DA release from residual neurons. However, chronic levodopa administration at concentrations sufficient to achieve symptomatic relief, particularly in late stage PD patients or those on long-term levodopa treatment, leads to the emergence of disabling motor side effects, termed levodopa-induced dyskinesia (LID).

SUMMARY

[0006] The present inventors have revealed that striatal cholinergic interneurons can powerfully inhibit dopamine release in the striatum after activating nicotinic acetylcholine receptors (nAChRs) on dopamine axons. Administration of a nAChR antagonist/blocker is expected to relieve an inhibition of dopamine release caused by striatal cholinergic interneurons, thereby providing an effective treatment for a condition or disorder in which reduced levels of dopamine are implicated. Thus, the present disclosure targets the reduced levels of dopamine seen in a number of conditions.

[0007] The present disclosure resides in the recognition that therapy involving the administration of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, results in an increase in the level of dopamine in the CNS. The administration of a nAChR antagonist/blocker itself targets the inhibition of dopamine release caused by striatal cholinergic interneurons acting at the nAChR.

[0008] Herein, the term “nicotinic acetylcholine receptor antagonist/blocker” (also known as nicotinic antagonist/blocker), refers to a compound which inhibits the action of acetylcholine (ACh) at nicotinic acetylcholine receptors. The term “antagonist/blocker” encompasses competitive antagonists and non-competitive antagonists.

Therapeutic Uses and Applications

[0009] In a first example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in the treatment of a condition or disorder in which reduced levels of dopamine are implicated.

[0010] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in the treatment of a condition or disorder in which reduced levels of dopamine in the central nervous system (CNS) are implicated.

[0010a] In one aspect, the present disclosure refers to use of mecamylamine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for increasing the level of dopamine in the CNS of a subject in the treatment of a condition or disorder in which reduced levels of dopamine in the CNS are implicated; wherein the condition or disorder is selected from dopamine deficiency, addiction (including binge eating, nicotine addiction and alcohol addiction), Alzheimer’s disease, attention deficit hyperactivity disorder (ADHD), bipolar disorder, dopa-responsive dystonia and DRD-plus, Huntington’s disease, multiple sclerosis, obsessive compulsive disorder (OCD), Parkinson’s disease (including resting tremor in Parkinson’s disease), schizophrenia, tics (i.e. a repetitive involuntary movement or sound), depression and reward deficiency syndrome.

[0011] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in the treatment of a condition or disorder in which reduced levels of dopamine in the brain are implicated.

[0012] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in the treatment of a condition or disorder in which reduced levels of dopamine in the striatum are implicated.

[0013] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in the treatment of a condition or disorder in which reduced levels of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra are implicated.

[0014] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in the treatment of a condition or disorder in which reduced levels of dopamine in the dorsal striatum (including the caudate and putamen) are implicated.

[0015] In further example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in increasing the level of dopamine in the CNS.

[0015a] In one aspect, the present disclosure refers to use of mecamylamine, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for increasing the level of dopamine in the CNS.

[0016] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in increasing the level of dopamine in the brain.

[0017] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in increasing the level of dopamine in the striatum.

[0018] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in increasing the level of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia, and/or the substantia nigra.

[0019] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in increasing the level of dopamine in the dorsal striatum (including the caudate and putamen).

[0020] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in increasing the level of dopamine in the CNS of a subject in the treatment of a condition or disorder in which reduced levels of dopamine in the CNS are implicated.

[0020a] In one aspect, the present disclosure refers to use of a pharmaceutical composition which comprises a mecamylamine, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable excipients, in the manufacture of a medicament for increasing the level of dopamine in the CNS of a subject in the treatment of a condition or disorder in which reduced levels of dopamine in the CNS are implicated; wherein the condition or disorder is selected from dopamine deficiency, addiction (including binge eating, nicotine addiction and alcohol addiction), Alzheimer's disease, attention deficit hyperactivity disorder (ADHD), bipolar disorder, dopa-responsive dystonia and DRD-plus, Huntington's disease, multiple sclerosis, obsessive compulsive disorder (OCD), Parkinson's disease (including resting tremor in Parkinson's disease), schizophrenia, tics (i.e. a repetitive involuntary movement or sound), depression and reward deficiency syndrome.

[0021] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in increasing the level of dopamine in the brain of a subject in the treatment of a condition or disorder in which reduced levels of dopamine in the brain are implicated.

[0022] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in increasing the level of dopamine in the striatum of a subject in the treatment of a condition or disorder in which reduced levels of dopamine in the striatum are implicated.

[0023] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in increasing the level of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra of a subject, in the treatment of a condition or disorder in which reduced levels of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra are implicated.

[0024] In another example of the disclosure there is provided a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in increasing the level of dopamine in the dorsal striatum (including the caudate and putamen) of a subject in the treatment of a condition or disorder in which reduced levels of dopamine in the dorsal striatum (including the caudate and putamen) are implicated.

[0025] In another example of the disclosure, there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in treatment of a subject suffering from a disorder associated with reduced levels of dopamine in the CNS.

[0026] In another example of the disclosure, there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in treatment of a subject suffering from a disorder associated with reduced levels of dopamine in the brain.

[0027] In another example of the disclosure, there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in treatment of a subject suffering from a disorder associated with reduced levels of dopamine in the striatum.

[0028] In another example of the disclosure, there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in treatment of a subject suffering from

a disorder associated with reduced levels of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra.

[0029] In another example of the disclosure, there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in treatment of a subject suffering from a disorder associated with reduced levels of dopamine in the dorsal striatum (including the caudate and putamen).

[0030] In another example of the disclosure there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in increasing the level of dopamine in the CNS.

[0031] In another example of the disclosure there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in increasing the level of dopamine in the brain.

[0032] In another example of the disclosure there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in increasing the level of dopamine in the striatum.

[0033] In another example of the disclosure there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in increasing the level of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra.

[0034] In another example of the disclosure there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in increasing the level of dopamine in the dorsal striatum (including the caudate and putamen).

[0035] In another example of the disclosure, there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in increasing the level of dopamine in the CNS, in the treatment of a subject suffering from a disorder associated with reduced levels of dopamine in the CNS.

[0036] In another example of the disclosure, there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt

thereof, in the manufacture of a medicament for use in increasing the level of dopamine in the brain, in the treatment of a subject suffering from a disorder associated with reduced levels of dopamine in the brain.

[0037] In another example of the disclosure, there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in increasing the level of dopamine in the CNS, in the treatment of a subject suffering from a disorder associated with reduced levels of dopamine in the CNS.

[0038] In another example of the disclosure, there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in increasing the level of dopamine in the striatum, in the treatment of a subject suffering from a disorder associated with reduced levels of dopamine in the striatum.

[0039] In another example of the disclosure, there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in increasing the level of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra, in the treatment of a subject suffering from a disorder associated with reduced levels of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra.

[0040] In another example of the disclosure, there is provided the use of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for use in increasing the level of dopamine in the dorsal striatum (including the caudate and putamen), in the treatment of a subject suffering from a disorder associated with reduced levels of dopamine in the dorsal striatum (including the caudate and putamen).

[0041] In another example of the disclosure, there is provided the use of a nAChR antagonist/blocker, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for increasing the level of dopamine in the CNS in the treatment of a condition or disorder in which reduced levels of dopamine in the CNS are implicated.

[0042] In another example of the disclosure, there is provided the use of a nAChR antagonist/blocker, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for increasing the level of dopamine in the brain in the treatment of a condition or disorder in which reduced levels of dopamine in the brain are implicated.

[0043] In another example of the disclosure, there is provided the use of a nAChR antagonist/blocker, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for increasing the level of dopamine in the striatum in the treatment of a condition or disorder in which reduced levels of dopamine in the striatum are implicated.

[0044] In another example of the disclosure, there is provided the use of a nAChR antagonist/blocker, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for increasing the level of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra in the treatment of a condition or disorder in which reduced levels of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra are implicated.

[0045] In another example of the disclosure, there is provided the use of a nAChR antagonist/blocker, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for increasing the level of dopamine in the dorsal striatum (including the caudate and putamen), in the treatment of a condition or disorder in which reduced levels of dopamine in the dorsal striatum (including the caudate and putamen) are implicated.

Methods of treatment

[0046] In another example of the disclosure there is provided a method of treating a condition or disorder in which reduced levels of dopamine in the CNS are implicated, said method comprising administering to a subject in need thereof a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof.

[0047] In another example of the disclosure there is provided a method of treating a condition or disorder in which reduced levels of dopamine in the brain are implicated, said method comprising administering to a subject in need thereof a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof.

[0048] In another example of the disclosure there is provided a method of treating a condition or disorder in which reduced levels of dopamine in the striatum are implicated, said method comprising administering to a subject in need thereof a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof.

[0049] In another example of the disclosure there is provided a method of treating a condition or disorder in which reduced levels of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra are implicated, said method comprising administering to a subject in need thereof a therapeutically effective amount of

a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof.

[0050] In another example of the disclosure there is provided a method of treating a condition or disorder in which reduced levels of dopamine in the dorsal striatum (including the caudate and putamen) are implicated, said method comprising administering to a subject in need thereof a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof.

[0051] In another example of the disclosure there is provided a method of increasing the level of dopamine in the CNS of a subject, the method comprising administering a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, to the subject.

[0052] In another example of the disclosure there is provided a method of increasing the level of dopamine in the brain of a subject, the method comprising administering a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, to the subject.

[0053] In another example of the disclosure there is provided a method of increasing the level of dopamine in the striatum of a subject, the method comprising administering a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, to the subject.

[0054] In another example of the disclosure there is provided a method of increasing the level of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigraof a subject, the method comprising administering a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, to the subject.

[0055] In another example of the disclosure there is provided a method of increasing the level of dopamine in the dorsal striatum (including the caudate and putamen)of a subject, the method comprising administering a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker, or a pharmaceutically acceptable salt thereof, to the subject.

[0056] In another example of the disclosure, there is provided a method of treating a condition or disorder in which reduced levels of dopamine in the CNS are implicated, said method comprising administering to a subject in need thereof a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker or a pharmaceutically acceptable salt thereof, wherein administration of nicotinic acetylcholine receptor antagonist/blocker increases the level of dopamine in the CNS.

[0057] In another example of the disclosure, there is provided a method of treating a condition or disorder in which reduced levels of dopamine in the brain are implicated, said method comprising administering to a subject in need thereof a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker or a pharmaceutically acceptable salt thereof, wherein administration of nicotinic acetylcholine receptor antagonist increases the level of dopamine in the brain.

[0058] In another example of the disclosure, there is provided a method of treating a condition or disorder in which reduced levels of dopamine in the striatum are implicated, said method comprising administering to a subject in need thereof a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker or a pharmaceutically acceptable salt thereof, wherein administration of nicotinic acetylcholine receptor antagonist/blocker increases the level of dopamine in the striatum.

[0059] In another example of the disclosure, there is provided a method of treating a condition or disorder in which reduced levels of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra are implicated, said method comprising administering to a subject in need thereof a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker or a pharmaceutically acceptable salt thereof, wherein administration of nicotinic acetylcholine receptor antagonist/blocker increases the level of dopamine in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra.

[0060] In another example of the disclosure, there is provided a method of treating a condition or disorder in which reduced levels of dopamine in the dorsal striatum (including the caudate and putamen) are implicated, said method comprising administering to a subject in need thereof a therapeutically effective amount of a nicotinic acetylcholine receptor (nAChR) antagonist/blocker or a pharmaceutically acceptable salt thereof, wherein administration of nicotinic acetylcholine receptor antagonist/blocker increases the level of dopamine in the dorsal striatum (including the caudate and putamen).

Conditions to be Treated

[0061] A number of conditions are associated with reduced levels of dopamine. The inventors have demonstrated that administration of a nAChR antagonist/blocker will act to increase the dopamine levels in the CNS (e.g. in the brain, including in the striatum) to treat such conditions. Suitably, the administration of a nAChR antagonist/blocker will act to increase the dopamine levels in the dorsal striatum, ventral striatum, ventral tegmental area, basal ganglia and/or the substantia nigra. Most suitably, the administration of a nAChR antagonist/blocker will act to increase the dopamine levels in the dorsal striatum (including the caudate and putamen).

[0079] According to a further example of the disclosure there is provided a pharmaceutical composition comprising a nAChR antagonist/blocker as defined hereinbefore, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable excipients.

[0080] Suitably, the pharmaceutical composition further comprises one or more additional pharmaceutically active agents, as defined herein.

[0081] Suitably, the pharmaceutical composition described herein is for use in the treatment of a condition or disorder defined herein.

[0082] The compositions of the disclosure may be in a form suitable for oral use (for example as tablets, lozenges, hard or soft capsules, aqueous or oily suspensions, emulsions, dispersible powders or granules, syrups or elixirs), for topical use (for example as creams, ointments, gels, or aqueous or oily solutions or suspensions), for administration by inhalation (for example as a finely divided powder or a liquid aerosol), for administration by insufflation (for example as a finely divided powder) or for parenteral administration (for example as a sterile aqueous or oily solution for intravenous, subcutaneous, intramuscular, intraperitoneal or intramuscular dosing or as a suppository for rectal dosing). The compositions of the disclosure may be in a form suitable for administration directly to the CNS (for example as a sterile aqueous or oily solution for local infusion to the CNS or direct injection to the CNS).

[0083] The compositions of the disclosure may be obtained by conventional procedures using conventional pharmaceutical excipients, well known in the art. Thus, compositions intended for oral use may contain, for example, one or more colouring, sweetening, flavouring and/or preservative agents.

[0084] An effective amount of a nAChR antagonist/blocker for use in therapy is an amount sufficient to treat or prevent a condition in which reduced levels of dopamine in the CNS are implicated, referred to herein, slow its progression and/or reduce the symptoms associated with the condition.

[0085] The amount of active ingredient that is combined with one or more excipients to produce a single dosage form will necessarily vary depending upon the individual treated and the particular route of administration. For Example, a formulation intended for oral administration to humans will generally contain, for example, from 0.5 mg to 0.5 g of active agent (more suitably from 0.5 to 100 mg, for example from 1 to 30 mg) compounded with an appropriate and convenient amount of excipients which may vary from about 5 to about 98 percent by weight of the total composition.

[0086] The size of the dose for therapeutic or prophylactic purposes of a nAChR antagonist/blocker will naturally vary according to the nature and severity of the conditions,

the age and sex of the animal or patient and the route of administration, according to well-known principles of medicine.

[0087] In using a nAChR antagonist/blocker for therapeutic or prophylactic purposes it will generally be administered so that a daily dose in the range, for example, 0.1 mg/kg to 75 mg/kg body weight is received, given if required in divided doses. In general lower doses will be administered when a parenteral route is employed. Thus, for example, for intravenous or intraperitoneal administration, a dose in the range, for example, 0.1 mg/kg to 30 mg/kg body weight will generally be used. Similarly, for administration by inhalation, a dose in the range, for example, 0.05 mg/kg to 25 mg/kg body weight will be used. Oral administration may also be suitable, particularly in tablet form. Typically, unit dosage forms will contain about 0.5 mg to 0.5 g of a nAChR antagonist/blocker.

Combinations

[0088] The nicotinic acetylcholine receptor antagonist/blocker treatment defined hereinbefore may be applied as a sole therapy or may involve, in addition to the nicotinic acetylcholine receptor antagonist/blocker, further agents that are conventionally used for the treatment of the condition concerned. Thus, the nicotinic acetylcholine receptor antagonist/blocker or pharmaceutical composition may be administered in combination with one or more additional pharmaceutically active agents.

[0089] Such conjoint treatment may be achieved by way of the simultaneous, sequential or separate dosing of the individual components of the treatment. Such combination products employ the nicotinic acetylcholine receptor antagonist/blocker within its approved dosage range described hereinbefore and the other pharmaceutically-active agent within its approved dosage range.

[0090] In a further example of the disclosure there is provided a nicotinic acetylcholine receptor antagonist/blocker, or a pharmaceutically acceptable salt thereof, in combination with another pharmaceutical agent for use in the treatment of a condition or disorder in which reduced levels of dopamine in the CNS are implicated. The condition or disorder may be any of those defined herein.

[0091] Suitably, the additional pharmaceutically active agent is an agent which increases the level of dopamine in the CNS by a different mechanism of action to the nicotinic acetylcholine receptor antagonist/blocker. Examples of such agents dopamine precursors (e.g. levodopa, co-careldopa, cobeneldopa), dopamine agonists (e.g. pramipexole, ropinirole, apomorphine, rotigine), MAO-B inhibitors (e.g. rasagiline, selegiline, safinamide),

COMT inhibitors (e.g. entacapone, opicapone), amantadine, anticholinergics (e.g. procyclidine, trihexyphenidyl) or Ritalin.

[0092] In a further example of the disclosure there is provided a nicotinic acetylcholine receptor antagonist/blocker, or a pharmaceutically acceptable salt thereof, for use in the treatment of Parkinson's Disease, in combination with a dopamine precursor (e.g. levodopa, co-careldopa, cobeneldopa), a dopamine agonist (e.g. pramipexole, ropinirole, apomorphine, rotigine), a MAO-B inhibitor (e.g. rasagiline, selegiline, safinamide), a COMT inhibitor (e.g. entacapone, opicapone), amantadine or an anticholinergic (e.g. procyclidine, trihexyphenidyl). Suitably, the nicotinic acetylcholine receptor antagonist/blocker, or a pharmaceutically acceptable salt thereof, is for use in the treatment of Parkinson's Disease, in combination with a dopamine precursor (e.g. levodopa, co-careldopa, cobeneldopa).

[0093] Herein, where the term "combination" is used it is to be understood that this refers to simultaneous, separate or sequential administration. In one example of the disclosure "combination" refers to simultaneous administration. In another example of the disclosure "combination" refers to separate administration. In a further example of the disclosure "combination" refers to sequential administration. Where the administration is sequential or separate, the delay in administering the second component should not be such as to lose the beneficial effect of the combination.

[0094] According to a further example of the disclosure there is provided a pharmaceutical composition which comprises a nicotinic acetylcholine receptor antagonist/blocker, or a pharmaceutically acceptable salt thereof, in combination with an agent which increases the level of dopamine in the CNS by a different mechanism of action to the nicotinic acetylcholine receptor antagonist/blocker, in association with a pharmaceutically acceptable diluent or carrier.

[0095] In another example, the disclosure relates to a therapeutic combination comprising a nicotinic acetylcholine receptor antagonist/blocker and a further agent which increases the level of dopamine in the CNS by a different mechanism of action to the nicotinic acetylcholine receptor antagonist/blocker.

BRIEF DESCRIPTION OF THE DRAWINGS

[0096] Embodiments of the invention are further described hereinafter with reference to the accompanying drawings, which are discussed below: