and the present invention seeks to provide alternative and more efficient ways to treat cognitive dysfunction.

Summary ~~of the invention~~

The present inventor has found that the combined use of the acetylcholine esterase inhibitor donepezil and vortioxetine gives rise to a synergistic increase in the extra-cellular level of acetylcholine in the brain.

Accordingly, in one ~~embodiment~~aspect, the present invention relates to a composition comprising vortioxetine and donepezil together with a pharmaceutically acceptable excipient.

In one embodiment, the ~~invention~~ disclosure relates to the use of vortioxetine and donepezil for the manufacture of a medicament for the treatment of cognitive dysfunction.

In one embodiment, the ~~invention~~ disclosure relates to a method for the treatment of cognitive dysfunction, the method comprising the combined administration of vortioxetine and donepezil to a patient in need thereof.

In one embodiment, the ~~invention~~ disclosure relates to vortioxetine and donepezil for the combined use in a method for the treatment of cognitive impairment.

In another aspect, there is provided the use of vortioxetine and donepezil for the manufacture of a medicament for the treatment of a disease selected from cognitive dysfunction; dementia in Alzheimer's disease; vascular dementia; dementia in Pick's disease; dementia in Creutzfeldt-Jakob disease; dementia in Huntington's disease; dementia in Parkinson's disease; dementia in HIV (human immunodeficiency virus); dementia in abusers (alcohol or drugs); MCI (mild cognitive impairment); cognitive dysfunction associated with depression; and cognitive dysfunction associated with schizophrenia.

Figures

Figure 1: The pharmacodynamic acetylcholine response in the ventral hippocampus in freely-moving rats after the combined administration of vortioxetine and donepezil. Figure 1A: Acetylcholine response at 0 mg/kg vortioxetine and 0 mg/kg donepezil (●); 0.3 mg/kg donepezil (▲); or 1 mg/kg donepezil (■). Figure 1B: Acetylcholine response at 5 mg/kg vortioxetine and 0.3 mg/kg donepezil (▲); and 1 mg/kg donepezil (■). Vehicle/vehicle (●) is included for reference. Figuge 1C: Acetylcholine response at 10 mg/kg vortioxetine and 0.3 mg/kg donepezil (▲); and 1 mg/kg donepezil (■). Vehicle/vehicle (●) is included for reference.

Figure 2: The pharmacodynamic acetylcholine response in the ventral hippocampus in freely-moving rats after the combined administration of vortioxetine and donepezil.

Figure 2A: Acetylcholine response at 0.3 mg/kg donepezil and 0 mg/kg vortioxetine (▲); 5 mg/kg vortioxetine (■); or 10 mg/kg vortioxetine (×).Vehicle/vehicle (●) is included for reference. Figure 2B: Acetylcholine response at 1 mg/kg donepezil and 0 mg/kg vortioxetine

Claims

1. A pharmaceutical composition comprising vortioxetine and donepezil together with a pharmaceutically acceptable excipient.

2. The composition according to claim one comprising 5-25 mg donepezil.

3. The composition according to claim 1 or 2 comprising 5-20 mg vortioxetine.

4. The use of vortioxetine and donepezil for the manufacture of a medicament for the treatment of a disease selected from cognitive dysfunction; dementia in Alzheimer's disease; vascular dementia; dementia in Pick's disease; dementia in Creutzfeldt-Jakob disease; dementia in Huntington's disease; dementia in Parkinson's disease; dementia in HIV (human immunodeficiency virus); dementia in abusers (alcohol or drugs); MCI (mild cognitive impairment); cognitive dysfunction associated with depression; and cognitive dysfunction associated with schizophrenia.

5. The use according to claim 4, wherein said medicament comprises 5-25 mg donepezil.

6. The use according to claim 4 or 5, wherein said medicament comprises 5-20 mg vortioxetine.

~~7. Vortioxetine and donepezil for use in a method for the treatment of a disease selected from cognitive dysfunction; dementia in Alzheimer's disease; vascular dementia; dementia in Pick's disease; dementia in Creutzfeldt-Jakob disease; dementia in Huntington's disease; dementia in Parkinson's disease; dementia in HIV (human immunodeficiency virus); dementia in abusers (alcohol or drugs); MCI (mild cognitive impairment); cognitive dysfunction associated with depression; and cognitive dysfunction associated with schizophrenia.~~

~~8. The use according to claim 7, wherein said donepezil is between 5 and 25 mg donepezil.~~

~~9. The use according to claim 7 or 8, wherein said vortioxetine is between 5 and 20 mg vortioxetine.~~

10. A method for the treatment of a disease selected from cognitive dysfunction; dementia in Alzheimer's disease; vascular dementia; dementia in Pick's disease; dementia in Creutzfeldt-Jakob disease; dementia in Huntington's disease; dementia in Parkinson's disease; dementia in HIV (human immunodeficiency virus); dementia in abusers (alcohol or drugs); MCI (mild cognitive impairment); cognitive dysfunction associated with depression; and cognitive dysfunction associated with schizophrenia, the method comprising the combined administration of vortioxetine and donepezil to a patient in need thereof.

11. The use according to claim 11, wherein said patient is administered 5-25 mg donepezil.

12. The use according to claim 10 or 11, wherein said patient is administered 5-20 mg vortioxetine.