

APPARATUS FOR REDUCING SYMPTOMS OF NEURODEGENERATIVE DISEASES

Field of the invention

5 The invention regards the treatment of symptoms of neurodegenerative diseases, in particular Parkinson's disease, or symptoms deriving from cerebral ischemia. In particular, the invention regards treatment to improve the mobility of patients affected by such diseases. Furthermore, the invention regards an apparatus for the implementation of such treatment.

Prior art

10 The most common therapy for Parkinson's disease is still the pharmacological treatment based on taking dopamine (L-dopa or levodopa), given that it is known that the disease is caused by the degeneration of the dopamine-producing neurons. This therapy is capable of limiting the symptoms, at least in the short term, but it has various and serious adverse effects among which
15 vomiting, anorexia, hypertension, psychological disturbance and arrhythmia. Generally, the patient is forced to take other drugs to control the adverse effects of the therapy. There is a considerable alternation of the patient's response, with periods of therapy refractoriness; furthermore, it is known that the efficiency of said therapy reduces considerably after a few years of treatment. There is
20 also a therapy based on direct electrical stimulation of the brain usually used in patients at an advanced stage of the disease and/or suffering from serious adverse effects of levodopa. Said therapy provides for surgical implantation of electrodes and thus it is extremely invasive. Other therapies are still at study level and quite far from practical availability for patients.

25 Hence, currently, the most common and actually the only means for symptomatic treatment of Parkinson's disease consists in drugs that must be taken continuously, such drugs creating dependence and causing serious

adverse effects.

There is a serious need for a therapy capable of reducing symptoms of Parkinson's disease. It is known that this disease may evolve slowly over several years, during which the patient gradually loses self-reliance due to tremors, rigidity, dyskinesia, postural and deglutition disorders, etc... In particular, the strong reduction of the mobility capacity has a negative effect on the independence of the patient. The patient suffers from slowness and difficulties to stand up, walk and turn around. Very often, the disease affects people at advanced age and worsens an already partly reduced mobility capacity. Within a few years, most of these people are no longer self-reliant and need almost constant assistance, with the ensuing high social costs. The pharmacological treatment used up to date does not satisfactorily meet this need.

Similar arguments may be raised regarding other neurodegenerative diseases or regarding the consequences of an ischemic attack which likewise reduce the mobility capacity and, thus, the self reliance of the patient. In these cases, either the drugs are not efficient or they cause serious adverse effects.

Summary of the invention

The inventors discovered a surprising improvement of the mobility capacity and more generally walking capacity, in patients affected by neurodegenerative diseases such as the Parkinson's disease, following a controlled and localised mechanical stimulation treatment of the foot. More in particular, said stimulation is localised at the tip of the big toe and an area of the sole of the foot which substantially corresponds to the lower big toe metatarsal joint.

The stimulation is carried out according to predetermined treatment parameters comprising at least the mechanical stimulation intensity, a stimulation sequence of said parts of the foot, the duration of each step of mechanical stimulation,

and optionally a repetition of the sequence for a defined number of cycles.

Preferably, the treatment sequence regards both the right and the left foot. More specifically, an aspect of the invention consists in a treatment comprising the steps of mechanically stimulating:

- 5 a) the tip of the right big toe:
- b) an area beneath the sole of the left foot corresponding to the lower left big toe metatarsal joint;
- c) an area beneath the sole of the right foot corresponding to the lower right big toe metatarsal joint;
- 10 d) the tip of the left big toe.

The term “mechanical stimulation” is used to indicate the attainment of an operating pressure, corresponding to feeling of a “stimulus” threshold by the patient. Regarding the present invention, such threshold is defined as the pain or stimulus threshold. The correct operating pressure shall be determined
15 depending on the case, given that it varies according to the patient’s clinical condition and in particular according to the age of the patient and the state of advancement of the neurodegenerative disease as well as subjective sensitivity. Generally, the attainment of said threshold corresponds to the occurrence of the patient’s reflex to withdraw the leg or foot. It was observed that by using – for
20 mechanical stimulation - 1.5 – 2.5 mm diameter spherical-headed tips, the force imparted to the tip in order to attain said operating pressure is usually comprised between 2 and 3.5 kg; However, a more or less intense stimulation may be used, without departing from the invention, depending on the subjective characteristics of the patient.

25 The treatment may be also performed manually but, preferably, it is automated by a series stimulators each provided with a member for contact with the foot,

for example a rounded-off tip.

The sequence preferably comprises the steps of stimulating said areas of the right and left foot following the order a), b), c), d), obtaining a mechanical stimulation, in the following order: right big toe tip, lower left big toe metatarsal joint, lower right big toe metatarsal joint, left big toe tip. However, such order shall not be considered limiting with respect to the present invention. The stimulation of the foot according to the invention may comprise any succession of stimulation on the parts of the foot defined above. For example, an inverse order may be followed from d) to a), or any other order may be followed.

More preferably, the treatment sequence is such that the abovementioned areas of the body are stimulated separately. This implies that at any time of the treatment, the mechanical stimulation is equivalent or greater than the operating (or threshold) pressure defined above in only one of the areas to be subjected to treatment, for example area a), b), c) or d). The "idle time" that elapses between the interruption of the stimulus in an area, for example area a), and the attainment of the operating pressure in the subsequent area, for example area b), is preferably about 1-2 seconds.

The duration and number of cycles may likewise be determined according to the overall clinical picture of the patient. In patients affected by Parkinson's disease optimal results were obtained with each stimulus lasting from 5 to 10 seconds, preferably 6 seconds, and the number of repetitions of said stimulation sequence a) - b) - c) - d) indicatively between 5 and 10 repetitions.

A preferred embodiment of the treatment, in particular for patients affected by Parkinson's disease, provides for repeating the stimulation sequence a) - b) - c) - d) for 5-10 cycles; stimulation using a 1.5 - 2.5 mm, preferably 1.8 mm, spherical-headed tip and the pressure to be determined on experimental basis, indicatively falling within 2 - 3.5 kg. Under particular conditions of hyposensitivity or hypersensitivity, values greater or lower than said limits -

herein indicated strictly for exemplification purposes – may be used.

A second aspect of the invention consists in an apparatus for performing the treatment described above. The apparatus may be made according to different variants from a construction point of view, not essential as regards with the invention. For example, the apparatus may comprise two devices respectively applicable to the right and left foot of the patient, or two accommodations for the feet, provided with the required mechanical stimulation devices, and a suitable control system.

According to a possible embodiment, an apparatus for mechanically stimulating the foot is provided, comprising at least one first mechanical stimulator arranged to operate, during use, on the tip of the big toe, and a second mechanical stimulator arranged to operate, during use, on an area localised beneath the sole of the foot and substantially corresponding to the lower big toe metatarsal joint; said apparatus further comprising a control system suitable to actuate said mechanical stimulators according to a treatment programme comprising at least one mechanical stimulation intensity, a predetermined sequence for stimulating said parts of the foot, a predetermined duration of each mechanical stimulation step, and optionally a repetition of said sequence.

According to the most preferred embodiment, provided for is an apparatus comprising a first mechanical stimulator, a second mechanical stimulator, a third mechanical stimulator, a fourth mechanical stimulator wherein: said first mechanical stimulator is arranged to operate, during use, on the tip of the right big toe of a patient; said second mechanical stimulator is arranged to operate, during use, in an area beneath the sole of the left foot corresponding to the lower big toe metatarsal joint; said third mechanical stimulator is arranged to operate, during use, in an area beneath the sole of the right foot corresponding to the lower big toe metatarsal joint; said fourth mechanical stimulator is arranged to operate, during use, on the tip of the left big toe; and furthermore

the control system is prearranged for the actuation of said first, second, third and fourth stimulator according to said treatment programme.

Preferably, the control system is prearranged for the sequence actuation of said first, second, third and fourth stimulator, causing the mechanical stimulation,
5 according to the predetermined sequence, of the areas of the body a), b), c), d) described above.

The apparatus preferably comprises suitable adjustment means for positioning the stimulators at the areas of the foot or feet subjected to treatment, for example the previously indicated zones a), b), c), d). Furthermore, the
10 apparatus preferably comprises suitable means for fastening against the feet to maintain the proper position during treatment, for example straps with adjustable fastening means or the like, as well as suitable means for adjusting and adapting to the morphology of the foot. In a preferred embodiment, for example, the apparatus comprises a front support – adjustable in a tilting
15 manner - for the toes, and a rear support for the heel area, also adjustable and spaceable from the front support, adapting to various sizes. More preferably, in order to facilitate selective stimulation of the tip of the toe, said toe support comprises a partitioning element or spacer for separating the toe from the rest of the toes, and allow accurate application of pressure on the tip of the toe.

The stimulators may be made according to per se known art and according to various embodiments, not essential as regards with the present invention. In a preferred embodiment, a stimulator is substantially made up of a motor which –
20 through a rotating spindle and a female-screw coupling – causes the translation of an actuator. The motor-actuator unit is mounted on adjustable supports.
25 Power supply is preferably low voltage (6-12 V) or battery powered.

Further construction details such as the use of non-allergic, easily washable material etc... and which are clear to a man skilled in the art, shall be provided for in compliance with the law and contingent requirements.

The control system preferably comprises at least one processing unit, an internal memory unit and a data interface connection with the external, of the per se known type such as for example a USB port, network plug or equivalent means for transmitting and receiving data. Said interface may be one or two-directional. Said interface may be used in particular for loading a specific programme, prepared by a specialist, for the patient. According to further variants, the apparatus may be controlled by a processor or by an external control unit. The control system may also comprise a function for the "historical" recording of the treatments on suitable storage means.

For example, the treatment therapy may comprise the following fundamental steps. The first step consists in performing neurological tests on the patient and determining the most suitable treatment parameters, in particular: detecting the stimulus threshold of the patient and determining the pressure and/or the travel of the actuators to attain the correct operating pressure; determining the duration of each stimulation and the number of cycles per treatment session. Thus, the specialist, may prepare a series of treatment parameters, for example with the help of a special software programme, and transfer them to the control system of the apparatus subject of the present invention. The apparatus may thus be used at home directly by the patient or by a person assisting the patient, without requiring any medical specialisation, given that it operates with a preloaded programme.

The invention has the evident capacity of obtaining surprising improvement of the mobility of patients affected by Parkinson's disease, as outlined more in detail in the following detailed description. In particular the treatment according to the invention is capable of reducing symptoms such as akinesia, tremors, slowness and rigidity of movement over time in a surprising and long-lasting manner. The treatment, based on a purely mechanical stimulation of selective areas of the foot, does not have the adverse effects of a pharmacological treatment; it is repeatable without limits and has no adverse effects.

A further and important advantage of the invention is that the treatment neither requires hospital facilities nor qualified personnel. The apparatus that provides the treatment is easy to manufacture and substantially requires power supply alone, which can be supplied from the mains or by batteries. The use of the apparatus and starting the treatment are possible even in the home environment, with apparent advantage in terms of self-reliance of the patient. This particularly important for controlling the symptoms of a disease such as the Parkinson's disease which, as known, is not fatal per se and may have a course characterized by slow advancement over time. The contribution of the specialist is limited to defining treatment parameters, which may be updated periodically and "loaded" into the internal memory of the control system; normal use is substantially attainable by anyone, due to the fact that the treatment parameters are preset and memorized in the machine.

Improvement is clearly observable especially regarding the patients' capacity to stand up, walk and turn around. As known, the ability to perform such tasks are strongly reduced and slowed down by the Parkinson's disease. It is deemed that the stimulation of the selected areas of the foot operates as a targeted stimulation of the nervous system and in particular of the areas of the brain having the task of controlling mobility, with the effect of temporarily compensating "regression" caused by the disease, without this being interpreted as restrictive as regards with the present patent. It has been observed that the effects generally last a few days; however, the treatment can be repeated frequently due to the substantial absence of contraindications and adverse effects.

A further advantage lies in the low cost, especially compared to the benefits obtained, hence making the treatment available to almost everyone.

Characteristics and advantages shall be more apparent from the following detailed description and with the help of the attached figures.

Brief description of the figures

Fig 1 schematically shows the use of a stimulation apparatus according to one of the various embodiments of the invention.

5 Fig 2 shows a simplified diagram of the control system of the stimulators in an apparatus according to the invention.

Fig 3 shows a possible form of the stimulation intensity curves over time.

Fig 4 shows one of the possible embodiments of an apparatus according to the invention.

Detailed description of a preferred embodiment

10 Fig 1 shows a device 1 applicable to the right foot P of a patient, and comprises an anatomic surface 2 for accommodating the foot, where two stimulators 3a, 3c are respectively positioned in a front area and in a central area of said surface 2. When the device 1 is correctly secured to the foot P, in the use position, the stimulator 3a is capable of causing a mechanical stimulus on the
15 tip of the big toe, while the stimulator 3c is capable of operating on an area of the sole substantially corresponding to the lower big toe metatarsal joint.

Said stimulators are made according to per se known art and may comprise, for example, an electric motor associated to a linear actuator, having a rounded tip contact member intended to exert pressure directly onto the tip of the big toe or
20 the metatarsal joint.

The surface 2 preferably comprises an adjustable front support for the toes and/or a separator for spacing the big toe from the other toes. The device 1 may be secured to the foot P, during treatment, using a fastening element of a per se known type (for example Velcro).

25 Preferably used for treatment is an apparatus 10 comprising two devices of the

type illustrated above, respectively one device 1 for the right foot and an analogous device 1' for the left foot comprising further mechanical stimulators 3b and 3d, as exemplified in the diagram of Fig. 2.

5 The apparatus 10 is provided with a control unit 4 which commands a series of mechanical stimulators 3a, 3b, 3c and 3d arranged to operate on the areas of the feet subjected to treatment. The first stimulator 3a operates on the tip of the right big toe; the second and the third stimulator 3b and 3c operate on areas beneath the sole of the feet corresponding to the lower metatarsal joint respectively of the right (stimulator 3b) and left (stimulator 3c) big toe. The
10 fourth stimulator 3d operates on the tip of the left big toe.

The control unit 4 commands the stimulators – in sequence – according to a predetermined treatment programme, which for example may be contained in an internal memory of the same control unit 4. The control unit 4 is also provided with at least one port 5 for communicating with the external
15 environment, according to a standard preferably selected from among the most common ones in the information technology industry (for example USB), so as to allow loading a treatment programme. Provided for in various embodiments may be ports even for remote connection, for example network plugs or equivalent connections according to the known art and the contingent
20 requirements.

An example of the actuation logic of the stimulators as a function of time t is given in Fig. 3. Each of the stimulators 3a – 3c comprises an actuator having a contact member, such as a rounded tip, capable of mechanically stimulating the foot. The intensity of the stimulation may be expressed in terms of force F
25 exerted by said actuator. In order to attain an effective outcome, such force must exceed a threshold F_s variable depending on the conditions of the patient, which must correspond to the pain or stimulus threshold, at which the patient shows an involuntary reflex of withdrawing the foot.

Curve A of Fig. 3 refers to the actuation of the first stimulator 3a having the task of stimulating the tip of the right big toes. The motor of the stimulator requires a transient time to attain the preset operating intensity, equivalent or slightly exceeding the threshold value F_s . Such intensity is maintained from a start of stimulus time t_i to an end of stimulus time t_f , for the duration of a single stimulus d typically amounting to a few seconds, for example 6 seconds.

The rising "ramp" of curve A corresponds to the time physically required by the actuator of the stimulator 3a to touch the tip of the big toe and attain the desired pressure. This time may for example amount to 1-2 seconds. At the end of treatment time, the stimulus intensity (curve A) decreases rapidly. Curve B shows the intervention of the subsequent stimulator according to the sequence preset for example in the stimulator 3b which operates on the area of the lower right big toe metatarsal joint. As can be seen, the stimulator 3b is preferably actuated slightly in advance (for example one second) with respect to the end of stimulus time stimulator 3a. Thus, the rising ramp of curve B is overlapped to the falling ramp of curve A, thus reducing absence of stimulus idle time t_m .

The same control logic is repeated when stimulators 3c and 3d intervene. The sequence is then repeated cyclically, for a variable number of cycles, for example 5-10 cycles. The overall duration of the treatment may thus amount to a few minutes, for example about 8-10 minutes.

One of the possible embodiments, is shown in Fig. 4 for indicative purposes. A device for applying the treatment to the right foot essentially comprises a base 11 for accommodating the foot, having a rear support 12 for accommodating the heel and a tiltable front support 13, for accommodating the toes. The rear support 12 is adjustable by making it slide into a slot 14 with respect to the base 11. The support 13 is pivoted to the sides 15 of the device, and it is tiltable for example between 0 and 90 degrees with respect to the support base 11 surface.

The stimulators 3a and 3c in the example are provided with actuators 16 and 17. The actuator 16 is fixed to the front support 13, and the actuator 17 is fixed beneath the base 11 and operates through an opening 18. Both actuators have an adjustable position through per se known means (for example stop screws).

5 Further characteristics, merely for exemplification purposes, are as follows. Each of the stimulators comprises a small electric motor with a rotating spindle which activates the respective actuator. The actuator is made up of a screw having an internal milling suitable to be accommodated over the spindle itself. The member intended to come into contact with the foot is obtained for example
10 from a solid bronze bar, with an internal threading suitable to engage the screw, and turned having a round-tipped end suitable to serve as a stimulator. The base of said bronze stimulator has two projections that serve as stop means, the entire assembly being guided by a Teflon guide which ensures that the actuator operates in an accurate and simple manner. The tip of the actuator
15 projects 0 to 20 mm from the containment cage.

It should be understood that the construction details may vary widely and thus they may be subjected to variations according to the applications of the known state of the art.

The treatment subject of the invention was applied to about 200 patients
20 affected by Parkinson's disease. The patients were treated by mechanically stimulating the areas of the right and left foot described previously above, following the a) b) c) d) sequence, each stimulus lasting about 5-6 seconds and with repetition of 5 cycles. All cases observed showed clear improvement of mobility with the duration of the effects varying between 2-3 days and about 7-
25 10 days depending on the patient and level of the disease progression.

CLAIMS

1. Method for treating mobility handicap in a patient affected by a neurodegenerative disease, comprising steps for controlled and localised mechanical stimulation of the foot, at a plurality of selected areas of the foot comprising at least the tip of the big toe and the lower big toe metatarsal joint, said method being implemented according to predetermined parameters comprising at least: a predetermined mechanical stimulation intensity, a predetermined sequence for stimulating said parts of the foot, a predetermined duration of each mechanical stimulation step, and optionally a repetition of said sequence.
2. Method according to claim 1, comprising steps for mechanically stimulating:
 - a) the tip of the right big toe;
 - b) an area beneath the sole of the left foot corresponding to the lower left big toe metatarsal joint;
 - c) an area beneath the sole of the right foot corresponding to the lower right big toe metatarsal joint;
 - d) the tip of the left big toe.
3. Method according to claim 2, wherein said mechanical stimulation steps are performed according to the following order a), b), c), d).
4. Method according to one of claims 1 to 3, wherein said mechanical stimulation steps comprise reaching an operating pressure or threshold pressure, corresponding to the patient feeling a stimulus.
5. Method according to claim 4, wherein each mechanical stimulation step is

operated by a respective contact member having a rounded or substantially spherical tip, having a diameter ranging between 1.5 to 2.5 mm, the force imparted to said contact member being comprised between 2 and 3.5 kg.

6. Method according to anyone of the preceding claims, wherein the mechanical stimulation steps have a substantially equivalent duration with respect to each other.

7. Method according to claim 6, wherein the mechanical stimulation steps have a duration in the range between 5 and 10 seconds.

8. Method according to anyone of the claims 4 to 7, wherein the mechanical stimulation steps are performed separately and in sequence, obtaining that at any time of the treatment, the mechanical stimulation be equivalent or greater than the operating pressure in only one of said areas of the body.

9. Method according to anyone of the claims 1 to 8, said neurodegenerative disease being the Parkinson's disease.

10. Apparatus (10) for mechanically stimulating the foot comprising at least one first mechanical stimulator (3a) arranged to operate, during use, on the tip of the big toe, and a second mechanical stimulator (3c) arranged to operate, during use, on an area localised beneath the sole of the foot and substantially corresponding to the lower big toe metatarsal joint; said apparatus further comprising a control system (4) suitable to actuate said mechanical stimulators according to a treatment programme comprising at least one mechanical stimulation intensity, a predetermined sequence for stimulating said parts of the foot, a predetermined duration of each mechanical stimulation step, and optionally a repetition of said sequence.

11. Apparatus according to claim 10, comprising a first mechanical stimulator (3a), a second mechanical stimulator (3b), a third mechanical stimulator (3c), a fourth mechanical stimulator (3d) wherein:

- said first mechanical stimulator (3a) is intended to operate, during use, on the tip of the right big toe of a patient;
- said second mechanical stimulator (3b) is intended to operate, during use, in an area beneath the sole of the left foot corresponding to the lower big toe metatarsal joint;
- said third mechanical stimulator (3c) is intended to operate, during use, in an area beneath sole of the right foot corresponding to the lower big toe metatarsal joint;
- said fourth mechanical stimulator (3d) is intended to operate, during use, on the tip of the left big toe;

and furthermore:

- the control system (4) is arranged for the actuation of said first, second, third and fourth stimulator (3a – 3d) according to said treatment programme.

12. Apparatus according to claim 11, wherein said control system (4) is arranged to obtain the actuation of said first, second, third and fourth stimulator in corresponding sequence.

13. Apparatus according to claim 11 or 12, wherein said control system is arranged to adjust the actuation of each of said stimulators to obtain a *predetermined threshold pressure*.

14. Apparatus according to claim 13, wherein said control system (4) is arranged to command said stimulators (3a – 3d) in sequence, in such a manner that said stimulators reach said threshold pressure in sequence, maintaining it for a predetermined period of time, and in such a manner that – at any time during the execution of a stimulation programme – only one of

said stimulators reaches said threshold pressure.

15. Apparatus according to claim 13 or 14, wherein each of said stimulators comprises a motor and linearly moving member for contact with the foot, said member having a tip for contact with the foot, said tip being rounded or substantially spherical.

16. Apparatus according to claim 15, said tip of the contact member having a diameter ranging between 1.5 and 2.5 mm, and said control system being arranged to adjust said motor to obtain a mechanical stimulation force between 2 and 3.5 kg.

17. Apparatus according to one of claims 10 to 16, wherein said control system (4) comprises at least a one-way or two-way data communication port (5).

18. Apparatus according to anyone of the claims 10 to 17, comprising a first device (1) for treating the right foot and a second device for treating the left foot, said first (3a) and said third stimulator being associated to the first device (1), and said second (3b) and fourth (3d) stimulator being associated to the second device.

19. Apparatus according to claim 18, wherein each of said first and second device comprises a base (11) for accommodating the foot, having an adjustable rear support (12) for accommodating the heel and a tiltable front support (13), for accommodating the toes.

20. A method for controlling an apparatus (10) for mechanically stimulating the foot according to one of claims 10 to 18, said method comprising the steps of activating said apparatus to mechanically stimulate:

a) the tip of the right big toe:

- b) an area beneath the sole of the left foot corresponding to the lower left big toe metatarsal joint;
- c) an area beneath the sole of the right foot corresponding to the lower right big toe metatarsal joint;
- 5 d) the tip of the left big toe;

according to treatment parameters comprising at least one predetermined mechanical stimulation intensity, a predetermined sequence for stimulating said parts of the foot, a predetermined duration of each mechanical stimulation step, and optionally a repetition of said sequence.

- 10 21. A method according to claim 20, wherein said sequence is sequence a) – b) – c) – d).