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A REVIEW TO UNDERSTAND EXCELSIOR ADVANCES AND INNOVATIVE DIAGNOSIS OF AMNESIA

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ABSTRACT

Several classes of memory loss have been reported which show that "Amnesia" is neurological disorder. Amnesia syndrome caused due to risk factors like stroke, traumatic brain injury, neurodegenerative diseases like Alzheimer's disease. The main perspective behind this study is based upon identifying the existing treatment or methods practised in hospitals and also new self-treatment or methods as there is no proper medication available to cure the disease.In amnesia disease hipocampus play a major role. As in most of the amnesic patients usually they regains their memories, but in some rare cases there may be problem occurs due to damage in hippocampus and these can make it so difficult to remember the old things or events. Hence, here we giving suggestions on psychiatric therapies to cure the disease on small scale. Also encapsulated the uses of some subclass of vitamin B and herbal medicines as supplement for the treatment of this disease and Scientists also performing global research on various features & type of amnesia by having approach towards the cognitive abilities, emotional state, physical & mental well-being of amnesic patient.

KEYWORDS: Memory, Hippocampus, Amnesia, Psychiatric therapy, Vitamin B.

INTRODUCTION

Amnesia is memory loss syndrome. It is also called as amnesic syndrome. People suffering from this disease are unable to collect and store information for longer time. Amnesia is a disease which was studied by the well know French psychologist Theodule-Armand Ribot. Henry Molaison was an American scientist who had undergone epilepsy surgery in the year 1953. The mission was to improve his epilepsy. At first, the surgery was thought to be

successful but later severe side effect were observed and they came to known that he was unable to create new memory.

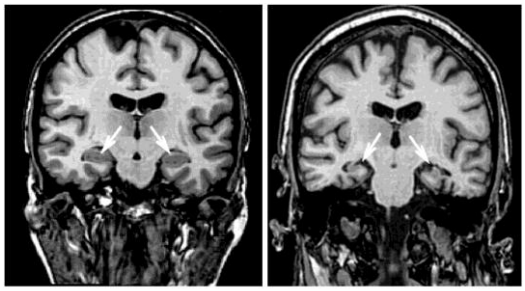

Fig 1: MRI view of amnesic brain (patients having hippocampal damage) as compare to healthy brain.

HOW DOES IT HAPPEN?

Amnesia results when there is damage to brain structure which controls our emotions and memories. It commonly occurs when there is injury to temporal lobe or to the hippocampus.

Causes

a) Brain injury
b) Epilepsy
c) Mild stroke
d) Alzheimer's diseases.

MEMORY

Different types of memories stored in human brain according to length of time.

- **Short term memory**: It is primary type of memory which holds very small amount of information for short period of time.
- **Long term memory**: It is stage of memory which leads to the storage of information for about long period of time or for more than few decades.

HIPPOCAMPUS

It is the part of brain which lies in the middle portion of the temporal lobe. It is derived from the Greek word "hippos" which means horse and "kampos" means sea monster. The structure of Hippocampus looks similar to the seahorse. Hippocampus is a part of limbic system which is associated with memory formation, functions of emotions and reaction.

Hippocampus detects various things which binds and converts it into whole experience and stores them.

Component of hippocampus:

- Cornu ammonis

a) CA1

b) CA2

c) CA3

d) CA4

- Hippocampal sulcus
- Subiculum
- Dentate gyrus

a) Fascia Dentata

b) Hilus (region CA4)

Hippocampus is made up of the following layers: Plexiform layer(external), Stratum oriens layer, Pyramidal cell layer, Stratum radiatum layer, Stratum lacunosum-molecular layer.

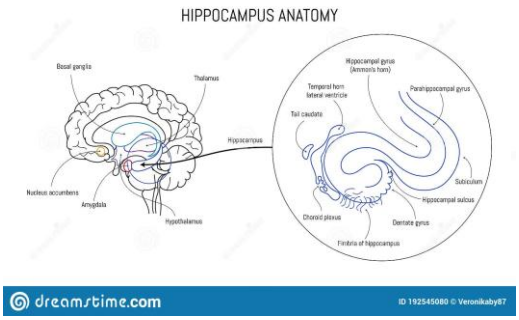

Fig. 2: anatomy & structure of hippocampus.

There are two types of memory which is regain by the process of Hippocampus: Declarative memory and spatial relationship memory. Person suffering from hippocampal damage will result in loss of declarative memory (events/data) and spatial relationship memory (direction/location).

Neurophysiology of Hippocampus

- In brain there are certain places where neurogenesis takes place from this one of it is Hippocampus.

- Hippocampus receives various signals from different parts of brain such as limbic system of nerves and external part of cerebrum and mostly it receives signals through entorhinal cortex i.e., medial temporal lobe and subiculum, which is the inferior part of entorhinal cortex.
- Entorhinal cortexes transmit the information towards the denate gyrus of hippocampus. Granule cells of denate gyrus send signal with secondary pyramidal cells i.e., CA1 and CA3 cells.
- Later the granule cells (cells which found on cerebellum) of the granule layer (the thin layer of stratum granulosum) project their axons known as mossy fibres. Activate CA3 pyramidal cells and hilar interneuron (nerves cells present in the brain).
- Then CA3 pyramidal cells activates CA1 pyramidal cells and then CA3 and CA1 pyramidal cells together activates other CA3 pyramidal cells and septum i.e., dividing wall between two chambers.
- Later CA1 pyramidal cells sends impulses away from central nervous system i.e., efferent fibres to inferior part of entorhinal cortex and several subcortical areas.
- Ion channel which crosses the plasma membrane are called as membrane ion channel. So, in the hippocampal neuron, mainly two membrane ion channels are present named as Ca2+ channels and K+ channels which are responsible for formation of neural activity.
- Interruption in major memory formation pathway of hippocampus causes anterograde amnesia.

Neurochemistry of hippocampus

Acetylcholine is the neurotransmitter which helps in the purpose of memory.

In brain there are several cholinergic areas present with distinct function such as some playing an important role in attention, learning and memory. So, in these various cholinergic areas of brain acetylcholine acts as neurotransmitter.

At the end terminal of cholinergic neuron acetylcholine activates the type of receptors i.e., muscarinic, and nicotinic which encodes the information for memory formation.

a) Nicotinic Receptor

Nicotinic acetylcholine receptor (nAChRs) is present on pre and post synaptic nerve terminal. They are ligand gated ion channel and moderate the neuromuscular transmission. They have been involved in the neural development, memory formation.

Upon binding of acetylcholine, nicotinic receptor opens the ion channel and allows the entry of sodium (Na+) ion which produces the net depolarization and generated the action potential in neuron.

They are found in the neuromuscular function of skeletal muscle that receive release of acetylcholine for muscular contraction.

They can be further divided into two types.

- **Neuronal receptor** – Receptor which are found in all over the central & peripheral nervous system & they are taking parts in process of synaptic transmission in which neurons communicate with one another.
- **Muscular receptor-** Receptor which are found in gap between motor nerves (nerve which send signals from CNS to different parts of the body) where they help to settle neuromuscular transmission (process of controlling muscle movement of body with the help of neurotransmitter).

From this two receptor muscular type receptors have five classes pf subunits which are α1, β1, ɣ, ε, and δ receptor composition (α1)2, β1, ɣ, δ is for the electrolytes and fetal muscles (muscles which help for the movement of foetus) whereas receptor composition (α1)2, β1, ε, δ., is for the adult muscles (like skeletal muscles, smooth muscles, etc.).

Neuronal receptors have 12 classes of subunits which are α2- α10 and β2- β4 like (α4)3 (β2)3, (α3)2(β4)3, α4α6β3(β2)2, (α7)5, and many others.

b) Muscarinic receptor

Muscarinic acetylcholine receptor (mAChRs) are associate with parasympathetic nervous system and defined under the G-protein coupled receptor. Muscarinic receptor indirectly opens the ion channel with the help of secondary messenger, therefore muscarinic receptor shows relatively slower response than nicotinic receptor. They are subdivided into 5 pharmacological types M1, M2, M3, M4 and M5. From which M1, M3 and M5 are stimulatory receptors and are made up of the Gq proteins whereas M2 and M4 are inhibitory receptors and are made up of Gi protein.

From all of this receptors, Mainly M1 receptor is use for the functions of learning and memory and this only receptor is broadly expressed in central nervous system.

- **M1 Receptor** – It is a G – Protein coupled receptor which found to bound with Gq protein and which is use to increase the response of phospholipase c. Also from long time ago it is identified as a therapeutic agent for development of learning disability in memory related disorder.

All others muscarinic receptors i.e M2,M3,M4 And M5 are useful for the functions of other organs in the body.

- **M2 Receptor** – It is coupled to Gi protein. Receptors are located in the heart and lungs and its increase heart rate.
- **M3 Receptor** – M3 Receptors are located in smooth muscles of blood vessels and also located in many glands and regulate phospholipase C enzyme.
- **M4 Receptor** – It is found around the CNS .It decreases the cAMP in the cell and shows inhibitory effect.
- **M5 Receptor** – Location of M5 Receptor is not known and it also regulate phospholipase C.

TYPES OF AMNESIA

1) RETROGRADE AMNESIA

It is a type of amnesia in which a person is unable to recall the memories which had already taken place years ago or in the childhood period. It happens due to the damage in the brain or due to the attack of any disease in the brain. It can give rise to trauma injury, stroke, or any other brain disease.

Symptoms

- confusion
- confabulation
- mental co-ordination
- trouble in recalling old memory.

Types

I. **Temporal graded (TGRA)-** Temporally graded retrograde amnesia is a phenomena of functional memory loss in which recent information is easily remembered than long term information.

II. **Focal-** Focal retrograde is ability to form new memory that is left undamaged. It is also called as isolated or pure retrograde amnesia.

III. **Dissociative** - (psychogenic amnesia) Person is unable to recollect personal information for e.g., Identity, or life history.

2) ANTEROGRADE AMNESIA

In anterograde amnesia person loses the capacity of forming a new memory and cannot sustain the recently learned action. It vanishes the short-term memory after certain time.

Symptoms

- Frustration
- Forgetfulness
- Recently learned things.
- Unable to recall new phone numbers.

3) TRANSIENT GLOBAL AMNESIA

It is a quick and limited period of memory loss. It does not include the quality of more common neurological condition (condition which affect the brain and nervous system) like, epilepsy or stroke. Transient global amnesia attack last for 2-8 hours. During this time, the person does not remember what happened in the last few minutes that mean person are unable to regain the recent information or activity which was happen (for example- where they are, how they got here, etc.) It simply vanishes because it has limited period of memory loss.

Symptoms

- Anxiousness
- Nausea

- Tiredness
- Confusion
- Migraine
- Sudden attack of memory loss

4) INFANTILE AMNESIA

Infantile amnesia is also called as childhood amnesia in which children or adults are unable to regain long term memory such as any event or function or any experience, etc, done by them in their childhood up to the age of 3 and this condition is strongly related with the quick forgetting which usually occur in childhood.

DIAGNOSIS

In addition to clinical study of memory disorder, the scientist may also find the physiological tests to determine the seriousness of amnesia.

A. CT Scan or MRI test – CT scan or MRI test is often used for the brain related disease which is done to identify any structural or functional abnormalities in any parts of the brain and that may be producing an effect in amnesia. For example, head injury, bleeding in the brain, etc., that may cause amnesia.

B. PET Scan- It is also known as Positron emission tomography. It is a useful technique for understanding the inner functioning of the body organs and tissues. A small Radioactive material called as radiotracer is into the vein to observe the blood flows inside organs and to understand the metabolization of the sugar in the brain.

C. Psychometric Testing- Psychometric tests are used to assess the patient's behaviour, skills, and mental capabilities. These tests are based upon psychological conditions, they include the activities such as logical thinking, memory games, puzzle solving. Psychometric tests help to measure the patient's aptitude and their cognitive abilities.

D. EEG test- It is also known as Electroencephalogram test which is often used to determine abnormal electric activities in the brain as recorded by electrodes is placed on scalp (this electrode do not generate electricity; they only record electrical activity) and further it is used as the indication of epilepsy or other neuronal disorder.

TREATMENT

Treatment on amnesia have not been develop but, in most cases, it heals on its own without any treatment or any specific medicine. To treat amnesia, we need to know it causes so that we can find a solution. There are some cognitive therapies that are available to treat amnesia, but they do not give definitive results.

1) Hypnosis- The treatment helps to reduce anxiety of person who is unable to recall important personal information or disconnected from reality.

2) Eye movement Desensitization and reprocessing: This method is for relieve of the stress related to the traumatic (serious) injury. In this method patient do this eye movements reduce the stressful emotional memories of past serious injury.

3) Cognitive therapy Is a psychological treatment that determine the ability of person to thought, solve problem. It is treatment of cognitive skill, helps patient to develop the skills, behaviour, emotion and enhance the brain concentration, to retrieve memory. Cognitive therapy can be extremely effective and is associated with certain form of memory loss. Person acquire the knowledge or techniques to overcome the daily challenges in amnesia.

4) Bilateral sound therapy - Is the part of EMDR(eye movement desensitisation reprocessing) therapy and brainspotting. Bilateral sound therapy involve the movement of sound from one ear to the other one in rhythmic pattern which used to activate the consolidate information from hemisphere of brain. This therapy helps to neutralize intense emotion, wrong perception, decrease worries, increase focus and also strengthen the long term memory.

5) Neurofeedback- It is non defensive and painless method which involves retraining of brain to function perfectly with the help of neuroplasticity technique in which brain determines itself and modify some changes in it related to learning and other daily activities which lead to the increase in capacity of identification and remembering information.

Self Treatment

1) Yoga - Yoga is Indian origin excercise which maintain the balance between mind and body.Yoga include focus, body posture, strength, and deep breathing. It help to reduce the stress & anxiety and promote the relaxation of whole body systems.

2) Meditation- It is a technique for resting the mind during Yoga which improves concentration and capacity to remain information active in one's mind. It helps to improve blood circulation in brain and focus on present occurring situations.

3) Diary writing- Writing a diary will help an amnesic patient to combine, secure and remember those thoughts which have recently happened. Some amnesic patients have chances of forgetting things in a single minute so they are able to make the video or recording of it. With the help of this technique they will be able to
recollect or remember the thoughts or incidents which will also help to improve thinking.

4) Sticky notes are used as reminder for amnesic patient. They can write their daily tasks on the small piece of paper and stick it somewhere where they can easily see it.

5) Get enough sleep- good sleep increases the capacity to regain memory. If we sleep after learning something or after experiencing any incident then sleeping factor can combine all of this information into memories and allowing person to store them in their brain so person who is suffering from any brain disease require optimal hours of sleep.

MEDICATION & SUPPLEMENT

There are currently no medication available that can cure amnesia.

B vitamin supplements helps to maintain general mental health, primarily it improve the cognitive functioning.

- **Vitamin B6** helps to build neurotransmitters that are important chemical messenger in the brain.
- **Vitamin B9** helps to repair brain cells that are further used to improve memory and concentration. Vitamin B9 reduces the homocysteine level (negatively affect the healthy functioning of the brain cells). It prevents anxiety and depression & enhance cognitive action.
- **Vitamin B12** - Vitamin B12 helps to maintain healthy nerve cells and red blood cells. Most commonly vitamin B12 deficiency is found in adults and vegetarian can cause various symptoms like memory loss, also low levels of Vitamin B12 is related to increase in the risk of amnesia. Like this in such cases vitamin B12 helps to improve memory function.
- **Ashwagandha**: is an ancient medicinal plant. It increases the level of acetylcholine in brain which linked to improve brain function and memory also.Ashwagandha can cross the blood-brain barrier and reduce inflammation in the brain. The beta amyloid plaque is toxic to the brain which is reduced by the effects of Ashwagandha. Dose of Ashwagandha in large amount should be avoided as it causes diarrhea, vomiting, nausea. It is not recommended for people suffering from hyperthyroidism and pregnant women.

- **Acetyl-L-carnitine:** Carnitine is an amino acid. It is found in red meat. Acetyl-L-carnitine (ALCAR) is modified from carnitine. Acetyl-L-carnitine improve mental functioning, memory and behavior. It improves long term thinking problems. It is used as an ancestor for acetylcholine.
- **Astaxanthin**- Astaxanthin is a red pigment of the keto carotenoid group found in the marine environment. It has anti-oxidative and anti-inflammatory property which helps to protect the cell from damage.Astaxanthin easily crosses the blood-brain barrier because its main target organ is the brain. Supplementation of astaxanthin is used to stimulate brain function and cognitive action, but higher doses may cause abdominal pain.
- **Vitamin B1** (Thiamine) is a water soluble. It plays an important role in the growth and various function of various cells. It is important in cases of forgetfulness, stress etc. Thiamine is mostly present in foods like whole grains, brown rise, nuts, soybeans etc. So lack of these vitamins B1 (Thiamine) can cause Wernicke's Korsakoff syndrome (it is brain disorder) which is described by memory problems and nerve damage. High doses of thiamine rarely improves memory loss. It is also used as a nutrient in a diet that makes brain so effective. Hence, there are chances of reducing memory related disorders.

CONCLUSION

In most of the condition amnesia heals itself i.e. People who is suffering with amnesia having the ability to remembering immediate information and they may still be able to form new memories. As well as there are so many researches have been continuing on amnesia but scientists can observe that there is severe loss in the capacity to receive new information and regain it. Hence currently along with medication there is no specific treatments are also available to cure disease and that's why along with medication finding the treatments are also challenging under the overall. Neurochemistry of brain especially hippocampal region.

However certain self-treatments are also there to cure amnesia like yoga, medication, diary writing, etc. and some therapeutical treatments are also use to cure the disease like cognitive therapy, occupational therapy, etc. In addition some natural supplements and vitamins are also useful for treating some types of amnesia but use of some supplements gives certain side effects on our body, For Example- vitamin B6 is failed to reduce memory loss problems and it gives side effects like headache, nausea, etc. Like these few more memory supplements are there that may also have some power but unluckily that all supplements are not successful. Therefore more research / studies needs to be done about these supplements and their effects.

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