Baclofen, a $GABA_B$ receptor agonist, is known to induce anterograde amnesia in rodents [11]. More recently, recurrent spells of amnesia have been reported in a woman subjected to intrathecal instillation of baclofen in the frame of a treatment for dystonia [12].Similarly, a clinical study about the effects of acamprosate on healthy young human subjects has shown that acamprosate impairs free recall, supporting the hypothesis that acamprosate impairs memory functions [13].

As shown herein, the inventors have found combinations of particular drugs that are efficient to stimulate cognition *in vivo*, particularly in healthy subjects, and which represent novel improved safe and efficient nootropic agents.

SUMMARY

One aspect of the invention relates to a use of a combination of at least two compounds selected from baclofen, acamprosate, cinacalcet, mexiletine, sulfisoxazole, and torasemide, or salt(s), prodrug(s), derivative(s), or sustained release formulation(s) thereof, for improving memory and/or memory related mental function performances in a subject not experiencing a condition which impairs his memory and/or memory related mental functions.

Another object resides in a composition comprising a combination of at least two drugs selected from baclofen, acamprosate, cinacalcet, mexiletine, sulfisoxazole, and torasemide, or salt(s), prodrug(s), derivative(s), or sustained release formulation(s) thereof, for use as a stimulator of cognitive function in a subject in need thereof.

Another object resides in a method for stimulating cognition in a subject in need thereof, comprising administering to the subject a combination of at least two drugs selected from baclofen, acamprosate, cinacalcet, mexiletine, sulfisoxazole, and torasemide, or salt(s), prodrug(s), derivative(s), or sustained release formulation(s) thereof.

In a preferred embodiment, the compositions for use herein comprise a combination of drugs selected from:

- baclofen and acamprosate,
- mexiletine and cinacalcet,
- baclofen and torasemide, or
- sulfisoxazole and torasemide.

Baclofen, a $GABA_B$ receptor agonist, is known to induce anterograde amnesia in rodents [11]. More recently, recurrent spells of amnesia have been reported in a woman subjected to intrathecal instillation of baclofen in the frame of a treatment for dystonia [12].Similarly, a clinical study about the effects of acamprosate on healthy young human subjects has shown that acamprosate impairs free recall, supporting the hypothesis that acamprosate impairs memory functions [13].

As shown herein, the inventors have found combinations of particular drugs that are efficient to stimulate cognition *in vivo*, particularly in healthy subjects, and which represent novel improved safe and efficient nootropic agents.

SUMMARY

In one aspect, there is provided a use of a combination of compounds selected from:

- baclofen and acamprosate,
- mexiletine and cinacalcet,
- baclofen and torasemide, or
- sulfisoxazole and torasemide,

for improving memory and/or memory related mental function performances in a subject not experiencing a disease selected from vascular dementia, senile dementia, age-associated memory impairment, Alzheimer's disease, Lewy body dementia, or mild cognitive impairment which impairs his memory and/or memory related mental functions.

One embodiment relates to a use of a combination of at least two compounds selected from baclofen, acamprosate, cinacalcet, mexiletine, sulfisoxazole, and torasemide, or salt(s), prodrug(s), derivative(s), or sustained release formulation(s) thereof, for improving memory and/or memory related mental function performances in a subject not experiencing a condition which impairs his memory and/or memory related mental functions.

Another object resides in a composition comprising a combination of at least two drugs selected from baclofen, acamprosate, cinacalcet, mexiletine, sulfisoxazole, and torasemide, or salt(s), prodrug(s), derivative(s), or sustained release formulation(s) thereof, for use as a stimulator of cognitive function in a subject in need thereof.

Another object resides in a method for stimulating cognition in a subject in need thereof, comprising administering to the subject a combination of at least two drugs selected from baclofen, acamprosate, cinacalcet, mexiletine, sulfisoxazole, and torasemide, or salt(s), prodrug(s), derivative(s), or sustained release formulation(s) thereof.

In a preferred embodiment, the compositions for use herein comprise a combination of drugs selected from:

- baclofen and acamprosate,
- mexiletine and cinacalcet,
- baclofen and torasemide, or
- sulfisoxazole and torasemide.

Claims

1. The use of a combination of compounds selected from:
   - baclofen and acamprosate,
   - mexiletine and cinacalcet,
   - baclofen and torasemide, or
   - sulfisoxazole and torasemide,

   ~~at least two compounds selected from baclofen, acamprosate, cinacalcet, mexiletine, sulfisoxazole, and torasemide, or salt(s), prodrug(s), derivative(s), or sustained release formulation(s) thereof,~~ for improving memory and/or memory related mental function performances in a subject not experiencing a ~~condition~~ disease selected from vascular dementia, senile dementia, age-associated memory impairment, Alzheimer's disease, Lewy body dementia, or mild cognitive impairment which impairs his memory and/or memory related mental functions.

2. The use of claim 1, wherein the memory related mental functions are cognitive tasks which are implicated or can sustain memory processes selected from learning, reasoning, alertness, attention, concentration, and/or language processing~~, and/or ability to cope with socio-professional burden~~.

3. The use of claim 1, wherein the memory is short-term memory and/or long-term memory.

~~4. The use of any one of the preceding claims, wherein said combination of at least two compounds comprises:~~
   - ~~baclofen and acamprosate,~~
   - ~~mexiletine and cinacalcet,~~
   - ~~baclofen and torasemide, or~~
   - ~~sulfisoxazole and torasemide,~~

   ~~or salt(s), prodrug(s), derivative(s), or sustained release formulation(s) thereof.~~

~~5.~~4. The use of any one of the preceding claims, wherein said combination further comprises at least one compound selected from methimazole, prilocaine, dyphylline, quinacrine, carbenoxolone, aminocaproic acid, cabergoline, diethylcarbamazine, cinacalcet, cinnarizine, eplerenone, fenoldopam, leflunomide, levosimendan, sulodexide, terbinafine, zonisamide, etomidate, phenformin, trimetazidine, mexiletine, ifenprodil, moxifloxacin, bromocriptine or torasemide.

~~6.~~5. The use of any one of the preceding claims, wherein said combination further comprises a racetam selected from levetiracetam, piracetam, pramiracetam, aniracetam or oxiracetam.

~~7.~~6. The use of any one of the preceding claims, wherein said compounds are formulated with a pharmaceutically acceptable carrier or excipient.

~~8.~~7. The use of any one of the preceding claims, wherein the compounds are formulated or administered together, separately or sequentially.

~~9.~~8. The use of claim ~~8~~7, wherein the compounds are formulated together in a same composition.

~~10.~~9. The use of any one of the preceding claims, wherein said compounds are administered repeatedly to said subject.

~~11.~~10. The use of anyone of claims 1 to ~~10~~9, wherein said subject has a need for a transient stimulation in memory, learning, or alertness performance.

~~12.~~11. The use of anyone of claims 1 to ~~10~~9, wherein said subject exhibits ~~transient memory loss caused by~~ hormonal changes or imbalances.

12. The use of anyone of claims 1 to 9, wherein said subject has to face with socio-professional burden.