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 ~~OF THE INVENTION~~

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 ~~of the invention~~ 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 ~~of the invention~~ 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 ~~in the invention~~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 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, to stimulate cognitive function in a healthy subject.

2. The use of claim 1, wherein the cognitive function is selected from memory, learning, reasoning, alertness, attention, concentration, language processing, and/or ability to cope with socio-professional burden.

3. The use of claim 2, wherein the memory is short-term memory and/or long-term memory.

4. The use of any one of the preceding claims wherein the composition comprises a combination of drugs selected from:
   - baclofen and acamprosate,
   - mexiletine and cinacalcet,
   - baclofen and torasemide, or
   - sulfisoxazole and torasemide.

5. The use of any one of the preceding claims wherein the composition comprises a combination of baclofen and acamprosate.

6. The use of claim 5, wherein the composition comprises baclofen and acamprosate as the only active agents.

7. The use of any one of the preceding claims, wherein the composition further comprises a pharmaceutically acceptable carrier or excipient.

8. The use of any one of the preceding claims, wherein the drugs in said composition are formulated or administered together, separately or sequentially.

9. The use of any one of the preceding claims, wherein the composition is administered repeatedly to the subject.

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

11. The use of anyone of claims 1 to 9, wherein the healthy subject exhibits transient memory loss caused by hormonal changes or imbalances, such as pregnancy, post-partum, in perimenaupose or menaupose.

12. The composition of anyone of claims 1 or 4 to 9, for use in the treatment of memory and/or memory related mental functions impairment, in a subject exposed or at risk to be exposed to a treatment or regimen having a potential negative effect on memory such as e.g., a toxic agent, drug withdrawal, or a dietary deficiency.

13. The composition of claims 1 or 4 to 9, for its use in treating learning, language, calculating and/or reading difficulties, for example, dyscalculia, dysorthographia or dyslexia in a subject suffering, having suffered, or at risk to suffer therefrom.

14. The composition of anyone of claims 1 or 4 to 9, for use in the treatment of memory and/or memory related mental functions impairment in a subject suffering, having suffered, or at risk to suffer from a psychiatric disorder, mental retardation, or hypothyroidism.

15. The composition for use of claim 14, wherein the mental retardation is selected from Rubinstein-Taybi's syndrome, Greig's syndrome, Apert's syndrome, Angelman's

syndrome, Coffin-Lowry's syndrome, Rett's syndrome, fragile X syndrome or William's syndrome.

16. The composition for use of claim 14, wherein the psychiatric disorder is selected from depression, psychotic disorders, attention deficit hyperactivity disorders, anxiety or obsessional compulsive disorders.

17. The composition for use of claim 12, wherein the toxic agent is selected from heavy metals, benzodiazepines, barbiturates, anti-seizure agents, first-generation antihistaminergics, anticholinergics, statins, and anesthetics.

18. The composition for use of anyone of claims 12-17, wherein memory is short term memory and/or long term memory.

19. The composition for use of anyone of claims 12-17, wherein memory related mental functions are learning, reasoning, alertness, attention, concentration, language processing, and/or ability to cope with socio-professional burden.

Claims

1. The 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.

2. The use of claim 1, wherein the memory related mental functions are selected from learning, reasoning, alertness, attention, concentration, 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. 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. 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. The use of any one of the preceding claims, wherein said compounds are formulated with a pharmaceutically acceptable carrier or excipient.

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

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

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

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

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