where you can mix the drug to be intake.

MOBILIZATION

At first independence in such life activity may be preserved, so it is necessary only to adopt some precaution to have a safe environments. The presence of more and more important mioclonies and atassia may take to difficult deambulation. Therefore at the beginning it might be necessary to be supported by someone who help the patient in his movements, while in an advanced phase of the disease, the use of a wheelchair may become essential.

PHOTOSENSIBILITY

It is important to consider this aspect to adopt tactics which may reduce the risk of seizures. Watching tv is one of the most common causes taking to a seizure for a patient suffering from a photosensitive epilepsy. It is important to sit far from the telescreen when watching tv to reduce the risk of a seizure. There is also a susceptibility to the light-dark transition which is named scotosensitivity.

Hints:

- * If is possible, choose a LCD (Liquid Crystal Display) telescreen
- * watch tv in a well-lighted room
- * put a small lamp on or near the television-set
- * do not sit too near the tv-set, at least 2,5 meters far
- * use the tv-remote control at a safe distance when zapping; if you get near the tv-set cover your eye by a hand. That will reduce the number of brain cells stimulated by the telescreen brightness.

Also using a computer may increase the risk of seizures, mostly if its images contain flash, intermittent, brightness or repetitive images or with high contrast. Videogames may increase the risk of seizures in cause of a photosensitive epilepsy.

Some hints to minimize the risk:

- * before playing control the videogame characteristics. In some of them there are instructions for use inside the packaging
- * do not play in tired, tiredness and or insomnia may increase the risk of seizures
- * have frequently break
- * play without food
- * playing video games in a well light room
- * stay as far away as possible from the monitor of the game
- * if possible, remembering to use the LCD to reduce the brightness and contrast
- * some people may want to cover one eye, for example using an ocular bandage, while playing to reduce the stimulus screen.

In vertigo, blurred vision, loss of consciousness or muscular spasm appear, stop immediately playing. Staring at pictures/images with a high contrast for a long time may increase the risk of seizures. E.g. white and black stripes, some materials or rich in drawing wallpapers ...

The sunlight through shutters or branches.

If there intermittent lights, cover your eyes by your hand and get far from the light source. Light-dark transition and viceversa must always be gradual never a sudden change.

INSOMNIA

The patient may be restless all night, this may be the worst problem for a carer.

Hints:

- * avoiding sleeping in the daytime
- * let the patient feel comfortable when it is time to go to bed.

HALLUCINATIONS

If the patient has hallucinations

Hints:

- * reassure the patient about his hallucination. Say you believe him
- * if the patient is frightened reassure him, a calm voice or a gentle touch may be useful
- * distract the patient, inviting to focus his attention on a real object in his room

GLOSSARY

ATAXIA: (from the Greek *ataxiā*, disorder) it is a disorder consisting in a progressive loss of muscle coordination which makes difficult to perform voluntary movements.

ATONIC SEIZURE: sudden loss of control of muscle tone which may cause falls on the ground

AUTOMATISM: involuntary psychomotor actions performer during a seizure. They may be simple (e.g. chewing - suction - deglutition movements) or complex (getting dressed undressed - deambulation - sometimes escape).

CLONE: it is constituted by a repetitive contraction of a muscle where the tendon is strained. It is often the result of an abnormal vivacity of reflexes.

CLONIA: must of people has experienced a sudden jerk in phase of sleeping. Even if this sudden muscle spasm is not epilepsy, it is similar to the one experienced by the patient who has mioclonic seizures

DELUSION: it is a perception disorder characterized by a modified elaboration of real sensorial stimula and by a wrong interpretation as a consequence real objects are perceived in a different way from reality; it may be connected to the peculiarity of the stimulus and to particular emotional or organic states.

DISARTRIA: By this word we refer to the disorders which affect the vocal emission of words due to parlysis of the musculature needed for the articulation, or to a bad movement coordination or on extrapiramidale kind disturbances.

EPG: (Endoscopic Percutaneous Gastrotomy): technique used in an enteral nutrition. An enteral nutrition by EPG represents an improvement as traditional nose-gastric probe is not well-tolerated, it is often accidentally removed, it may move to bronchial organs, causing decubits ulcer and gastro esophageal reflux. Thanks to an EPG the patient may carry out activities and have the same life style in the period before gastotomy.

FARMDRUG RESISTANCE: Epilepsies are neurologic diseases characterized by repente seizures due to excessive discharge of cell groups into the central nervous system. In epilepsies, these events are often associated with consciousness alterations, involuntary movements and, sometimes convulsions. 30-40% of people affected by epilepsies show a difficult control of seizures also after intaking one or more therapies at the maximum tolerated dosage, causing a “drug resistance”. This is probably due to the numerous causes of the disease and to the possible presence of injuries or anomalies in the central nervous system. Moreover it is possible that genetic factors contribute to determine a “drug resistance” , modifying the distribution of drugs in the brain or changing the nervous structures (mostly the receptor ones), where the same drugs work.

HALLUCINATION: sensation or perception with no object. Hallucination may be “simple” (bright twinkle, buzzing...) or “complex” (scene at the cinema, music...)

MIOCLONIA: it may defined as a sharp, rapid, arrhythmic and involuntary contraction of a muscle portion (parcellare mioclonia) or o fan entire muscle or muscle group. Jerk may be symmetric, repetitive, at regular or irregular intervals, they appear at rest or during a voluntary activity and may be stimulated by emotional, cognitive, tactile acoustic or visual impulses.

Mioclonic spasms may manifest in a short absence of contraction, contractions are called positive mioclone, relaxations or tone loss, negative mioclone.

MIOCLONIC SEIZURE: short or strong sudden contractions may affect the whole body or only a part of it. A muscle contraction may be so intense to cause a fall. Mioclonic seizures may affect all body, but generally they affect one or both limbs, waist and sometimes head. The muscle contraction may be so intense to cause a fall. Mioclonic seizures usually appear in the morning. They are short but they may be very frustrating (e.g. they may cause spilling of drinks or similar accidents)

NGP: (nosegastro probe) rubber or silicone catheter which is introduced through nasal passage to reach the stomach. It is used in enteral nutrition.

PHOTOSENSITIVITY: photosensitivity is an anomalous reaction of the brain to an intermittent light stimulation (ILS) or to a light stimulus of various nature, which manifests or simply as an EEG alteration or as an easily recognizable seizure. Photosensitivity is often present in patients affected by generalized epilepsy, but it may be present in healthy people too.

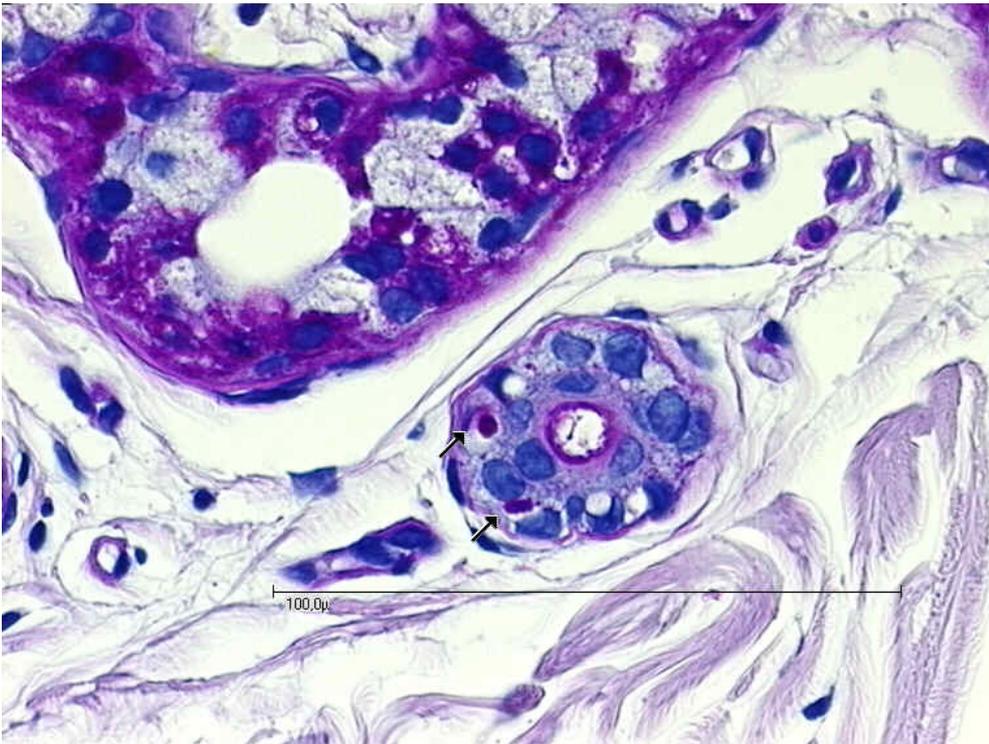
RECESSIVE AUTOSOMICA: it is a pathology which manifests only when the DNA alteration is present in both the elements of a couple of chromosomes. Therefore the disease appears only if there are two copies of the affected gene.

SCOTOMA: reduction of visual field (sight vanishes in some areas) there are positive scotomas, which result in dark or coloured spots on the observed objects and negative scotomas, characterized by a lack of vision corresponding to their projection in the space. Absolute scotomas, if each visual perception is lost only for colours (or some colours) whereas white colour is perceived. There may a particular light sensation lasting some minutes, which has often the appearance of a flaming circle bow, formed by the connection of various broken lines. This is said "shining scotoma".

SCOTOSENSITIVITY: it is an anomalous brain reaction due to the sudden passage light/dark or dark/light. It may be considered a sub-kind of photosensitivity.

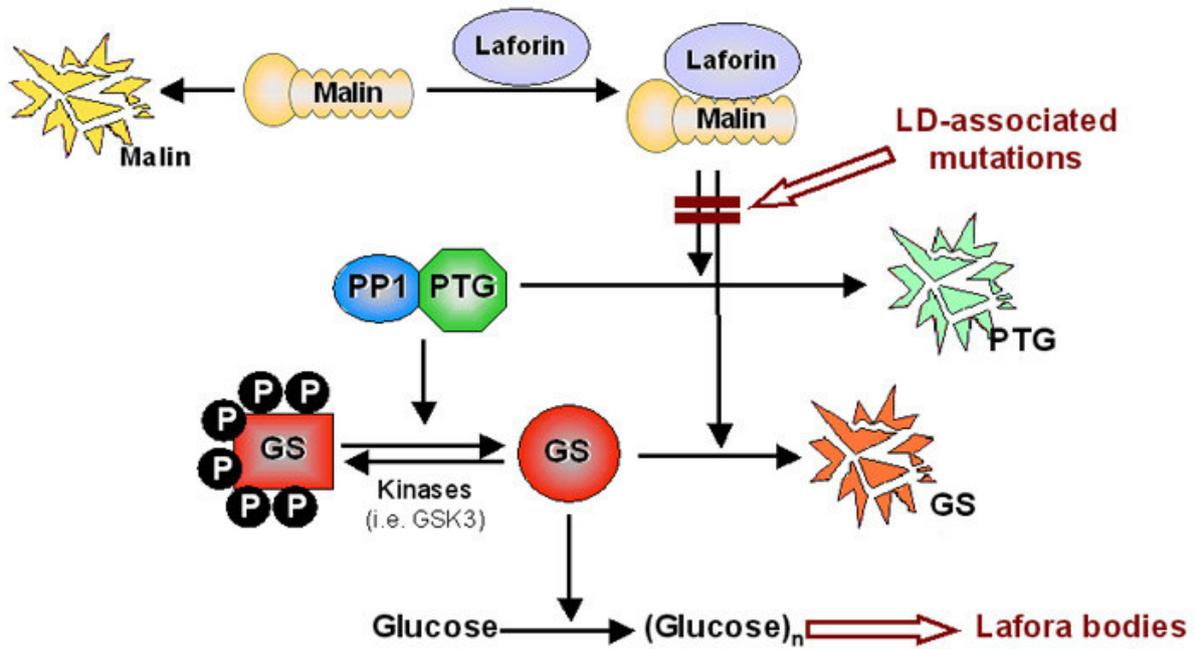
TONIC SEIZURE: tonic seizures cause muscle stiffness. The body stiffens and a patient, as a consequence, may fall if not helped. Usually tonic seizures last less than 20 seconds and they often appear during sleeping.

FIGURE A



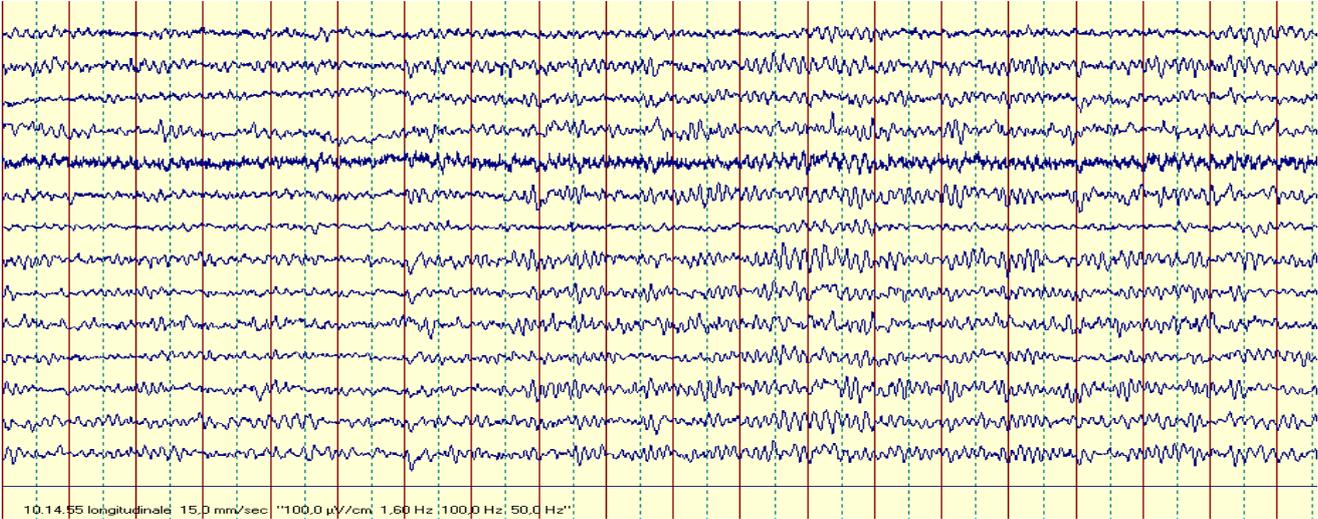
Example of electron microscopy which revealed the Lafora bodies inside the cell

SCHEME B



Lafora disease is due to alterations which affect one of the two known genes both situated on the sixth chromosome called EPM2A (discovered in 1998) and EPM2B (or NHLRC1 discovered in 2003) and that cause a wrong functioning in the protein which they produce, respectively Laforin and Malina. (see B scheme).

EEG THE FIRST CONSULTATION



EEG AFTER 34 MONTHS



Example diary description of the crisis

Aura(sensations that precede the crisis): _____

State body:

- | | | |
|--|--|--|
| <input type="checkbox"/> Still | <input type="checkbox"/> Fall | <input type="checkbox"/> Automatic actions |
| <input type="checkbox"/> Snap | <input type="checkbox"/> Stiffness | <input type="checkbox"/> Clonie |
| <input type="checkbox"/> Sound emitted | <input type="checkbox"/> Sensations felt | <input type="checkbox"/> Other |

Position and actions of the individual parts of the body:

Head _____ Eyes _____ Mouth _____
Body _____ Hands _____ Arms _____
Legs _____ Other _____

Loss of contact with the environment:

- YES NO Total Partial

Shooting mode:

- | | | |
|------------------------------------|-------------------------------------|--|
| <input type="checkbox"/> Immediate | <input type="checkbox"/> Slow | <input type="checkbox"/> After _____ minutes |
| <input type="checkbox"/> Sleep | <input type="checkbox"/> Sleepiness | <input type="checkbox"/> Other _____ |

Source of information:

- Patient Family Friends Bystanders
 Other _____

Contact your doctor:

- YES NO

Decisions: _____

Comments: _____

Concurrent situations:

- Mestrual _____
 Fever _____
 Therapy is not taken _____
 Other drugs taken _____
 Alcohol _____
 Stress _____
 Tiredness _____
 Modification meals _____
 Sleepiness _____
 Change in duration and quality of sleep _____

 Changes in mood _____
 Unpleasant news _____
 Other _____

Our location:
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