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 healthy 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.

The ~~invention~~ disclosure is particularly suited to stimulate (*e.g.*, improve, enhance or increase) memory, learning, reasoning, alertness, attention, concentration, language processing, and/or the ability to cope with socio-professional burden in said subject.

The disclosure ~~invention~~ is particularly suitable for use in healthy subjects who have no known clinical signs of a disease (particularly subjects who do not suffer from vascular dementia, senile dementia, age-associated memory impairment, Alzheimer's disease, Lewy body dementia or mild cognitive impairment), and who only have a need for improved or stimulated cognitive capacities, either temporarily, or for longer periods of time.

The disclosure ~~invention~~ may also be used, either in a curative or preventive regimen, in subjects having, having had, or at risk of having particular disorders which affect cognition such as a psychiatric disorder, mental retardation, chemical induced memory disturbances or amnesia, a dietary or metabolism deficiency, a learning, language, calculating and/or reading disability, or drug withdrawal.

The disclosure ~~invention~~ may be used in any mammalian subject, preferably in human subjects.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1: Baclofen and acamprosate combinations are efficient in significantly improving learning and working memory performances (in T-maze alternation task) of mice whatever the concentrations tested (cf. table I) and regardless duration of treatment (from 7 days (dark grey bars) or 2 hours (light grey bars) before the test); black bar: vehicle dosed animals; * : significantly different from vehicle, ANOVA and Dunnett's test).

Figure 2: Baclofen and acamprosate, when combined and administered once only 2 hours before the test, act synergistically for improving learning and working memory performances (in T-maze alternation task). A significant positive effect of baclofen (BCL) and acamprosate (ACP) combinations is observed for very low doses (dark grey bars) whereas, at such concentrations, no significant improvement is observed for any one of the

Claims

1. The 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 healthy 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~~.

2. The use of claim 1, wherein said subject is not suffering from vascular dementia, senile dementia, age-associated memory impairment, Alzheimer's disease, Lewy body dementia, or mild cognitive impairment.

~~2.~~3. The use of claim 1 or 2, 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.

~~3.~~4. The use of any one of claims 1 to 3, wherein the memory is short-term memory and/or long-term memory.

~~4.~~5. 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.

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

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

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

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

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

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

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

~~12.~~ 13. The use of anyone of claims 1 to ~~9~~10, wherein said subject has to face with socio-professional burden.