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"MANAGEMENT OF HEALTHY BRAINS IN COMPARISON WITH THE PHARMACOLOGICAL WAYS IN THE MANAGEMENT OF PARKINSON'S DISEASES AND IMPAIRMENTS OF MEMORY" A REVIEW

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ABSTRACT

The human brain is the command center for the nervous system and empower thinking, memory, movement, and emotions by a tricky function that is the biological evolution of highest product. To sustain a healthy brain during one's life is the topmost aim in ensuing health and endurance. The load of disorders related to neurological diseases and demand for the preservation of brain health raise by the ages of population. It is therefore necessary to understand what healthy brain is and why it is necessity. This article aims to describe healthy brain, analyse the effect of major neurological disorders on brain health, and discuss how these disorders might be treated and prevented.

KEYWORDS: Meningitis, cognitive impairment; Rey-Osterrieth complex figure test, neurodegenerative disorders.

INTRODUCTION

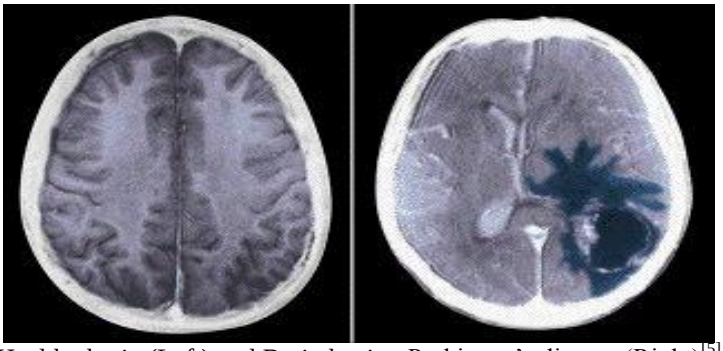
According to the updated explanation of WHO in 1948 regarding health that "a state of complete mental, physical, and social well-being and not simply the absent of disease or infirmity".

To maintain a healthy life depends on following factors which may vary from times to time and impact direct the healthy brain to sustain and plague.

1. Physical Health: Physical activity is here defined as all form of movement associated with an increase of energy expenditure. It includes spontaneous physical activity and organized non-competitive forms of physical activity including exercise, physical education classes, and sport. In Europe, the term sport was once used to describe all forms of vigorous physical activity[1], but we have followed the recommendation of an international consensus conference and restrict this term to physical activities performed individually or in teams and involving some form of competition.[2]
2. Mental health: Mental health, would be the special case obtained by focusing on the functions of mental processes; and so there is such a thing as mental health if there are mental functions.
3. Social health.
4. Economic health, etc.

All these are required to maintain and measuring the health, depends on the capacity, state and health of brain.Currently, there is no universally accepted definition of healthy brain. Ultimate current definitions have only a general explanation of how brain functions normally or indicate one or two proportion of healthy brain. According to the United States of Centers for Disease Control and Prevention a brain health is an ability to implements all the mental processes of ability to determine and judge, cognition, use language, and remember and memorize things.[3] The optimal brain health defined as "balance performance levels among all people at that age who are free of known brain or other organ system diseases in terms of reject from function levels, or as competence to perform all actions that the individual wishes to begin" stated by the American Heart Association/American Stroke Association (AHA/ASA) presidential advisory.[4],,

The brain is a complicated organ and has at least three levels of functions that affect all facet of our daily lives: analysis of senses and management of movement; cognitive maintenance, emotional, and mental processes; and management of normal behaviour and social awareness. Healthy brain may therefore be brief as the conservation of optimal brain integrity, cognitive and mental function at a given age in the nonappearance of apparent brain diseases that affect functions of normal brain.



Healthy brain (Left) and Brain having Parkinson's disease (Right)[5]

Effect of major brain diseases on healthy brain.

Certain brain diseases may disturb functions of normal brain and affect humans' healthy life. Medically, brain diseases that induce normal brain dysfunction can be classified into three groups.

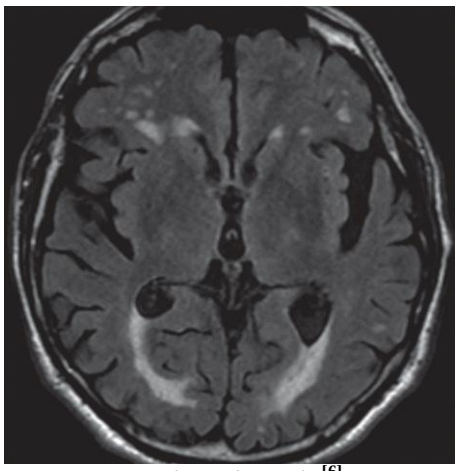
• Brain diseases with undisguised damage to brain structures, such as traumatic brain injury, cerebrovascular diseases, brain tumours, and communication, meningitis and sensory disorders etc.

• Brain functions disorders with measurable loss of brain connections or networks, such as neurodegenerative diseases (eg, Alzheimer's disease, Parkinson's disease, etc) and mental disorders (eg, schizophrenia, depression, bipolar disorder, alcoholism, and drug abuse, etc)

• Another brain disorders without measurable functional or structural impairment, such as migraine and sleep disorders, severe headache.

These brain diseases may have diverse or common reactions on healthy brain and it's functions. For example, Alzheimer's disease is the main type of dementia, with a decline in different discipline of cognitive function. Mind diseases may cause dysfunction in reward processing, execution, and emotional regulations.

In addition to physical disability, gait, aphasia and balance problems, and cerebrovascular diseases may start to dementia and cognitive impairment, which are ignored by both doctors and patients.



Parkinson's brain[6]

Deteriorate and overload of brain diseases

Human Deterioration is mainly imitating in the expression of brain Deterioration and disgrace of brain function. The number of people aged 60+ years and over worldwide was around 900 million in 2015 and is predict to grow to two billion by 2050.[7] With the enhance in population Deterioration and growth, the overload of brain diseases and challenges to the safety of healthy brain steeper growth. Community with brain diseases will have cognitive or mental disorders, physical disability, and social dysfunction and be a huge economic burden.

According to the Global Burden of Diseases study universally, neurological disorders where the major cause of disability adapt life years (276 million) and the second major cause of death (9 million) in 2016.[8] Stroke, migraine, Alzheimer's disease, Meningitis and other dementias contributes the largest neurological disability adapt in life years.[8]

About every one in four adults will have a stroke in their lifetime, from the age of 25 years and beyond.[9] Around 50 million people worldwide were living with dementia in 2018, and the number will increase more than triple to 152 million by 2050.[10] In the following decades, governments will face more demand for treatment, rehabilitation, and support services for brain diseases.

Scope and objections of further future research on healthy brain

Exist of Scope and objections in the determination of healthy brain, the mechanism of dysfunction and brain function, and paths to enhance brain health are.

• Loss of metrics or weapon to complete assess or evaluate healthy brain.

• Insufficient knowledge about the mechanisms of dysfunction and brain function.

• Few effective ways to prevent and handle dysfunction of brain in some large neurological disorders, such as dementia

• Need to specifically secure functions of brain for people with brain diseases.

Briefing and developing ideal healthy brain require the scientific assessment of healthy brain. However, it is tough to fully assess or quantify healthy brain through

one metric owing to the complicated aspects of healthy brain. Many structured or semi structured applications have been established to test brain health by self-assessments or close family member evaluations of daily function or abilities. In recent decades new structural and functional brain mapping procedures have been applied to assess network of brain sincerity and functional connectivity.[11]

However, these objective or subjective evaluation have both stability and instability. For example, scales such as the mini-mental state assessments and Montreal cognitive evaluations are smooth and easy to appliances but are used only as universal screening instruments for cognitive impairment; Rey-Osterrieth complex figure test, trail making A and B, tests such as the digit span, Stroop task, Boston naming test, verbal fluency test, and clock drawing test are used generally to evaluate one or two specific regions of memory, visuospatial, attention, language, and executive function; and brain mapping techniques, although non-invasive and objective, still have drawback of test contraindications, lack of temporal or spatial resolution, high false research rates, and motion artefact which limit their clinical revolutions.

Other complications in assessments of healthy brain is that culture, ethnicity, age, and geography location specific variations exist in the consciousness of excellent healthy brain. Consolidation of patient examination of function of brain, such as self-perception of cognitive function and quality of life, should also be contemplated when measuring brain health.

Global acceptable, age appropriate, and sensitive metrics or instruments, multidimensional, multidisciplinary are required to comprehensively quantify and monitor function of brain and health of brain.

We want a higher quality understanding for the mechanisms of brain function and dysfunction, to improv. optimal healthy brain, Sadly, least is known about the mechanism of the brain and its functions that how it working. Although we have made reasonable developments in recent decades, in neuroscience.

Still, we cannot totally decode the relations between activity across the interconnected networks of neurons of spatiotemporal patterns and thoughts or the cognitive and mental conditions of a person.[12]

In brain simulation and artificial intelligence, new research provides a vital measurement to understand biological brains, and vice versa.[13,14] In the European Union and China Brain Project it was mentioned that the development of brain simulation, and inspired brain computation, and intelligent machines was emphasised.[12,15]

Simultaneously, the working about the brain dysfunction in few brain disorders are still not well known, specifically for neurodegenerative and mental disorders. Also, study of the mechanisms of brain disorders may indicate new ways for the treatment and improvement of function of brain. Brain imaging based cognitive neuroscience may resolve the highlights of mechanism of brain of cognitive dysfunction and provide a solution to develop a biological structure for fidelity biomarkers of mental diseases.[16]

Most frequent neurological diseases, such as Alzheimer's disease, cerebrovascular diseases and, have complex aetiopathologies, involves typically in spatial-temporal interactions of environmental and genetics factors. These disorders could be more readily examinates by clear modelling cross species, greater efficiency in testing innovative therapies and leading to better understanding of their mechanisms.

Anyhow, a single genetic factor could account for the progression of disease monogenic neurological diseases. This research may find a window to increases the examinations of common general brain health and neurological disorders, as discussed by Chen and colleagues elsewhere in this series.[17]

Most frequent brain disorders, such as Alzheimer's disease and cerebrovascular diseases, have complicated aetiopathologies, environmental consideration and typically containing spatial-temporal cooperation of genetic disorders. Anyhow, a single genetic aspect may lead for the progression of disease with monogenic neurological disorders.

These brain disorders may be more easily researched by uncomplicated modelling of cross species, increasing to better understanding of their greater effects and mechanisms in the testing experiments for treatments. Such investigations may bring a skylight to increase the investigation of general healthy brain and common brain diseases.[17]

1. Alzheimer's disease:
2. Cerebrovascular diseases:
3. Genetic disorders:

Few effective accesses are presents to block and investigate dysfunction of brain in some main brain and neurological diseases, such as dementia and Alzheimer's disease. Neurons are not sustainable, and dysfunction of brain is always certain permanent. Some recent research showing amyloid clearance and the selective blocking of protein of tau aggregation failed to permits cognition or revise disease progression in patients with mild Alzheimer's disease and other brains diseases.[18,19]

New thoughts have focused on other ability to investigation and treatment of therapeutic targets, such as inflammation, and the gut microbiome and vascular dysfunction, as discussed by Shi and colleagues.[20]

In some, recent research it was showed that the previous impairment of cognition was introduced by the destructions of neurovascular integrity of unit of mechanisms, which may cause the breakdown of the blood-brain barrier and hypoperfusion and subsequent destructions in the clearance of proteins in the brain.[21, 22]

Blood-Brain Barrier.
There are some factors involved in the maintenance and keeping the mind healthy. They are mentioned below:

1. Physical activity
2. Mental exercise
3. A healthy diet
4. Nutrition
5. Social interaction
6. Ample amount of sleep
7. Relaxation
8. Control of vascular risk factors.

The AHA/ASA presidential advisory suggested that there are followings factors to maintain and operate simple brain health.

1. Non-smoking
2. Appropriate body mass index
3. Blood pressure
4. Total cholesterol
5. Physical activity
6. Healthy diet
7. Blood glucose

Some investigation of Pan and colleagues consider how this may indicate a new dawn of blocking of some brain dysfunction by preventing vascular risk factors and cognitive impairment and cerebrovascular diseases.[23]

For other brain disorders with potential treatment approaches, the main aim is to sustain brain function and maintenance. Defectiveness of function of brain due to damage of anatomical structural is underrated in patients with brain disorders such as brain tumours, trauma, seizures and epilepsy, etc.

In recent years, effective targets for brain disorders have changed from fixing on survival or life prediction to maintaining structures of brain and functions of brain to work in proper manner. Preservation of proper functions of brain function requires an understanding of the refined relation between advanced technologies to visualise brain structure-function relations and brain structure and function to maintain healthy brain.[24]

Other example of the circumstances associated with preservation of functions of brain is unpredictability in the treatment of response in epilepsy and seizures management. Current standard care for epilepsy and seizures depends on a clinical trial and misunderstanding of approach of subsequent regimens of antiseizure and anti-epilepsy medications and treatments. Delay in time due to these treatment approach which means that such treatments and medications may be ineffective and irreversible damage may occur.

i) Epilepsy
ii) Seizures

Chen and colleagues define how recent advances in personalised epilepsy and seizures based on management on patient derived stem cells, artificial intelligence, genomics is bringing some hope to overcome this crisis in epilepsy and seizures management and commitment for a more effective strategy and treatments.[25, 26, 27]

Healthy brain is defined as the conservation aspects of multidimensional brain function. However, many brain disorders may affect health of brain in one or more form of functions of brain.

Analysing and enhancing and promoting the function and health of the brain, the most difficult organ in the human body, will have a sensational tremor on society and science and medicine.[28]

In the past several years, a large number of scales of healthy brain derives have been launched in many countries to enhance the development of neuroscience and brain protection and brain simulation.[12]

However, several challenges are occurred by the different points, research directions of brain program in different countries. In the face of these challenges, Liu and colleagues discussed that collaboration on healthy brain clinical trials is urgently needed in this highly advanced increasing populations in world.

Parkinson's diseases and impairments of memory

Parkinson's disease (PD) is a neurodegenerative disease which stimulate memory progressiveness and impairment of memory. This may generally manage by using some non-pharmacological and pharmacological treatments in a proper manner. Mainly to focus on one aspect of impairments, or class of drug for treatment or management, we will deliver a broad aspect to know how different classes of pharmacological drugs or medications may increase different types of memory and its functioning. The development of increase the cognitive treatment is the first move towards the researching on what and how pharmacological compounds may alter the ability to memorize the things, ability to keep multiple tasks in mind, alter the impairments of memory in laboratory animals that may be used to decrease the impairments in functions of those patients suffering from neurodegenerative disorders. Which include perceptions of memory, consideration, working of memory, and the flexibility behavioural of different components. Class of drugs which are mainly used to treat memory impairment and Parkinson's disease are as follows.

1. Antidiabetic
2. Antiepileptic's
3. Antipsychotic

4. Antidepressants
5. Orexin-1 and other various medications.

The main attention is to arrange on compare and contrast the certain drugs to shows more effects on different diseases like impairments of memory and functions of brain, focusing on issues related to methodological way which associated with to defines this type of research, investigate the tasks used to determines these functions, and findings for upcoming research and review.

The study of the neuropharmacological basis of maintaining and managing the impairments of memory, and human primates and **Parkinson's** disease in a collective way to identified targets that will hopefully effective to open new ways for the treatment of cognitive disabilities in persons affected by mental disorders.

A process of management of storing information in a regular track by which one becomes attentive of their objects and views and surroundings.[32] We can define learning as procurring new or making partial changes to living knowledge, skill and demeanour. It enhance due to experience as it is a long term change in internal representation Memory is the process in which captured information is descrambled, stored and regained.[33]

By means of senses, the sensory memory act as a buffer forstimuli. The exact copy of sensory memory is what is perceive with the eye or perceive with the ear. For a few hundred milliseconds to one or two seconds, sensory memory holds sensory information.[34, 35]

To provide environment for temporary recall of the information, short term memory act as a scratchpad. It may archive that we see in the street like face of any human, any house or a contactable number, email id etc, but due to sensitive to disruption this information will stay for second to hours. Long term memory keeps the data for days, weeks, year and even for life time consolidated, its capacity is unlimited. The transfer of short-term memory to long term memory will occur after a short period of time. Only recall is necessary for the long-term potentiation without wasting time.[36, 35, 37]

The temporary loss of memory due to bilateral damage to the brain especially the limbic system known as Amnesia. It's generally of three types which are as follows.
1. Transient global amnesia,
2. Anterograde (loss of new information),
3. Retrograde (loss of old or previous information).[38]

To perform/acts or functioning daily activities (get dressed, take food and any official or daily work) in Dementia is difficulty to take places. Areas involved for cognitive in dementia disorder include – apraxia, aphasia, and many other chief functions.[39]

An idiopathic disease of the nervous system characterized by both motor and non-motor system manifestations known as Parkinson's disease (PD). It is also known as chronic progressive neurodegenerative disorder that happens mostly in older persons but that can occur in much younger patients now a days. It is called as the second most common neurodegenerative disease.[40]

Other neurodegenerative disorders can imitator idiopathic Parkinson's disease (PD) which included followings.
1. Dementia with Lewy Bodies (DLB),
2. Corticobasal Degeneration (CBD),
3. Multiple System Atrophy (MSA)
4. Progressive Supranuclear Palsy (PSP).

Our focus of this review will be the pharmacological ways in the management of Parkinson's diseases or impairments of memory and not these other parkinsonian-like syndromes.

The common neurodegenerative disease after Alzheimer's disease is Parkinson's disease, with an estimated average incidence of 20/100 000 and a prevalence of 150/100 000. It is clinically represented by asymmetrical onset of rigidity, bradykinesia, and usually, resting tremor. The most common clinical features cause the death of dopaminergic neurones in the substantia nigra of the human midbrain. Lewy bodies are appeared in an extent of surviving neurones. At the pathological level, there are some overlapping with other neurodegenerative disorders which including Alzheimer's disease, and this was used to support the view that these diseases may share some common pathogenetic mechanisms.[41]

In every 100 persons one person is affected by Parkinson's disease (PD) which range above the age of 65 years, making it the most common second neurodegenerative disease after Alzheimer's disease. Parkinson's disease (PD) is a disease of the central nervous system that may increase to severe difficulties with body activities. The present available treatments help to improve the functional capacity of the patient for a very certain period of time; however, the modification in the progression of the neurodegenerative process is not done. The need for new and more effective medications and treatments is consequently receiving a great deal of attention and therefore being aimed to huge research.

This review concisely compiles the limitations of currently available therapies and the most recent research regarding neuroprotective agents, antioxidants, and various techniques available for the management of PD.[42]

A progressive neurological disorder that characterised by tremor, rigidity, and slowness of movements, which

associated with progressive loss of neuronal substantia nigra and other brain structures are known as Parkinson's disease (PD). Non-motor features which included dementia and dysautonomia, occur more, especially in advanced stages of disease. Parkinson's disease is not observed as a single disease stuff and the meaning does not necessarily mean the same for all health care professional and research scholars.

Some health care professional and research scholars use the strict term to define the clinical diagnosis and may welcome some different pathological substrates for underlying the syndrome. That term will only use for those cases which are idiopathic parkinsonism associated with Lewy body accepted in the nigra cells and in other brain cells regions.

The term Parkinson's disease refer to a clinical condition which generally progressive parkinsonism of unresolved cause of without features expressive of an alternative diagnosis responded to dopaminergic treatment which associated with reduction of neurons of brainstem and with Lewy body accepted in some of the remaining nerve cells.[43, 44]

Almost 0.3 percent which is an estimated prevalence in the U.S. population is affected with Parkinson's disease which is a progressive neurodegenerative disorder.[45] This prevalence increases from 4 to 5 percent in those populations which is older than 85 years. The main characteristic neuropathologic features are the degeneration in the substantia nigra of dopaminergic neuron and the inclusions (Lewy bodies) in the residual dopaminergic neurons in presence of eosinophilic intracytoplasmic.[46] Mostly Family health care professional or physicians should have a good knowledge and understanding of Parkinson's disease because of its increasing prevalence as the population ages. They can generally treatment the individual to decrease symptoms while try to maintain motor and nonmotor complications.[47, 48] Treatment can be more complicated as the disease progresses, and may be required a subspecialist for co-management. To help patients to maintain maximal autonomy and quality of life is the primary aim of any health care professional.
A common neurodegenerative disorder as a synucleinopathy with a prevalence of 160/100 000 in Western Europe rising to 4% of the population over 80 is known as Parkinson's disease (PD).[49] The management of PD for neurologists and general physicians is likely to primary aim and an important and challenging condition of medical practice with an ageing population. In the last few decades our understanding in the pathogenesis of the disease has been developed with the identification of several gene mutations which may sprinkle more light on the mechanisms of pathogenesis in rare cases of Parkinson's disease (PD).

Symptoms of Parkinson's Disease[50]
Parkinson's disease (PD) progresses slowly as a movement disorder. Firstly, some people observe a sense of weakness, walking difficulty, and muscles stiffness. Some people notice a tremor feeling of the head or hands. Parkinson's disease (PD) is a progressive disorder with sudden worsen of symptoms. Followings are the general symptoms of Parkinson's disease.

- Voluntary movement's slow, basically in the initiation of walking or rolling over in bed.
- Facial expression decrease, speech monotonous, and eye blinking decrease.
- Poor arm swing with shuffling gait and posture stooped
- Unbalanced; rising difficulty from a sitting position
- Continuous motion of "pill-rolling" of the thumb and forefinger
- Abnormal pain or stiffness in the trunk and limbs
- Swallowing problems in later stages
- Light headed or fainting during standing (orthostatic hypotension)

Drugs used in the treatment of Parkinson's disease[51]

- Levodopa
- Dopamine agonists
- Glutamate antagonist
- Anticholinergics
- COMT inhibitors
- MAO-B inhibitors
- Dopaminergic Medications

LEVODOPA
A most common drug used during the progressive stages of PD is Levodopa (L-dopa).It is not activated until it crosses the blood brain barrier via active transport, hence L-dopa is considered as a prodrug.[52] The main purpose to use Levodopa is to restore depleted levels of dopamine of the substantia nigra at the presynaptic terminal, which restores functional movement.[53] This treatment will relieve symptoms of Parkinson's disease, such as rigidity and freezing.[54]

If a patient develop tolerance with L-dopa, or adverse drug effects become present with this drug alone, then combinations of drugs like Benserazide and Carbidopa (LD-CD) can be used in the periphery to prevent the further premature breakdown.[55] Benserazide with levodopa known as co-beneldopa. Carbidopa with levodopa known as co-careldopa.

An optimal single oral dosing of LD-CD is generally between 97.5 mg-390 mg, and 25mg-100mg twice daily/thrice daily for either sustained release or immediate release.[56]

Its volume of distribution generally around 28.5 L and the plasma half-life clearance is 1.8 hours. Hence, frequent dosage is required generally. Approximately 72 ml/min is the renal clearance of L-dopa.[53]

As levodopa is not combined with a partner drug, many of the adverse effects were present. The most common adverse effects known during a physical therapy include gastrointestinal distress due to the enteral administration, end of dose akinesia, and a tolerance after around 3-4 years, cardiac difficulties, gait disturbances due to dyskinesias. During the peak time of this drug administering physical therapy treatment helps to subside these ends of dose side effects.[54] It can be used at all stages of the condition. Levodopa converts into dopamine by human body because it is a chemical building-block. Dopamine is replaced which is lost in Parkinson's.

Some of the common examples of branded and unbranded forms of levodopa are followings.

- Co-beneldopa (Madopar, Madopar CR)
- Co-careldopa (Caramet CR, Duodopa, Sinemet, Sinemet CR, Kinson)
- Co-careldopa plus entacapone (Stalevo)

Madopar and Sinemet

Mostly patient took Madopar and Sinemet without experiencing sickness or nausea by them. Patients taking these medications will experience long-term improvement, especially in slowness of movement and stiffness. Firstly, a low dose was started in initial phase. This will increase gradually patients and physicians or specialist agree that your symptoms are under control. It is available in capsules formulation, which is unbroken, tablets or dispersible tablets, which can be dissolved in water. Sinemet taken in as a pill form. Different strengths were available in market for both medications.

Controlled release Madopar and Sinemet

Controlled release preparations let the levodopa enter into patient body slowly instead of all at once. Dosing time will be increase which depends on severity or seriousness of patient's symptoms. It is generally used when no effect of L-Dopa will shown during the use of standard dose of levodopa. It can reduce involuntary movements (dyskinesia) sometimes.

Side effects and problems experienced by the use of levodopa

Initially patients may feel sickness or nausea. Most people will bypass if patient's body adjusts with medication. The dose of levodopa needs to be adjusted by the severity or seriousness of Parkinson's progresses.
L-Dopa is absorbed through the gut, hence some patient experienced constipation or other stomach problems during the uptake of the medication.

Some other side effects or problem developed during the uptake of the medication included:

- Confusion
- Hallucinations and delusions
- Mood swings
- Psychological changes
- Sleepiness, fainting or dizziness

Side effects may vary in patients by changing dose, formulations or frequency. Other types of drug may be used in combination with levodopa, if single L-Dopa shows less effect or ineffective. Impulsive and compulsive behaviour may be experienced when given L-Dopa in a combination with a dopamine agonist.

MAO-B inhibitors

These medications were used in patients having PD due to potential disease modifying and neuroprotective effects of Monoamine Oxidase B Inhibitors, such as Selegiline and Rasagiline.[57] This is a class of drugs having a potential disease modifier because it have ability to inhibit the monoamine oxidase type B (MAO-B) enzyme present in the brain, which naturally breaks down dopamine in PD.[57] The effects of dopamine at the CNS synapse increased by inhibiting the breakdown of the MAO-B enzyme.[58, 59] By decreasing the oxidation of dopamine, MAO-B inhibitors exhibit neuroprotection which preventing the excessive production of free radicals, while prolonging the effects of endogenous dopamine.[60, 61] It can be used as an initial treatment of Parkinson's Disease or may be combined with L-Dopa in order to decrease motor fluctuations.[57]

It is a irreversible and selective Monoamine Oxidase B Inhibitors, Selegiline distributed to tissues throughout the body including the brain before absorbed in the GI tract.[62] Selegiline promote insomnia by metabolized L-amphetamine-like metabolites.[57] It is metabolized in the liver and then excreted through kidneys.[62] It has 10% bioavailability by oral route and 59 L/min oral clearance rate.[63] The initial therapeutic dose is 10mg/day with half-life of 10 hours.[57]

The other selective and irreversible MAO-B inhibitor is Rasagiline, which metabolized into aminoindan in the liver by cytochrome p450 type 1A2. It does not have the amphetamine-like effects which is shown by Selegiline. It is 35% bioavailability by oral route and shows its therapeutic maximum effect after 0.5-1 hour with oral clearance rate of 94.3 L/day. The recommended dose is 0.5-1 mg/day with half-life of 1.5-3.5 hours.[64]

Levodopa used as adjunct with Selegiline and Rasagiline to decrease motor fluctuations in patients with Parkinson's (57). Due to their selective ability, these two drugs are safe compared with other MAO inhibitors. Most Common side effects of other MAO-B Inhibitors like dizziness, headache, GI distress, and sedation.[65] It is mainly used to treat symptoms of Parkinson's.

Some generic and brand drug names are.

- Rasagiline (Azilect)
- Selegiline (Eldepryl, Zelapar)

Advantages and disadvantages of MAO-B inhibitors.
It can be used in all stages of Parkinson's with combinations also.

It is available as tablets or also a form that dissolves on the tongue, for patient having trouble swallowing.
MAO-B inhibitors can decrease fluctuations in effectiveness of drugs.
When selegiline taken along with levodopa, some serious side effects like dyskinesias (involuntary movements), hallunications or vivid dreaming occur sometimes which will be more worsen.
It has drug interaction with antidepressant, which raise blood pressure to a dangerous level.

When Rasagiline taken as treatment of PD without levodopa, the most common side effects are:

- Headache
- Aching joints
- Indigestion
- Flu-like symptoms
- Depression
- Uncontrolled movements and accidental falls.

Dopamine agonists medications

The most common class of drugs used during the treatment of PD is Dopamine agonists medications.[66,67] It actively increases the dopamine receptors in the brain to develop more in-vivo dopamine. Apomorphine is one of the premier drugs due to having powerful modulating capabilities of motor fluctuation, which seen in the end of dose dyskinesias generated by anti-parkinsonian medications like L-Dopa.[68] Apomorphine is generally given by subcutaneous route of cyclic frequency of an average of 16 hours per day at a rate of 3-6 mg/hr.[69] Further the drug takes approximately 15-20 minutes to reach its maximum bioavailability within the bloodstream having the half-life of about 30-40 minutes. Apomorphine available in injection formulation or as a continuous infusion under the skin.

Some common and main side effects of this medication include somnolence, and psychiatric disorders, such as confusion and hallucinations and withdrawal.[68,69]

Some examples of branded and unbranded dopamine agonists are.

- Bromocriptine (Parlodel)
- Cabergoline (Cabaser)
- Pramipexole (Sifrol, Sifrol SR)
- Rotigotine (NeuproPatan)
- Apomorphine (Movapo)

Some common side effects and problems of dopamine agonists are.

- Nausea and vomiting
- Constipation
- Headaches
- Drowsiness and sudden ‘attacks’ of sleepiness
- Dizziness or fainting due to low blood pressure
- Hallucinations or delusions and confusion
- Existing dyskinesias (involuntary movements) becoming more troublesome initially

Some impulsive or compulsive behaviours occurred by the use of this medication like increased desire to gamble or engage in sexual activity. This behaviour may often develop slowly so not seems to be a problem immediately. If experienced with this side effect, dose will be decreases or stopped to stop the behaviour.

Anticholinergic Medications

Anticholinergic medications used to mitigate the motor symptoms of Parkinson’s disease. Some important class of medications used as Anticholinergic medications are Benztropine mesylate, Biperiden, Diphenhydramine, and Trihexyphenidyl. The main and effective mechanism of action is not known. There is a assumptions that anticholinergic medications inhibits disproportionate acetylcholine action from the basal ganglia, specifically involuntary muscle movement due to competitive antagonists of muscarinic receptors. The maximum bioavailability range from 30-70% when used by oral route. It is absorbed into the brain and produce a high volume of distribution, then excretes via N-dealkylated and hydroxylated metabolites. Kidneys help to process excretion of the parent drug.

Each drugs have its own separate side effects. The most common side effects of anticholinergic medications include memory issues, drowsiness, sedation, urinary retention, constipation, blurred vision, tachycardia, and delirium.[70]

It is a type of drug, which is less commonly used to prescribed now to treat the symptoms of Parkinson’s.

Some examples of branded and unbranded anticholinergics are.

- Orphenadrine (Biorphen, Disipal,)
- Procyclidine (Arpicolin, Kemadrin)
- Trihexyphenidyl (Broflex, Artane)

It is useful in the early stages of Parkinson’s having mild symptoms which helps to improve tremor more than stiffness and slowness.

Anticholinergics can reduce bladder contractions which cause a urgent and frequent urge to urinate.

Some common side effects and problems with anticholinergics are.

Confusion, dry mouth, constipation and blurred vision.
It interacts with levodopa absorption in the small bowel, which decrease the effectiveness of Madopar or Sinemet, which is the forms of levodopa.
It is not a first choice for older people with Parkinson’s because there is an more risk of memory loss and, in men, more issue with urinating.

Glutamate Antagonists

One of the most common glutamate antagonists available in market is Amantadine, which is used to treat Parkinson’s symptoms. Amantadine is the generic name,

also available under the brand name of Symmetrel. The mechanisms of action od these drugs is completely unknown or not understood yet, but it may modify certain chemicals levels in the brain.

It may show the stimulatory effect and can help to reduce the tiredness. It is used to treat tremor and muscles stiffness and it can decrease unwanted involuntary movements without worsen the other symptoms.

Some common side effects and problems with glutamate antagonist.

It is not a first-choice drugs for the treatment of Parkinson's and has a limited action.

- Blurred vision, fainting, confusion or dizziness.
- Swelling of the ankles or a mottled appearance on the skin of the lower leg.

CONCLUSION

After review the management and treatment for both the conditions i.e Healthy brain and Parkinson's disease and memory impairment, it was observed that the management to maintain the healthy brain for normal brain functioning is easier and easy to adopt. However, the management and treatment for Parkinson's disease is difficult and hard to maintain the consistency throughout the treatment. Also the side effect of drugs used in Parkinson's disease will more harmful and sometimes near to death. We will avoid to experience the Parkinson's disease by the regular minimum maintains of healthy brain from the affecting factors.

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