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Description

DEVICE FOR INDUCING HIGH-FREQUENCY OSCILLATIONS IN A BRAIN

Field of the Invention

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[0001] This application claims priority of Luxembourg Patent Application number LU503626, filed on 13 March 2023 and European Patent Application EP 23179351.4. The entire disclosure of the Luxembourg Patent Application number LU503626 and European Patent Application EP 23179351.4 is hereby incorporated herein by reference

10 [0002] The invention comprises a device for inducing ripples in a brain of a subject, a system for improving a memory retention of an object, and a method for inducing the ripples in the brain of the subject.

Background of the Invention

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[0003] US Patent application US 2023/0022546 A1 (Cognito Therapeutics Inc.) is directed to neural stimulation via non-invasive sensory stimuli. The non-invasive stimuli can reduce neuroinflammation, improve synaptic plasticity and stimulate neural networks. Cerebral insults contribute to brain atrophy. The non-invasive stimuli can improve microglial-mediated clearance of the cerebral insults, thereby preventing a progression of brain atrophy. The non-invasive stimuli induce synchronized gamma oscillations in at least one region of the brain in a subject. The non-invasive stimuli can adjust, control, or manage the frequency of the synchronized gamma oscillations, i.e., the neural oscillations, to provide effects to one or more cognitive states or cognitive functions of the brain. The non-invasive stimuli can simultaneously mitigate or prevent adverse consequences resulting from a progression of brain atrophy one a cognitive state or on a cognitive function.

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[0004] US Patent application US 2013/0338738 A1 (Garcia Molina et al.) relates to a device and a corresponding method for cognitive enhancement of a user. The user is going to execute a cognitive activity. The device for effective cognitive enhancement comprises a light unit for providing an imperceptible light stimulation to the user. The device further comprises a control unit for controlling said light unit to provide said imperceptible light stimulation less than 5 seconds before the execution of the cognitive activity by the user.

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[0005] US Patent application US 2010/0331912 A1 (Tass et al.) discloses a device and a method for providing stimulation signals that reset a phase of a neuronal activity of neurons in a brain of a patient. The device includes a control unit and a stimulation unit. The stimulation unit has a plurality of stimulation elements. Each stimulation element generates
5 visual stimulation signals that reset the phase of the neuronal activity of the neurons when the signals are taken up via the eye of the patient. The visual stimulation signals are transmitted to the neurons, which exhibit a pathologically synchronous and oscillatory neuronal activity in a psychiatric or neurological disease. The control unit is further capable of actuating the stimulation unit such that the stimulation elements generate the visual
10 stimulation signals with a time offset in respect to one another and/or with differing phase and/or with differing polarity.

[0006] Teeuwen et al. in “A neuronal basis of iconic memory in macaque primary visual cortex”, *Current Biology* 31, 5401–5414 (2021), accessible at <https://doi.org/10.1016/j.cub.2021.09.052> define different types of memory. These are long-
15 term memory, working memory and iconic memory. The long-term memory is stored in patterns of connections with different strengths between neurons in the neocortex and is arranged by the hippocampus. The working memory is stored in the ongoing activity of the neurons. Neural correlates of the working memory are primarily in higher cortical areas, e.g., the frontal, parietal and temporal cortex, of the neocortex hierarchy. Teeuwen et al. teach
20 that the iconic memory is a short-lasting high-capacity form of memory with neural correlates in the primary visual cortex (V1) of the brain. This means that the iconic memory can maintain a large amount of information and visual details of an object for a short period of time. The iconic memory is located in low-level visual areas of the brain and is briefly stored in the brain. The iconic memory decays over time. This decay results in a decrease in
25 the storage capacity of the iconic memory. The iconic memory is short-lasting. The iconic memory cannot be stored entirely as the working memory.

[0007] Teeuwen et al. further disclose that a decay time of the iconic memory is longer than a duration of activity of single neurons in the V1 region. In other words, retention of the image in the iconic memory is not only dependent on the activity of the single neurons in
30 the V1 region. During persistence of the image in the iconic memory, there must therefore be a communication between multiple brain regions to exchange information about the image between the V1 region and other brain structures.

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[0008] Teeuwen et al. further disclose that the iconic memory is influenced by the overwriting effect of a newly presented object. The iconic memory is further influenced by directing attention to an object or parts of an object. Attention refers to a brain cognitive function which strengthens a neural representation of a viewed object or diminishes the neural representation by putting an attentional weight on the viewed object.

[0009] The newly presented object abolishes the iconic memory and erases a representation of the previous image in the primary visual cortex (V1). The attention interacts with the iconic memory to boost relevant V1 activity.

[0010] Teeuwen et al. hypothesize that a timescale to process the information and to permanently store the information in the brain increases when the information passes from the iconic memory in primary visual cortex (V1) to higher visual cortical areas, e.g., V3-V5, of the brain and working memory, e.g., the frontal, parietal, and temporal cortex, of the neocortex hierarchy.

[0011] Teeuwen et al. disclose that the most stable form of the short-term visual memory is the working memory. An object presented to the working memory is kept in the working memory. A newly presented object can be received by the working memory and the working memory is not overwritten by the newly presented object. However, the working memory has a limited capacity for storing the presented objects. The storage capacity of the working memory is only around seven to nine objects of a complex visual object.

[0012] Neurons in the frontal cortex, parietal cortex and medial temporal lobe of the brain play a prominent role in maintaining working memory neural representations, i.e., the strength of connections between the neurons in the neocortex. The working memory neural representations have to be represented in the brain by an ongoing synchronous activity of the neurons. This means that networks of the neurons that contain the working memory need to be constantly active for the duration of the memory, usually in the range of a few minutes.

[0013] The short-term working memory therefore requires communication between the multiple brain regions. The multiple brain regions collectively organize the storage and maintenance of sensory information. Liebe et al. in "Theta coupling between V4 and prefrontal cortex predicts visual short-term memory performance". Nat Neurosci 15, 456–462 (2012). <https://doi.org/10.1038/nn.3038> have suggested that a rhythmic oscillatory synchronization underlies the communication between the multiple regions in the brain. The

communication between the multiple brain regions is, according to Liebe et al., responsible for learning and for a permanent formation of the long-term memory.

[0014] Battaglia et al. in “The hippocampus: hub of brain network communication for memory” Trends in Cognitive Science, 15(7), 310-318 (2011),
5 <https://doi.org/10.1016/j.tics.2011.05.008> disclose that synchronization of neuron assemblies by oscillations of neural activity enables encoding and recalling the long-term memory. Sharp-wave-ripples (SWRs) are one type of these oscillations of neural activity that synchronize the brain structures relevant for long-term memory. These brain structures are the hippocampus and the neocortex.

10 [0015] Buzsáki in “Hippocampal sharp-wave-ripple: A cognitive biomarker for episodic memory and planning,” Hippocampus 25(10), 1073-1188 (2015).
<https://onlinelibrary.wiley.com/doi/10.1002/hipo.22488> discloses that naturally occurring SWRs are short oscillations with a duration of 40 - 100 ms. The short oscillations comprise a large amplitude negative polarity deflection of 1 – 2 mV, and a synchronous high-
15 frequency oscillation of the electrical local field potential of the CA1 region of the hippocampus. The naturally occurring SWRs occur most frequently during sleep, or during awake resting periods.

[0016] Logothetis et al. in “Hippocampal–cortical interaction during periods of subcortical silence,” Nature 491, 547–553 (2012). <https://doi.org/10.1038/nature11618> disclose that a
20 synergistic interaction between thalamus and neocortex may be orchestrating a communication between the hippocampus, in particular the CA1 region, and the neocortex. The communication between the hippocampus and the neocortex may be facilitated by silencing the output of subcortical centers. The subcortical centers are involved in sensory processing. A mechanism of silencing and reactivating the brain would cause minimal
25 interference in the brain and would enable consolidation of the long-term memory.

[0017] Logothetis et al. disclose that naturally occurring SWRs are thought to be involved in the off-line memory consolidation. Logothetis et al. define the naturally occurring SWRs to be a combination of aperiodic and recurrent oscillations of large deflections, i.e., sharp waves, and synchronous high-frequency oscillations, i.e., ripples, in the electrical activity of
30 the hippocampus. The high frequency oscillations have a frequency in a range of 80 to 250 Hz that depends on the anatomical site in the brain, for example, in the CA1 region and in the CA3 region of the hippocampus, or in the entorhinal cortex. The naturally occurring

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SWR depends on an animal state, for example, whether the animal, (or human), is alert or anaesthetized. The naturally occurring SWR also depends on the animal species.

[0018] Logothetis et. al. show by functional magnetic resonance imaging (fMRI) which areas of the brain are active or silent when the naturally occurring SWRs occur in the brain.

5 The whole neocortex of the brain of a subject is active, except the V1 region and the subcortical areas. The activation of the neocortex perhaps represents the communication between the multiple regions in the brain.

[0019] The information is stored during the naturally occurring SWRs in neural networks of the hippocampus, presumably from all relevant cortical areas, which are in "active" state.

10 However, the iconic memory, which is stored in the V1 region for a very short time, for example 100 ms, never entirely gets to more stable forms of visual memory, e.g., the working memory. The reason why full details of information in the iconic memory are not available to more stable forms of memory is maybe that the iconic memory comprises too much information and/or comprises sensory input noise. The information in the iconic memory
15 and/or the sensory input noise could cause an interference with the information stored during the naturally occurring SWRs.

[0020] A suppression of the V1 region during the naturally occurring SWRs could facilitate the communication between the hippocampus and all relevant neocortical areas. This suppression could facilitate consolidating the long-term memory.

20 [0021] Behrens et al. "Induction of sharp-wave-ripple complexes in vitro and reorganization of hippocampal networks", Nature Neuroscience, 8(11), 1560-1567 (2005). <http://www.nature.com/articles/nn1571> disclose that it is possible to artificially induce SWRs with various invasive stimulation methods. These artificially induced SWRs have the same temporal and spectral properties as naturally occurring SWRs. The onset of the
25 artificially induced SWRs can be caused by an external stimulus, on the contrary to the naturally occurring SWRs.

[0022] The number of the SWRs is correlated with the number of remembered long-term memory items, as disclosed in Norman et al., "Hippocampal sharp-wave-ripples linked to visual episodic recollection in humans", Science, 365(6454), eaax1030 (2019).

30 <https://doi.org/10.1126/science.aax1030><https://doi.org/10.1126/science.aax1030>. An increased number of the SWRs could facilitate consolidating the long-term memory.

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[0023] Ripples, i.e., synchronous high frequency oscillations in the frequency range of the SWRs, occur in the entire brain, e.g., in the neocortex or in the hippocampus. The ripples can be one of neocortical ripples or hippocampal SWRs. The neocortical ripples occur before the SWRs in the hippocampus during waking. The neocortical ripples can therefore induce the SWRs in the hippocampus. The SWRs in the hippocampus occur before the neocortical ripples during consolidation and recall. This reflects the information flow during the encoding, the consolidation, and the recall of the long-term memory, as disclosed in Dickey et al., “Widespread ripples synchronize human cortical activity during sleep, waking, and memory recall”, PNAS, 119(28), e2107797119 (2022).
10 <https://doi.org/10.1073/pnas.2107797119>.

[0024] The neocortical ripples in the visual areas (V1) of the neocortex can be generated by using a visual input. The visual input is used to induce synchronous high frequency oscillations in the frequency range of the SWRs of humans. The frequency range of the neocortical ripples is above 80 Hz in the V1 region, when induced by high frequency visual flickering stimulation at frequencies between 80 Hz and 250 Hz.
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[0025] The artificial induction of the SWRs by using the visual input has two potential problems. A first problem is that the high frequency visual flickering stimulus may not pass through the retina of an eye. The retina of the eye is the first stage of the visual system of the brain. The cone photoreceptors of the retina have a peak response latency of approximately 10 ms. This creates a low-frequency filter of 100 Hz to a visual stimulation of a high frequency, as disclosed by Schneeweis et al., “Photovoltage of rods and cones in the macaque retina”. Science, 268(5213), 1053–1056.
20 <https://doi.org/10.1126/science.7754386>.

[0026] A second problem is that it is not sure whether the V1 region of the brain is able to process the high frequency visual flickering stimulus even if the high frequency visual flickering stimulus passes through the retina.
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[0027] There is therefore a need to develop a system for inducing the SWRs in the hippocampus. There is a need for inducing non-invasively the SWRs in the hippocampus. There is a need to develop a system to preserve an image in the primary visual cortex region of the brain. This allows preservation of the information captured by the primary visual cortex in the iconic memory to obtain a more stable form of memory. The more stable form
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of memory is, for example, the working memory. The preservation of the information is further conducted before the iconic memory decays.

Summary of the Invention

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[0028] A device for inducing ripples (i.e. neocortical ripples and/or sharp-wave ripples (SWRs)) in a brain of a subject is taught in this disclosure.

[0029] Ripples refer to synchronous, oscillatory neural activity of the brain with a frequency between 80 and 250 Hz.

10 [0030] Neocortical ripples refer to synchronous, oscillatory neural activity of the neocortex of a brain with a frequency between 80 and 250 Hz.

[0031] SWRs refer to synchronous, oscillatory neural activity of the hippocampus of a brain with a frequency between 80 and 250 Hz.

[0032] The device comprises a light source. The light source is adapted for generating light.

15 The generated light has at least two light variations. The at least two light variations are selected from at least two of a spatial variation, a temporal variation, a wavelength spectrum variation, an intensity variation, or a polarization variation. The at least two light variations are selected for inducing the ripples in the brain. The generated light generates a visual stimulation in the brain at the frequency of the ripples.

20 [0033] The device enables inducing non-invasively the ripples in the brain of a subject by using the visual system of the brain.

[0034] In one aspect, the generated light generates the visual stimulation in the brain at the frequency of the ripples so that different cells of the retina of the subject are activated sequentially.

25 [0035] The induced ripples enable passing the limitations of the retina of the subject.

[0036] The induced ripples in a V1 region of the brain enable improvement of communication of the large-capacity iconic memory to the downstream areas of the brain, e.g., in the CA1 region. The induced ripples, i.e., oscillatory events, may trigger crosstalk between the V1 region and higher areas of the brain to pass on the information of the iconic

30 memory that would not get a chance to be passed on in a natural case.

[0037] In one aspect, the light source is one of a stroboscope, an electronic display, a light-emitting diode, a panel of multiple light-emitting diodes, an electronic display comprising multiple light-emitting diodes, a liquid crystal display, or a laser diode.

[0038] In one aspect, the at least two light variations are a spatial variation and a temporal variation.

[0039] In a further aspect, the device comprises a piezoelectric device for vibrating the light source.

[0040] A system for improving memory retention of an object is also taught in this disclosure. The object is substantially located in the center of a visual field of a subject. The system comprises a light source adapted to generate light in a peripheral field of the subject. The generated light has at least two light variations. The at least two light variations are selected from at least two of a spatial variation, a temporal variation, a wavelength spectrum variation, an intensity variation, or a polarization variation. The at least two light variations are selected for inducing the ripples in a brain of the subject. As noted above, the generated light generates a visual stimulation in the brain at the frequency of the ripples.

[0041] In one aspect, the device is used for at least one enhancement of the iconic memory of the subject, improvement of the performance of the subject in memorizing a higher number of elements in an image, transformation of iconic memory into working memory, transformation of working memory to hippocampal or long-term memory, transformation of hippocampal memory to long-term memory, transformation of spatial memory into long term memory, prevention or treatment of Alzheimer's disease, prevention or treatment of aging effects on memory or other cognitive functions of the brain of the subject, prevention or treatment of effects of dementia on memory or other cognitive functions of the brain, training of the memory of the subject to learn lost identities of faces memories, memorizing image pairs, vocabulary pairs, or a combination thereof.

[0042] A method for inducing ripples in a brain of a subject is further taught in this disclosure. The method comprises illuminating alternately different cells of the retina of the subject from a light source. The light source is adapted for generating light. The generated light has at least two light variations. The at least two light variations are selected from at least two of a spatial variation, a temporal variation, a wavelength spectrum variation, an intensity variation, or a polarization variation. As noted above, the generated light generates

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a visual stimulation in the brain at the frequency of the ripples, thereby inducing the ripples in the brain.

[0043] In one aspect, the ripples are selected from one of neocortical ripples or hippocampal SWRs.

5 [0044] In one aspect, the method comprises, prior to the step of illuminating alternately the different cells of the retina, a step of measuring a brain activity of the subject, measuring an oscillatory brain rhythm of the subject, and thereby illuminating alternately the different groups of cells based on the oscillatory brain rhythm and/or based on the properties of the brain activity. The properties of the brain activity comprise amplitude, frequency, phase, and
10 synchrony.

[0045] A head-mounted device or a screen-mounted device comprising the device is further taught in this disclosure. The head-mounted device or the screen-mounted device is used for replacing sleep, mimicking sleep, learning during sleep, or memory consolidation during sleep.

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Description of the figures

[0046] Fig. 1 shows a view of a device for artificially inducing ripples in a brain of a subject.

[0047] Fig. 2 shows a system for improving memory retention of an object.

20 [0048] Fig. 3 shows a view of a head-mounted device comprising the device for artificially inducing the ripples.

[0049] Fig. 4 shows a view of a screen-mounted device comprising the device for artificially inducing the ripples.

25 [0050] Figs. 5 and 6 shows a flow chart describing a method for artificially inducing the ripples in the brain of the subject.

[0051] Fig. 7 shows a combination of a temporal variation and one or more of a spatial variation, a wavelength spectrum variation, an intensity variation, or a polarization variation.

30 [0052] Fig. 8 show results from one electrophysiological experiment indicating the number of artificially induced SWRs in mice following a high-frequency visual stimulation with a temporal and a spatial variation compared to a control condition.

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[0053] Fig. 9 show results from one electrophysiological experiment indicating the number of artificially induced SWRs in humans following a high-frequency visual stimulation with a temporal and a spatial variation compared to a control condition.

[0054] Fig. 10 show results from one magnetoencephalography experiment indicating the number of artificially induced SWRs in humans following a high-frequency visual stimulation with a temporal and a spatial variation compared to a control condition.

[0055] Fig. 11 shows the results from one behavioral experiment indicating the memory recall performance following a high-frequency visual stimulation with a temporal and a spatial variation compared to a sham condition.

[0056] Fig. 12 shows a virtual reality (VR) glass, an augmented reality (AR) glass, a mixed reality (MR) glass, an extended reality (XR) glass, or data glasses, comprising the device for artificially inducing the ripples.

[0057] Fig. 13 shows a head-mounted device.

[0058] Fig. 14 shows the training and testing performance of a recurrent neural networks (RNN) in detecting the signal in the oscillatory brain rhythm, which is considered to be a correlate for the SWR, from a power spectrum of electroencephalographic signals recorded from the surface of the head of the subject.

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Detailed description of the invention

[0059] The invention will now be described on the basis of the drawings. It will be understood that the embodiments and aspects of the invention described herein are only examples and do not limit the protective scope of the claims in any way. The invention is defined by the claims and their equivalents. It will be understood that features of one aspect or embodiment of the invention can be combined with a feature of a different aspect or aspects and/or embodiments of the invention.

[0060] Fig. 1 shows a view of a device 10 for ripples in a brain 15 of a subject 20. The device 10 comprises a light source 30 generating light having at least two light variations. The at least two light variations are selected from at least two of a spatial variation, a temporal variation, a wavelength spectrum variation, an intensity variation, or a polarization variation.

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[0061] In one example, the at least two light variations are a combination of a temporal variation and one or more of a spatial variation, a wavelength spectrum variation, an intensity variation, or a polarization variation.

[0062] The device 10 uses the visual system of the brain 15 to non-invasively induce ripples
5 in the brain 15 of the subject 20.

[0063] Using a visual input from the visual system of the brain 15 with a visual stimulation at high frequency in the frequency range of the ripples allows the induction of the ripples.

[0064] The retina 25 of the eye 22 is a first stage of the visual system of the brain 15. The different cells of the retina, for example, cone photoreceptors of the retina 25, have a peak
10 response latency of approximately 10 ms. This creates a low-frequency filter of 100 Hz to high-frequency visual stimulation. Sequential activation of the different cells of the retina allows passing the limitations of the retina 25. The different cells of the retina could be neighboring retinal cells, different color receptor cells, or a random selection of retinal cells. In other words, the induction of the ripples by using the visual input stimulates areas of the
15 retina 25 in such a manner that the stimulated areas receive sufficient time to reach the peak response before a further stimulus arrives at the same previously stimulated area.

[0065] The generated light generates a visual stimulation in the brain 15.

[0066] A temporal variation refers to a change of activity of the light source 30 over time. A spatial variation refers to a change of spatial location of the light source 30 or a direction
20 of the light generated by the light source 30 over time. A wavelength spectrum variation refers to a change of the wavelength of the light source 30 over time. An intensity variation refers to a change of the light brightness or the luminosity of the light source 30 over time. A polarization variation refers to a change of the direction of a light wave of the light source 30 over time.

[0067] The visual stimulation is generated, in one aspect, by a temporal variation in the frequency of the ripples, and by a light variation selected from at least one of a spatial variation, a wavelength spectrum variation, an intensity variation, or a polarization variation. The visual stimulation may sequentially stimulate the different cells of the retina, i.e., different areas of the retina 25. This leads to passing the limitations of the retina 25 to induce
30 synchronous high-frequency oscillations in the brain 15 of the subject 20.

[0068] The visual stimulation is generated, in one further aspect, by a temporal variation in the frequency of the ripples and a light variation selected from at least one of a spatial

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variation, a wavelength spectrum variation, an intensity variation, or a polarization variation may artificially induce synchronous high-frequency oscillations, i.e., ripples, in a V1 region of the brain. This visual stimulation can induce the SWRs in the hippocampus of the brain.

[0069] The visual stimulation generated by a temporal variation at a frequency below the
5 frequency range of the ripples and the SWRs is not able to artificially induce high-frequency oscillations and is not able to induce the ripples in a V1 region of the brain. The visual stimulation generated by a temporal variation below the frequency range of the ripples and the SWRs is further not able to induce the SWRs in the hippocampus of the brain 15.

[0070] The visual stimulation generated by a temporal variation and no selection of at least
10 one of a light variation from at least one of a spatial variation, a wavelength spectrum variation, an intensity variation, or a polarization variation, is not able to stimulate different areas of the retina 25, in such a sequence that the stimulated different areas receive sufficient time to reach the peak response before a further stimulus arrives at the same previously stimulated area.

[0071] The device 10 comprises, for example, a piezoelectric device 40. The piezoelectric
15 device 40 can vibrate the spatial location of the light source 30 or the direction of the light from the light source 30. i.e., the generated light.

[0072] Most naturally occurring ones of the SWRs occur during sleep or quiet rest. The device 10 can be used to increase the number of the SWRs by artificially inducing the SWR.

[0073] Mimicking refers to an operation of the device 10 to increase the number of the
20 SWRs. The device 10 can replace the function of sleep to generate the SWRs.

[0074] The naturally occurring SWRs in the brain 15 are very high frequency oscillations, for example the frequency of the naturally occurring SWR is between 80 Hz and 250 Hz. The naturally occurring SWRs are short in length, for about 50 ms, and occur up to 100 times
25 in a minute. The naturally occurring SWRs occur especially during sleep and during a resting state of the brain.

[0075] Artificially inducing the SWRs means increasing the number of the SWRs during and/or after the use of the device 10 compared to a time before the use of the device 10.

[0076] The generated light having the temporal variation and a light variation of at least one
30 of a spatial variation, a wavelength spectrum variation, an intensity variation, or a polarization variation generates a visual stimulation in the brain 15 at the frequency range of the ripples, for example, at a frequency range between 80 and 250 Hz. The visual stimulation

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can generate high frequency oscillations, i.e., ripples, in the V1 region. The visual stimulation can further induce the SWRs in the hippocampus.

[0077] Fig. 8 shows the number of the SWRs recorded from the hippocampus of mice during the visual stimulation with light having a temporal variation and a spatial variation on a 240
5 Hz refresh rate gaming monitor. The number of the SWRs during the visual stimulation is higher than during a resting baseline phase.

[0078] The frequency of the temporal variation of the visual stimulus can be selected according to the frequency of the SWRs of the species in which the visual stimulus is applied.

[0079] The term “flickering” refers to the temporal variation of the visual stimulus. The
10 frequency of the temporal variation of the visual stimulus is, for example, between 80 and 240 Hz. The temporal variation of the visual stimulus is, for example, combined with the spatial variation. The temporal variation of the visual stimulus combined with the spatial variation is, for example, the frequency of the entire visual stimulus divided by the number of the spatial variations.

[0080] In one non-limiting example, the entire visual stimulus has a frequency of 180 Hz and comprises 4 spatial variations. Thus, the temporal variation combined with the spatial variation is 180 Hz divided by 4, ergo 45 Hz. Fig. 7 shows the temporal variation (Variation
1) of each of 4 spatial variations (Variation 2).

[0081] In some aspects, the temporal variation of the visual stimulus is combined with the
20 wavelength spectrum variation. The temporal variation of the visual stimulus combined with the wavelength spectrum variation is, for example, the frequency of the entire visual stimulus divided by the number of wavelength spectrum variations. In one non-limiting example, the entire visual stimulus has a frequency of 180 Hz and comprises 2 wavelength spectrum variations. Thus, the temporal variation combined with the wavelength spectral variation is
25 180 Hz divided by 2, ergo 90 Hz.

[0082] In some aspects, the temporal variation of the visual stimulus is combined with the intensity variation. The temporal variation of the visual stimulus combined with the intensity variation is the frequency of the entire visual stimulus divided by the number of intensity variations. In one non-limiting example, the entire visual stimulus has a frequency of 180
30 Hz and comprises 2 intensity variations. Thus, the temporal variation combined with the intensity variation is 180 Hz divided by 2, ergo 90 Hz.

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[0083] In some aspects, the temporal variation of the visual stimulus is combined with the polarization variation. The temporal variation of the visual stimulus combined with the polarization variation is the frequency of the entire visual stimulus divided by the number of polarization variations. In one non-limiting example, the entire visual stimulus has a frequency of 180 Hz and comprises 2 polarization variations. Thus, the temporal variation combined with the polarization variation is 180 Hz divided by 2, ergo 90 Hz.

[0084] The V1 region of the brain was found out to be able to handle a frequency of oscillations of the artificially induced SWRs of at least 80 Hz. This frequency is measured in the electrical activity of the brain after generating a flickering stimulus in combination with a spatial variation on a 240 Hz refresh rate gaming monitor.

[0085] The artificially induced SWRs comprises properties that depend on the duration, the exact frequency, the timing of the naturally occurring SWRs in relation to the visual stimulus, i.e., latency, and the number of occurrences of the naturally occurring SWRs in the brain. The artificially induced SWRs were found to have, for example, the same frequency as the naturally occurring SWRs.

[0086] The device 10 and the light source 30 can be standalone devices, i.e., the device 10 and the light source 30 do not need a controlling computer system to work. The light source 30 is, in one example, an industrial device from Rheintacho Messtechnik GmbH. The light source 30 is, for example, a stroboscope with a flickering light of a frequency of at most 20 kHz. The light source 30 is, in a further example, an electronic display or a light-emitting diode (LED). The light source 30 is, in a further example, a panel comprising multiple light-emitting diodes (LEDs), a display comprising multiple light emitting diodes (LEDs), a liquid crystal display (LCD), or a laser diode. The light emitted by the light source 30 is, for example, polarized light or flickering light. The flickering light of the light source 30 flickers so that the flickering light stimulates the retina 25 of the subject 20 with a high frequency of, for example, 120 Hz.

[0087] The colors of the light source 30 are, for example, red and green. Changing alternately the colors of the light source 30 enable targeting of different types of photoreceptors of the retina 25. This different targeting lets one cell of the retina 25 recover while another cell of the retina 25 is stimulated. A high temporal frequency can be achieved by changing colors of the light source 30 at a frequency, for example, of 120 Hz.

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[0088] The high frequency component of the light source 30 is normally removed by the low-pass filter (LPF) property of the retina 25. It is known that the retina 25 removes frequencies of above 100 Hz. Different groups of cells in the retina 25 can be alternately stimulated in order to give resting time to one cell while stimulating a different cell. This leads to a maximum temporal frequency of 100 Hz when stimulating the whole retina 25, because of the aforementioned low-pass filter property. In other words, this means that a higher temporal frequency of over 100 Hz cannot be reached (due to the LPF property of the retina 25) if different types of cells (i.e., the photoreceptors in the retina 25) or different areas of the retina 25 at different time points are not targeted.

10 [0089] In one non-limiting example, the device 10 further comprises a rotating device 50 located between the light source 30 and the eyes 22 of the subject 20. In one example, the rotating device 50 is a rotating disc. In a further example, the rotating device 50 is a cylinder coated with reflective surfaces. The cylinder can be a three dimension (3D) printed cylinder. In a further example, the rotating device 50 is a hexagonal cylinder.

15 [0090] The rotating device 50 has, in a further example, alternating transparent shapes and untransparent shapes, like a checkerboard pattern. The transparent shapes and untransparent shapes have a specific design of size, dimension, and form. In one non-limiting example, the shape is a circular wedge with an outer length of 1 cm, an edge length of 13 cm, and 6 alternating transparent and untransparent stripes with a length of 1 cm.

20 [0091] In a further non-limiting example, the rotating device 50 is a translucent disc made of, for example, acrylic glass. The rotating device 50 has, in the example, the untransparent shape comprising black ink named “off” fields. The remaining shapes of the rotating device 50 are the transparent shapes and are named “on” field.

[0092] In another example, the rotating device 50 has shapes of different colors. The shapes of different colors alternate to make the checkerboard pattern on the rotating device 50.

[0093] In one example, the rotating device 50 comprises alternating tinted filters of at least two different colors.

[0094] In a non-limiting example, the rotating device 50 comprises alternating holes and surfaces. In one example, the rotating device 50 is made of wood with a thickness of 2.5 mm. In one example, the rotating device 50 is designed so that one cycle of “on” and “off” is synchronized with the “on” and “off” cycle of the stroboscope light-emitting diode (LED).

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[0095] The method for artificially inducing the SWRs will now be described in connection with Fig. 5.

[0096] The method comprises illuminating in step S1000 alternately different ones of the cells of the retina 25 of the subject 20 from the light source 30. This illumination thereby
5 induces in step S1202 the SWRs in the brain 15.

[0097] In one non-limiting example, the step of illuminating S1000 alternately different groups of cells comprises illuminating S1001 the rotating device 50 that comprises a checkerboard pattern on the surface of the rotating device 50. The checkerboard pattern generates alternating “on” fields and “off” fields.

10 [0098] The different ones of the cells of the retina 25 are either illuminated by the “on” field or are blocked by the “off” field.

[0099] The step of illuminating S1001 the rotating device 50 is contiguous with a step of rotating S1002 the rotating device 50. This rotating step S1002 results in that the cells of the retina 25 see the “opposite” field after the rotation S1002. One cell of the retina 25 sees, for
15 example, an “off” field after the rotation S1002 if the cell of the retina 25 was illuminated S1001 by an “on” field. That corresponds to one cycle of “on” and “off” stimulus for that given cell in the retina.

[00100] The rotating device 50 rotates in the step S1002 so that the cells of the retina 25 see this cycle in a subsequent order and this means that alternate different groups of cells in the
20 retina 25 are illuminated.

[00101] The rotating disc 50 is rotated in step S1002 in a fast way (e.g., 600-720 rounds per minute for a stimulation of the retina of 120 Hz) to induce artificially the SWRs that have the same properties, for example the same frequency, of the naturally occurring SWRs.

[00102] Fig. 6 shows the method comprising prior steps of measuring S802 a brain activity
25 of the subject 20 followed by measuring, in step S804, an oscillatory brain rhythm 70 of the subject 20, and thereby illuminating in the aforementioned step S1000 alternately the different groups of cells based on the measured oscillatory brain rhythm 70. The measurement step S804 comprises, for example, measuring the frequency, phase, and amplitude of the oscillatory brain rhythm 70.

30 [00103] Fig. 2 shows a system 100 for improving memory retention of an object 110. The system 100 comprises the rotating device 50 and the light source 30 located behind the

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rotating device 50. The light source 30 is located in the visual field 21 of the subject 20. The object 110 is substantially located in the center of the visual field 21.

[00104] Fig. 6 shows the method comprising placing in step S2000 an object 110 in substantially the center of a visual field 21 of the subject 20 for a period of time. The step
5 S2000 is followed by the illuminating step S1000 for illuminating the different groups of cells alternately in peripheral areas of the retina 25 of the subject 20 for the period of time. The illumination step S1000 is followed by an inducing step S1202 for artificially inducing the SWRs in the brain 15 of the subject 20.

[00105] The method is, in one example, used in an improvement of the performance of the
10 subject 20 in memorizing a higher number of elements in an image. The placing step S2000 of the object 110 followed by the illuminating step S1000 opens in a very short window of opportunity, i.e., 100 ms, for the V1 region to transfer the very short-lasting information located in the V1 region, in form of iconic memory, to the higher areas of the brain 15. The transfer occurs during and after artificially inducing the SWRs in the inducing step S1202.
15 The rest of the memorizing happens naturally in the brain 15. The method enables to facilitate an information transfer from the V1 region to higher area of the brain shortly after visual image presentation.

[00106] In one example, the method is used in a “visual mode”. The visual mode is, for example, the mode for memorizing elements from the object 110. The object 110 can be in
20 the example a visual object with multiple memorable items in the object, such as a matrix of letters or composition of icons. The method of the visual mode comprises looking in the step S1000 at the object 110 for a very short length of time, e.g., 100 ms and actively memorizing the object 110. That means that the subject 20 makes a cognitive effort to memorize the object 110 after looking at the object 110.

25 [00107] The step S1000 is followed by artificially inducing the SWRs in the brain 15 in the inducing step S1202. The inducing step S1202 replaces the active phase in the brain 15 during which the subject 20 becomes engaged in actively memorizing the object 110.

[00108] In another example, the method is used in a “non-visual mode”. The non-visual mode is, for example, learning vocabulary for a foreign language. The inducing step S1202
30 induces the SWRs and plays a role of repeating a pair of words loudly to actively memorizing the pair of words by sending a visual image of the pair of words presented to the user, immediately after the presentation of the pair of words to the subject 20. The presentation

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occurs precisely before the decaying period of the V1 region to the higher areas of the brain 15, so that the brain is let to consolidate the pair of words.

[00109] The device 10 is used, for example, for enhancement of the iconic memory of the subject 20. The device 10 increases, in one example, the time in which the object 110 is
5 stored in the iconic memory, i.e., 100 ms. Thus, a consolidation of the memory is enhanced by providing more time for the brain 15 to pass the information to the higher brain areas and/or to more stable form of memory, i.e., the working memory. The device 10 increases in a further example the capacity of the iconic memory by improving the performance of the subject 20 in memorizing a higher number of elements in the image of the object 110.

10 [00110] The device 10 is used, in another example, for memory transformation. The device 10 can be used to transform one form of memory, i.e., iconic memory, to another form of memory, i.e., hippocampal long-term memory, by inducing the SWRs after presenting an image to the subject 20. This would replace the active memorizing by the subject 20 with an induction of the SWRs in the step S1202. The artificially induced SWRs transfers the
15 information from the short-term iconic memory to a more stable, long-term form of memory in higher cortical areas of the brain 15 and possibly in the hippocampus.

[00111] The device 10 is used, in a further example, to prevent or treat Alzheimer Disease (AD). Zhen et al. in “Normal and Abnormal Sharp Wave Ripples in the Hippocampal-Entorhinal Cortex System: Implications for Memory Consolidation, Alzheimer’s Disease,
20 and Temporal Lobe Epilepsy”. *Frontiers in Aging Neuroscience*, 13, 683483 (2021). <https://doi.org/10.3389/fnagi.2021.683483> state that the naturally occurring SWRs system in AD is undermined.

[00112] Neurodegenerative diseases, such as AD, are characterized by a marked loss of neural and glial substance. It is known that various metabolites accumulate inside brain cells,
25 forming neurofibrillary Tau protein tangles, and accumulate outside of the brain cells, forming β amyloid ($A\beta$) plaques. These metabolites have neurotoxic effects leading to further cell death, as taught by Hardy, J. A., & Higgins, G. A. in “Alzheimer’s Disease: The Amyloid Cascade Hypothesis”. *Science*, 256(5054), 184–185 (1992). <https://doi.org/10.1126/science.1566067>. Severe cognitive decline is a hallmark of AD, and
30 the subjects suffer from progressive dementia, marked by impaired spatial orientation (i.e., the subject has difficulty in determining the position of the subject in space and in determining spatial relationships of objects), memory loss, and learning problems.

[00113] It is unknown whether the A β plaques play a prominent role in the degenerative process of AD after disease initiation. A β cascade hypothesis was one of the original ideas for the cause of the physiological mechanism of AD, as disclosed by Spires-Jones et al. in “The Intersection of Amyloid Beta and Tau at Synapses in Alzheimer’s Disease”. *Neuron*, 82(4), 756–771 (2014). <https://doi.org/10.1016/j.neuron.2014.05.004>. It was originally thought that deposit of the A β plaques in the brain of the subject triggered a series of events that lead to death of neurons and dementia.

[00114] More recently, the role of synaptic loss in AD pathophysiology has come into focus, as taught by Tzioras et al. in “Synaptic degeneration in Alzheimer disease”. *Nature Reviews Neurology*, 19(1), 19–38 (2023), <https://doi.org/10.1038/s41582-022-00749-z>. Synaptic loss is the loss of connections (i.e., synapses) between neurons of the brain of the subject. SWRs may play a central role in impaired synaptic plasticity, as taught by Caccavano et al. in “Inhibitory Parvalbumin Basket Cell Activity is Selectively Reduced during Hippocampal Sharp Wave Ripples in a Mouse Model of Familial Alzheimer’s Disease”. *The Journal of Neuroscience*, 40(26), 5116–5136 (2020). <https://doi.org/10.1523/JNEUROSCI.0425-20.2020> and Sanchez-Aguilera et al. in “Sharp Wave Ripples in Alzheimer’s Disease: In Search of Mechanisms”. *The Journal of Neuroscience*, 41(7), 1366–1370 (2021). <https://doi.org/10.1523/JNEUROSCI.2020-20.2020>. Synaptic plasticity refers to the ability of the synapses in the brain to be strengthened or weakened over time. One line of research with respect to glial cells points towards a specific role of oligodendrocytes and towards a loss of axonal myelin sheaths in AD, impairment of SWRs, described by Steadman et al., in “Disruption of Oligodendrogenesis Impairs Memory Consolidation in Adult Mice”. *Neuron*, 105(1), 150-164.e6. (2020), <https://doi.org/10.1016/j.neuron.2019.10.013>, and improvement of memory and SWRs with increased myelination, described by Chen et al. in “Enhancing myelin renewal reverses cognitive dysfunction in a murine model of Alzheimer’s disease”. *Neuron*, 109(14), 2292-2307.e5 (2021). <https://doi.org/10.1016/j.neuron.2021.05.012>. The impaired SWRs appear to play a central role on mechanisms of the AD pathophysiology. Based on these observations, the inventors have concluded that targeting generation of the impaired SWRs via brain stimulation could help to alleviate symptoms of AD in the subjects.

[00115] A β is a neuropeptide derived from the amyloid-beta precursor protein (APP). The APP occurs in 60-70% of vertebrates similar to humans. It is known that the APP has a critical physiological function as disclosed in Tharp & Sarkar, “Origins of amyloid- β ”. *BMC*

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Genomics, 14(1), 290 (2013). <https://doi.org/10.1186/1471-2164-14-290>, but its functional role is controversial and unclear. Accumulation of the A β in AD appears to be one of the earliest biomarkers in the subject to indicate onset of the AD. It has been seen that the accumulation of the A β disrupts the SWR and appear to impair memory formation. It has
5 been concluded that an imbalance between a synthesis of the A β and clearance of the A β from the brain is a potential cause of a A β plaque formation.

[00116] The glymphatic system has been found to have a role in the A β plaque formation. Natale et al. in “Glymphatic System as a Gateway to Connect Neurodegeneration from Periphery to CNS”. *Frontiers in Neuroscience*, 15, 639140 (2021).
10 <https://www.frontiersin.org/articles/10.3389/fnins.2021.639140/full> have reported that the glymphatic system possibly removes excessive A β from the brain to the cerebrospinal fluid (CSF). The function of the glymphatic system is therefore thought to clean toxins into the CSF and this cleaning is found to mostly occur during slow-wave-sleep (SWS). It is also found that, during inducing the SWRs, memory consolidation occurs as disclosed in Branger
15 et al., “Relationships between sleep quality and brain volume, metabolism, and amyloid deposition in late adulthood”. *Neurobiology of Aging*, 41, 107–114 (2016). <https://doi.org/10.1016/j.neurobiolaging.2016.02.009>. An increase of the SWRs for the subject suffering from AD might be a compensatory mechanism to counter a reduced density of SWRs in the subject. The impairment of SWRs appears to cause an impaired encoding,
20 an impaired consolidation, and an impaired retrieval of memory as disclosed in Cushing et al., “Impaired Hippocampal-Cortical Interactions during Sleep in a Mouse Model of Alzheimer’s Disease”. *Current Biology*, 30(13), 2588-2601.e5 (2020). <https://doi.org/10.1016/j.cub.2020.04.087>. Experimental work in humans indicates that visual stimulation can drive flow of the CSF in the brain, as disclosed in Williams et al.,
25 “Neural activity induced by sensory stimulation can drive large-scale cerebrospinal fluid flow during wakefulness in humans”. *PLOS Biology*, 21(3), e3002035 (2023). <https://doi.org/10.1371/journal.pbio.3002035>. Targeting the impaired generation SWRs with artificially induced SWR increases the clearing of A β by activating the glymphatic system, while at the same time increasing the SWRs density. The inventors have concluded
30 that an increase of the SWRs density would further alleviate the AD memory pathology, i.e., the decline in the function of the memory observed by the subjects with AD.

[00117] White matter impairment, i.e., alteration of a myelination of central nervous axons, has also been identified in AD in addition to the aforementioned degeneration of neural tissues. The myelination is implicated in supporting the structure of the axons in the brain. The axons are long slender projections of neurons in the brain which transmit electrical impulses within the brain. Degradation of the myelin leads to a reduction of the speed of transmission of the electrical signal along the central nervous axons.

[00118] Experimental research points to experience-related changes in the myelination indicating that changes in the myelination play an important role in neural plasticity and memory as disclosed in Xin & Chan, "Myelin plasticity: Sculpting circuits in learning and memory". Nature Reviews Neuroscience, 21(12), 682–694 (2020).
<https://doi.org/10.1038/s41583-020-00379-8>.

[00119] It has also been found that the myelin is needed to facilitate the generation of the SWRs. Glia cell loss impairs renewal of the axonal myelination as well as impairs SWRs and associated memory formation.

[00120] The inventors concluded that an increase in myelinations will lead to improvement of memory and to an SWRs functionality, thereby countering the AD pathology. Chen et al. in "Enhancing myelin renewal reverses cognitive dysfunction in a murine model of Alzheimer's disease". Neuron, 109, 2292-2307 (2021) showed in a mouse model of AD that simulating renewal of the myelin in the mouse can improve memory performance and increase the SWRs density and frequency. Increasing the SWRs density promotes activity of the glia cell and the axonal remyelination for improving neural network functionality and memory formation.

[00121] Molecular changes and cellular degeneration are at the core of current AD models, but synaptic dysfunction may be detectable before e.g., clinically relevant deposition of the A β plaques is observed. Cellular alterations cause changes in the synaptic activity. The synaptic activity altering molecular structure and function causes the cellular alterations as disclosed in Iaccarino et al. "Gamma frequency entrainment attenuates amyloid load and modifies microglia". Nature, 540(7632), 230–235 (2016).
<https://doi.org/10.1038/nature20587>. Neuroplastic deficits are prominent at early stages of AD and link A β and Tau to cognitive decline. The inventors have concluded that the dysfunction of the synapses might be a link between neuropathology and cognitive symptoms considering early changes in the synaptic activity in AD and the synaptic loss

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across different molecular pathologies in AD. Experimental evidence points towards a critical role of the SWRs in triggering and tuning of the synaptic plasticity. The inventors have therefore concluded that artificially inducing the synaptic plasticity by artificially inducing SWRs counter early pathological synapse loss in AD. The early counter of pathological synapse loss in AD provides a prolongation of normal functioning considering neuropathological changes and prevents neurodegenerative progression of AD.

5 [00122] The device 10 can artificially induce SWRs in a pace and temporal pattern which is required by the cortical network to compensate the lack of naturally occurring SWRs in the brain 15 with AD. The device 10 can further be used in a “pace-maker” manner, comparable to a heart pacemaker concept.

[00123] The device 10 can be used in prevention or treatment of effects of dementia on memory or other cognitive functions of the brain. The presence of the SWRs declines indeed by aging.

[00124] The device 10 can be used, in another example, for training the memory of the subject 20 to learn lost face identity memories, memorizing image pairs, vocabulary pairs, or a combination thereof.

[00125] In this example, the device 10 can be used to memorize image pairs in a naïve subject 20. The subject 20 is presented with several pairs of images in a training phase. The training phase is the phase during which the subject 20 learns the information. The pairs of images are divided into a first subgroup of the image pairs and a second subgroup of the image pairs. An SWR is induced after a display of the image pairs for the first subgroup of the image pairs. For the second subgroup of image pairs, there is no SWR induced after the display of the image pairs. The subject 20 responds in a test phase to the test pair with yes or no. The test pair indicates if the test pair includes two images which have been shown in the training phase. If the test pair is among the first subgroup of image pairs during which an artificially induced SWR was induced, it is to be expected that the subject 20 should be able to remember the images better. The subject should then be able to provide more correct answers to the first subgroup of image pairs presented with the artificially induced SWRs than to a second subgroup of the image pairs presented without artificially induced SWRs stimulation. This improvement is due to the first subgroup of image pairs with the artificially induced SWR being memorized better.

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[00126] The SWR occurs naturally during resting states of the brain 15 and particularly during sleep. The device 10 can be used to increase the number of the SWRs by artificially inducing the SWRs. Mimicking means that the device 10 can be used to increase the number of the SWRs. Thus, the device 10 can replace the function of sleep to generate the SWRs.

5 [00127] In one example, the artificially inducing SWRs in the brain 15 in any state, i.e., wake state or sleeping state, enables people with sleep deficits, or with a poor-quality sleep, to benefit from memory consolidation during sleep. The head-mounted device 200 can further be a memory booster, or a memory consolidator. The head-mounted device 200 enables replacing sleep, mimicking sleep, and learning during sleep.

10 [00128] The head-mounted device 200 is implemented, in a further example, as a virtual reality (VR) glass, an augmented reality (AR) glass, a mixed reality (MR) glass, an extended reality (XR) glass or data glasses. In one example, the VR glass, the AR glass, the MR glass, the XR glass or the data glasses are implemented as standalone wearables with a dedicated processing unit, standalone wearables with a power supply. Other implementations include
15 but are not limited to housings enabling holding a separate device or a light source, such as a smartphone. The head mounted device 200 could also be connected to an external processing unit or are connected to a power unit, such as a computer.

[00129] In one example, the head-mounted device 200 further comprises optomechanical components to project light to the visual field 21, for example to the peripheral areas of the
20 retina 25 of the visual field 21. The optomechanical components are, for example, Micro Electromechanical Systems (MEMS), light projection components or integrated light sources in glass lenses, such as micro- and pico-LEDs.

[00130] In one example, a smartphone is placed in the center of the rotating device 50.

[00131] Fig. 3 shows a head-mounted device 200 comprising the device 10. The device 10
25 is, in one example, light-sealed to the head-mounted device 200.

[00132] The head-mounted device 200 is, in one aspect, worn by the subject 20 to improve memory and learning. A visual or auditory content to be learnt is presented to the subject 20 in a temporal relation to the light source 30 generating the visual stimulation. The temporal relation is, for example, a time window of a range of 1000 ms – 3000 ms after the visual or
30 auditory content is presented to the subject 20. The head-mounted device should be worn for a time between 1 min and 60 min and during times of the day when the subject 20 is relaxing or resting.

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[00133] The head-mounted device 200 is, in another aspect, worn by the subject 20 to prevent AD or at least to prevent the AD from advancing. The head-mounted device 200 is worn by the subject 20 for a defined period of time and at a defined time of the day, while the high frequency visual stimulation is not necessarily paired with learning the visual or auditory content.

[00134] Fig. 4 shows a screen-mounted device 201 comprising the device 10. In one example, the screen-mounted device 201 is used for memory enhancement.

[00135] Fig. 7 shows the combination of the temporal variation and one or more of the spatial variation, the wavelength spectrum variation, the intensity variation, or the polarization variation, applied with the device 10.

[00136] An example is provided below. Flickering visual stimulation targeting the entire visual field 21 can evoke steady-state visual evoked potentials (SSVEPs) up to approximately 100 Hz, as disclosed in Herrmann, C. S., "Human EEG responses to 1-100 Hz flicker: resonance phenomena in visual cortex and their potential correlation to cognitive phenomena", *Experimental Brain Research*, 137(3-4), 346-353 (2001), accessible under <https://doi.org/10.1007/s002210100682>.

[00137] Artificially enhancing these oscillations could artificially induce SWRs and potentially boost perception and information absorption.

[00138] A combination of a stroboscope as light source 30 with a rotating disc with opaque and transparent sections as rotating device 50 was built. The stroboscope was an industrial device from Rheintacho Messtechnik GmbH. The combination enables to selectively and sequentially target the different cells of the retina 25 with high-frequency flickering light with a frequency of 120, 165, 180 or 190 Hz.

[00139] Ones of the cells in the retina 25 were stimulated every 10 ms. Different groups of the cells were stimulated at a later time (i.e., lag) of one of 8.33 ms, 6.06 ms, 5.55 ms, or 5.26 ms, i.e., 120, 165, 180 and 190 Hz. Sixty trials of two seconds of the aforementioned stimulation frequencies were carried out (i.e., 240 trials in total). 64-channel EEG from ten participants was recorded in the 240 trials. Spatially selective SSVEPs were successfully recorded for 120 Hz and 180 Hz stimulation with a parieto-occipital topography.

[00140] On the other hand, in a further four trials of thirty seconds, in which 64-channel EEG was recorded from six participants, high-frequency SSVEP responses at 180 Hz to stimulation at 180 Hz were successfully measured.

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[00141] Electrophysiological experiments in humans and mice showed that a high-frequency visual flickering stimulation above 80 Hz in combination with a spatial variation can induce the SWRs in the hippocampus, as disclosed in Figs. 8, 9, and 10. The electrophysiological experiments demonstrate that the problem of passing the retina 25, inducing the high-frequency oscillation in the visual cortex, and inducing the SWR in the hippocampus can be solved by combining the high-frequency visual flickering stimulation with an equally high-frequency change in one of or a combination of a spatial variation, a wavelength spectrum variation, an intensity variation, or a polarization variation.

[00142] In a one example, the light-emitting diode display generated light to project a spatial pattern on the retina 25 of mice. The light-emitting diode display used was an industrial device from ASUS. The light-emitting diode display generated the high-frequency flickering light at frequencies of 144 Hz, 180 Hz, and 240 Hz, enabling selectively and alternately illumination of different groups of the cells in the retina 25 of mice.

[00143] The cells in the retina 25 of mice were stimulated every 22.22 ms. The different cells of the retina 25 were stimulated at a lag of 6.94 ms, 5.55 ms, or 4.16 ms, i.e., at 144 Hz, 180 Hz, or 240 Hz, for fifty trials of two seconds. Signals from intracranial electrodes implanted in the right hippocampus of six mice were recorded.

[00144] Fig. 8 shows that an increase in the SWRs in the local field potential of the hippocampus in mice compared to a resting state condition prior to the stimulation was recorded for 144 Hz stimulation.

[00145] In a further instance, the light-emitting diode display generated light to project a spatial pattern on the retina 25 of humans. The light-emitting diode display used was an industrial device from Samsung. The device generated a high-frequency flickering light at 120 Hz, 144 Hz, and 180 Hz enabling selectively and alternately illumination of different groups of the cells in the retina 25.

[00146] The cells in the retina 25 were stimulated every 22.22 ms. Different groups of the cells in the retina 25 were stimulated at a lag of 8.33 ms, 6.94 ms, or 5.55 ms, i.e., at 120 Hz, 144 Hz, or 180 Hz, for seventy trials of two seconds. Electrical activity of the brain was recorded from intracranial electrodes implanted in the left hippocampus of two human participants.

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[00147] Fig. 9 shows that an increase in SWR in the electrical activity of the hippocampus in two human participants compared to a resting state condition prior to the stimulation was recorded for 120 Hz stimulation.

5 [00148] In a further instance, the light-emitting diode display generated light to project a spatial pattern on the retina 25 of humans. The light-emitting diode display used was an industrial device from ViewPixx Technologies. The device 10 generated a high-frequency flickering light at 120 Hz and 180 Hz enabling selectively and alternately illumination of different ones of the cells of the retina 25.

10 [00149] The cells in the retina 25 were stimulated every 22.22 ms. The different ones of the different cells of the retina 25 were stimulated at a lag of 8.33 ms or 5.55 ms, i.e., at 120 Hz or 180 Hz, for one hundred trials of two seconds. 306-channel Magnetoencephalography (MEG) from six participants was recorded. Spatially selective SSVEPs were successfully recorded for 120 Hz and 180 Hz stimulation with an occipital topography.

15 [00150] Fig. 10 shows that an increase in the SWR in the magnetic field of the electrical activity of the hippocampus in six human participants compared to a resting state condition prior to the stimulation was recorded for 120 Hz stimulation.

[00151] In a further instance, the light-emitting diode display generated light to project a spatial pattern on the retina 25. The light-emitting diode display used was an industrial device from ASUS. The light-emitting diode display generated a high-frequency flickering
20 light at 120 Hz enabling selectively and alternately illumination of the different cells of the retina 25 of humans.

[00152] The cells in the retina 25 were stimulated every 22.22 ms. The different ones of the different cells of the retina 25 were stimulated at a lag of 8.33 ms, i.e., at 120 Hz for five trials of sixty seconds. Before the stimulation, 17 participants learned a list of words. After
25 the stimulation, these participants recalled the previously learned words in the presented order.

[00153] Fig. 11 shows an increase in the correct recall of the word order by the participants following the stimulation compared to a sham stimulation control condition in the same participants.

30 [00154] Spatially selective noninvasive visual stimulation was used as a tool to artificially boost naturally occurring high-frequency oscillations during stimulus processing, attentional

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information selection, and memory. Targeted therapeutic interventions based on the device 10 could be possible, for example, for temporally specific visual stimulation.

[00155] Fig. 12 shows a view of a virtual reality (VR) glass, an augmented reality (AR) glass, a mixed reality (MR) glass, an extended reality (XR) glass, or data glasses comprising the device 10 for artificially inducing the ripples in the brain. The device 10 is made of two lenses 220. The device 10 further comprises projectors 210. The projectors 210 comprises the light source 30. The generated light from the light source 30 is projected on the lenses 220 or in the lenses 220. The generated light is illustrated in a non-limiting aspect as squares on the lenses 220.

10 [00156] Fig. 13 shows a view of the head-mounted device 200 chosen from one of the virtual reality (VR) glass, the augmented reality (AR) glass, the mixed reality (MR) glass, the extended reality (XR) glass, or the data glasses. The head-mounted device 200 comprises the device 10 for artificially inducing the ripples on the head of the subject 20. The head-mounted device 200 further comprises a screen 230 for generating stimulation of the retina
15 25 of the subject 20.

[00157] In one aspect, the step of measuring S802 the brain activity of the subject 20 comprises measuring a signal in the oscillatory brain rhythm, which is considered to be a correlate for the SWR. The correlate of the SWR is recorded with electroencephalographic methods from the surface of the head of the subject 20. The alternately illumination of the
20 different cells of the retina 25 can be adjusted, so that the number of the measured SWR correlates increases.

[00158] In one further aspect, the correlate of the SWR is recorded with electroencephalographic methods from the surface of the head of the subject 20 by computing the power spectrum of the recorded signal.

25 [00159] In a further non-limiting aspect, the computing of the power spectrum of the recorded signal can be achieved by training recurrent neural networks (RNN) to detect the correlates of the SWR. Experimental results shown on Fig. 14 discloses that training an RNN on the power spectrum of electroencephalographic signals achieves more than 80% accuracy of detecting SWR.

30

Reference numerals

	10	device
	15	brain
5	20	subject
	21	visual field
	22	eyes
	25	retina
	26	cell
10	30	light source
	31	first light source
	32	second light source
	40	piezoelectric device
	50	rotating device
15	70	motor
	80	microcontroller
	100	system
	110	object
	200	head-mounted device
20	201	screen-mounted device
	210	projector
	220	lenses
	230	screen

Claims

1. A device (10) for inducing ripples in a brain (15) of a subject (20), the device (10)
5 comprising a light source (30), wherein
the light source (30) is adapted for generating light,
the generated light having at least two light variations, the at least two light variations
are selected from at least two of a spatial variation, a temporal variation, a wavelength
spectrum variation, an intensity variation, or a polarization variation;
10 wherein the at least two light variations are selected for inducing the ripples in the
brain (15); and
the generated light generates a visual stimulation in the brain (15) at the frequency
of the ripples.
- 15 2. The device (10) of claim 1, wherein the ripples are selected from one of neocortical
ripples or hippocampal sharp-wave ripples (SWRs).
3. The device (10) of claim 1 or 2, wherein the generated light generates the visual
stimulation in the brain (15) at the frequency of the ripples so that different cells of
20 the retina (25) of the subject (20) are activated sequentially.
4. The device (10) of any one of the above claims, wherein the at least two light
variations are selected from a temporal variation and at least one of a spatial
variation, a wavelength spectrum variation, an intensity variation, or a polarization
25 variation.
5. The device (10) of any one of the above claims, wherein the generated light generates
the visual stimulation at the frequency range of between 80 and 250 Hz.
- 30 6. The device (10) of any one of the above claims, wherein the light source (30) is one
of a stroboscope, an electronic display, a light-emitting diode (LED), a panel of

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multiple light-emitting diodes, an electronic display comprising multiple light-emitting diodes, a liquid crystal display (LCD) or a laser.

- 5 7. The device (10) of any one of the above claims, wherein the at least two light variations are a spatial variation and a temporal variation.
8. The device (10) of any one of the above claims, further comprising a piezoelectric device (40) for vibrating the light source (30).
- 10 9. A system (100) for improving memory retention of an object (110), the object (110) being substantially located in the center of a visual field (21) of a subject (20);
- the system (100) comprising a light source (30) adapted to generate light in a peripheral field of the subject (20), the generated light having at least two light
- 15 variations;
- the at least two light variations are selected from at least two of a spatial variation, a temporal variation, a wavelength spectrum variation, an intensity variation, or a polarization variation;
- wherein the at least two light variations are selected for inducing ripples in a brain
- 20 (15) of the subject (110); and
- the generated light generates a visual stimulation in the brain (15) at the frequency of the ripples.
- 25 10. The device (10) of any one of claims 1 to 8 for use in at least one of enhancement of the iconic memory of the subject (20), improvement of the performance of the subject (20) in memorizing a higher number of elements in an image, transformation of iconic memory into working memory, transformation of working memory to hippocampal or long-term memory, transformation of hippocampal memory to long-term memory, transformation of spatial memory into long term memory, prevention
- 30 or treatment of Alzheimer's disease (AD), prevention or treatment of aging effects on memory or other cognitive functions of the brain (15) of the subject (20), prevention or treatment of effects of dementia on memory or other cognitive

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functions of the brain, training of the memory of the subject (20) to learn lost identities faces memories, memorizing image pairs, vocabulary pairs, or a combination thereof.

5 11. Use of the device (10) of any one of claims 1 to 8 for at least one of enhancement of the iconic memory of the subject (20), improvement of the performance of the subject (20) in memorizing a higher number of elements in an image, transformation of iconic memory into working memory, transformation of working memory to hippocampal or long-term memory, transformation of hippocampal memory to long-
10 term memory, transformation of spatial memory into long term memory, prevention or treatment of Alzheimer's disease (AD), prevention or treatment of aging effects on memory or other cognitive functions of the brain (15) of the subject (20), prevention or treatment of effects of dementia on memory or other cognitive functions of the brain, training of the memory of the subject (20) to learn lost
15 identities faces memories, memorizing image pairs, vocabulary pairs, or a combination thereof.

12. A method for inducing ripples in a brain (15) of a subject (20), the method comprising:
20 illuminating (S1000) alternately different cells of the retina (25) of the subject (20) from a light source (30), wherein the light source (30) is adapted for generating light, the generated light having at least two light variations, the at least two light variations are selected from at least two of a spatial variation, a temporal variation, a wavelength spectrum variation, an intensity variation, or a polarization variation;
25 wherein the at least two light variations are selected for inducing the ripples in the brain (15);
the generated light generates a visual stimulation in the brain (15) at the frequency of the ripples;
thereby inducing (S1202) the ripples in the brain (15).

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13. The method of claim 12, wherein the ripples are selected from one of neocortical ripples or hippocampal sharp-wave ripples (SWRs).

14. The method of claim 12 or 13, wherein the generated light generates the visual stimulation in the brain (15) at the frequency of the ripples so that different cells of the retina (25) of the subject (20) are activated sequentially.
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15. The method of any one of claims 12 to 14, wherein the at least two light variations are selected from a temporal variation and at least one of a spatial variation, a wavelength spectrum variation, an intensity variation, or a polarization variation.
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16. The method of any one of claims 12 to 15, wherein prior to the step of illuminating (S1000) alternately different cells of the retina (25), the method comprises:
measuring (S802) a brain activity of the subject (20);
measuring (S804) an oscillatory brain rhythm (70) of the subject (20); and
thereby illuminating (S1000) alternately the different cells of the retina (25) based
15 on the oscillatory brain rhythm (70) and/or based on the properties of the brain activity.
17. The method of any one of claims 12 to 16, further comprising
placing (S2000) an object (110) in the center of a visual field (21) of the subject (20)
20 for a period of time t ; and
the different cells of the retina (25) are illuminated (S1000) alternately in the peripheral retina (25) of the subject (20) for the period of time t .
18. A head-mounted device (200) or screen-mounted device (201) comprising the device
25 (10) of any one of claims 1 to 8, or the system (100) of claim 9.
19. The head-mounted device (200) of claim 18 for one or more of replacing sleep, mimicking sleep, learning during sleep, memory consolidation during sleep or a combination thereof.