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Regimen of Parkinson's Disease and Alzheimer's Disease

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Abstract: *Neurodegenerative diseases Alzheimer's disease and Parkinson's disease (PD) are characterised by low levels in the brain of the neurotransmitters acetylcholine (ACH) and dopamine (DA). Natural products continue to provide useful drugs in their own right but also provide templates for the development of other compounds. An effective therapy for these diseases is highly sought. Current treatment brings only temporary symptomatic relief and does not result in halting the progression of these diseases. To gain a better understanding of the current therapeutic frontier for the treatment of ad and PD. One of the main limitations of these treatments is the low concentration. That drugs reach in the central nervous system after systemic administration. Indeed, the presence of biological barriers, particularly the blood-brain barrier (BBB), this review discusses the increasing evidence for a role of both mitochondrial dysfunction and oxidative damage in contributing to!-amyloid deposition in Alzheimer's disease.*

Keywords: Parkinson's disease, Alzheimer's disease, neurodegenerative disorders, Dopaminergic agonists, pathogenesis, cholinergic compounds

I. INTRODUCTION

Parkinson's disease and Alzheimer's disease (ad) are the two most common neurodegenerative diseases associated with age. PD is primarily a movement disorder and at least 1% of people suffer from it by age 70 years [1]. This affirmation is substantiated in the literature. In 2015, there were 46.8 million ad patients worldwide with direct and indirect costs to society of 81,800 million USD[2], neurodegenerative disorders (NDDS) are characterized by aprogressive loss of neuron structure or function which is often associatedwith neuron death [3] alzheimer's disease (ad) and parkinson's disease (PD) are the two commonest age-related NDDS characterized by prominent neurodegeneration in selective neural systems [4] therapies used today are only relief based and are unable to halt the progression of PD and ad. Therefore, there is a great need to find new effective regenerative therapeutic strategies that can stop the development and progression of these neurodegenerative diseases and that will improve a patient's quality of life. Over the past 20 years, a substantial progression in our understanding of the molecular mechanisms underlying pd and ad has been achieved, enabling the development of novel therapeutic strategies to cure these diseases. The main hallmarks of both disorders is neuronal degeneration and neuronal death; therefore, cell replacement strategies are currently regarded as a potential therapy by either transplanting embryonic stem cells or neural progenitors [5]

II. NEURODEGENERATIVE DISEASE

2.1 Parkinson's Disease

In Parkinson's disease, dopaminergic neurons in the substantial nigra are affected by a degeneration process leading to motor and non-motor disturbances. Animal and in vitro studies have demonstrated a beneficial effect of ketone bodies on the course of pd. 1-methyl-4-phenyl-1,2, 3, 6-tetrahydropyridine (MPTP) produced the death of dopaminergic substantial nigral cells, both in vitro and in vivo, producing a syndrome indistinguishable from Parkinson's disease. It was shown that beta-hydroxybutyrate acts in vitro as a neuroprotective agent against the toxicity of MPTP on dopaminergic neurons [17] its characteristic feature is an increasing tremor in resting limbs and a rigidity, known as

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dyskinesia, particularly exhibited as a shuffling gait, but it is also associated with the degeneration of cognitive function and memory. It is thought that oxidative stress in the substantial nigra plays a significant role in the loss of neurons which produce da [19]

2.2 PD: use of Dopaminergic Agonists

The structure-activity relationships of compounds which are agonists at the da receptor are generally accepted to be the two Ortho OH groups on the aromatic ring which bind with serine residues 505 and 508, the aromatic ring enabling hydrophobic interactions with a phenylalanine at 617 and, in the terminal position of the ethyl amino group attached to the aromatic ring. Da itself is quite unstable and cannot cross the blood brain barrier. However, it can be formed within the brain by conversion of its precursor l-DOPA it is found in commercially viable amounts in various species of bean, notably *mucuna* spp., and this has been used as a commercial source, although the drug is now mainly obtained by synthesis. L-dopa is often given together with another analogue of da, carbidopa 35, which is not dopaminergic but which inhibits dopa decarboxylase and so, by maintaining levels of L-dopa in the blood, prolongs its activity. When L-dopa is given over long periods of time, it is common for a sudden decline in sensitivity to occur from time to time and this is called the 'on-off" effect. [20]

Pathogenesis

PD is a progressive disease and clinical symptoms, such as rest tremor, rigidity, balance impairment and slowness of movement, only manifest in the late stages. Break and colleagues described in detail six stages of the disease based on the pathological hallmarks, that is, α-synuclein build up in the levy bodies (lb) and levy neuritis (lN) and degeneration of the dopaminergic (danergic) neurons in the substantial nigra (sn) [6] the cause of PD in the majority of the patients suffering from the non-hereditary form of the disease is as yet unknown. A role of environmental factors in the development of the disorder has been suggested. In the early twentieth century, it has been observed that a viral infection can cause nigral degeneration [7] in the past 10 years, genetic mutations were identified that cause or are involved in pd. Single point mutations in the α-synuclein, parkin, dj-1, pten-induced putative kinase 1 (pink-1), dardarin (lrrk2) [1] and ubiquitin carboxyl-terminal esterase l1 (uch-l1)[8] interestingly, different variants of semaphoring 5a were associated with PD in a Taiwanese population. However, this could not be confirmed in a finish population study, prompting a debate regarding this gene and its role in pd development [9]

Regimen

All current PD therapies focus on restoring the da levels by either the oral administration of the da precursor levodopa (L-dopa), which supplements the low level of endogenous da, or inhibition of the breakdown of endogenous da by treatment with the monoamine oxidase type b (MOA-b) inhibitor, selegiline. Da agonists are also used to directly stimulate the da receptors [1, 10] surgical treatment by deep brain stimulation is practiced to further modify dyskinesia and decrease the 'off' time [11]

III. ALZHEIMER'S DISEASE

Ad is a neurodegenerative disease which is associated with progressive deficit regarding verbal and visuospatial memory as well as other cognition domains. The hallmark pathology involves an accumulation of □ß plaques and neurofibrillary tangles, as well as neurochemical
Deficits and other neuropath logical processes, including inflammation [18]

3.1 Ad: the use of Cholinergic Compounds

The rationale underlying the use of cholinergic compounds is that they are agonists of the nicotinic cholinergic receptor and so compensate for the low levels of ach. The binding of ach. To the receptor is shown diagrammatically although these compounds have been suggested as valuable agents in treating ad, because they also appear to inhibit fibrillary tangle and amyloid production, success has been limited as far as clinical studies are concerned, although results in animals were initially promising [21]

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Pathogenesis

The classical pathological changes in the brain of ad patients include deposition of α-amyloid plaques, the presence of neurofibrillary tangles, gliosis and neuronal atrophy.

The neuronal degeneration and loss of synapses progresses over time and are widespread in ad, beginning with the entorhinal cortex and hippocampus and progressing to the neocortex, amygdala, thalamus and sn[12] genetic screenings have so far revealed the causative role of three genes in early-onset familial ad. Missense mutations in presenilin 1 (ps1), presenilin 2 (ps2) and the amyloid precursor protein (app) gene all caused autosomal dominant ad [13] oxidative stress and an impaired ubiquitin–proteasome system have also been implicated in ad [13]

Regimen

Currently, there is no cure for ad and today's treatments bring relatively small symptomatic relief to the patients, without having an effect on the progression of the disease. The most common therapy is the prescription of acetyl cholinesterase inhibitors, such as donepezil, tacrine or rivastigmine, which reduce the rate of acetylcholine breakdown and increase its concentration in the brain, resulting in a modest cognitive improvement [14]

Drug penetration of the BBB

Unlike most other mammalian organs, the brain is separated from blood circulation by physiological barriers; a drug must be able to cross such barriers to gain access to brain tissue .drugs are likely to exert their pharmacological effects only if they have a proper chance of engaging with their molecular targets at the site of action in the body. This is true for all drug targets, including those residing within the cns [15] the third process (active transfer) requires an energy source (atp) and can transfer molecules via a carrier against a gradient. The bbb is an outlier because bbb epithelial cells form tj effectively precluding

Par cellular diffusion [16]

IV. CONCLUSION

The field of cell replacement and gene therapy as a new therapy for pd and ad has evolved enormously over the last years. Currently, no cure is available for these diseases. The cell-replacement and gene-therapy strategies reported so far result in complete rescuing or restoration and functional repair of the damaged brain areas. Targeting molecular mechanisms with current genome-wide genotyping of large populations of patientt.

Applied knowledge regarding nanotechnology and materials science must be taken into account when designing transport and BBB penetration. Regarding the treatment of the major diseases involved, it can be said that chemotherapy of ad with cholinesterase inhibitors is unlikely to develop very much further since effective agents such as glutamine have been introduced.

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