(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
11 March 2010 (11.03.2010)

PCT

(10) International Publication Number
WO 2010/027266 A1

(51) International Patent Classification:
A61K 31/197 (2006.01) *A61P 25/00* (2006.01)
A61K 31/198 (2006.01) *A61P 25/08* (2006.01)
A61K 31/4415 (2006.01)

(21) International Application Number:
PCT/NL2009/050535

(22) International Filing Date:
4 September 2009 (04.09.2009)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
08163730.8 5 September 2008 (05.09.2008) EP

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

(54) **Title**: MEANS AND METHODS FOR COUNTERACTING NEUROLOGICAL DISORDERS

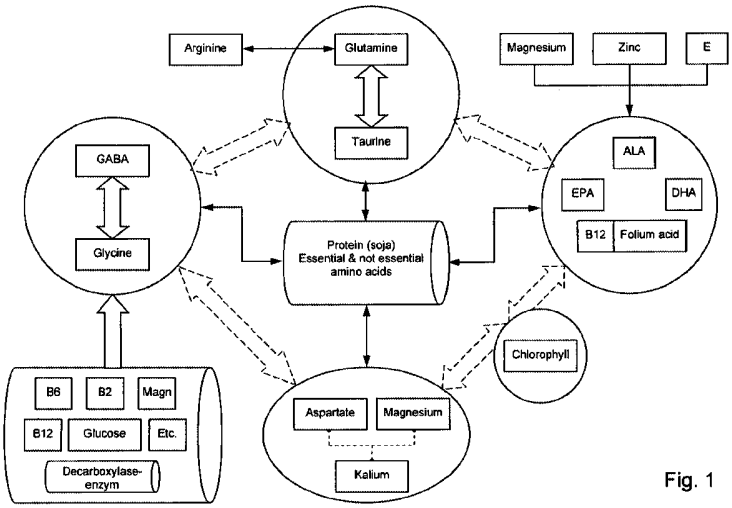

Fig. 1

(57) **Abstract**: The invention provides means and methods for treating neurological disorders, and/or alleviating at least one symptomof a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, brain systems,nerve cellsand/or nerve systems. Drug combinations are provided which appear to be more effective then current treatments.

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Title: Means and methods for counteracting neurological disorders

The invention relates to the fields of biology and medicine. More particularly, the invention relates to neurological disorders.

The term "neurological disorder" involves impaired function of brain cells, impaired function of nerve cells and/or impaired transmission of neurological impulses. It embraces a wide variety of disorders of the nervous system.

The nervous system is a network of specialized nerve cells that conduct impulses from or to areas of the body to the brain and spinal cord and within the brain. It is composed of neurons and other specialized cells, like glial cells and neuroglia, that aid in the function of the neurons. Nerve cells are interconnected in complex arrangements and use electrochemical signals to transmit impulses between cells, they respond to a great variety of stimuli and form neural circuits that regulate an organism's perception and behavior. The nervous system is connected into many systems that function together.

The human nervous system can be grouped into the central nervous system, the peripheral nervous system and the autonomic nervous system.

The central nervous system (CNS) of vertebrates contains the majority of the nervous system, and consists of the brain (in vertebrates which have brains), and the spinal cord (which is a long, thin, tubular bundle of nerves that is an extension of the central nervous system from the brain and is enclosed in and protected by the bony vertebral column. The CNS is contained within the dorsal cavity, with the brain within the cranial cavity, and the spinal cord in the spinal cavity. The CNS is covered by the meninges. The brain is also protected by the skull, and the spinal cord is also protected by the vertebrae. The main function of the spinal cord is transmission of neural inputs between the periphery and the brain). The central nervous system has, together with the peripheral nervous system, a fundamental role in the control of behavior.

The peripheral nervous system (PNS) resides or extends outside the central nervous system (CNS), to serve the limbs and organs. Unlike the central nervous system, however, the PNS is not protected by bone, leaving it exposed to mechanical injuries.

The autonomic nervous system (ANS), also called visceral nervous system, is the part of the peripheral nervous system that acts as a control system in the body. The activities of the ANS are generally performed without conscious control or sensation. The ANS for instance affects heart rate, digestion, respiration rate, salivation, perspiration and the diameter of the pupils. Whereas most of its actions are involuntary, some, such as breathing, work in tandem with the conscious mind.

Vertebrate brains are extremely complex. For example, the human brain contains roughly 100 billion neurons, linked with up to 10,000 connections each. The brain is composed of two broad classes of cells, neurons and glia, both of which contain several different cell types which perform different functions. Interconnected neurons form neural networks (or neural ensembles). These networks are similar to man-made electrical circuits in that they contain circuit elements (neurons) connected by biological wires (nerve fibers). These do not form simple one-to-one electrical circuits like many man-made circuits, however. Typically neurons connect to at least a thousand other neurons. These highly specialized circuits make up systems which are the basis of perception, different types of action, and higher cognitive function. Neurons are the cells that convey information to other cells; these constitute the essential class of brain cells. Neurons are electrically excitable cells in the nervous system that process and transmit information. Neurons are the core components of the brain, the vertebrate spinal cord, the invertebrate ventral nerve cord, and the peripheral nerves. A number of different types of neurons exist: sensory neurons respond to touch, sound, light and numerous other stimuli effecting sensory organs and send signals to the spinal cord and brain, motor neurons receive signals from the brain and spinal cord and cause muscle contractions and effect glands, Interneurons connect neurons to other neurons with in the brain and spinal cord.

In addition to neurons, the brain contains glial cells in a roughly 10:1 proportion to neurons. Glial cells are non-neuronal cells that provide support and nutrition, maintain homeostasis, form myelin, and participate in signal transmission

in the nervous system. Glial cells ("glia" is Greek for “glue”) provide support and protection for neurons. They are thus known as the "glue" of the nervous system. The four main functions of glial cells are to surround neurons and hold them in place, to supply nutrients and oxygen to neurons, to insulate one neuron from another, and to destroy pathogens and remove dead neurons. Glial cells create the insulating myelin, provide structure to the neuronal network, manage waste, and clean up neurotransmitters. Most types of glia in the brain are present in the entire nervous system. Exceptions include the oligodendrocytes which myelinate neural axons (a role performed by Schwann cells in the peripheral nervous system). The myelin in the oligodendrocytes insulates the axons of some neurons. White matter in the brain is myelinated neurons, while gray matter contains mostly cell soma, dendrites, and unmyelinated portions of axons and glia. The space between neurons is filled with dendrites as well as unmyelinated segments of axons; this area is referred to as the neuropil.

The junction between two neurons is called a synapse. There is a very narrow gap (about 20nm in width) between neurons which is called the synaptic cleft, where an action potential is transmitted from one neuron to a neighboring one. They do this by relaying the message with the use of neurotransmitters which the next neuron then receives, known as a nerve impulse. The nerve impulse is determined by the neurotransmitter which carries the message to its appropriate destination. These nerve impulses are a change in ion balance in the nerve cell, which the nervous system then interprets. The fact that the nervous system uses a mixture of electrical and chemical signals makes it incredibly fast, which is necessary to acknowledge the presence of danger such as, for example, a hand touching a hot stove. If the nervous system was only comprised of chemical signals, the body would not tell the arm to move fast enough to escape dangerous burns. So the speed of the nervous system is a necessity for life.

In mammals, the brain is surrounded by connective tissues called the meninges, a system of membranes that separate the skull from the brain. This three-layered covering is composed of (from the outside in) the dura mater, arachnoid mater, and pia mater. The arachnoid and pia are physically connected and thus often

considered as a single layer, the pia-arachnoid. Below the arachnoid is the subarachnoid space which contains cerebrospinal fluid, a substance that protects the nervous system. Blood vessels enter the central nervous system through the perivascular space above the pia mater. The cells in the blood vessel walls are joined tightly, forming the blood-brain barrier which protects the brain from toxins that might enter through the blood. Hypersensitivity of the dura mater and/or the pia mater results in various neurological symptoms, such as for instance seizures as a result of temperature changes. The symptoms are partly similar to Hydrocephalus. Hydrocephalus can be caused by impaired cerebrospinal fluid (CSF) flow, reabsorption, or excessive CSF production. When disorders of CSF flow occur, they may therefore affect not only CSF movement, but also the intracranial blood flow, with subsequent neuronal and glial vulnerabilities. The venous system is also important in this equation. There is some relationship between CSF disorders, including hydrocephalus and impaired CSF lymphatic transport. An individual suffering from hydrocephalus may have motivation and visual problems, problems with coordination, and may be clumsy. About one in four develops epilepsy.

The brain is bathed in CSF, which circulates between layers of the meninges and through cavities in the brain called ventricles. It is important both chemically for metabolism and mechanically for shock-prevention. For example, the human brain weighs about 1-1.5 kg or about 2-3 lb. The mass and density of the brain are such that it will begin to collapse under its own weight if unsupported by the CSF. The CSF allows the brain to float, easing the physical stress caused by the brain's mass.

Vertebrate brains receive signals through nerves arriving from the sensors of the organism. These signals are then processed throughout the central nervous system; reactions are formulated based upon reflex and learned experiences. A similarly extensive nerve network delivers signals from a brain to control important muscles throughout the body. Anatomically, the majority of afferent and efferent nerves (with the exception of the cranial nerves) are connected to the spinal cord, which then transfers the signals to and from the brain.

Sensory input is processed by the brain to recognize danger, find food, identify potential mates, and perform more sophisticated functions. Visual, touch, and

auditory sensory pathways of vertebrates are routed to specific nuclei of the thalamus and then to regions of the cerebral cortex that are specific to each sensory system, the visual system, the auditory system, and the somatosensory system. Olfactory pathways are routed to the olfactory bulb, then to various parts of the olfactory system. Taste is routed through the brainstem and then to other portions of the gustatory system.

To control movement the brain has several parallel systems of muscle control. The motor system controls voluntary muscle movement, aided by the motor cortex, cerebellum, and the basal ganglia. The system eventually projects to the spinal cord and then out to the muscle effectors. Nuclei in the brain stem control many involuntary muscle functions such as heart rate and breathing. In addition, many automatic acts (simple reflexes, locomotion) can be controlled by the spinal cord alone.

Brains also produce a portion of the body's hormones that can influence organs and glands elsewhere in a body—conversely, brains also react to hormones produced elsewhere in the body. In mammals, the hormones that regulate hormone production throughout the body are produced in the brain by the structure called the pituitary gland.

Evidence strongly suggests that developed brains derive consciousness from the complex interactions between the numerous systems within the brain. Cognitive processing in mammals occurs in the cerebral cortex but relies on midbrain and limbic functions as well. Among "younger" (in an evolutionary sense) vertebrates, advanced processing involves progressively rostral (forward) regions of the brain.

Hormones, incoming sensory information, and cognitive processing performed by the brain determine the brain state. Stimulus from any source can trigger a general arousal process that focuses cortical operations to processing of the new information. This focusing of cognition is known as attention. Cognitive priorities are constantly shifted by a variety of factors such as hunger, fatigue, belief, unfamiliar information, or threat. The simplest dichotomy related to the processing of threats is the fight-or-flight response mediated by the amygdala and other limbic structures.

Neurological disorders are disorders that affect the central nervous system, the peripheral nervous system, and/or the autonomic nervous system. Neurological disorders involve a wide variety of different conditions. Non-limiting examples include

muscle spasms and cramps, paralysis, dystrophy, dystonia, ataxia, behavioral/cognitive syndromes, headache disorders such as migraine, cluster headache and tension headache, epilepsy, traumatic brain injury, whiplash, neurodegenerative disorders, including Alzheimer's disease and Parkinson's disease, cerebrovascular disease, such as transient ischemic attack and stroke, sleep disorders, cerebral palsy, movement disorders, demyelinating diseases of the central nervous system, such as multiple sclerosis (MS), and demyelinating diseases of the peripheral nervous system, such as Guillain-Barré syndrome and chronic inflammatory demyelinating polyneuropathy (CIDP), spinal cord disorders caused by trauma, disorders of peripheral nerves, muscle disorders (myopathy), disorders of neuromuscular junctions, exciting injuries to the brain, spinal cord and peripheral nerves, altered mental higher status, and speech and language disorders.

Current treatments of neurological disorders, which are often directed at suppressing the symptoms of the disease rather than curing the underlying cause, for instance include drugs against epileptic seizures, cramps and/or spasms such as carbamazepine, phenytoin, quinine and Baclofen, and surgery such as vagus nerve stimulation. However, the symptoms of various neurological conditions can be counteracted to a limited extent only. Patients often have to accept impaired mental and/or physical capabilities and a decreased quality of life.

It is an aim of the present invention to provide alternative and/or improved therapies against neurological disorders.

The present inventor has developed therapies which are capable of alleviating neurological disorder-related symptoms such as, preferably, symptoms of myelin damage-related disorders, whiplash, dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS). Moreover, said therapies are capable of restoring sense and motion, demonstrating that the therapies according to the present invention are also capable of inducing and/or enhancing the repair and/or production of myelin, brain cells, brain systems, nerve cells and/or nerve

systems. The present inventor has developed novel combinations of medicaments which appear to be more effective then current treatments. The present invention provides the insight that neurological disorders are particularly well treated by increasing the glycine level and increasing the gamma amino butyric acid (GABA) level in an individual suffering from such neurological disorder. One aspect of the invention therefore provides a method for treating a neurological disorder, and/or alleviating at least one symptom of a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, at least one brain system, nerve cells and/or at least one nerve system, comprising increasing the glycine level and the GABA level in an individual in need thereof. Preferably, the vitamin B6 level in said individual is increased as well in order to obtain even better results. In one embodiment, said glycine level and said GABA level are increased by administering to said individual a therapeutically effective amount of glycine and GABA (or an analogue or metabolite thereof, preferably Baclofen).

Said individual is preferably a human individual. Before the present invention, a combination of glycine (especially at a high dose of at least 20 mg/kg/day) and GABA (or an analogue or metabolite of GABA) has never been administered to human individuals because severe side effects were feared, as explained in more detail below. According to the present invention, however, such combination does not involve unacceptable side effects. Contrary, beneficial results are obtained.

One aspect of the present invention thus provides a combination comprising glycine, or an analogue or metabolite thereof, and gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, which analogue or metabolite of GABA is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell. Said GABA analogue preferably comprises 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen). According to the present invention a high glycine dosage of at least 20 mg/kg/day is preferably used in order to obtain particularly good results.

Glycine (abbreviated as Gly or G) with the formula NH_2CH_2COOH is the smallest of the 20 amino acids commonly found in proteins. Because it has specialized structural properties in protein architecture, this compact amino acid is often evolutionarily conserved. For example, cytochrome c, myoglobin, and hemoglobin all contain conserved glycines. Glycine is the only natural amino acid that is not chiral.

Most proteins contain only small quantities of glycine. A notable exception is collagen, which contains about 35% glycine. In its solid, i.e., crystallized, form, glycine is a free-flowing, sweet-tasting crystalline material.

Glycine is an inhibitory neurotransmitter in the central nervous system, especially in the spinal cord, brainstem, and retina. When released into a synapse, glycine binds to a receptor of an adjacent nerve cell (neuron). When glycine receptors are activated, chloride enters the neuron via ionotropic receptors. As a result, the membrane of said neuron becomes more permeable to chloride ions and the membrane is hyperpolarized, causing an inhibitory postsynaptic potential (IPSP).

As a result, said neuron is less likely to fire. Hence, undesired impulses are counteracted. Glycine is currently prescribed against spasms and MS. According to some studies it may have anti-psychotic and anti-schizophrenia activity as well. It is known to readily cross the blood-brain barrier and can therefore be given orally.

According to one aspect according to the present invention, glycine (or an analogue or metabolite thereof) is combined with gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite of GABA is capable of specifically binding a GABA receptor of a brain cell or nerve cell. GABA is the chief inhibitory neurotransmitter in the mammalian central nervous system. It plays an important role in regulating neuronal excitability throughout the nervous system. GABA is also directly responsible for the regulation of muscle tone.

In spastic cerebral palsy in humans, GABA cannot be absorbed properly by damaged nerve rootlets corresponding to affected muscles, which leads to hypertonia in those muscles. Disrupted GABAergic signaling has been implicated in numerous and varied neurological and psychiatric pathologies including movement and anxiety disorders, epilepsy, schizophrenia, and addiction.

In vertebrates, GABA acts at inhibitory synapses in the brain by binding to specific transmembrane receptors in the plasma membrane during both pre- and postsynaptic neuronal processes. This binding causes the opening of ion channels to allow the flow of either negatively-charged chloride ions into the cell or positively-charged potassium ions out of the cell. This action results in a negative change in the transmembrane potential, usually causing hyperpolarization. Three general classes of

GABA receptors are known: $GABA_A$ and $GABA_C$ ionotropic receptors, which are ion channels themselves, and $GABA_B$ metabotropic receptors, which are G protein-coupled receptors that open ion channels via intermediaries (G proteins).

Neurons that produce GABA as their output are called GABAergic neurons, and have chiefly inhibitory action at receptors in the adult vertebrate. Medium Spiny Cells are a typical example of inhibitory CNS GABAergic cells. In the hippocampus and neocortex of a mammalian brain, GABA has primarily excitatory effects early in development, and is in fact the major excitatory neurotransmitter in many regions of the brain prior to the maturation of glutamate synapses

Organisms synthesize GABA from glutamate using the enzyme L-glutamic acid decarboxylase and using pyridoxal phosphate as a cofactor. It is worth noting that this process converts the principal excitatory neurotransmitter (glutamate) into the principal inhibitory one (GABA).

Since GABA barely crosses the blood-brain barrier, it is normally synthesized in the brain. Drugs that act as agonists of GABA (also called herein GABA analogues or GABA agonists) typically have relaxing, anti-anxiety and anti-convulsive effects. One preferred GABA analogue, known in the art, is 4-amino-3-(4-chlorophenyl)-butanoic acid. This drug is called Baclofen. Baclofen is prescribed as a muscle relaxant and antispasticity agent. Like GABA, Baclofen does not readily cross the blood-brain barrier. Therefore, Baclofen is preferably administered directly into the intrathecal space surrounding the spinal cord.

Baclofen (brand names are also Kemstro and Lioresal) affects the spinal cord, which is the main connection between the brain and the rest of the body. The spinal cord plays a role as a reflex system that functions as a feedback loop. In a natural situation, GABA slows this reflex circuit down. Baclofen mimics these effects of GABA. The dose of intrathecal Baclofen necessary to slow down the reflex circuit is variable but is generally one thousand times (three orders of magnitude) smaller than the oral dose of Baclofen.

Baclofen is a direct agonist of $GABA_B$ receptors, which upon activation utilize a G-protein coupled mechanism to increase transmembrane potassium conductance

through specific ion channels. Since potassium has a positive charge, and since intracellular potassium concentrations are normally at least ten times that of the extracellular environment, opening potassium channels has an inhibitory, hyperpolarizing effect on a cell's resting electrochemical potential. This tends to decrease the rate of neuronal action potentials, which accounts for Baclofen's anti-spastic effects.

According to a preferred embodiment according to the present invention, intrathecal Baclofen is used in combination with oral glycine. In a particularly preferred embodiment, intrathecal Baclofen is used in combination with oral glycine and vitamin B6 (or an analogue or metabolite of any of these compounds).

Although both glycine and GABA are well known transmitters for the nerve system a combination of glycine and Baclofen has not been administered to human individuals before the present invention. Until the present invention, severe adverse side effects were feared, especially when Baclofen is administered intrathecally (the effect is generally one thousand times bigger as compared to oral administration) and especially when a high dosage of glycine is used. Adverse effects of a combination of glycine and Baclofen were feared.

The present inventor, however, who is himself diagnosed with complex regional pain syndrome (CRPS) involving whiplash, epileptic seizures, dystrophy, dystonia, muscle spasms and cramps, paralysis, ataxia and hypersensitivity, has provided the insight that a combination comprising glycine and Baclofen, preferably in combination with vitamin B6 (or analogues or metabolites thereof) surprisingly well alleviates symptoms of neurological disorders without severe side effects. As described in more detail in the Example, after the inventor underwent intrathecal administration of Baclofen and oral administration of glycine and vitamin B6 his condition improved significantly. The number and duration of his epileptic seizures diminished and he regained his capability of moving his toes, feet and legs.

After treatment during one and a halve (1 ½) year with oral Baclofen, with a follow up of four and a halve (4 ½) years of treatment with intrathecal Baclofen,

glycine and vitamin B6, the administration of Baclofen was discontinued due to a defect of the pump for intrathecal administration. According to the present invention, however, a combination comprising glycine and vitamin B6 (or analogues or metabolites thereof) has the same kind of positive effects (in kind, not necessarily in amount) and gives a proper follow up after a combination comprising Baclofen, glycine and vitamin B6, since the inventor retained his capability of moving his toes, feet and legs while the number and duration of his epileptic seizures remained diminished as compared to his situation before administration of any of the above mentioned combinations.

Accordingly, in one aspect the invention provides a method for treating a neurological disorder, and/or alleviating at least one symptom of a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, nerve cells, at least one brain system and/or at least one nerve system, comprising administering to an individual in need thereof:

- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell. This combination preferably also comprises a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof. Said analogue of GABA preferably comprises 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen).

In one particularly preferred embodiment a combination comprising Baclofen, glycine and vitamin B6 is used. Further provided is therefore a method for treating a neurological disorder, and/or alleviating at least one symptom of a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, nerve cells, at least one brain system and/or at least one nerve system, comprising administering to an individual in need thereof a therapeutically effective amount of:

- glycine, or an analogue or metabolite thereof, and
- vitamin B6, or an analogue or metabolite thereof, and
- Baclofen, or an analogue or metabolite thereof.

As stated before, after initial treatment with said combination, it is possible to discontinue the administration of Baclofen while maintaining positive therapeutic effects.

Also provided is a combination comprising glycine, or an analogue or metabolite thereof, and gamma amino butyric acid (GABA) or an analogue or metabolite of GABA (preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen)) which analogue is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell. Said combination preferably also comprises vitamin B6, or an analogue or metabolite thereof. One preferred embodiment of the present invention provides a combination comprising glycine, or an analogue or metabolite thereof, and vitamin B6, or an analogue or metabolite thereof, and Baclofen, or an analogue or metabolite thereof. These combinations are particularly suitable for counteracting neurological disorders and/or the symptoms thereof. Furthermore provided is therefore a combination as mentioned above for use as a medicament.

The above mentioned combinations are particularly suitable for the preparation of a medicament. Also provided is therefore a use of a combination comprising glycine, or an analogue or metabolite thereof and gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, which analogue is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, for the preparation of a medicament, a combination of medicaments, or a kit of parts for treating a neurological disorder, and/or alleviating the symptoms of a neurological disorder, and/or inducing or enhancing the repair or production of myelin, brain cells, at least one brain system, nerve cells and/or at least one nerve system. As said before, said GABA analogue preferably comprises 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen). Said combination preferably also comprises vitamin B6, or an analogue or metabolite thereof.

As used herein, the term “treating a neurological disorder” comprises counteracting a neurological disorder. Hence, complete recovery is not necessary as long as a patient’s status is improved. A neurological disorder is defined herein as a

disorder of the central, peripheral, and/or autonomic nervous system, involving impaired function of brain cells, impaired function of nerve cells and/or impaired transmission of neurological impulses. When an individual suffers from a neurological disorder, signal transmission between at least some brain cells and/or nerve cells is at least in part impaired or increased as compared to a natural, healthy situation. As used herein, a neurological order is preferably a disorder involving damage of myelin, damage of brain cells, damage of nerve cells, damage of a brain system, damage of a nerve system, death of brain cells, a decrease of brain cells, death of nerve cells and/or a decrease of nerve cells.

Said neurological disorder most preferably comprises a whiplash, a myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS).

Hence, one embodiment of the invention provides a method for treating whiplash, myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS), comprising administering to an individual in need thereof:

- a therapeutically effective amount of glycine, or an analogue or metabolite thereof (preferably in combination with a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof), and a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell. In one particularly preferred embodiment a combination comprising glycine, vitamin B6 and Baclofen is administered to said individual. Subsequently, after positive therapeutic effects have been achieved, the administration of Baclofen is optionally discontinued.

Also provided is a use of

- a therapeutically effective amount of glycine, or an analogue or metabolite thereof

(preferably in combination with a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof), and a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell for the preparation of a combination of medicaments or a kit of parts for treating a whiplash, a myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS). In one particularly preferred embodiment a combination comprising glycine, vitamin B6 and Baclofen is used for the preparation of said combination of medicaments or said kit of parts. All of the above mentioned conditions improved after administration of glycine in combination with Baclofen and vitamin B6 to the present inventor. Even after subsequent discontinuation of Baclofen the symptoms remained alleviated. In another preferred embodiment, a combination comprising glycine, vitamin B6 and Baclofen is used for the preparation of a combination of medicaments or a kit of parts for treating multiple sclerosis. Symptoms of MS are also alleviated by a combination according to the invention.

Dystonia (or muscle dystonia) is defined as any disorder involving abnormal muscle tone of one or more muscles and/or muscle spasms. Dystonia is a neurological movement disorder in which sustained muscle contractions cause twisting and/or repetitive movements and/or abnormal postures. The disorder may be inherited or caused by other factors such as birth-related or other physical trauma, infection, poisoning (eg. lead poisoning) or reaction to drugs.

The causes of dystonia are not yet known or understood; however, they are categorized as follows on a theoretical basis:

Primary dystonia is suspected to be caused by a pathology of the central nervous system, likely originating in those parts of the brain concerned with motor function, such as the basal ganglia, and the GABA producing Purkinje neurons. The precise cause of primary dystonia is unknown. In many cases it may involve some genetic predisposition towards the disorder combined with environmental conditions.

Secondary dystonia refers to dystonia brought on by some identified cause, usually involving brain damage, or by some unidentified cause such as chemical imbalance. Some cases of (particularly focal) dystonia are brought on after trauma, are induced by certain drugs (tardive dystonia), or may be the result of diseases of the nervous system such as Wilson's disease.

(Muscle) dystrophy is defined herein as at least partial degeneration of at least one muscle. (Muscle) dystrophy may have various causes. As used herein, the term "muscle dystrophy" is defined as a muscle dystrophy involving a neurological disorder, preferably muscle dystrophy associated with and/or resulting from brain damage and/or nerve damage and/or myelin damage.
Complex Regional Pain Syndrome (CRPS) is a chronic progressive neurological disease characterized by severe pain, swelling and changes in the skin. The cause of this syndrome is currently unknown. Precipitating factors include illness, injury and surgery, although there are documented cases that have no documentable injury to the original site.

As used herein, the term "brain system" refers to distinct systems formed by neurons which express a certain type of neurotransmitter. Neurons expressing certain types of neurotransmitters form distinct systems which are called brain systems or neurotransmitter systems. Activation of a brain system causes effects in large volumes of the brain, called volume transmission.

Major brain systems are the noradrenaline (norepinephrine) system, the dopamine system, the serotonin system and the cholinergic system. Drugs targeting the neurotransmitter of such systems affects the whole system, which explains the mode of action of many drugs. Cocaine, for example, blocks the reuptake of dopamine, leaving these neurotransmitters in the synaptic gap longer. Prozac is a selective serotonin reuptake inhibitor (SSRI), hence potentiating the effect of naturally released serotonin. Diseases may affect specific brain systems. For example, Parkinson's disease is at least in part related to failure of dopaminergic cells in deep-brain nuclei, for example the substantia nigra. Treatments potentiating the effect of dopamine precursors have been proposed and effected, with moderate success.

Table 1 shows a brief comparison of the major brain systems:

Table 1

Brain systems		
System	Origin	Effects
Noradrenaline system	locus coeruleus	• arousal • reward
	lateral tegmental field	
Dopamine system	dopamine pathways: • mesocortical pathway • mesolimbic pathway • nigrostriatal pathway • tuberoinfundibular pathway	motor system, reward, cognition, endocrine, nausea
Serotonin system	caudal dorsal raphe nucleus	Increase introversion, mood, satiety, body temperature and sleep, while decreasing nociception.
	rostral dorsal raphe nucleus	
Cholinergic system	pontomesencephalotegmental complex	• learning • short-term memory • arousal • reward
	basal optic nucleus of Meynert	
	medial septal nucleus	

The term "nerve system" is defined herein as the CNS, PNS or ANS.

As used herein, the term "vitamin B6" embraces a group of closely related chemical compounds with related names - non limiting examples include pyridoxine, pyridoxal and pyridoxamine - that are transformed within the body to yet another form of vitamin B6, pyridoxal phosphate that acts as a coenzyme.

Vitamin B6 is a water-soluble vitamin. Pyridoxal phosphate (PLP) is the active form and is a cofactor in many reactions of amino acid metabolism, including transamination, deamination, and decarboxylation. PLP also is necessary for the enzymatic reaction governing the release of glucose from glycogen.

Vitamin B6 was discovered in the 1930s during nutrition studies on rats. The vitamin was named pyridoxine to indicate its structural homology to pyridine. Later it was shown that vitamin B6 could exist in two other, slightly different, chemical forms, termed pyridoxal and pyridoxamine. All three forms of vitamin B6 are precursors of an activated compound known as pyridoxal 5'-phosphate (PLP), which plays a vital role as a cofactor of a large number of essential enzymes in the human body. As used herein, the term "vitamin B6" encompasses pyridoxine, pyridoxal, pyridoxamine and pyridoxal 5'-phosphate (PLP).

Enzymes dependent on PLP focus a wide variety of chemical reactions mainly involving amino acids. The reactions carried out by the PLP-dependent enzymes that act on amino acids include transfer of the amino group, decarboxylation, racemization, and beta- or gamma-elimination or replacement. Such versatility arises from the ability of PLP to covalently bind a substrate, and then to act as an electrophilic catalyst, thereby stabilizing different types of carbanionic reaction intermediates.

Vitamin B6 is especially important to the function of the central nervous system, skin, and blood. As used herein, the term "vitamin B6" also encompasses analogues and metabolites of vitamin B6. Such analogues are capable of performing the same function as vitamin B6 in kind, not necessarily in amount. A non-limiting example of an analogue of vitamin B6 is pyridoxal phosphate with a substitution so that the overall function is not seriously affected.

A metabolite of a compound is defined herein as either a molecule which is formed when said compound is processed *in vivo*, or a substance which, after processing *in vivo*, results in the formation of said compound. After administration of a substance such as for instance a prodrug to an animal, said substance is sometimes

altered within said animal. Said substance is for instance cleaved, resulting in the therapeutically active drug of interest. As another example said substance is modified by conjugation with an endogenous molecule such as for instance glucuronic acid, glutathione and/or sulfate. A metabolite resulting from such modification may subsequently be cleaved, and/or a cleavage product may subsequently be modified.

As used herein, a metabolite of vitamin B6 is defined as any compound which, after processing *in vivo*, results in the formation of pyridoxal phosphate.

In a particularly preferred embodiment, a method according to the invention further comprises administering to said individual a therapeutically effective amount of glutamine and/or arginine and/or taurine.

According to the present invention, a combination comprising: 1) glycine or an analogue or metabolite thereof, and 2) Vitamin B6, or an analogue or metabolite thereof and 3) GABA or a GABA analogue or metabolite such as Baclofen and 4) at least one compound chosen from the group consisting of glutamine and arginine and taurine, provides improved results in treating a neurological disorder, and/or alleviating the symptoms of a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, nerve cells, at least one brain system and/or at least one nerve system. The same holds true for a combination comprising 1) glycine and 2) vitamin B6 and 3) at least one compound chosen from the group consisting of glutamine and arginine and taurine. In one embodiment, a combination comprising glycine and vitamin B6 and at least one compound chosen from the group consisting of glutamine and arginine and taurine is used after initial therapy comprising said combination and Baclofen. Of course, any of these compounds may be replaced by therapeutically effective analogues and/or metabolites thereof.

Glutamine is a precursor of GABA and has an anti-depressive effect. Glutamine is the most abundant naturally occurring, non-essential amino acid in the human body and one of the few natural amino acids which are capable of directly crossing the blood-brain barrier. In the body it is circulating in the blood as well as stored in skeletal muscles.

Glutamine and glutamate are both used for the production of GABA in the brain.

Glutamine has a variety of biochemical functions. It is a substrate for DNA synthesis and plays a major role in protein synthesis. It is also a primary source of fuel for enterocytes (cells lining the inside of the small intestine). Glutamine is furthermore a precursor for rapidly dividing immune cells, thus aiding in immune function. Glutamine is also involved with regulation of acid-base balance in the kidney by producing ammonium. It is an alternative source of fuel for the brain and helps to block cortisol-induced protein catabolism.

The present inventor has shown that addition of glutamine to anti-neurological disorder therapy provides improved results. The number and duration of his epileptic seizures even further diminished and his movement capabilities improved. Glutamine is advantageous because of his blood/brain crossing capacity and because it is a natural ingredient that the brain uses for forming a natural GABA. Furthermore, without wishing to be bound to theory, the inventor believes that neurological disorders mentioned herein before involve a huge deficiency of several natural c.q. ortomolecular compounds such as glutamine. Long term shortage of such compounds results in a generalized or specific deregulation of the brain and triggers seizures. Glutamine has a positive effect on epileptic and dystonic seizures, especially in combination with taurine (explained in more detail below). According to the present invention, glutamine and taurine are forming a cluster, meaning that they enhance each other's effects when present in certain ratio, and are therefore preferably used in a fixed ratio. The ratio glutamine:taurine is preferably between 1:1 and 4:1, more preferably about 2:1 – 3:1, when both glutamine and taurine are administered via the same route of administration, preferably via oral administration. Said cluster effect has increased benefits to reduction of the seizures and also on regaining of movement capabilities, reflexes etc. If glutamine is combined with at least two compounds selected from the group consisting of glycine, GABA (or Baclofen) and vitamin B6, the regaining of neurological functions improves rapidly. Preferably, taurine is used as well.

A minimal oral dosage of 20 mg/kg/day glutamine stimulates the production of hormones which has a positive effect on forming of GABA.

Administration of glutamine has an extra benefit because the (human) body is capable of forming arginine from glutamine. Arginine is classified as a semi essential

or conditionally essential amino acid, depending on the developmental stage and health status of the individual. Arginine is firstly oxidized into N-hydroxyl-arginine, which is then further oxidized to citrulline concomitant with release of nitric oxide. Proteins that normally contain citrulline residues include myelin basic protein (MBP). Therefore, arginine is also beneficial for improving neurological conditions. In one embodiment, therefore, arginine is administered to an individual as well, either in combination with glutamine or in place of glutamine. The ratio arginine:taurine is preferably between 1:1 and 4:1, more preferably about 2:1 – 3:1 when both arginine and taurine are administered via the same route of administration, preferably via oral administration.

Further provided is therefore a method for treating a neurological disorder, and/or alleviating at least one symptom of a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, nerve cells, at least one brain system and/or at least one nerve system, comprising administering to an individual in need thereof:

- a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine and/or arginine, or an analogue or metabolite thereof, and
- preferably, a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof.

Also provided is a combination comprising:

- a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and

- a therapeutically effective amount of glutamine and/or arginine, or an analogue or metabolite thereof, and
- preferably, a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof.

The above mentioned combination for use as a medicament is also provided. In one embodiment, said combination is used for the preparation of a combination of medicaments (kit of parts) for treating a neurological disorder, and/or alleviating the symptoms of a neurological disorder, and/or inducing or enhancing the repair or production of myelin, brain cells, at least one brain system, nerve cells and/or at least one nerve system. Of course any of the above mentioned compounds may be replaced by therapeutically effective analogues and/or metabolites thereof.

Said neurological disorder preferably comprises at least one of the conditions as described herein before. Moreover, the use of glycine, glutamine and/or arginine, vitamin B6 and Baclofen is preferred. One particularly preferred embodiment of the invention therefore provides a method for treating whiplash, myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS), comprising administering to an individual in need thereof:

- a therapeutically effective amount of 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), and
- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine and/or arginine, and
- preferably, a therapeutically effective amount of vitamin B6.

The inventor has shown that the beneficial effects are also experienced when the Baclofen is subsequently omitted. Further provided is therefore a method for treating whiplash, myelin damage-related disorder, muscle dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS), comprising administering to an individual in need thereof:

- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine and/or arginine, and
- a therapeutically effective amount of vitamin B6.

Said individual has preferably been treated with Baclofen before the above mentioned treatment.

Also provided is a combination comprising
- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine and/ or arginine, and
- a therapeutically effective amount of vitamin B6 and
- optionally, a therapeutically effective amount of 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen). The above mentioned combination for use as a medicament is also provided. Said combination is preferably used for the preparation of a combination of medicaments (kit of parts) for treating whiplash, myelin damage-related disorder, muscle dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS).

Of course, any of these compounds may be replaced by therapeutically effective analogues and/or metabolites thereof.

In yet another preferred embodiment, taurine is used. Taurine is a non-protein amino acid. It is an end product of cysteine-metabolism and the principal free intracellular amino acid in many tissues. Taurine has antioxidant and membrane-stabilizing activities. Taurine also reacts as a glycine receptor

It has until the present invention not been prescribed for alleviating the effects of a neurological disorder in humans.

According to the present invention, a combination comprising: 1) glycine and 2) GABA or a GABA analogue such as Baclofen, preferably in combination with vitamin B6, and 3) glutamine and/or arginine and 4) taurine is particularly suitable for treating a neurological disorder and/or alleviating at least one symptom of a neurological disorder, and/or inducing or enhancing the repair and/or production of

myelin, brain cells, nerve cells, at least one brain system and/or at least one nerve system.

Further provided is therefore a method for treating a neurological disorder, and/or alleviating at least one symptom of a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, nerve cells, at least one brain system and/or at least one nerve system, comprising administering to an individual in need thereof:

- a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine and/or arginine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of taurine, or an analogue or metabolite thereof, and
- preferably, a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof.

The inventor has shown that the beneficial effects are also experienced when the Baclofen is subsequently omitted. Further provided is therefore a method for treating a neurological disorder, and/or alleviating at least one symptom of a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, nerve cells, at least one brain system and/or at least one nerve system, comprising administering to an individual in need thereof:

- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine and/or arginine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of taurine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof.

Said individual has preferably been treated with Baclofen before the above mentioned treatment. Of course, as already stated before, any of these compounds may be replaced by therapeutically effective analogues and/or metabolites thereof.

Also provided is a combination comprising:

- a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine and/or arginine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of taurine, or an analogue or metabolite thereof, and
- preferably, a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof.

The above mentioned combination for use as a medicament is also provided. In one embodiment, said combination is used for the preparation of a combination of medicaments (kit of parts) for treating a neurological disorder, and/or alleviating the symptoms of a neurological disorder, and/or inducing or enhancing the repair or production of myelin, brain cells, at least one brain system, nerve cells and/or at least one nerve system.

Said neurological disorder preferably comprises at least one of the conditions as described herein before. Moreover, the use of glycine, glutamine/arginine, taurine, vitamin B6 and Baclofen is preferred. One particularly preferred embodiment of the invention therefore provides a method for treating whiplash, myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS), comprising administering to an individual in need thereof:

- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine and/or arginine, and
- a therapeutically effective amount of taurine, and
- a therapeutically effective amount of vitamin B6 and
- a therapeutically effective amount of 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen).

As said before, the inventor has shown that the beneficial effects are also experienced when the Baclofen is subsequently omitted. Further provided is therefore a method for treating whiplash, myelin damage-related disorder, muscle dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS), comprising administering to an individual in need thereof:
- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine and/or arginine, and
- a therapeutically effective amount of taurine, and
- a therapeutically effective amount of vitamin B6.

Said individual has preferably been treated with Baclofen before the above mentioned treatment. Of course, as already stated before, any of these compounds may be replaced by therapeutically effective analogues and/or metabolites thereof.

Also provided is a combination comprising:
- a therapeutically effective amount of 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), and
- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine and/or arginine, and
- a therapeutically effective amount of taurine, and
- preferably a therapeutically effective amount of vitamin B6. The above mentioned combination for use as a medicament is also provided. Said combination is preferably used for the preparation of a combination of medicaments (kit of parts) for treating myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or

complex regional pain syndrome (CRPS). These are the conditions of the present inventor which particularly improved after administration of a combination according to the present invention. In another embodiment, said combination is used for the preparation of a combination of medicaments (kit of parts) for treating multiple sclerosis.

For epilepsy, additional insights are provided by the present invention. In one embodiment, a combination comprising glutamine and taurine is used in order to counteract epileptic seizures. Said combination preferably also comprises GABA or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell. In a preferred embodiment, said combination also comprises vitamin B6. A particularly preferred embodiment provides a method for counteracting epileptic seizures, comprising administering to an individual in need thereof a therapeutically effective amount of glutamine, taurine and Baclofen. Preferably, the number and/or duration of epileptic seizures are counteracted. Most preferably, vitamin B6 is also administered to said individual. Also provided is a combination comprising:

- a therapeutically effective amount of glutamine and/or arginine, and
- a therapeutically effective amount of taurine, and
- a therapeutically effective amount of Baclofen. Said combination preferably also comprises vitamin B6. The above mentioned combination for use as a medicament is also provided. Said combination is preferably used for the preparation of a combination of medicaments (kit of parts) for treating epilepsy.

Yet another embodiment provides a use of glycine, taurine and either glutamine and/or arginine in order to counteract epilepsy. Said combination preferably also comprises vitamin B6. A further embodiment therefore provides a method for counteracting epileptic seizures, comprising administering to an individual in need thereof a therapeutically effective amount of glycine, taurine, vitamin B6, in combination with glutamine and/or arginine. Also provided is a combination comprising:

- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of taurine, and

- a therapeutically effective amount of glutamine and/or arginine, and
- a therapeutically effective amount of vitamin B6.

The above mentioned combination for use as a medicament is also provided. Said combination is preferably used for the preparation of a combination of medicaments or a kit of parts for treating epilepsy.

Of course, any of these compounds may be replaced by therapeutically effective analogues and/or metabolites thereof.

The present invention furthermore provides the insight that addition of magnesium and/or aspartate and/or kalium to any combination of medicaments provided herein furthermore improves the efficiency of counteracting neurological disorders. For instance, after addition of magnesium, the present inventor experienced further improvements, in particular concerning muscle movements. Furthermore edema in his legs was significantly reduced. His former size 46 became size 42.

Magnesium is needed for more than 300 biochemical reactions in the body. It helps maintaining normal muscle and nerve function, keeps heart rhythm steady, supports a healthy immune system, and keeps bones strong. Magnesium also helps regulating blood sugar levels, promotes normal blood pressure, and is known to be involved in energy metabolism and protein synthesis.

Magnesium effects muscle relaxation through direct action on the cell membrane. Mg++ ions close certain types of calcium channels, which conduct a positively charged calcium ion into the neuron. With an excess of magnesium, more channels will be blocked and the nerve will have less activity.

Aspartate (the conjugate base of aspartic acid) stimulates NMDA receptors, though not as strongly as the amino acid neurotransmitter glutamate does. It serves as an excitatory neurotransmitter in the brain and is an excitotoxin.

Aspartic acid is non-essential in mammals, being produced from oxaloacetate by transamination. In plants and microorganisms, aspartic acid is the precursor to several amino acids, including four that are essential: methionine, threonine, isoleucine, and lysine.

Potassium and kalium allow muscle contraction and transmission of nerve impulses in animals through action potentials. By nature of their electrostatic and

chemical properties, K^+ ions are larger than Na^+ ions, and ion channels and pumps in cell membranes can distinguish between the two types of ions, actively pumping or passively allowing one of the two ions to pass, while blocking the other.

A method according to the invention, further comprising administering to said individual a therapeutically effective amount of magnesium and/or aspartate and/or kalium, is therefore also herewith provided. In one embodiment, magnesium ascorbate is administered. Magnesium ascorbate provides both magnesium and vitamin C (as ascorbate). This provides the advantage that vitamin C levels are raised as well, which is, amongst other things, beneficial for metabolic reactions. The combination of magnesium and ascorbate or vitamin C has the effect that less - if any - magnesium needs to be administered separately (for instance in liquid form or via intramuscular administration). For instance, the amount of magnesium in 6 grams magnesium ascorbate is 390 mg (which is already 130% of the Recommended Daily Intake (RDI)) and the amount of ascorbatic acid is 5610 mg (which is as much as 9350% RDI).

Further provided is therefore a method for treating a neurological disorder, and/or alleviating at least one symptom of a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, nerve cells, at least one brain system and/or at least one nerve system, comprising administering to an individual in need thereof:

- a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine and/or arginine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of magnesium (preferably magnesium ascorbate) and/or aspartate and/or kalium, and
- preferably, a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof. Preferably, taurine is administered as well.

Also provided is a combination comprising:

- a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine and/or arginine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of magnesium (preferably magnesium ascorbate) and/or aspartate and/or kalium, and
- preferably, a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof. Said combination preferably also comprises taurine. Also provided is therefore a combination comprising:
- optionally, a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine and/or arginine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of magnesium (preferably magnesium ascorbate) and/or aspartate and/or kalium, and
- preferably, a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof, and
- a therapeutically effective amount of taurine.

The above mentioned combinations for use as a medicament are also provided. In one embodiment, such combination is used for the preparation of a combination of medicaments or kit of parts for treating a neurological disorder, and/or alleviating the symptoms of a neurological disorder, and/or inducing or enhancing the repair or

production of myelin, brain cells, at least one brain system, nerve cells and/or at least one nerve system.

Said neurological disorder preferably comprises at least one of the conditions as described herein before. Moreover, the use of glycine, glutamine/arginine, taurine, magnesium, vitamin B6 and Baclofen is particularly preferred. One particularly preferred embodiment of the invention therefore provides a method for treating a whiplash, a myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension, spasm and/or complex regional pain syndrome (CRPS), comprising administering to an individual in need thereof:

- a therapeutically effective amount of 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), and
- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine and/or arginine, and/or taurine
- a therapeutically effective amount of magnesium (preferably magnesium ascorbate) and/or aspartate and/or kalium, and
- preferably, a therapeutically effective amount of vitamin B6. In one embodiment, taurine and glutamine (or arginine) are both administered. Further provided is therefore a method for treating a whiplash, a myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension, spasm and/or complex regional pain syndrome (CRPS), comprising administering to an individual in need thereof:

- a therapeutically effective amount of 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), and
- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine and/or arginine, and
- a therapeutically effective amount of taurine, and
- a therapeutically effective amount of magnesium (preferably magnesium ascorbate) and/or aspartate and/or kalium, and
- preferably, a therapeutically effective amount of vitamin B6.

Also provided is a combination comprising:

- a therapeutically effective amount of 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), and
- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine and/or arginine, and/or taurine
- a therapeutically effective amount of magnesium (preferably magnesium ascorbate) and/or aspartate and/or kalium, and
- preferably, a therapeutically effective amount of vitamin B6. In one embodiment said combination comprises both taurine and glutamine (or arginine). Further provided is therefore a combination comprising:
- a therapeutically effective amount of 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), and
- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine and/or arginine, and
- a therapeutically effective amount of taurine, and
- a therapeutically effective amount of magnesium (preferably magnesium ascorbate) and/or aspartate and/or kalium, and
- a therapeutically effective amount of vitamin B6.

The above mentioned combinations for use as a medicament are also provided. Such combination is preferably used for the preparation of a combination of medicaments or kit of parts for treating a whiplash, a myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, hypersensitivity of the dura mater, spasm, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS).

In yet another embodiment, any of the above mentioned combinations is combined with alpha-lipoic acid. Alpha lipoic acid (ALA) is a natural fatty acid. It is involved in energy production since it converts glucose into energy. Alpha lipoic acid is also an antioxidant. Alpha lipoic acid functions in water and fat, unlike more common antioxidants and it is able to recycle antioxidants such as vitamin C and glutathione. Glutathione is an important antioxidant that helps the body to eliminate potentially harmful substances. Alpha lipoic acid increases the formation of glutathione.

One of the most visible roles of lipoic acid is as a cofactor in aerobic metabolism, specifically the pyruvate dehydrogenase complex. Lipoate participates in transfer of acyl in 2-oxoacid dehydrogenases (2-OADH) and in transfer of methylamine groups in glycine cleavage complexes (GCV), which are protein complexes that catalyze the reversible oxidation of glycine. In the glycine cleavage complex methylamine is transferred from lipoate to tetrahydrofolate (THF) yielding methylene-THF and ammonia. Methylene-THF is then used by serine hydroxymethyltransferase (SHMT) to synthesize serine from glycine. Serine is important in metabolism in that it participates in the biosynthesis of purines and pyrimidines. It is also the precursor to several amino acids, including glycine, cysteine, and, in bacteria, tryptophan. It is also the precursor to numerous other metabolites, including sphingolipids. Serine is also a precursor to folate, which is the principal donor of one-carbon fragments in biosynthesis.

Hence, alpha lipoic acid enhances methylation processes. A compound capable of enhancing methylation processes (such as alpha lipoic acid) is particularly beneficial for improving neurological disorders, amongst other things via DNA damage repair.

Further provided is therefore a method, combination, use or kit of parts according to the invention, further comprising (administering to said individual) a therapeutically effective amount of alpha-lipoic acid.

In a further preferred embodiment, any of the above mentioned combinations is combined with acetyl-L-carnithine, which enhances fatty acid oxidation and has neuroprotective benefit. Carnitine is a quaternary ammonium compound biosynthesized from the amino acids lysine and methionine. In living cells, it is required for the transport of fatty acids from the cytosol into the mitochondria during the breakdown of lipids (or fats) for the generation of metabolic energy. Vitamin C (ascorbic acid) is essential for the synthesis of carnitine.

Acetyl L-carnitine stimulates the production of acetylcholine or ACh (muscarinic acetylcholine receptor and nicotinic acetylcholine receptor) which is a neurotransmitter that is important for excitation and contraction of the muscle. Acetylcholine mediates fast synaptic transmission at all neuromuscular junctions.

Studies of rat aging have suggested that the use of acetyl-L-carnitine and lipoic acid results in improved memory performance and delayed structural mitochondrial decay. Further provided is therefore a method, combination, use or kit of parts according to the invention, further comprising (administering to said individual) a therapeutically effective amount of acetyl-L-carnithine.

Furthermore, any of the above mentioned combinations is preferably combined with methionine and/or selenium methionine. Methionine is an essential amino acid, which is not synthesized by humans. Methionine is a precursor of glutathione, which is a potent antioxidant. Methionine is also a histidine inhibitor and it detoxifies heavy metal toxins and diminishes muscle weakness. Together with cysteine, methionine is one of two sulfur-containing amino acids. Its derivative S-adenosyl methionine (SAM) serves as a methyl donor. Hence, addition of methionine or an analogue or a metabolite thereof also enhances methylation processes, which is particularly beneficial for improving neurological disorders, amongst other things via DNA damage repair. Methionine is furthermore an intermediate in the biosynthesis of cysteine, carnitine, taurine, lecithin, phosphatidylcholine, and other phospholipids.

Further provided is therefore a method, combination, use or kit of parts according to the invention, further comprising (administering to said individual) a therapeutically effective amount of methionine.

Another amino acid which is preferably combined with a combination according to the present invention is tryptophan. This is also an essential amino acid. Tryptophan is an important building block in protein biosynthesis. Moreover, tryptophan is a biological precursor for the neurotransmitter serotonin. Serotonin, in turn, can be converted to melatonin, which hormone is important in the regulation of circadian rhythms. Tryptophan is also a precursor of Niacin (Vitamin B3), which is involved in the repair of DNA, and of Auxin, which is essential for cell growth.

Tryptophan synthase catalyzes the formation of tryptophan from indole and the amino acid serine. Further provided is therefore a method, combination, use or kit of parts according to the invention, further comprising (administering to said individual) a therapeutically effective amount of tryptophan.

In yet another embodiment, a combination according to the present invention is combined with selenium. Selenium is important for cellular function and it forms the active center of the enzyme glutathione peroxidase which protects organisms from oxidative damage. Selenium is a component of the unusual amino acids selenocysteine and selenomethionine. Selenium is a trace element nutrient which functions as cofactor for reduction of antioxidant enzymes such as glutathione peroxidases. Selenomethionine is an amino acid containing selenium. The L-isomer of selenomethionine, known as Se-met and Sem, is a common natural food source of selenium. *In vivo*, selenomethionine is randomly incorporated instead of methionine and is readily oxidized.

Further provided is therefore a method, combination, use or kit of parts according to the invention, further comprising (administering to said individual) a therapeutically effective amount of selenium.

The present inventor has experienced that a combination of alpha-lipoic acid, acetyl-L-carnithine, methionine, tryptophan and selenium, together with glycine, glutamine, vitamin B6 and magnesium, significantly improved his condition, even after the Baclofen pump had become dysfunctional.

Further provided is therefore a method for treating a neurological disorder, and/or alleviating at least one symptom of a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, nerve cells, at least one brain system and/or at least one nerve system, comprising administering to an individual in need thereof:

- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of magnesium (preferably magnesium ascorbate), and
- a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof, and
- a therapeutically effective amount of alpha-lipoic acid, and

- a therapeutically effective amount of acetyl-L-carnithine or an analogue or metabolite thereof such as acetylcholine, and
- a therapeutically effective amount of methionine, and
- a therapeutically effective amount of tryptophan or an analogue or metabolite thereof such as serotonin, and
- a therapeutically effective amount of selenium, and
- optionally, a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell.

Also provided is a combination comprising:
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of magnesium (preferably magnesium ascorbate), and
- a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof, and
- a therapeutically effective amount of alpha-lipoic acid, and
- a therapeutically effective amount of acetyl-L-carnithine or an analogue or metabolite thereof such as acetylcholine, and
- a therapeutically effective amount of methionine, and
- a therapeutically effective amount of tryptophan or an analogue or metabolite thereof such as serotonin, and
- a therapeutically effective amount of selenium, and
- optionally, a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell.

The above mentioned combination for use as a medicament is also provided. In one embodiment, such combination is used for the preparation of a combination of medicaments or kit of parts for treating a neurological disorder, and/or alleviating the symptoms of a neurological disorder, and/or inducing or enhancing the repair or production of myelin, brain cells, at least one brain system, nerve cells and/or at least one nerve system.

Said neurological disorder preferably comprises at least one of the conditions as described herein before. One particularly preferred embodiment of the invention therefore provides a method for treating a whiplash, a myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension, spasm and/or complex regional pain syndrome (CRPS), comprising administering to an individual in need thereof:

- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of magnesium (preferably magnesium ascorbate), and
- a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof, and
- a therapeutically effective amount of alpha-lipoic acid, and
- a therapeutically effective amount of acetyl-L-carnithine or an analogue or metabolite thereof such as acetylcholine, and
- a therapeutically effective amount of methionine, and
- a therapeutically effective amount of tryptophan or an analogue or metabolite thereof such as serotonin, and
- a therapeutically effective amount of selenium, and
- optionally, a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-

butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell.

Also provided is a use of a combination comprising:
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of magnesium (preferably magnesium ascorbate), and
- a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof, and
- a therapeutically effective amount of alpha-lipoic acid, and
- a therapeutically effective amount of acetyl-L-carnithine or an analogue or metabolite thereof such as acetylcholine, and
- a therapeutically effective amount of methionine, and
- a therapeutically effective amount of tryptophan or an analogue or metabolite thereof such as serotonin, and
- a therapeutically effective amount of selenium, and
- optionally, a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell,

for the preparation of a combination of medicaments or kit of parts for treating a whiplash, a myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, hypersensitivity of the dura mater, spasm, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS).

In one embodiment, any of the above mentioned combinations is combined with soy protein. A method according to the invention, further comprising administering to said individual a therapeutically effective amount of soy protein, is therefore also herewith provided. Soy proteins provide several amino acids and essential minerals to

the body within a very short time, and can be seen as a short boost. It is therefore advantageously used in addition to the above mentioned ingredients.

The present invention furthermore provides the insight that addition of an omega-3 polyunsaturated fatty acid (also called a long chain omega-3 fatty acid) to any combination of medicaments provided herein furthermore improves the efficiency of counteracting neurological disorders. Omega-3 polyunsaturated fatty acids are a family of unsaturated fatty acids that have in common a carbon–carbon double bond in the $n-3$ position; that is, the third bond from the methyl end of the fatty acid. Omega-3 fatty acids are considered essential fatty acids. They are essential to human health but cannot be manufactured by the body. For this reason, omega-3 fatty acids must be obtained from food. Omega-3 fatty acids can be found in fish, such as salmon, tuna, and halibut, other marine life such as algae and krill, certain plants (including purslane), and nut oils. Omega-3 fatty acids play a crucial role in brain function as well as normal growth and development. There are three major types of omega 3 fatty acids that are ingested in foods and used by the body: alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). Once eaten, the body converts ALA to EPA and DHA, the two types of omega-3 fatty acids more readily used by the body. After addition of ALA to his diet, the present inventor experienced further improvements; particularly his capability of standing and moving his legs and feet were much improved. Furthermore, hypersensitivity of his legs was significantly diminished. If an omega-3 polyunsaturated fatty acid is added to a combination of medicaments according to the invention, it is highly recommended to administer vitamin B12 as well. Vitamin B-12 is a vitamin which is important for the normal functioning of the brain and nervous system, and for the formation of blood. It is normally involved in the metabolism of most kinds of cells of the body, especially affecting DNA synthesis and regulation, but also fatty acid synthesis and energy production. A common form of the vitamin, cyanocobalamin, does not occur in nature, but is used as a supplement and food additive, due to its stability. It is converted to other forms of the vitamin which are actually used in chemical reactions in the body. The term vitamin B-12, known as vitamin B_{12} (commonly B_{12} or B-12 for short) refers to all forms of the vitamin. Vitamin B-12 is the most chemically complex of all the

vitamins. The structure of B-12 is based on a corrin ring, which is similar to the porphyrin ring found in heme, chlorophyll, and cytochrome. The central metal ion is cobalt.

The use of folic acid is also highly recommended. Folic acid (also known as Vitamin M and Folacin) and Folate (the anion form) are forms of the water-soluble Vitamin B_9. These occur naturally in food and can also be taken as supplements.

Folate is necessary for the production and maintenance of new cells. This is especially important during periods of rapid cell division and growth such as infancy and pregnancy. Folate is needed to synthesize DNA bases (most notably thymine, but also purine bases) needed for DNA replication.

Further provided is therefore a method according to the invention, further comprising administering to said individual a therapeutically effective amount of an omega-3 polyunsaturated fatty acid (also called a long chain omega-3 fatty acid), said omega-3 polyunsaturated fatty acid preferably comprising alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and/or docosahexaenoic acid (DHA), preferably in combination with a therapeutically effective amount of vitamin B12 and/or folic acid. More preferably, said omega-3 polyunsaturated fatty acid is combined with a therapeutically effective amount of at least one compound selected from the group consisting of vitamin B12, folic acid, vitamin E, zinc and magnesium. In one embodiment, said omega-3 polyunsaturated fatty acid is combined with vitamin B12 and folic acid. In another preferred embodiment, said omega-3 polyunsaturated fatty acid is combined with vitamin B12, folic acid, vitamin E, zinc and magnesium.

Further provided is therefore a method for treating a neurological disorder, and/or alleviating at least one symptom of a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, nerve cells, at least one brain system and/or at least one nerve system, comprising administering to an individual in need thereof:

- a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a

GABA receptor of a brain cell or nerve cell, and
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine and/or arginine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of magnesium and/or aspartate and/or kalium, and
- a therapeutically effective amount of at least one omega-3 polyunsaturated fatty acid, preferably a composition comprising ALA, EPA and/or DHA, and
- preferably, a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof. In a further preferred embodiment, taurine is administered as well.

Further provided is therefore a method for treating a neurological disorder, and/or alleviating at least one symptom of a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, nerve cells, at least one brain system and/or at least one nerve system, comprising administering to an individual in need thereof:
- a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine and/or arginine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of taurine, and
- a therapeutically effective amount of magnesium and/or aspartate and/or kalium, and
- a therapeutically effective amount of at least one omega-3 polyunsaturated fatty acid, preferably a composition comprising ALA, EPA and/or DHA, and
- preferably, a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof.

Also provided is a combination comprising:

- optionally, a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine and/or arginine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of magnesium and/or aspartate and/or kalium, and
- a therapeutically effective amount of at least one omega-3 polyunsaturated fatty acid, preferably a composition comprising ALA, EPA and/or DHA, and
- a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof. Said combination preferably also comprises taurine. In a particularly preferred embodiment, said combination also comprises vitamin B12, folic acid, vitamin E and/or zinc.

Also provided is therefore a combination comprising:

- a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of glutamine and/or arginine, or an analogue or metabolite thereof, and
- a therapeutically effective amount of taurine, and
- a therapeutically effective amount of magnesium and/or aspartate and/or kalium, and
- a therapeutically effective amount of at least one omega-3 polyunsaturated fatty acid, preferably a composition comprising ALA, EPA and/or DHA, and
- preferably, a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof, and

- preferably, a therapeutically effective amount of vitamin B12, folic acid, vitamin E and/or zinc.

The above mentioned combinations for use as a medicament are also provided. In one embodiment, such combination is used for the preparation of a combination of medicaments (kit of parts) for treating a neurological disorder, and/or alleviating the symptoms of a neurological disorder, and/or inducing or enhancing the repair or production of myelin, brain cells, at least one brain system, nerve cells and/or at least one nerve system.

Said neurological disorder preferably comprises at least one of the conditions as described herein before. Moreover, the use of glycine, glutamine/arginine, taurine, magnesium, a composition comprising ALA and/or DHA and/or EPA, vitamin B6 and Baclofen is particularly preferred. One particularly preferred embodiment of the invention therefore provides a method for treating a whiplash, a myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS), comprising administering to an individual in need thereof:

- a therapeutically effective amount of 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), and
- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine or arginine, and
- a therapeutically effective amount of magnesium, and
- a therapeutically effective amount of alpha-linolenic acid, and/or DHA and/or EPA, and
- preferably, a therapeutically effective amount of vitamin B6 and
- preferably, a therapeutically effective amount of vitamin B12, folic acid, vitamin E and/or zinc. Preferably, taurine is administered as well. Further provided is therefore a method for treating myelin damage-related disorder, (muscle) dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS),

comprising administering to an individual in need thereof:

- a therapeutically effective amount of 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), and
- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine and/or arginine, and
- a therapeutically effective amount of taurine, and
- a therapeutically effective amount of magnesium, and
- a therapeutically effective amount of alpha-linolenic acid and/or DHA and/or EPA, and
- preferably, a therapeutically effective amount of vitamin B6 and
- preferably, a therapeutically effective amount of vitamin B12, folic acid, vitamin E and/or zinc.

Said combination preferably comprises at least vitamin B12 and folic acid. In one embodiment, vitamin B12 is used instead of DHA or EPA.

Also provided is a combination comprising:

- a therapeutically effective amount of 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), and
- a therapeutically effective amount of glycine, and
- a therapeutically effective amount of glutamine and/or arginine, and
- a therapeutically effective amount of magnesium, and
- a therapeutically effective amount of alpha-linolenic acid and/or DHA and/or EPA, and
- preferably, a therapeutically effective amount of vitamin B6. Said combination preferably also comprises taurine.

In one embodiment said combination also comprises vitamin B12, folic acid, vitamin E, zinc and/or magnesium. Said combination preferably comprises at least vitamin B12 and folic acid. In another preferred embodiment, vitamin B12 is used instead of DHA or EPA.

The above mentioned combination for use as a medicament is also provided. Said combination is preferably used for the preparation of a combination of medicaments (kit of parts) for treating myelin damage-related disorder, whiplash,

muscle dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS).

According to another aspect of the present invention, the beneficial effects of drug combinations according to the present invention are furthermore enhanced by chlorophyll. Chlorophyll is a green pigment found in most plants, algae, and cyanobacteria. Chlorophyll is the molecule that absorbs sunlight and uses its energy to synthesise carbohydrates from CO_2 and water. Chlorophyll is known for its detoxifying capability. Chlorophyll is a chlorin pigment, which is structurally similar to and produced through the same metabolic pathway as other porphyrin pigments such as heme. At the center of the chlorin ring is a magnesium ion. Chlorophyll is similar to the human hemoglobin but has a magnisium core instead of an iron one.

The use of chlorophyll in therapy against anti-neurological disorders has not been described before. Further provided is therefore a method according to the invention, further comprising administering to said individual a therapeutically effective amount of chlorophyll. A combination or use according to the invention, wherein said combination further comprises chlorophyll, is also provided, as well as a combination or use according to the invention, wherein said combination comprises a therapeutically effective amount of glycine and a therapeutically effective amount of Baclofen and a therapeutically effective amount of glutamine and/or arginine and/or taurine and/or magnesium and/or aspartate and/or kalium and/or soy protein and/or omega-3 polyunsaturated fatty acid, said omega-3 polyunsaturated fatty acid preferably comprising alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and/or docosahexaenoic acid (DHA). In one embodiment said combination also comprises vitamin B12 and folic acid. In another preferred embodiment, vitamin B12 is used instead of DHA or EPA.

Dose ranges and modes of administration of the above mentioned components of combinations according to the invention can of course vary to some extent, for

instance dependent on the weight and age of the patient and the kind and severity of his/her neurological disorder and the mode of administration.

Glycine is preferably administered orally in a dose of about 20-60 mg/kg/day, preferably about 30-50 mg/kg/day, more preferably about 35-45 mg/kg/day. Glycine readily crosses the blood-brain barrier. Glycine for oral administration is readily available in the art. Of course, all other routes of administration can be used, such as for instance injections. In such case, the dose will mostly be adapted. Suitable doses for different routes of administration are either known in the art or readily determined in the clinic using well known rising doses studies. Preferably, a dosage of glycine is used which corresponds to an oral dosage of 20-60 mg/kg/day. This means that a dosage is used which results in a similar effect of glycine as compared to the effect that is obtained with oral administration of glycine in a dosage of 20-60 mg/kg/day.

Baclofen is preferably administered directly into the intrathecal space surrounding the spinal cord because Baclofen does not readily cross the blood-brain barrier. Baclofen is thus preferably administered intrathecally. A preferred dosage is between 0.75 – 20 microgram/kg/day.

The dosage of Baclofen for intrathecal administration can be much higher (up to about 20 microgram/kg/day) as compared to dosages for oral administration (up to about 0.70 – 1.20 microgram/kg/day). Intrathecal use of drugs has the benefit that the blood/brain barrier does not need to be crossed. When Baclofen is administered intrathecally, varying doses are preferably administered initially in order to establish an optimal dose for a given patient.

Glutamine, arginine and taurine are capable of crossing the blood-brain barrier and are therefore preferably administered orally. Glutamine and/or arginine are preferably administered orally in a dose of about 20-60 mg/kg/day, preferably about 30-50 mg/kg/day. Taurine is preferably administered orally in a dose of about 5-30 mg/kg/day, preferably about 10 – 20 mg/kg/day. Of course, other routes of administration can be used, such as for instance injections. In such case, the dose will mostly be changed. As said before, suitable doses are either known in the art or readily determined in the clinic using well known rising doses studies. Preferably, a dosage of glutamine and/or arginine is used which corresponds to an oral dosage of 20-

60 mg/kg/day. This means that a dosage is used which results in a similar effect of glutamine and/or arginine as compared to the effect that is obtained with oral administration of glutamine and/or arginine in a dosage of 20-60 mg/kg/day. The same holds true for taurine: a dosage of taurine is preferably used which corresponds to an oral dosage of 5-30 mg/kg/day. This means that a dosage is used which results in a similar effect of taurine as compared to the effect that is obtained with oral administration of taurine in a dosage of 5-30 mg/kg/day.

If magnesium and/or aspartate and/or kalium are administered orally, they are preferably combined with a compound that enhances their capability of crossing the blood-brain barrier. Non-limiting examples of such compounds are vitamin B12 and docosahexaenoic acid. As conservation compound, Solutio methylparabeni concentrate may be used. Of course, other known compounds capable of enhancing crossing of the blood-brain barrier are suitable as well. If magnesium is administered orally, a dose of about 5- 50 mg/kg/day is preferably used. Said dose is preferably about 20-40 mg/kg/day.

It is also possible to use other routes of administration, which will often influence the optimal doses. Suitable doses are either known in the art or readily determined in the clinic using well known rising doses studies. Preferably, a dosage of magnesium is used which corresponds to an oral dosage of 5-50 mg/kg/day. This means that a dosage is used which results in a similar effect of magnesium as compared to the effect that is obtained with oral administration of magnesium in a dosage of 5-50 mg/kg/day. For instance, if magnesium is administered via an injection (preferably intramuscularly or subcutaneously), a dose of about 2-10 mg/kg/day is suitable. Said dose is preferably about 4-8 mg/kg/day, more preferably about 5-6 mg/kg/day.

Alpha-lipoic acid, acetyl-L-carnithine, methionine, tryptophan and selenium are preferably administered orally. Alpha-lipoic acid is preferably administered orally in a dose of about 5-30 mg/kg/day, preferably about 10-20 mg/kg/day. Acetyl-L-carnithine is preferably administered orally in a dose of about 5-45 mg/kg/day, preferably about 20-40 mg/kg/day. Methionine is preferably administered orally in a dose of about 4-20 microgram/kg/day, preferably about 5-16 microgram/kg/day. Tryptophan is preferably administered orally in a dose of about 5-35 mg/kg/day,

preferably about 10-30 mg/kg/day. Selenium is preferably administered orally in a dose of about 4-20 microgram/kg/day, preferably about 5-16 microgram/kg/day. Vitamin C is preferably administered orally in a dose of about 20 – 100 mg/kg/day, preferably about 20-40 mg/kg/day.

As outlined above, it is also possible to use other routes of administration, which will often influence the optimal doses. Suitable doses are either known in the art or readily determined in the clinic using well known rising doses studies. Preferably, dosages are used which correspond to the above mentioned oral dosages of alpha-lipoic acid, acetyl-L-carnithine, methionine, tryptophan, selenium and/or vitamin C.

In a preferred embodiment, specific ratios between individual components are used. The use of fixed ratios is preferred because, according to the present invention, certain types of amino acids, vitamins and minerals form clusters when administered in combination with each other in certain dosages. Components of the same cluster enhance each other's effects when present in a certain ratio. Hence, the overall effects of a combination of compounds of the same cluster are larger than the sum of the effects of each individual compound when administered separately. Moreover, different clusters are also capable of enhancing each other's effect if the components of each cluster are present in certain ratios.

Hence, the use of ratios which allow beneficial cluster effects are preferred in the used circumstances. According to the invention, glutamine forms a cluster with taurine. Furthermore, glycine, Baclofen and vitamin B6 form a cluster. Additionally, glycine forms a cluster with magnesium. Vitamin C, selenium and tryptophan also form a cluster, as well as acetyl-L-carnithine, alpha-lipoic acid and methionine.

According to the invention, therefore, in embodiments wherein taurine as well as glutamine or arginine are administered via the same route of administration, the ratio between glutamine and taurine and/or the ratio between arginine and taurine is preferably between 1:1 and 4:1, more preferably about 2:1-3:1. Of note, this ratio is preferably applied if glutamine and taurine are both administered orally and within a time frame of 1- 1½ hours. Glutamine administered outside this time frame is preferably not taken into account for determining said ratio. Furthermore, in embodiments wherein magnesium as well as glycine is administered via the same

route of administration, preferably orally, the ratio between magnesium and glycine is preferably between 1:4 and 2:1, more preferably between 1:3 and 1:1.In embodiments wherein glycine as well as aspartate is administered via the same route of administration, preferably orally, the ratio between glycine and aspartate is preferably between 2:1 and 4:1, more preferably about 3:1.

Moreover, in embodiments wherein vitamin C, selenium and tryptophan are administered via the same route of administration, preferably orally, the ratio between vitamin C (in mg) and selenium (in μg) and tryptophan (in mg) is preferably between 10: 1: 5 and 4: 1: 2, more preferably between 8: 1: 4 and 6: 1: 3.

Finally, in embodiments wherein acetyl-L-carnithine, alpha-lipoic acid and methionine are administered via the same route of administration, preferably orally, the ratio between acetyl-L-carnithine (in mg) and alpha-lipoic acid (in mg) and methionine (in μg) is preferably between 8: 4: 1 and 3: 1.5: 1, more preferably between 6: 3: 1 and 4: 2: 1.

According to the present invention, the above mentioned ratios result in particular good therapeutic effects, while adverse side effects are at least in part avoided. As mentioned before, if different routes of administration are used, the dosages will be adapted. Therefore, in such cases, the above mentioned ratios will change accordingly. However, if the route of administration of both components of any of the above mentioned combinations is the same, said ratio preferably remains the same. For instance, the ratio between magnesium and glycine remains preferably the same when both magnesium and glycine are administered by injection instead of orally.

Figure 1 shows a schematic, non-limiting, overview of possible embodiments according to the present invention. Of course, a patient does not need to be provided with all the listed compounds. Figure 1 merely provides a non-limiting overview of various embodiments according to the invention. Components shown in a circle form a cluster. However, because of the simplification to show the principle, it is not possible to depict all relations. An example is the glycine-magnesium and the glycine-vitamin B6 clustering. Figure 1 should be seen as a non-limiting indication of the principle of cluster forming.

Further provided is a kit of parts comprising a therapeutically effective amount of:

* glycine, and
* glutamine and/or arginine, and
* taurine and/or chlorophyll,

the kit of part preferably also comprising:

- a therapeutically effective amount of vitamin B6, and/or
- a therapeutically effective amount of vitamin B12 and folic acid, and/or
- a therapeutically effective amount of magnesium and/or aspartate and/or kalium, and/or
- an omega-3 polyunsaturated fatty acid (also called a long chain omega-3 fatty acid), said omega-3 polyunsaturated fatty acid preferably comprising alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and/or docosahexaenoic acid (DHA), preferably in combination with a therapeutically effective amount of at least one compound selected from the group consisting of vitamin B12, folic acid, vitamin E, zinc and magnesium, and/or
- soy protein, and/or
- gamma amino butyric acid (GABA) or an analogue of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue is capable of specifically binding a GABA receptor of a brain cell or nerve cell.

As described above, a method, combination or use according to the invention is preferably used for counteracting a myelin damage-related disorder, whiplash, dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS).

The invention is further explained in the following example. This example does not limit the scope of the invention, but merely serves to clarify the invention.

Brief description of the drawing

Figure 1: non-limiting overview of possible embodiments according to the present invention. The drawing indicates relations between several compounds of various clusters.

Example

On the 7th of November 2000 the present inventor was involved in a car accident in the Netherlands. With a speed between 80 a 130 km/h a car crashed at two non driving cars, including the car of the inventor, on the sub highway. The driver who caused the accident was drunk. The present inventor was transported to the hospital. After 1 h it was no longer possible to move his neck (this would last for more than 4 years) and there were major concentration problems, etc. At first he was diagnosed with a complex whiplash with no expectation on recovery from this. After 1 ¾ year and a very progressive situation, he was finally diagnosed with CRPS class 1 (secondary generalized dystonic reflex dystrophy), primary due to a whiplash movement. This was fully related to the accident. Although the new medication (Baclofen) was successful at that moment, the progressive situation could not be stopped. The future would be: no longer being able to move and becoming completely dependable to others in a bed laying situation.

After an experimental operation (implantation of a Baclofenpomp) and complications during and after the operation, the inventor was fully dependable on an electric wheelchair, but he could use his right hand and he could again use his face; this fulfilled the expectations. Complications after the operation were, however, paralysis of the lower body and epileptic attacks induced by movements and displacements. Final result in 2004, was a very serious handicap with particularly the next parameters:

- Generalized Posttraumatic dystrophy, cold form.
- Generalized dystonia. Result: forced poses over whole corpus inclusive impaired face functions (talking, eating, drinking, seeing, mimicry). After an experimental operation in 2004, a Baclofenpomp was implanted, where after the inventor was again able to use his face functions (eating, drinking, speak etc) and to use his right hand/arm.
- Paralysed from L1 level, because of a not recognized and afterwards not decompressed Quada equina syndrome.
- Ataxia, due to intoxications of medications.

- Epileptic (Status epileptic) seizures and proximal dystonic seizures. During 2 – 3 h a day (maximum 4, 5 h a day). Triggered by movements and reflex epileptic seizures. A third cause is medication (Baclofen). 1/3 of all patients have seizures, Baclofen is known for this site effect.
- Permanent leakage of brain liquid (Liquor hypotension) and reactions of the dura mater and the pia mater.
- Neurological body functions in poor condition. Left hand/arm in forced position. No reflexes, bad coordination.
- Neuropsychological test (belonging to 1% slowest people of the population). Before the accident the inventor was capable of working and thinking on university + level.

In 2004, the doctors were afraid to give more and other medications due to strong reactions. After experimenting with various dosages of the Baclofen pump the inventor started in January 2005 with his own search for recovery. His main goal was to reduce the many epileptic seizures, which occurred daily and lasted for up to 2 ½ hrs. It took ½ year research before he started experimenting with glycine on his own body.
(Before that he tried a high dosage vitamin B6 and later a multivitamin composition in combination with the Baclofen (400 microgram a day). Although it resulted in less seizures and a short period of no seizures all results were gone as soon as the dosage of the Baclofen or vitamin B6 was changed).

The inventor believed that a certain level of vitamins and minerals is beneficial to improve metabolism of the body and brain and is preferably brought to a certain level to have optimal benefit. It is also in a way a start point for possible recovery. As known, several body systems and processes are reduced during illness and sleep. If there is not a certain level of vitamins and minerals then after prolonged periods of time a deficiency is the result and such deficiency is an extra trigger for adverse neurological reactions. The inventor therefore used vitamin B6. Beneficial effects were indeed obtained using vitamin B6 in a high dosage up to 500 mg a day.
By accident the inventor found out that stopping with the combination Naproxen and Pantorc (which he had been using for some time) had a positive result on his seizures. This effect was for about 1 month. At this point the inventor stopped with all pain

medication. Searching for solutions the inventor wanted to try another neurotransmitter besides Baclofen. Glycine seemed to be a possibility. But there was no research result available answering the question whether a GABA analogue and glycine could be used together, especially not in combination with a high dosage of vitamin B6 and/or other vitamins. Nevertheless, the inventor tried it with a glycine dosage of 500 mg/day and a vitamin B6 dosage of 200 mg/day. Shortly thereafter, the vitamin B6 was replaced by multivitamin tablets. The inventor took two tablets per day. One multivitamin tablet comprises:

Vitamin A, 1200 ug - 150% Recommended Daily Intake (RDI)
Vitamin D, 5ug- 100% RDI
Vitamin E, 83.9 mg – 840% RDI
Vitamin C, 250 mg – 417% RDI
Thiamine (vitamin B1), 80 mg – 5714% RDI
Riboflavin (vitamin B2), 80 mg – 5000% RDI
Niacin (Vitamin B3), 80 mg – 444% RDI
Vitamin B6, 80 mg – 4000% RDI
Folic acid, 400 ug – 200% RDI
Vitamin B12, - 80 ug – 8000% RDI
Biotin 80 ug – 53% RDI
Pantothenic acid (vitamin B5), 80 mg – 1333% RDI
Calcium 8 mg – 1% RDI
Iron 2 mg – 14% RDI
Magnesium 6 mg – 2% RDI

Hence, with the multivitamin tablets the inventor had a vitamin B6 dosage of 160 mg/day.

The Baclofen pump at that time delivered 390 microgram/day. Surprisingly, remarkable results were obtained. Within 8 hours the inventor was able to lift his left arm up while he had a frozen shoulder and dystonic problems with using this arm. Moreover, he was not only able to use his left shoulder but also the durations of his seizures shortened and the seizures were less heavy. One part of his body seemed to

react on the Baclofen and another part on the glycine or the combinations of Glycine/Baclofen/vitamin B6 and multivitamins. After two weeks the blood levels stabilized. Then, a remarkable and unpleasant side effect occurred. The duration of the seizures increased again and the seizures became much heavier. After the inventor stopped with the glycine the seizures reduced to the level before taking the glycine. Analyzing everything he came to the conclusion that both neurotransmitters (glycine and Baclofen) cooperated at certain dosages but could also oppose each other's activity at different dosages. By reducing the Baclofen by 10 microgram per 3 months and adding glycine he was able to find a Baclofen dosage that cooperated with a low level of glycine and vitamin B6/multivitamins. His internationally famous and well-known neurological doctor was positive over his first results and he told the inventor that as far as he knew the inventor was the first person in the world that used this combination of Baclofen and glycine.

In the year 2006 there were positive but also negative issues around his neurological disorders. During the summer period June/July/August the situation became worse. Several less optimistic points were noted, see below. The level of medication at that time was:

- 350 microgram of Baclofen per day
- 1000 mg glycine per day, and
- 160 mg B6 and other high dosage of vitamins/minerals (see above mentioned list of multivitamin tablets)

The weight of the inventor was 115 kg.

The extra neurological problems that occurred:

- Temporarily paralysed left arm/hand during 6-8 hrs a day.
- Longer duration of the attacks with increased intensity (of 2 a 3 hours to 4 a 4 ½ hour per day)
- Regularly short bumps/attacks during the day. During this period he did not leave his house because of the high frequency.

Since the accident the inventor had been suffering from a lack of gnostic sensitivity of his body. With the above mentioned medication, he regained feeling, which was considered a positive result. However this had as consequence that his lower body became extremely sensitive.

On the inventor's request the dosage of Baclofen was reduced to 340 micrograms a day. This took place on 16 August 2006. On 11 October 2006 the output of the Baclofen pump was reduced to 330 micrograms a day. During 2 ½ months the dosage of glycine was increased to 3000 milligrams a day (dosage of 3000 mg/day reached on 8 November 2006). On 1 December 2006 the glycine dosage was increased to 4000 milligrams a day. Suddenly the inventor was totally free of seizures. This lasted for a longer period.
During the period between August and December 2006 it was apparent that a different situation was underway. Each upgrade with 500 mg glycine gave a short improvement but was not lasting until 4000 mg/day was reached. The dosage of vitamin B6 was 160 mg a day, the dosage of vitamin B12 was 160 microgram a day, the dosage of vitamin B9 or folic acid was 800 microgram a day, and the dosage of vitamin E was 167.8 mg/day.

The first benefits on the first of December 2006 were:

- Clarity of his mind had improved
- Functions of his left hand had improved
- Conscience loss as a result of hypersensitivity disorder was significantly decreased, strong pain reduction
- No seizures during longer period
- Positive effect on temporally paralysis
- Positive effect on Dystonia.
- Bodyfunctions and strength had improved.
- First small reactions of a toe of both feet, after having been paralyzed for several years.

During the period between December 2006 and April 2007 the effects became less and the inventor was again confronted with seizures. However, they were much less and less heavy than before. The positive effects on his arms and legs and the reactions in his toes decreased. If he did not use the glycine and the vitamins, he obtained a condition as bad as in 2004.
Using the glycine and the vitamins again resulted in quick recovery to the level of April 2007.

In April the glycine dosage was brought to 4500 milligrams a day. This improved the use of his toes and even his heels gave reactions. The hypertension became worse. An unexpected phenomenon was introduced. During the seizures both legs reacted. Both legs sometimes even reacted simultaneously. Hence, both sites of the brain give similar reactions. Firstly the inventor started to increase the vitamin B6 level to 400 milligrams/day to acidify the muscles. The reactions became more controllable. As soon this phenomenon became controllable the vitamin B6 level was reduced to 160 milligrams a day and the inventor started with glutamine to improve control. Within 3 months the dosage of glutamine was brought up to 3000 milligrams/day. The others dosages of glycine, Baclofen, and vitamins remained the same and are at this moment still on the same level, because it was important to keep the existing levels stable at this point.
Adding glutamine gave the following amazing results:

- A minimal frequency of seizures.
- Better coordination over the entire body
- Movements become more natural.
- Simultaneous movements possible with both arms and legs.
- Able to move feet and pull up both legs.
- Reduction of oedema, specifically in the legs.
- Less dystonic and dystrophic reactions.

In July 2007 the inventor started to add taurine. The reason was that the inventor believed that certain types of amino acids and vitamins and/or minerals form certain clusters on certain levels. He had the point of view that glutamine forms a cluster with taurine, like glycine, Baclofen and vitamin B6. The amino acids are preferably in

a specific ratio for optimal results.

The results of adding taurine were in October 2007 (dosage 1500 milligrams a day) as follows:

- Further improvement of the earlier mentioned results with glutamine
- Positive influence on Liquor hypotension and dura mater and pia mater
- Improvement in thinking and calculating capability. Until then the inventor was not capable to calculate without any tool.
- Change in hypersensitivity; not stable, depending on taurine level.
- Regaining of reflexes over the body
- 4 months seizure free

Just adding taurine by drinking a Red Bull does not help. Again the cluster forming is important. Glutamine and taurine are preferably taken together for optimum effect. Glutamine can be added separately after some time 1 – ½ hours. It then works separately from taurine or the glutamine/taurine cluster.

In October 2007 the inventor started with magnesium (in this case magnesium sulphate) in liquid form. The intended dosage was 1500 milligrams a day. If needed the dosage would be increased to 4500 milligrams a day. Again is a cluster forming expected; this time between magnesium and glycine.

In January 2008 the following results were obtained:

- The weight of the inventor is meanwhile 108 kg
- Coordination of the muscles is improved
- Dystonie and dystrophy are significantly diminished
- Edema is almost gone. From size 46 back to size 42. Reduction was reached in both legs/feet.
- Improvement duration of the movement of legs.
- Endurance improved.
- More possibilities to do something during the day.
- First time standing on both feet.
- Improvement sexuality, until then as normal for paralysed people and/or qauda syndrom.

In spite of the improvement the seizures came back. A relation between the winter period and the type of reactions during the seizures was established.

In January 2008 the inventor started with using oil to add ALA, EPA, DHA. Positive influence had been found by accident. During New Year the inventor had eaten something with a high dosage of oil. Suddenly his capabilities improved during two days and subsequently decreased as fast as they had increased. Analysing what aspect of his diet had changed, the inventor obtained the insight that oil, specifically omega 3 and or 6 fatty acids, are beneficial. The ALA and the forming of EPA and or DHA was further analysed by using a specific type of oil. In this case Walnut oil was used. (line seed oil has a higher DHA amount, but line seed oil involves the risk of prostate cancer). Result of using Walnut oil was that the inventor's capabilities improved rapidly again.

Results of adding ALA, EPA, DHA were:

- Within 3 weeks capable to stand and to keep standing in balance without help
- Knee bending from standing position.
- Walking a few steps sideward at his bed.
- Hypersensitivity of legs was gone.

The positive effects are probably also enhanced because of the high amounts of vitamin B12 and vitamin B9 (folic acid). The dosages remained the same as before. Both vitamin B12 and DHA are capable to cross the blood-brain barrier. It looks like that they are also positively influenced by each other when used in high amounts. Glutamine was brought up to 4000 miligrams a day.

In January 2008 it appeared that the Baclofen pump had given problems during the last months. The pump is filled with 18 millilitres of Baclofen. When refilling took place, it appeared that the pump still contained 13 millilitres. The amount that should have been left was 8.2 milliliters. Hence, the pump had not worked properly during a longer period. Surprisingly the inventor's condition improved a couple of weeks after the redraw. The capabilities of the inventor improved. Normally, a

problem with the Baclofen pump had severe effects within a very short period. This time, however, the combination of medicines according to the invention had taken over the task of the pump and even improved the living conditions in a remarkable way.

The doctor was surprised but also very positive. Although it was unknown what would happen when the pump was refilled.
When the pump was working again, the inventor reacted on the pump after 1 hour. He had strong reactions and he was totally drugged. But during therapy he was suddenly able to walk a few steps forward. The next day he was able to use his legs to step out of his bed and could stand beside it. This was until then not possible. Within a week he was able to "walk" during four minutes beside his bed. He was also able to stand up 20 times from a chair. A very rapid improvement took place.
However after 1 ½ weeks he became ill. His improved capabilities had disappeared. During refill again was concluded that the pump had only had a short working period. From the 18 millilitres still 17 ml was left in the pump. The level should be 8.0 ml at that time.

It was concluded that the pump failed again. Recalculation shows that the pump had worked properly during 1 ½ week after refill. Again redraw effects occurred, but again without severe consequences.
After four months, however, the inventor had achieved the same improvement as compared to the 1 ½ week rapid improvement with a working Baclofen pump, during the last week of January, in combination with the other medicines according to the invention.

During the period February and April 2008 the inventor started to use a high concentrate form of DHA. He started with 100 milligrams/day; later he used 200 milligrams/day. This addition brought him to an improved level of his functions, which were then the same as they had been during the last period that the Baclofen pump worked. His pain level was reduced to 2. Before he started his therapy according to the present invention, his pain was up to 9. His capability to walk has now been increased to walking 2 ½ minutes and 30 times standing up from a chair.

To speed up recovery, he took for a short period soy protein, he found out that this has great benefits for quick recovery, but soy protein is preferably not used in combination with a high dosage of DHA.

The doctor did not want to replace the Baclofen pump. The risks were too high and the current improvements were so high that this couldn't be achieved by the pump alone.

Meanwhile in April/May 2008 the inventor added his last ingredient to his trial; chlorophyll. Firstly because of its detoxifying capability but when the dosage was increased other beneficial goals where achieved. These improvements are:

- Better awakening in the morning
- Increased strength
- Total improvement of all neurological complications
- Going up to 8 minutes walking with help
- Few meters walking without help.
- Practising to go up stairs, 15 times 1 step for each foot

Situation in September 2008

In September 2008 the cocktail of the present inventor had several ingredients and made that he could not only move his legs, stand and walk a few steps, but also that his reflexes and coordination were back. Major improvements are accomplished.
His therapy in September 2008:

- 4500 mg glycine per day, and
- 4000 mg glutamine per day, and
- 1500 mg taurine per day, and
- 2 tablets of multivitamin max. (incl. vitamin B6, B12, folic acid, vitamin E and zinc) per day (see earlier multivitamin list for dosages), and
- 1500 mg magnesium in liquid form per day, and
- 300 mg of a high concentrate form of DHA/day, and

- chlorophyll (1560 mg/day)
- 20 milligrams walnut oil a day

On the first of September 2008 he started with experimenting with intramuscular administration of magnesium (500 mg/day), instead of the oral dosage, in order to improve efficacy.

At this moment the Baclofen pump is not working properly. Before the present invention, the inventor would have had severe redraw effects, possibly resulting in death, but fortunately this is now not the case. One year ago the lack of Baclofen would have been a catastrophe. Without Baclofen the inventor would have been a vegetable, but the cocktail according to the present invention is now taking over and makes that there are no big differences. It is expected that with a properly working pump the effects would be even bigger.

Major Benefits until September 2008 (without trying to be complete)

- Recovery of nerves after being paralysed. Able to stand and walk during therapeutic sessions (up to 40 meters) without helping tools and the inventor is shortly able to go upstairs.
- Recovery of reflexes in both arms.
- Reduction of dystrophy
- Reduction of oedema.
- Reduction of dystonic reactions.
- Improved coordination.
- Reduction of ataxia
- Pain level from nine to two
- Improved speech
- Reduction of reactions caused by liquor hypotension and meninges
- Controllable Epileptic (Status epileptic) seizures and proximal dystonic seizures.
- Again working and thinking on university level.

Situation in September 2009

Meanwhile, the inventor has continued his investigation. He has now discontinued the use of taurine, DHA, chlorophyll and walnut oil, while maintaining his improved condition. During a period of 6 weeks (January/February 2009) he stopped with every medication. This was done in order to give his body time to use its own strength and capability to recover. No side effects occurred besides the fact that the inventor became a little bit less flexible. This period was also a preparation time for starting phase two.

Phase two started with vitamin C and selenium. Then tryptophan was added. This combination worked well but gradually more attacks occurred. This happened in combination with again having awakening problems because of increasing liquor hypotension problems during the night. However, the inventor's capabilities during the day improved. Particularly the night/sleep situation gave problems. Discomforts such as awakening problems, attacks and dystonic problems in his face recurred. Therefore, glycine and glutamine were again added. This helped but was not sufficient.

In his attempt to solve this problem the inventor combined methionine, acetyl L-carnitine and alpha liponic acid. (In an earlier stage he experimented with these medications separately with temporally results).

This combination resulted not only in awakening without any problems but also his capabilities to move improved very rapidly. Within one week he was able to improve his walking from maximally 60 meters to 270 meters. One week later this resulted in 360 meters walking in one single attempt and approximately one month later the inventor could even walk 550 meters! Until now (approximately one and a half month after start) the results remain and give a good hope for the future.

Alpha-liponic acid and methionine were added mainly because of their glutathion increasing capacity and their capability of enhancing methylation processes (which is beneficial for DNA repair). Acetyl-L-carnithine was added because it enhances fatty acid oxidation and has neuroprotective benefits and forms acetylcholine.

Selenium was added because it forms the active center of the enzyme glutathione peroxidase which protects organisms from oxidative damage.

Tryptophan was added because this is converted into serotonine *in vivo* which, in turn, is converted to melatonin. It was therefore expected that the inventor would sleep and awake more easily. Although these effects were not completely accomplished due to the liquor hypothension, it will be an additional benefit for people who don't have this specific problem.

The inventor has also replaced the magnesium in liquid form by magnesium ascorbate in order to obtain more vitamin C. The overall vitamin C dosage has now been increased from 500 mg/day to 4250 mg/day. The inventor has furthermore reduced the glycine and glutamine dosages to 3000 mg/day. This appears to be sufficient. Moreover, he now takes 1 multivitamin tablet per day instead of two tablets.

His therapy in September 2009:

- 3000 mg glycine per day, and
- 3000 mg glutamine per day, and
- 1 tablet of multivitamin max. (incl. vitamin B6, vitamin C, vitamin B12, folic acid, vitamin E and zinc) per day (see earlier multivitamin list for dosages), and
- 4000 mg magnesium ascorbate per day, and
- 1500 mg alpha-lipoic acid per day, and
- 3000 mg acetyl-L-carnithine per day, and
- 600 microgram L-methionine per day, and
- 600 microgram selenium per day, and
- 2000 mg tryptophan per day

The weight of the inventor is 105 kg.

Major Benefits until September 2009 (without trying to be complete)

As compared to September 2008, the condition of the inventor has been further

improved. In addition to the improvements in September 2008, described above, the inventor is now capable of walking at least 360 - 550 meters. In the morning he awakes more easily. Furthermore, the number of seizures is still reduced.

In conclusion, using combinations according to the invention the inventor has significantly improved his quality of life. Instead of no longer being able to move and becoming completely dependable to others in a bed laying situation, the inventor is now capable of standing and walking and using his arms and hands. He is again capable of working, something that was deemed impossible before the present invention.

Claims

1. A method for treating a neurological disorder, and/or alleviating at least one symptom of a neurological disorder, and/or inducing or enhancing the repair and/or production of myelin, brain cells, at least one brain system, nerve cells and/or at least one nerve system, comprising increasing the glycine level and the gamma amino butyric acid (GABA) level in an individual in need thereof, preferably in a human individual.
2. A method according to claim 1, further comprising increasing the vitamin B6 level in said individual.
3. A method according to claim 1 or 2, comprising administering to said individual:
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and/or
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof, and a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell.
4. A method according to any one of claims 1-3, further comprising administering to said individual a therapeutically effective amount of glutamine and/or arginine and/or taurine, or an analogue or metabolite thereof.
5. A method according to any one of claims 1-4, further comprising administering to said individual a therapeutically effective amount of magnesium and/or aspartate and/or kalium, or an analogue or metabolite thereof, optionally in combination with soy protein.
6. A method according to any one of claims 1-5, further comprising administering to said individual a therapeutically effective amount of magnesium ascorbate and/or

alpha-lipoic acidand/or acetyl-L-carnithine (and/or an analogue or metabolite of acetyl-L-carnithine such as acetylcholine) and/or methionine and/or tryptophan (and/or or an analogue or metabolite of tryptophan such as serotonin) and/or selenium.

7. A method according to any one of claims 1-6, further comprising administering to said individual a therapeutically effective amount of an omega-3 polyunsaturated fatty acid (also called a long chain omega-3 fatty acid), said omega-3 polyunsaturated fatty acid preferably comprising alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and/or docosahexaenoic acid (DHA), preferably in combination with a therapeutically effective amount of at least one compound selected from the group consisting of vitamin B12, folic acid, vitamin E, zinc and magnesium.

8. A method according to any one of claims 1-7, further comprising administering to said individual a therapeutically effective amount of chlorophyll.

9. A combination comprising:

- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and/or
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof, and a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell.

10. A combination comprising:

- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and/or

- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof, and a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell,

for use as a medicament.

11. Use of a combination comprising:

- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell, and/or
- a therapeutically effective amount of glycine, or an analogue or metabolite thereof, and a therapeutically effective amount of vitamin B6, or an analogue or metabolite thereof, and a therapeutically effective amount of gamma amino butyric acid (GABA) or an analogue or metabolite of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue or metabolite is preferably capable of specifically binding a GABA receptor of a brain cell or nerve cell,

for the preparation of a medicament for treating a neurological disorder, and/or alleviating the symptoms of a neurological disorder, and/or inducing or enhancing the repair or production of myelin, brain cells, at least one brain system, nerve cells and/or at least one nerve system.

12. A combination or use according to any one of claims 9-11, wherein said combination also comprises a therapeutically effective amount of glutamine and/or arginine and/or taurine and/or chlorophyll.

13. A combination or use according to any one of claims 9-12, wherein said combination also comprises a therapeutically effective amount of magnesium and/or aspartate and/or kalium, optionally in combination with soy protein.

14. A combination or use according to any one of claims 9-13, wherein said combination also comprises a therapeutically effective amount of magnesium

ascorbate and/or alpha-lipoic acid and/or acetyl-L-carnithine (and/or an analogue or metabolite of acetyl-L-carnithine such as acetylcholine) and/or methionine and/or tryptophan (and/or or an analogue or metabolite of tryptophan such as serotonin) and/or selenium.

15. A combination or use according to any one of claims 9-14, wherein said combination also comprises a therapeutically effective amount of an omega-3 polyunsaturated fatty acid (also called a long chain omega-3 fatty acid), said omega-3 polyunsaturated fatty acid preferably comprising alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and/or docosahexaenoic acid (DHA), preferably in combination with a therapeutically effective amount of at least one compound selected from the group consisting of vitamin B12, folic acid, vitamin E, zinc and magnesium.

16. A method, combination or use according to any one of claims 1-15, wherein:

- the amount of glycine to be administered is about 20-60 mg/kg/day, preferably about 30-50 mg/kg/day, more preferably about 35-45 mg/kg/day when glycine is administered orally, and/or wherein the dosage of glycine corresponds to an oral dosage of about 20-60 mg/kg/day, preferably about 30-50 mg/kg/day, more preferably about 35-45 mg/kg/day, and/or
- wherein the amount of glutamine and/or arginine to be administered is about 20-60 mg/kg/day, preferably about 30-50 mg/kg/day when glutamine and/or arginine are administered orally, and/or wherein the dosage of glutamine and/or arginine corresponds to an oral dosage of about 20-60 mg/kg/day, preferably about 30-50 mg/kg/day, and/or
- wherein the amount of Baclofen to be administered is about 0.75-20 microgram/kg/day when Baclofen is administered intrathecally, and/or wherein the dosage of Baclofen corresponds to an intrathecal dosage of 0.75-20 microgram/kg/day, and/or
- wherein the amount of taurine to be administered is about 5-30 mg/kg/day, preferably about 10-20 mg/kg/day when taurine is administered orally, and/or wherein the dosage of taurine corresponds to an oral dosage of about 5-30 mg/kg/day, preferably about 10-20 mg/kg/day, and/or
- wherein the amount of magnesium to be administered is about 5-50 mg/kg/day, preferably about 20-40 mg/kg/day, when magnesium administered orally, and/or

wherein the dosage of magnesium corresponds to an oral dosage of 5-50 mg/kg/day, preferably about 20-40 mg/kg/day, and/or

- wherein the amount of alpha-lipoic acid to be administered is about 5-30 mg/kg/day, preferably about 10-20 mg/kg/day when alpha-lipoic acid is administered orally, and/or wherein the dosage of alpha-lipoic acid corresponds to an oral dosage of about 5-30 mg/kg/day, preferably about 10-20 mg/kg/day, and/or

- wherein the amount of acetyl-L-carnithine to be administered is about 5-45 mg/kg/day, preferably about 20-40 mg/kg/day when acetyl-L-carnithine is administered orally, and/or wherein the dosage of acetyl-L-carnithine corresponds to an oral dosage of about 5-45 mg/kg/day, preferably about 20-40 mg/kg/day, and/or

- wherein the amount of methionine to be administered is about 4-20 microgram/kg/day, preferably about 5-16 microgram/kg/day when methionine is administered orally, and/or wherein the dosage of methionine corresponds to an oral dosage of about 4-20 microgram/kg/day, preferably about 5-16 microgram/kg/day, and/or

- wherein the amount of tryptophan to be administered is about 5-35 mg/kg/day, preferably about 10-30 mg/kg/day when tryptophan is administered orally, and/or wherein the dosage of tryptophan corresponds to an oral dosage of about 5-35 mg/kg/day, preferably about 10-30 mg/kg/day, and/or

- wherein the amount of selenium to be administered is about 4-20 microgram/kg/day, preferably about 5-16 microgram/kg/day when selenium is administered orally, and/or wherein the dosage of selenium corresponds to an oral dosage of about 4-20 microgram/kg/day, preferably about 5-16 microgram/kg/day, and/or

- wherein the amount of vitamin C to be administered is about 20 – 100 mg/kg/day, preferably about 20-40 mg/kg/day when vitamin C is administered orally, and/or wherein the dosage of vitamin C corresponds to an oral dosage of about 20 – 100 mg/kg/day, preferably about 20-40 mg/kg/day.

17. A method, combination or use according to any one of claims 1-16, wherein the ratio between glutamine and taurine or the ratio between arginine and taurine is between 1:1 and 4:1, preferably about 2:1-3:1, when glutamine and taurine or

arginine and taurine are administered via the same route of administration, preferably orally.

18. A method, combination or use according to any one of claims 1-17, wherein the ratio between magnesium and glycine is between 1:4 and 2:1, preferably between 1:3 and 1:1, when magnesium and glycine are administered via the same route of administration, preferably orally.

19. A method, combination or use according to any one of claims 1-18, wherein said neurological disorder comprises a myelin damage-related disorder, whiplash, dystrophy, dystonia, paralysis, quada equina syndrome, ataxia, epilepsy, multiple sclerosis, hypersensitivity disorder, spasm, hypersensitivity of the dura mater, hypersensitivity of the pia mater, liquor hypotension and/or complex regional pain syndrome (CRPS).

20. A kit of parts comprising a therapeutically effective amount of:

* glycine, and
* glutamine and/or arginine, and
* taurine and/or chlorophyll,

the kit of part preferably also comprising:

- a therapeutically effective amount of vitamin B6, and/or
- a therapeutically effective amount of vitamin B12 and folic acid, and/or
- a therapeutically effective amount of magnesium and/or aspartate and/or kalium, and/or
- an omega-3 polyunsaturated fatty acid (also called a long chain omega-3 fatty acid), said omega-3 polyunsaturated fatty acid preferably comprising alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and/or docosahexaenoic acid (DHA), preferably in combination with a therapeutically effective amount of at least one compound selected from the group consisting of vitamin B12, folic acid, vitamin E, zinc and magnesium, and/or
- soy protein, and/or
- gamma amino butyric acid (GABA) or an analogue of GABA, preferably 4-amino-3-(4-chlorophenyl)-butanoic acid (Baclofen), which analogue is capable of specifically binding a GABA receptor of a brain cell or nerve cell.

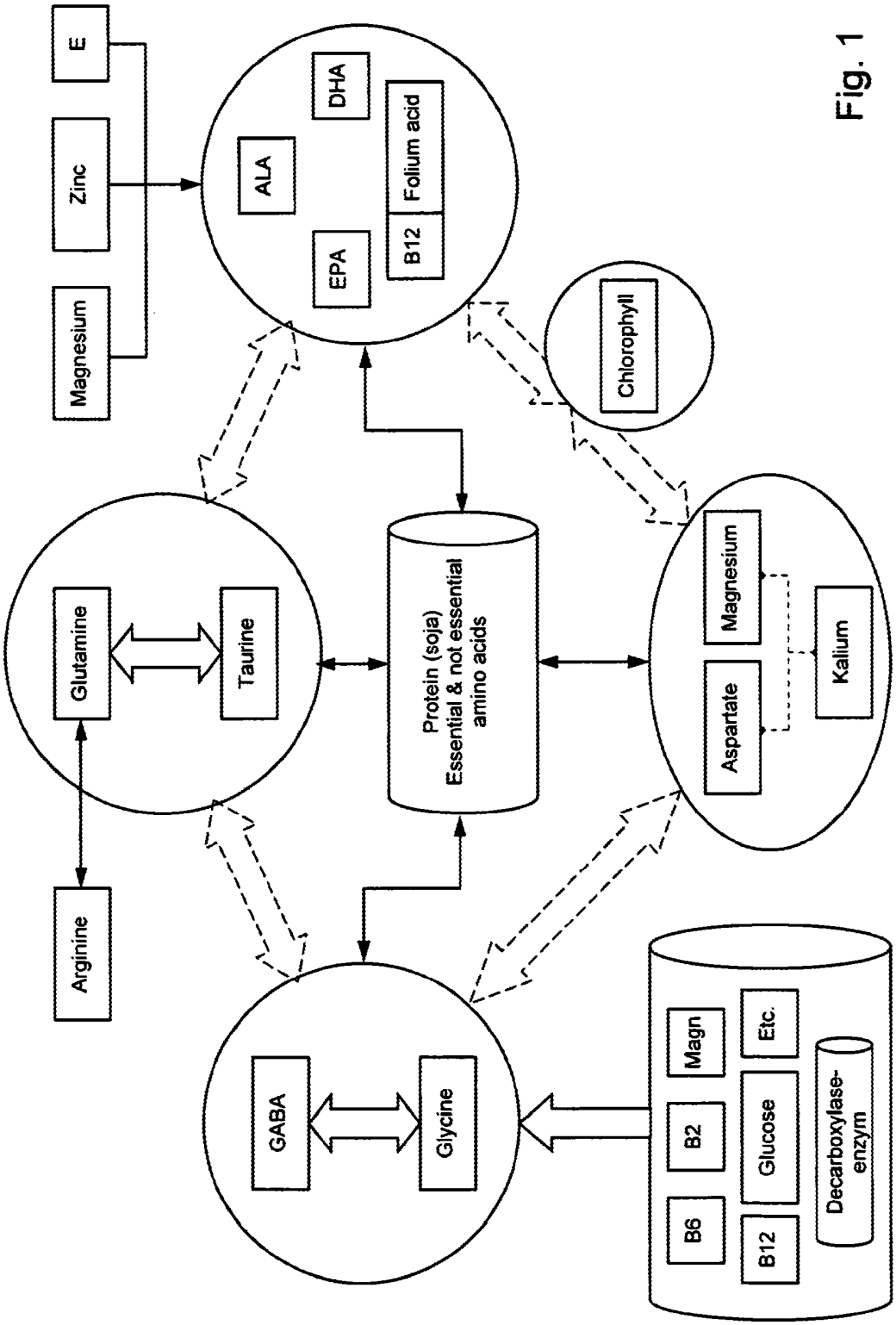
E
Zinc
Magnesium
DHA
ALA
Folium acid
EPA
B12
Chlorophyll
Glutamine
Taurine
Protein (soja)
Essential & not essential
amino acids
Magnesium
Kalium
Aspartate
Arginine
GABA
Glycine
Magn
Etc.
B2
Glucose
B6
B12
Decarboxylase-
enzym

Fig. 1

INTERNATIONAL SEARCH REPORT

International application No
PCT/NL2009/050535

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/197 A61K31/198 A61K31/4415 A61P25/00 A61P25/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, EMBASE, CHEM ABS Data, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 01/10432 A1 (UAB RESEARCH FOUNDATION [US]; MEYTHALER JAY M [US]; PEDUZZI JEAN [US]) 15 February 2001 (2001-02-15) page 6 - paragraph 2 figure 1	1-20
Y	ZUNIGA ROBERT E ET AL: "Intrathecal baclofen: A useful agent in the treatment of well-established complex regional pain syndrome" REGIONAL ANESTHESIA AND PAIN MEDICINE, vol. 27, no. 1, January 2002 (2002-01), pages 90-93, XP002502892 ISSN: 1098-7339 the whole document	1-20

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

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"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 December 2009	04/01/2010

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Büttner, Ulf

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	ALCANIZ-FOLCH ET AL: "804 USE OF INTRATHECAL BACLOFEN IN THE CASE OF A PATIENT WITH FOCAL DYSTONIA" EUROPEAN JOURNAL OF PAIN, SAUNDERS, LONDON, GB, vol. 10, 1 September 2006 (2006-09-01), page S209, XP005741898 ISSN: 1090-3801 the whole document	1-20
Y	AWAAD Y ET AL: "Progressive dystonia in a child with chromosome 18p deletion, treated with intrathecal baclofen" JOURNAL OF CHILD NEUROLOGY, DECKER PERIODICALS, HAMILTON, CA, vol. 14, no. 2, 1 February 1999 (1999-02-01), pages 75-77, XP009098835 ISSN: 0883-0738 Progressive dystonia treated with intrathecal baclofen ; page 77 - last paragraph	1-20
Y	DYKSTRA D D ET AL: "Treatment of cervical dystonia and focal hand dystonia by high cervical continuously infused intrathecal baclofen: A report of 2 cases" ARCHIVES OF PHYSICAL MEDICINE AND REHABILITATION, W.B. SAUNDERS, vol. 86, no. 4, 1 April 2005 (2005-04-01), pages 830-833, XP004836048 ISSN: 0003-9993 the whole document	1-20
Y	WO 02/43507 A (HEALTH RES INST [US]; WALSH WILLIAM JOHN [US]; USMAN ANJUM IONA [US]) 6 June 2002 (2002-06-06) claims 41,42	1-20
Y	US 2003/194453 A1 (COLEMAN HENRY D [US] ET AL) 16 October 2003 (2003-10-16) paragraph [0014] examples	1-20
Y	WO 2007/145520 A (NUTRICIA NV [NL]; HARTOG ANITA [NL]) 21 December 2007 (2007-12-21) page 5, line 25 - line 32	1-20
Y	WO 2008/010222 A (UNIV RAMOT [IL]; UNIV BAR ILAN [IL]; BIOLINERX LTD [IL]; NUDELMAN ABRA) 24 January 2008 (2008-01-24) page 25, line 7 - line 10	1-20

-/--

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 2008/100727 A (UNIV COLUMBIA [US]; CLEVELAND W LOUIS [US]) 21 August 2008 (2008-08-21) page 4 - page 5	1-20
Y	CHERUBINI E ET AL: "The action of glycine on rat epileptic foci" NEUROSCIENCE LETTERS, LIMERICK, IE, vol. 21, no. 1, 1 January 1981 (1981-01-01), pages 93-97, XP023799011 ISSN: 0304-3940 [retrieved on 1981-01-01] page 96	1-20
Y	WO 2007/096694 A (VERGARA RAMIRO [CO]) 30 August 2007 (2007-08-30) claims	1-15
Y	AKHONDIAN J ET AL: "High-dose oral pyridoxine in treatment of paediatric recurrent intractable seizures" EPILEPSIA, vol. 45, no. Suppl. 3, 2004, page 159, XP002502891 & 6TH EUROPEAN CONGRESS ON EPILEPTOLOGY; VIENNA, AUSTRIA; MAY 30-JUNE 03, 2004 ISSN: 0013-9580 the whole document	1-20
Y	WO 2007/098020 A (RELIANT PHARMACEUTICALS INC [US]; KIRCHER CHRISTOPHER [US]; PRETORIUS) 30 August 2007 (2007-08-30) claims	4,11
Y	WANG WEI-SHU ET AL: "Oral glutamine is effective for preventing oxaliplatin-induced neuropathy in colorectal cancer patients." THE ONCOLOGIST MAR 2007, vol. 12, no. 3, March 2007 (2007-03), pages 312-319, XP002560323 ISSN: 1083-7159 page 314 - last paragraph	4,12, 16-17

-/--

INTERNATIONAL SEARCH REPORT

International application No
PCT/NL2009/050535

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WOLF S ET AL: "Chemotherapy-induced peripheral neuropathy: Prevention and treatment strategies" EUROPEAN JOURNAL OF CANCER, PERGAMON PRESS, OXFORD, GB, vol. 44, no. 11, 1 July 2008 (2008-07-01), pages 1507-1515, XP022808031 ISSN: 0959-8049 [retrieved on 2008-06-18] page 1508, column 1 page 1508, column 2 page 1511, column 1, paragraph 2	4-7, 12-17,20
Y	HAWKINS J E ET AL: "On the efficacy of asparagine, glutamine, gamma-aminobutyric acid and 2-pyrrolidinone in preventing chemically induced seizures in mice" CLINICA CHIMICA ACTA, ELSEVIER BV, AMSTERDAM, NL, vol. 2, no. 6, 1 December 1957 (1957-12-01), pages 481-484, XP023618337 ISSN: 0009-8981 [retrieved on 1957-12-01] figure 1	4-7, 12-17,20
Y	WO 00/44361 A2 (LAXDALE LIMITED [GB]; PEET MALCOLM [GB]; VADDADI KRISHNARAO SITAMRAO [) 3 August 2000 (2000-08-03) claims	7,15,20

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/NL2009/050535

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0110432 A1	15-02-2001	AU 771115 B2	11-03-2004
		AU 6764500 A	05-03-2001
		CA 2378955 A1	15-02-2001
		EP 1202720 A1	08-05-2002
		JP 2003506407 T	18-02-2003
		NZ 517407 A	31-10-2003
		US 2006142396 A1	29-06-2006
WO 0243507 A	06-06-2002	AU 3652702 A	11-06-2002
US 2003194453 A1	16-10-2003	US 2004213829 A1	28-10-2004
WO 2007145520 A	21-12-2007	EP 2032170 A1	11-03-2009
WO 2008010222 A	24-01-2008	AU 2007274583 A1	24-01-2008
		CA 2659521 A1	24-01-2008
		EP 2051735 A2	29-04-2009
		WO 2008010223 A2	24-01-2008
		KR 20090048462 A	13-05-2009
		US 2009304584 A1	10-12-2009
WO 2008100727 A	21-08-2008	NONE	
WO 2007096694 A	30-08-2007	NONE	
WO 2007098020 A	30-08-2007	EP 1984029 A2	29-10-2008
		JP 2009532663 T	10-09-2009
WO 0044361 A2	03-08-2000	AT 300296 T	15-08-2005
		AU 3065700 A	18-08-2000
		BR 0007743 A	27-11-2001
		CA 2360776 A1	03-08-2000
		CN 1338929 A	06-03-2002
		CN 1739496 A	01-03-2006
		CZ 20012695 A3	13-02-2002
		DE 60021525 D1	01-09-2005
		DE 60021525 T2	01-06-2006
		DK 1148873 T3	28-11-2005
		EE 200100387 A	17-02-2003
		EP 1148873 A2	31-10-2001
		ES 2246825 T3	01-03-2006
		HK 1039564 A1	09-12-2005
		HR 20010558 A2	31-08-2002
		HU 0105215 A2	29-05-2002
		IS 5988 A	29-06-2001
		JP 2002535355 T	22-10-2002
WO 0044361 A2		MX PA01007662 A	24-06-2003
		NO 20013546 A	25-09-2001
		NZ 513172 A	31-10-2003
		PT 1148873 E	30-11-2005
		SK 10392001 A3	05-02-2002
		TR 200102170 T2	21-12-2001
		TR 200504156 T2	21-07-2006
		TW 228041 B	21-02-2005
		UA 76405 C2	17-12-2001
		US 2008200547 A1	21-08-2008
		US 6384077 B1	07-05-2002

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/NL2009/050535

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
		ZA 200106105 A	30-04-2003