NANOPARTICLES FOR USE FOR ENHANCING BRAIN PERFORMANCES OR FOR TREATING STRESS

SUMMARY

The present invention relates to the medical field, in particular to the enhancement of brain performances and to the treatment of pathological stress. ~~More specifically~~In one example, the present invention relates to use of a nanoparticle or nanoparticles' aggregate for the prevention or treatment of a symptom of pathological stress selected from deterioration in learning and memory capacity in a subject, when the nanoparticle or nanoparticles' aggregate is to be exposed to an electric field, wherein the nanoparticle's or nanoparticles' aggregate's material is gold or ~~for use in enhancing brain performances or in prevention or treatment of pathological stress in a subject when the nanoparticle or nanoparticles' aggregate is exposed to an electric field/stimulus, wherein the nanoparticle's or nanoparticles' aggregate's material is selected from a conductor material, a semiconductor material,~~ an insulator material with a band gap Eg equal to or above 3.0 eV and with a relative dielectric constant ε_{ijk} equal to or below 100, the relative dielectric constant ε_{ijk} being measured between 20°C and 30°C and between 10^2 Hz up to the infrared frequency, which is ZrO_2 or HfO_2~~with a dielectric constant ε_{ijk} equal to or above 200, and an insulator material with a dielectric constant ε_{ijk} equal to or below 100. It further relates to compositions and kits comprising such nanoparticles and/or nanoparticles' aggregates as well as to uses thereof~~.

In another example, the present invention relates to use of a composition in the manufacture of a medicament for the prevention or treatment of a symptom of pathological stress selected from deterioration in learning and memory capacity in a subject exposed to an electric field, wherein the composition comprises nanoparticles and/or nanoparticles' aggregates and a pharmaceutically acceptable support, and wherein the nanoparticle's or nanoparticles' aggregate's material gold, or an insulator material with a band gap Eg equal to or above 3.0 eV and with a relative dielectric constant ε_{ijk} equal to or below 100, the relative dielectric constant ε_{ijk} being measured between 20°C and 30°C and between 10^2 Hz up to the infrared frequency, which is ZrO_2 or HfO_2,and the nanoparticles or nanoparticles' aggregates are exposed to an electric field.

BACKGROUND

With advancing comprehension of neuroscience, brain can be thought as an electric network, coding and transmitting information through its electric wires, neurons. Connectivity between neurons is simple and complex at the same time: simple because it lies on influx/efflux of ions inside neurons, which result in action potentials (or "spikes" of electric activity); complex because the brain network is composed of hundreds of billion neurons, which form nodes, hubs and modules that demonstrate

coordinated interactions, at various spatial and temporal scales (*Fornito* et al., *Nature Reviews Neuroscience, 2015, 16, 159-172: The connectomics of brain disorders*). Neural communication depends on the anatomical components that connect individual neurons (structure) and on the process of transmitting information (function). Both aspects affect the overall performance of the nervous system. Neuronal interactions are traduced by oscillations of the brain electric activity pattern, which oscillations are measurable typically by electroencephalogram (EEG). Different frequency bands of oscillations are observed: delta, theta, alpha, beta, gamma (*Ward* et al., *Trends in Cognitive Sciences, 2003, 7(12), 553-559: Synchronous neural oscillations and cognitive processes*). Structurally, the most striking neuroanatomical feature of the brain is the abundant connectivity between neurons, which reflects the importance of neural communication. Synchronization of oscillations ("synchrony") between one brain area and another seems to constitute the last level of information coding [first level (neuron): action potentials; second level (neuronal network(s)): neuronal oscillations] by bringing spatio-temporal coordination (*Engel* et al., *Nature Reviews Neuroscience, 2001, 2, 704-716: Dynamic predictions: oscillations and synchrony in top-down processing*). Importantly, evidence is emerging that a delicately balanced pattern of synchronization and desynchronization in space and time is fundamental to the functional performance of the nervous system (*Schnitzler* et al., *Nature Reviews Neuroscience, 2005, 6, 285-296: Normal and pathological oscillatory communication in the brain*).

CLAIMS

1. Use of a nanoparticle or nanoparticles' aggregate in the manufacture of a medicament for ~~enhancing learning, memorizing and attention in a subject suffering of an altered brain functional activity or for~~ the prevention ~~–~~or treatment of a symptom of pathological stress selected from deterioration in learning and memory capacity in a subject, when the nanoparticle or nanoparticles' aggregate is to be exposed to an electric field, wherein the nanoparticle's or nanoparticles' aggregate's material is ~~selected from a metal having a standard reduction potential E° above 0.2 or an organic material having contiguous sp2 hybridized carbon centers in its structure as a conductor material, a semiconductor material with a band gap Eg below 3.0 eV, an insulator material with a band gap Eg equal to or above 3.0 eV and with a relative dielectric constant ε_{ijk} equal to or above 200, and~~ gold or an insulator material with a band gap Eg equal to or above 3.0 eV and with a relative dielectric constant ε_{ijk} equal to or below 100, the relative dielectric constant ε_{ijk} being measured between 20°C and 30°C and between 10^2 Hz up to the infrared frequency, which is ZrO_2 or HfO_2.

2. Use according to claim 1, wherein the nanoparticle and/or nanoparticles' aggregate is coated with a biocompatible agent conferring a neutral surface charge, or with a biocompatible agent conferring a negative surface charge.

3. Use according to claim 2, wherein the biocompatible agent conferring a neutral surface charge is a hydrophilic agent displaying a functional group selected from an alcohol (R-OH), an aldehyde (RCOH), a ketone (R-CO-R), an ester (R-COOR), an acid (R-COOH), a thiol (R-SH), a saccharide, glucose, fructose, ribose, an anhydride (RCOOOC-R), or a pyrrole.

4. Use according to claim 3, wherein R is selected from a thiol, a silane, a carboxylic or a phosphate group.

5. Use according to claim 2, wherein the biocompatible agent conferring a negative surface charge is a phosphate or a sulphate.

~~1.~~6. Use according to claim 5, wherein the biocompatible agent conferring a negative surface charge is selected from a polyphosphate, a metaphosphate, or a pyrophosphate.

~~2.~~7. The use according to any one of claims 1 to 6, wherein the electric field is to be applied through transcranial electric stimulation or transcranial magnetic stimulation.

~~3. The use according to claim 1 or 2, wherein the metallic element of the metal having a standard reduction potential E° above 0.2 is Ir, Pd, Pt, Au, or a mixture thereof, or the organic material having contiguous sp2 hybridized carbon centers in its structure consists of polyaniline, polypyrrole, polyacetylene, polythiophene, polycarbazole and/or polypyrene.~~

~~4. The use according to anyone of claims 1-3, wherein the nanoparticle's or nanoparticles' aggregate's material consists of an element from group IVA of the Mendeleev's periodic table, or in a mixed composition of elements from group III and V of the Mendeleev's periodic table, or in a mixed composition of elements from group II and VI of the Mendeleev's periodic table.~~

~~5. The use according to claim 4, wherein the nanoparticle's or nanoparticles' aggregate's material consists of an element from group IVA of the Mendeleev's periodic table and is doped with a charge carrier selected from Al, B, Ga, In and P.~~

~~6. The use according to anyone of claims 1-5, wherein the insulator material with a band gap Eg equal to or above 3.0 eV and a relative dielectric constant ε_{ijk} equal to or above 200 is a dielectric material which is a mixed-metal oxide selected from $BaTiO_3$, $KTaNbO_3$, $KTaO_3$, $SrTiO_3$ and $BaSrTiO_3$.~~

~~7. The use according to anyone of claims 1-5, wherein the insulator material with a band gap Eg equal to or above 3.0 eV and the relative dielectric constant ε_{ijk} is equal to or below 100 is a dielectric material which is selected from a metal oxide, a mixed metal oxide, the metallic element of which is from period 3, 5 or 6 of the Mendeleev's periodic table or a lanthanide, and a carbon material.~~

8. The use according to anyone of claims 1 to 7, wherein the nanoparticle or nanoparticles' aggregate also enhances physical performances, ~~–~~sense perception and/or decision making of the subject.

9. Use of a composition in the manufacture of a medicament for ~~enhancing learning, memorizing and attention in a subject suffering of an altered brain functional activity or in~~ the prevention or treatment of a symptom of pathological stress selected from deterioration in learning and memory capacity in a subject exposed to an electric field, wherein the composition comprises nanoparticles and/or nanoparticles' aggregates and a pharmaceutically acceptable support, and wherein the nanoparticle's or nanoparticles' aggregate's material is ~~selected from a metal having a standard reduction potential E° above 0.2 or an organic material having contiguous sp2 hybridized carbon centers in its structure as a conductor material~~gold, ~~a semiconductor material with a band gap Eg below 3.0 eV, an insulator material with a band gap Eg equal to or above 3.0 eV and with a relative~~

~~dielectric constant ε_{ijk} equal to or above 200, and~~or an insulator material with a band gap Eg equal to or above 3.0 eV and with a relative dielectric constant ε_{ijk} equal to or below 100, the relative dielectric constant ε_{ijk} being measured between 20°C and 30°C and between 10^2 Hz up to the infrared frequency, which is ZrO_2 or HfO_2, and the nanoparticles or nanoparticles' aggregates are to be exposed to an electric field.

10. The use according to claim 9, wherein the nanoparticle and/or nanoparticles' aggregate is coated with a biocompatible agent conferring a neutral surface charge, or with a biocompatible agent conferring a negative surface charge.

11. The use according to claim 10, wherein the biocompatible agent conferring a neutral surface charge is a hydrophilic agent displaying a functional group selected from an alcohol (R-OH), an aldehyde (RCOH), a ketone (R-CO-R), an ester (R-COOR), an acid (R-COOH), a thiol (R-SH), a saccharide, glucose, fructose, ribose, an anhydride (RCOOOC-R), or a pyrrole.

12. The use according to claim 11, wherein R is selected from a thiol, a silane, a carboxylic or a phosphate group.

13. The use according to claim 10, wherein the biocompatible agent conferring a negative surface charge is a phosphate or a sulphate.

14. The use according to claim 13, wherein the biocompatible agent conferring a negative surface charge is selected from a polyphosphate, a metaphosphate, or a pyrophosphate.

15. ~~10.~~ The use of any of claims 9 to 14, wherein the composition comprises at least two distinct nanoparticles and/or nanoparticles' aggregates, each nanoparticle or nanoparticles' aggregate consisting of a distinct material selected from ~~a metal having a standard reduction potential E° above 0.2 or an organic material having contiguous sp2 hybridized carbon centers in its structure as a conductor material, a semiconductor material with a band gap Eg below 3.0 eV, an insulator material with a band gap Eg equal to or above 3.0 eV and with a relative dielectric constant ε_{ijk} equal to or above 200, and an insulator material with a band gap Eg equal to or above 3.0 eV and with a relative dielectric constant ε_{ijk} equal to or below 100, the relative dielectric constant ε_{ijk} being measured between 20°C and 30°C and between 10^2 Hz up to the infrared frequency~~ gold, ZrO_2 or HfO_2.

~~11. A kit for use in enhancing learning, memorizing and attention in a subject suffering of an altered brain functional activity or for use in prevention or treatment of pathological stress in a subject, wherein the kit comprises at least two distinct nanoparticles and/or nanoparticles' aggregates, each nanoparticle or nanoparticles' aggregate consisting of a distinct material selected from a metal having a standard reduction potential E° above 0.2 or an organic material having contiguous sp2 hybridized carbon centers in its structure as a conductor material, a semiconductor material with a band gap Eg below 3.0 eV, an insulator material with a band gap Eg equal to or above 3.0 eV and with a relative dielectric constant ε_{ijk} equal to or above 200, and an insulator material with a band gap Eg equal to or above 3.0 eV and with a relative dielectric constant ε_{ijk} equal to or below 100, the relative dielectric constant ε_{ijk} being measured between 20°C and 30°C and between 10^2 Hz up to the infrared frequency, and wherein the nanoparticles or nanoparticles' aggregates are exposed to an electric field.~~