Dementia

Excerpt from www.alzheimer.ca:

Dementia is an umbrella term for a variety of brain disorders. Symptoms include loss of memory, judgment and reasoning, and changes in mood and behaviour. Brain function is affected enough to interfere with a person's ability to function at work, in relationships or in everyday activities.

Several conditions produce symptoms similar to dementia. These can include depression, thyroid disease, infections or drug interactions. Early diagnosis is essential to make sure that people with these conditions get the right treatment.

Alzheimer's disease is a fatal, progressive and degenerative disease that destroys brain cells. It is the most common form of dementia, accounting for 64 per cent of all dementias in Canada.

Alzheimer's disease is not a normal part of aging. Symptoms include having difficulty remembering things, making decisions and performing everyday activities. These changes can affect the way a person feels and acts. There is currently no way to stop the disease, but research is improving the way we provide care and will continue to search for a cure.

Vascular dementia (VaD), also called multi-infarct dementia, occurs when the cells in the brain are deprived of oxygen. A network of blood vessels called the vascular system supplies the brain with oxygen. If there is a blockage in the vascular system, or if it is diseased, blood is prevented from reaching the brain. As a result, cells in the brain die, leading to the symptoms of dementia. After Alzheimer's disease, VaD is the second leading form of dementia, accounting for up to 20% of all cases.

When Alzheimer's disease and VaD occur at the same time, the condition is called "mixed dementia".

Lewy body dementia is a form of dementia that occurs because of abnormal deposits of a protein called alpha-synuclein inside the brain's nerve cells. These deposits are called "Lewy bodies," after the scientist who first described them. The deposits interrupt the

brain's messages. Lewy body dementia usually affects the areas of the brain that involve thinking and movement. Why or how Lewy bodies form is unknown.

Lewy body dementia can occur by itself, or together with Alzheimer's disease or Parkinson's. It accounts for 5-15% of all dementias.

Creutzfeldt-Jakob disease (CJD) is a rare form of deadly dementia that comes on fast. It is caused by infectious proteins called prions. Prions are proteins that are naturally in the brain and are normally harmless. When they are not shaped properly, however, they can have devastating effects. They can attack the brain, kill cells and create gaps or holes in brain tissue.

Huntington's disease is an inherited disease that causes certain nerve cells in the brain to waste away. People are born with the defective gene, but symptoms usually don't appear until middle age.

HD is a familial disease, passed from parent to child through a mutation in the normal gene. Anyone with a parent with Huntington's has a 50 percent chance of inheriting the gene, and everyone who inherits it will eventually develop the disorder. In about 1 to 3 percent of cases, no history of the disease can be found in other family members.

Wernicke's encephalopathy is a degenerative brain disorder caused by the lack of thiamine (vitamin B1). It may result from alcohol abuse, dietary deficiencies, prolonged vomiting, eating disorders, or the effects of chemotherapy.

Down syndrome is a genetic disorder that affects about one in every 800 live births in Canada. It is the most common genetic cause of severe learning disabilities in children and can cause developmental delays, learning difficulties, health issues and some physical abnormalities.

People with Down syndrome have an extra copy of the 21st chromosome. Because of recent medical advances, people with Down syndrome are living longer, usually into their 50's.

The incidence of Alzheimer's disease in people with Down syndrome is about three to five times greater than the general population. As with Alzheimer's disease, the risk increases with age.

The link between Alzheimer's disease and Down syndrome lies in the 21st chromosome. The protein that leads to the development of plaques in the brain, a hallmark characteristic of Alzheimer's disease, is located on that chromosome. Since people with Down syndrome have an additional copy of the 21st chromosome, they are prone to an over-production of the protein. Not everyone with Down syndrome, however, develops Alzheimer's disease.

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The endogenous cannabinoid system and the basal ganglia. biochemical, pharmacological, and therapeutic aspects.

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Abstract

New data strengthen the idea of a prominent role for endocannabinoids in the modulation of a wide variety of neurobiological functions. Among these, one of the most important is the control of movement. This finding is supported by 3 lines of evidence: (1) the demonstration of a powerful action, mostly inhibitory in nature, of synthetic and plant-derived cannabinoids and, more recently, of endocannabinoids on motor activity; (2) the presence of the cannabinoid CB(1) receptor subtype and the recent description of endocannabinoids in the basal ganglia and the cerebellum, the areas that control movement; and (3) the fact that CB(1) receptor binding was altered in the basal ganglia of humans affected by several neurological diseases and also of rodents with experimentally induced motor disorders. Based on this evidence, it has been suggested that new synthetic compounds that act at key steps of endocannabinoid activity (i.e., more-stable analogs of endocannabinoids, inhibitors of endocannabinoid reuptake or metabolism, antagonists of CB(1) receptors) might be of interest for their potential use as therapeutic agents in a variety of pathologies affecting extrapyramidal structures, such as Parkinson's and Huntington's diseases. Currently, only a few data exist in the literature studying such relationships in humans, but an increasing number of journal articles are revealing the importance of this new neuromodulatory system and arguing in favour of the funding of more extensive research in this field. The present article will review the current knowledge of this neuromodulatory system, trying to establish the future lines for research on the therapeutic potential of the endocannabinoid system in motor disorders.

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Cannabinoid control of motor function at the basal ganglia.

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Abstract

Classic and novel data strengthen the idea of a prominent role for the endocannabinoid signaling system in the control of movement. This finding is supported by three-fold evidence: (1) the abundance of the cannabinoid CB1 receptor subtype, but also of CB2 and vanilloid VR1 receptors, as well as of endocannabinoids in the basal ganglia and the cerebellum, the areas that control movement; (2) the demonstration of a powerful action, mostly of an inhibitory nature, of plant-derived, synthetic, and endogenous cannabinoids on motor activity, exerted by modulating the activity of various classic neurotransmitters; and (3) the occurrence of marked changes in endocannabinoid transmission in the basal ganglia of humans affected by several motor disorders, an event corroborated in animal models of these neurological diseases. This three-fold evidence has provided support to the idea that cannabinoid-based compounds, which act at key steps of the endocannabinoid transmission [receptors, transporter, fatty acid amide hydrolase (FAAH)], might be of interest because of their potential ability to alleviate motor symptoms and/or provide neuroprotection in a variety of neurological pathologies directly affecting basal ganglia structures, such as Parkinson's disease and Huntington's chorea, or indirectly, such as multiple sclerosis and Alzheimer's disease. The present chapter will review the knowledge on this issue, trying to establish future lines for research into the therapeutic potential of the endocannabinoid system in motor disorders.

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The endocannabinoid system as a target for the treatment of motor dysfunction.

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Abstract

There is evidence that cannabinoid-based medicines that are selective for different targets in the cannabinoid signalling system (e.g. receptors, inactivation mechanism, enzymes) might be beneficial in basal ganglia disorders, namely Parkinson's disease (PD) and Huntington's disease (HD). These benefits not only include the alleviation of specific motor symptoms [e.g. choreic movements with cannabinoid receptor type 1 (CB(1))/transient receptor potential vanilloid type 1 agonists in HD; bradykinesia with CB(1) antagonists and tremor with CB(1) agonists in PD], but also the delay of disease progression due to the neuroprotective properties demonstrated for cannabinoids (e.g. CB(1) agonists reduce excitotoxicity; CB(2) agonists limit the toxicity of reactive microglia; and antioxidant cannabinoids attenuate oxidative damage). In addition, extensive biochemical, anatomical, physiological and pharmacological studies have demonstrated that: (i) the different elements of the cannabinoid system are abundant in basal ganglia structures and they are affected by these disorders; (ii) the cannabinoid system plays a prominent role in basal ganglia function by modulating the neurotransmitters that operate in the basal ganglia circuits, both in healthy and pathological conditions; and (iii) the activation and/or inhibition of the cannabinoid system is associated with important motor responses that are maintained and even enhanced in conditions of malfunctioning and/or degeneration. In this article we will review the available data regarding the relationship between the cannabinoid system and basal ganglia activity, both in healthy and pathological conditions and will also try to identify future lines of research expected to increase current knowledge about the potential therapeutic benefits of targeting this system in PD, HD and other basal ganglia disorders.

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