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dementia

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What is Dementia?

By Brady Bateman

Dementia is an overarching term, which refers to a number of specific medical conditions, including Alzheimer's disease. Dementia refers to a set of symptoms, which are associated with a progressive deterioration of cognitive abilities affecting daily activities.

Dementia is caused by various brain diseases and injuries and can be identified by symptoms including memory loss, judgement and reasoning problems and changes in behaviour, mood and communication skills.

Common types of dementia include:

- Vascular dementia
- Lewy body dementia
- Frontotemporal dementia
- Alzheimer's disease dementia
- Mixed dementia (a combination of more than one type)

Signs and Symptoms of Dementia

Cognitive decline must be present in two of four essential cognitive functions[1]

1. Memory
2. Language/speech
3. Visual processing
4. Planning capacity/ability to carry out complex tasks)

While each of the dementia subtypes has a unique clinical pattern, there are many overlapping signs and symptoms including:

- Lack of focus
- Lack of attention
- Forgetfulness
- Personality changes
- Confusion
- Communication difficulties
- Loss of spatial awareness (no longer oriented in time and space)

Dementia can affect anyone

An estimated 47 million people worldwide were living with dementia as of 2015.[2] More than 500,000 Canadians are living with dementia, with the number expected to rise to over 900,000 by 2030.[3]

The causes of dementia are not all specifically known, and there is currently no cure for Alzheimer's disease, the most common type of dementia. Risk factors for the development of dementia include age, sex and genetics. Depending on the type of dementia, research points to preventable factors including unhealthy diet, severe brain injury, physical inactivity and environmental factors.

Roughly 25,000 Canadians are diagnosed with dementia yearly, with 65% of those diagnosed over the age of 65 being women. Although the majority of those diagnosed with dementia are over the age of 65, a small number of people in their 40s and 50s can and do develop dementia. This is known as young onset dementia.

Young onset dementia accounts for an estimated 2 to 8% of all dementia cases. Currently, at least 16,000 Canadians under the age of 65 are living with young onset dementia.[4]

Living with Dementia

Dementia is progressive, meaning that the condition of individuals diagnosed with dementia will continue to decrease as the disease progresses. As more brain cells become damaged and eventually die, symptoms of dementia gradually increase. That is why an early dementia diagnosis is so important.

Almost half (48.4%) of Canadians aged 35 years or older with dementia reported having fair or poor general health according to the Canadian Chronic Disease Surveillance System. Almost one-third (29.7%) of those individuals reported having mood disorders. Dementia was associated with high levels of overall disability and specific functional impairments, including:

- 58.4% of Canadians with dementia reported urinary incontinence
- 37.0% reported moderate or severe pain and discomfort
- 31.7% reported bowel incontinence

It was estimated as part of this study that men with dementia would lose on average 16.0 years of life in full health due to disability and premature death, and that women would lose 15.2 years on average.[5]

The Cost of Dementia in Canada

According to the microsimulation analysis of the National Population Health Study of Neurological Conditions, total health care system costs and out of pocket costs of caring for people with dementia were $10.4 billion in 2016, and are projected to double by 2031.[3]

The cost associated with caring for those with dementia are estimated to be more than five times greater than for those who are dementia-free, with the largest contributors to cost being long-term care and home care.

An additional 19.2 million hours of informal unpaid caregiver time in 2011 was valued at $1.2 billion in cost and is projected to double by 2031.

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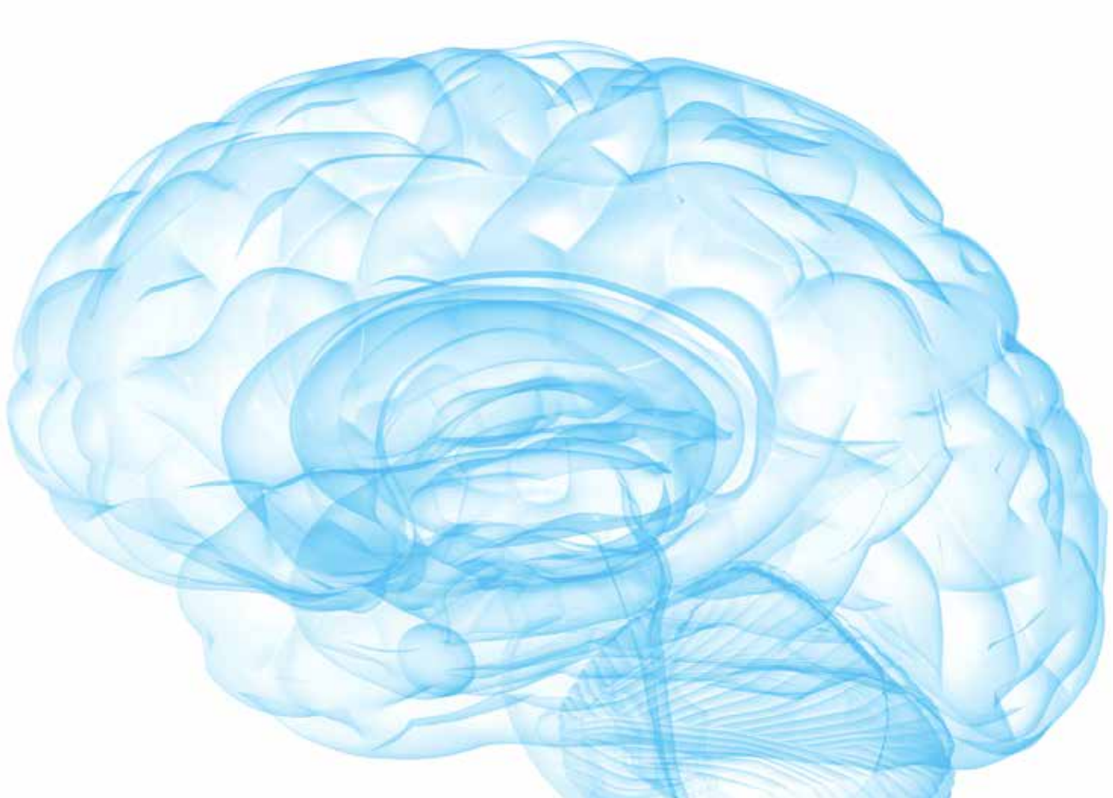
The Genetic Relationship with Dementia

By NavNirat Nibber, ND



Important Definitions

Dementia Syndrome

An umbrella term used to describe a change in the levels of cognitive function without a change in consciousness; this cognitive decline relates to underlying neurodegenerative diseases.

Dementia subtypes include Alzheimer's disease (AD), frontotemporal lobar degeneration (FTLD), vascular dementia (VD), dementia with Lewy bodies and Parkinson's associated dementia (PD). Each of these subtypes have distinct pathophysiology, and protein deposition leading to neurodegeneration that leads to formation of disease- therefore, different genes influence risk to varying degree. Further mixed dementias are common namely AD and cerebrovascular disease.[1-4]

Penetrance

A term that defines the probability that a mutation in a disease-defining gene will result in the development of that phenotype.[1]

Mendelian Diseases

These diseases are defined as a single-gene disease due to a mistake or mutation that will have strong penetrance leading to the clinical development of disease (or the disease phenotype). These are autosomal dominant genes with high penetrance and are often rare within populations.[1]

Complex or Polygenic Diseases

This disease category relates to the multiple genes that have varying penetrance on disease phenotype and are often understood as genetic modifiers that may or may not contribute to disease processes.[1,2]

Sporadic vs Genetic Disease

Referring to the etiology for the development of disease. Sporadic disease related to development of disease independent of family history while genetic diseases confer a family history and the presence of disease producing alleles.[2]

Allele

A version or variant of a gene. Every individual inherits two alleles of each gene. When they are the same, they are considered homozygous for this gene, while two different alleles are termed heterozygous. Often between heterozygous alleles, one may be dominant.[1]

Single Nucleotide Polymorphisms (SNP)[2]

These are differences at a single point in the genetic sequence of a gene that can lead to alterations in the genes end product.

Three categories of genetic impact have arisen:[1]

1. The first is locus heterogeneity- whereby mutations on different genes can lead to the same histopathology (or tissue alteration)
2. Next is allelic heterogeneity: where different mutations (or variants) on the same gene have differing histopathologic outcomes
3. Finally, scientists have identified phenotypic heterogeneity: a phenomena that causes one genetic mutation to result in two or more different histopathologic outcomes (likely dependent on other factors such as environment or other genetic alterations)

Assessment Tools and Genetic Testing

Dementia syndrome has varying presentations. Physicians determine presence and or degree of cognitive decline using a number of validated cognitive tests such as the Montreal Cognitive Assessment (MoCA), Mini-Mental State Exam (MMSE), and the Mini-Cog.[3] While these tests are helpful to assess mild to severe cognitive impairment and are often used in practice, they are subject to human error. Advances in the human genome and have identified a number of key genes which if modified can contribute to pathophysiology and disease phenotypes. When combined with cognitive testing and thorough family history, molecular genetic testing provides more accurate insights into individual risk.[1-3] Further, studies defining the impact of lifestyle and environment on genetic expression of variants to disease phenotypes also elucidates the complexity of diseases and modifiable factors. That being said, there is still much to uncover about this relationship. Recently two large-scale retrospective cohort studies examined the impact of modifiable risk factors depending on genetic predisposition and arrived at very different conclusions.

The first was a large observational study, published in 2019 of 6300 individuals greater than 55 years old, known as the Rotterdam Study, conducted by Licher et al.[4] which assessed dementia incidence over 15 years. Researchers considered single genetic risk of 27 genetic variants in the absence of known modifiable risks such as diet, social isolation, smoking, diabetes, and depression to determine disease onset and progression. The study concluded that those with low genetic risk could modestly reduce risk by modifying lifestyle changes, however; high-risk genetic groups (those with the ApoE4 allele) were not responsive to lifestyle changes relating to dementia incidence.

While another study published in 2020, a UK biobank study of 196,383 subjects of European ancestry were observed in this 10-year retrospective study.[5] This study differed from the Rotterdam study in that multiple genes associated with dementia were assessed to determine the genetic risk (known as polygenic scoring) and concluded that the modifiable lifestyle factors affect the dementia risk irrespective of genetic risk categorisation.

Ultimately, while the two studies differ in scope and conclusions regarding the degree of impact of lifestyle on genetic risks, both these studies will serve as the basis for future meta-analysis and clinical studies to clearly establish this relationship and speak to the breadth of information still unknown.[3]

The Related Genes

As discussed, the pathophysiology of dementia subtypes has distinct genes, variants or alleles of genes, and pathologic outcomes. However, we know that genetic variants that confer disease are those that cause distinct proteinopathies.[1,2] These deficiencies in protein formation, shape, size, clearance, or function results in deposits forming in various sites in the brain and resulting in neurodegeneration. These genes may regulate immune function, neuronal lipid and cholesterol metabolism, synaptic function and neuronal endocytosis. Below are some of the predominant genes involved in each dementia subtype (though it is important to note this is not a comprehensive list).

- **Alzheimer's Disease (AD):** a form of dementia with the main differentiating feature of the deposition of abnormal protein plaques (known as beta-amyloid and neurofibrillary tangles) in the central nervous system.[1,2] Therefore genes regulating the accumulation, or clearance were evaluated for risk.[1]

- **Amyloid precursor protein (APP) gene:** These mediate an important physiological process that degrades and clears the amyloid beta protein and prevents plaque formation as well as local metabolism of the tau protein. Mutations in these genes attribute to earlier onset AD diagnoses as they can alter the cleavage and solubility making the proteins more aggregate prone. These mutations are rare though inherited in an autosomal dominant nature and have quite a high effect size.

- **Presenilin-1 (PSEN1) and presenilin-2 (PSEN2) genes**: Like the APP genes, mutations in these genes have a high effect size due to their autosomal dominant inheritance. Therefore, presence of point mutation is strongly related to development of early onset AD (<60yo). The pathological changes to tissue that arises from these mutations are similar to those seen in APP gene mutations as well.[2]

- **APO E:** This gene involved in transcribing proteins in glial cells, which metabolize cholesterol in neurons, is considered an important marker of risk as it can mediate beta aggregation and poor clearance depending on the allele. This gene has four known variants (E1-4), with the majority of the population exhibiting ApoE3, however the rare homozygous occurrence of the E4 has a high penetrance. While the ApoE2 allele seems to confer some degree of protection against development of the disease.[2,3,6]

- **Gene modifiers:** This group of genes are less strongly correlated with disease potential and have more complex roles in various aspects of gene progression. Genetic counsellors therefore assess these results within the context of other lifestyle and environmental risk factors. This complexity likely also accounts for the difference in findings of the aforementioned studies linking impact of lifestyle on genetic risk groups. Further risks from these gene mutations are more strongly associated with late onset cases of AD and include genes such as: GAB2, EPHA1, CD33, ABCA7, CD2AP, CR1, MTHFD1L CD33, BIN, CLU, EPHA1, SORL1, PICALM, MAPT, MS4A4/6E2.

Frontotemporal Lobar Degeneration (FTLD)

Research into this subtype of dementia has also found specific genes associated with disease progression. This dementia subtype is characterised by degeneration in the frontal and temporal regions of the brain, which are normally involved in speech and language, and is more common in dementias occurring earlier than 65 years old.[2] Therefore, patients suffering from FTLD demonstrate significant changes in communication while memory may be relatively less impacted. Genes associates with FTLD were discovered to have strong autosomal dominant family history, in addition to the PSEN1&2 genes the three primary genes associated with FTLD are: microtubule-associated protein tau (*MAPT*), granulin (*GRN*), and chromosome 9 open reading frame 72 (*C9orf72*). Notably, various mutations in the MAPT gene all seem to have very different pathological outcomes (allelic heterogeneity) and are known as tauopathies which has become a significant focus for clinical research over the last decade.

Dementia with Lewy bodies

This dementia subtype results in the deposition of α-synuclein in Lewy bodies in the brain- such pathologies are considered "Lewy body diseases" (DLB) and also include Parkinson's disease dementia (PDD). DLB is defined as dementia following motor impairment within a year while in PDD, the dementia onset occurs after a year of motor impairment symptoms arise. The genetic link between pathophysiology of DLB and PDD has been established though rather than single genes with large impact, there seems to be e more complex polygenic interplay between genes such as: *LRRK2*, *SNCA*, *PLA2G6*, *C19ORF12* and certain *GBA* mutations.[1, 2,6,7]

The Role of Genetic Counselling

With increased access to a simple genetic test, individuals have insights into their genetic data like never before. While this presents an opportunity to understand risks for prevention, family planning and health optimisation, it also presents a challenge for genetic counsellors who are often frantically sought to alleviate undue anxieties from misinterpreted data. Physicians strive to contextualise the genetic information with environmental and lifestyle risks, framing the genetic data as a sort of blueprint. Patients often see certain buzz genes that may clinically have associations with disease processes though the true risk has not yet been determined. Consider that we are still within the infancy of our understanding on this amazing and complex topic.[9] The interactions between mutations on different genes and clinical consequences is still being uncovered for many processes. Exemplified by the fact that ApoE testing is not clinically recommended (rather relegated to the research sector.) The REVEAL study from 2008[8] examined the health behaviour impact of ApoE4 allele status on 162 patients. They found that there was no clear effect on short-term anxiety or depression, subjects were also at high risk of incorrectly recalling clinical implications and education on the status following the clinical discussion not proper recall. However, individuals in the E4 positive group did appear to engage in healthier behaviours in an effort to offset the perceived risk. Ultimately, genetic counselling with qualified professionals ensures the appropriate framing and context for determining genetic risk for dementia in relation to personal and family history, as well as clinical presentation and progression.[9]

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The Impact of **Dementia** on **Families**

By Krista Powell

Living with dementia can be a frustrating, frightening and lonely experience, not only for the person with the disease but for family members and caregivers as well. Being a dementia caregiver comes with many emotions from anger to anxiety and despair. It can also be isolating, as it may be difficult to express these feelings to outsiders for fear of judgement or lack of understanding. Balancing the demands of caring for your declining loved one with career, family and other responsibilities is a challenging task.

It can be easy to feel overwhelmed at the enormity of undertaking the care of a person with dementia. While this is a difficult journey, it can also be a rewarding one. Keeping things in perspective and finding the bright spots in dark times is easier said than done, but some of the following information may be helpful.

1. **Understanding the symptoms.** Dementia is more than just forgetfulness. Your loved one will experience a wide range of symptoms. There may be behavioral changes and personality differences. They may feel the need to repeat actions over and over without being able to explain why. Some dementia sufferers experience hallucinations or delusions, while others may exhibit changes in sexual activity or conduct. Many will become confused easily or lose their way when out on their own. Discussing your loved one's symptoms with them and their healthcare practitioner will help all of you be prepared.
2. **Communicating effectively.** Through the stages of dementia from diagnosis to end of life care learning what to expect is important. Communication with your loved one, especially in the early stages, will help both of you through the difficult times. Keep in mind that they may be resistant to talking about their diagnosis. Don't force the issue, but take any opportunities that do arise to listen to their fears and concerns, even if they don't seem grounded in reality. Often they are aware that they have said the wrong word or lost their train of thought and they too are surprised and confused by it. If possible, discuss the future with them and learn about their wishes for end of life care.
3. **Making safety a priority.** As your loved one experiencing the symptoms of cognitive and physical decline, keeping them safe becomes more important than ever. This may mean making changes around the house like removing loose carpets that could cause a trip or fall, changing locations for power tools or chemicals in workspaces or removing locks from interior doors. Be on the lookout for potential hazards and address them promptly. Consider getting a locating device for your loved one. This can allow them their independence but still enable you to monitor their location. People with dementia can also be vulnerable to cyber attacks. If possible, try to monitor internet access and review interactions to reduce risk of identity theft or credit card fraud.
4. **Knowing when to look for full-time care.** There is no perfect time to transition your loved one to a full-time care facility. If the stress of being a caregiver has begun to affect you physically or if you are frequently feeling overwhelmed, it may be time to consider a change. The decision is difficult and can come with a host of emotions including guilt, sadness and relief, but be sure to take into consideration the needs of your loved one, and your own. Discuss it with your family and healthcare practitioner and take time to find a facility that works for everyone. The Caregiver Stress Checklist on alzheimers.ca is a helpful tool in the determination process.
5. **Taking time for yourself.** There is an immense mental, emotional and physical toll being a primary caregiver to someone with dementia takes. If may feel as though your own needs are unimportant compared with those of your loved one but that is not the case. Taking time for yourself is healthy and necessary. Make your life as easy as possible and keep these things in mind:
    - See your own healthcare practitioner regularly – make sure you make your own health a priority. You'll be a much better caregiver if you are healthy, both mentally and physically. Make sure you are eating right and exercising at least three times a week.
    - Try to get as much sleep as possible – getting up frequently at night with your loved one might be part of your routine. Ask a family member to take the night shift occasionally or consider a night nurse once or twice a week if that is financially viable. Your sleep is important to your overall health.
    - Maintain social connections – even just a quick coffee or chat with a friend will help restore some balance in your life. Be honest with them about how you're doing and don't worry about seeming like you have it all together. True friends will understand.
    - Forget "normal" – accept all your feelings, positive, negative and everything in between. There is no right way to process your complex emotions so be gentle with yourself.
    - Reach out to other family members for support – no one person should have to be fully responsible for care. Include family members in decision-making, progress reports, doctor's visits and let them know when you need a break.
    - Ask for help when you need it – make use of any community resources available to you. Some programs offer meal assistance or help with grocery shopping and household chores.
    - Join a support group – connecting with other caregivers is so important. They can share knowledge, expertise and advice on specific caregiving situations.

Caring for someone with dementia is difficult. Remember that you are not alone. Websites like alzheimer.ca can provide many online resources and connect you with your local society. Finding people you can talk to about the journey you are on, who can share and understand the experience is invaluable. Sometimes just being able to say the words aloud can help you feel less isolated. The resources listed below may offer some guidance and assistance.

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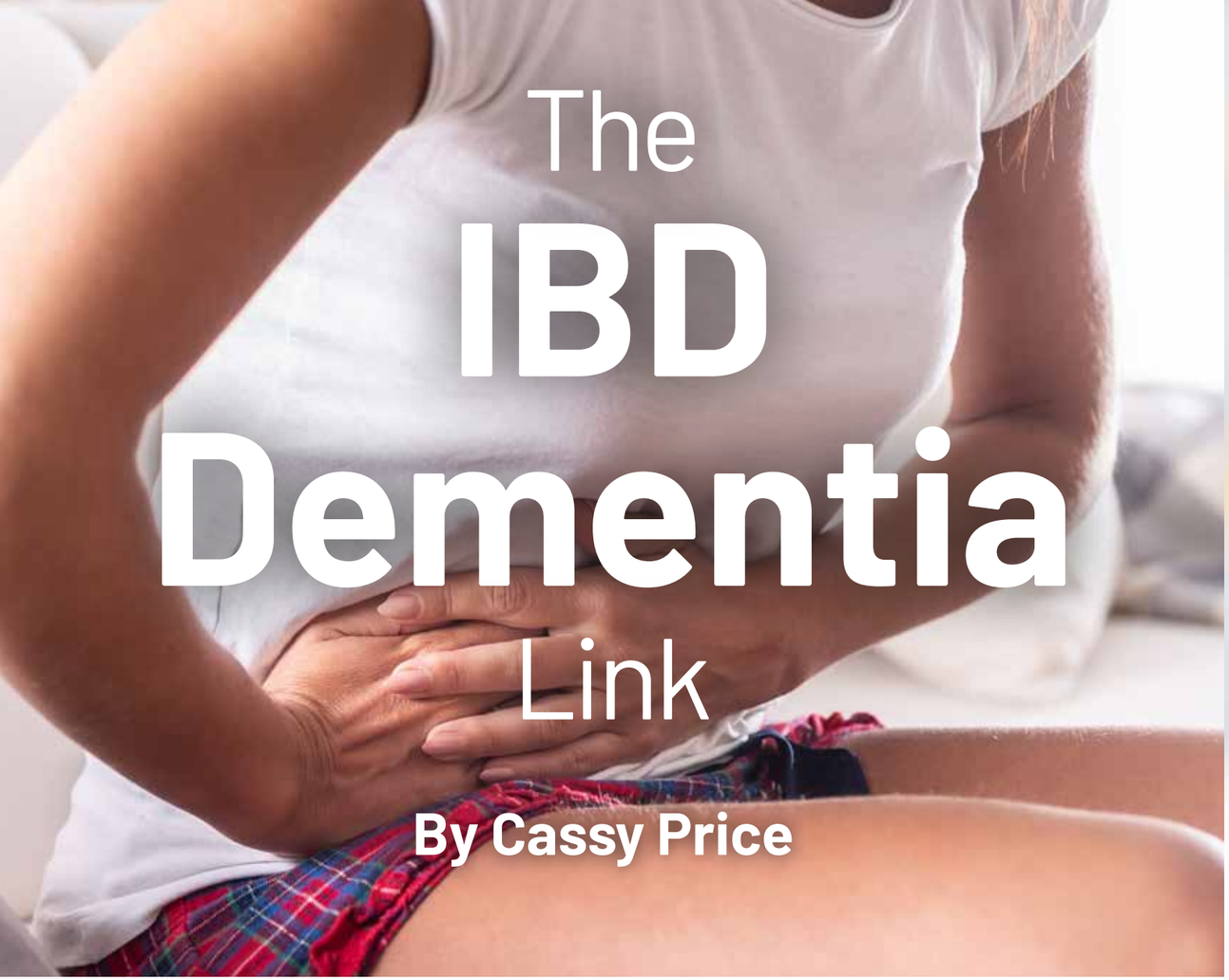

The IBD Dementia Link

By Cassy Price

Inflammatory bowel disease (IBD) is a term for two conditions, Crohn's disease and ulcerative colitis, that are characterized by chronic inflammation of the gastrointestinal (GI) tract. When there is inflammation in the GI tract, there is increased permeability of the gut. It is becoming fairly well known that the bidirectional communication between the central nervous system (CNS) and the gut microbiota plays a pivotal role in human health.

Chronic gut inflammation increases intestinal permeability, leading to the release of more pro-inflammatory factors in the CNS. Several studies have provided considerable evidence of the effect of gut microbiota on the CNS, as well as its neuroinflammatory role in neurodegenerative diseases.[1] Animal models have demonstrated that infection mediated chronic gut inflammation can lead to significant changes in behaviour including anxiety. When bacteria mediated inflammation is present in the gut, decreases to short-chain fatty acid production as well as increased inflammatory signalling molecules and bacterial peptides modulate brain plasticity and cognitive function.[1,2]

Dementia vs. Alzheimer's Disease

While the terms "Alzheimer's disease" and "dementia" are often used interchangeably, it's important to know there is a difference between the two. Dementia is not a single disease, but rather is a set of symptoms that are caused by disorders affecting the brain. Alzheimer's disease is a chronic neurodegenerative disease, and a form of dementia, that destroys brain cells, causing thinking ability and memory to deteriorate over time.

There are over 500,000 Canadians living with dementia today with 25,000 more receiving diagnosis each year. The annual cost to Canadians to care for those living with dementia is over $12 billion.[3] Roughly 60% to 80% of dementia cases are Alzheimer's disease.[4] In the United States, there are close to six million living with the disease with around 16 million people providing unpaid care for people with Alzheimer's.

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IBD in Dementia Pathogenesis

A population-based cohort study demonstrated significant association between IBD and subsequent development of dementia. Dementia was diagnosed at as much as seven years earlier among patients with IBD, and disease risk appeared to increase with IBD persistance.[5] The researchers speculate chronic inflammation and disruptions to the gut's microbial flora may explain the findings. Nonetheless the findings only represent a correlation rather than a true cause and effect. Further research would be needed to clarify the relationship between IBD and dementia. It is also of note that the health records used in this study didn't include diet and exercise information. Diet and exercise influence on the GI flora is well documented and future observational studies should attempt to include recreational and dietary behaviours.

Another observational study found those with IBD were six times as likely to develop Alzheimer's disease than those without the GI condition. Those with IBD were also more than three times as likely to develop other forms of dementia. The longer someone had IBD after diagnosis, the more likely they were to develop dementia.[5] These findings, though they do not prove cause and effect, did suggest an association between gut inflammation and the development of dementia.

Immuno-dysregulation

About two thirds of people with Alzheimer's disease are women.[6] Similarly, IBD is more prevalent in females compared with males[7] This parallel may be coincidence, however, studies have found possible factors that play into this gender disparity.

Researchers have found that hormonal factors may predict who will have changes in the brain. Study results show changes in biomarkers in the brain suggesting menopausal status may be the best predictor of Alzheimer's related brain changes in women,[6] signifying that in order to effect true change in Alzheimer's disease risk, interventions must be considered earlier in a woman's life to have the most benefit. Several lines of evidence suggest that estrogens play a role in the modulation of immune responses and may be related to the etiology of IBD.[8-13]

It has been implied that sex hormones such as estrogen, and progesterone play a positive modulatory role on epithelial wound healing. The data also demonstrated that sex hormones may protect epithelial barrier cells from damage inflicted by Endoplasmic Reticulum (ER) stress, occurring when the capacity of the ER to fold proteins becomes saturated.[14]

Secondary systemic amyloidosis (SSA) is a rare but severe complication of IBD. The exact cause of SSA is unknown, yet, people are more likely to develop SSA if they suffer from long-term infection or inflammation, suggesting a connection to immune function.

This disorder results in abnormal protein build-up in tissues and organs. Clumps of the abnormal proteins are called amyloid deposits.[15] Further studies are needed to explore this association, however it would be interesting to see the research furthered in terms of the connection to Alzheimer's disease which is also characterized by amyloid deposits. The prevalence of amyloidosis among IBD patients is 0.53%, although epidemiological data suggest that it may be under-diagnosed.[16]

Vitamin D

Another consideration is the role vitamin D plays in immune regulation. A recent meta-analyses confirms that low serum vitamin D concentrations are associated with prevalent Alzheimer disease dementia and cognitive impairment.[17]

Research on animals suggest that vitamin D deficiency may be involved in the degeneration of neurons and loss of cognitive functions.[18] There is also experimental evidence supporting a role for vitamin D in calcium channel regulation, neuroprotection, and immunomodulation in the central nervous system which also implies that low vitamin D status may precede or contribute to cognitive dysfunction with age.[19]

Vitamin D deficiency has also been implicated in IBD due to its immune-modulatory and anti-inflammatory effects. Beneficial effects of vitamin D in IBD are supported by pre-clinical studies, notably with mouse models, where the active form of vitamin D, 1,25-dihydroxyvitamin D (1,25-(OH)2D) has been shown to regulate gastrointestinal microbiota function, and promote anti-inflammatory, tolerogenic immune responses.[20] Vitamin D levels are also associated with relapse rates in Crohn's disease.[21,22]

Conclusion

Dementia is a complex issue that has a significant economical burden on our society. Though there is not a clear cause and effect currently determined there are several promising avenues to be further explored. With Canada spending about $41 million on dementia research each year, through the Canadian Institutes of Health Research (CIHR), and the United States spending roughly $1.9 billion annually, we hope to see more breakthroughs that further our understanding of these diseases. With greater understanding of the pathogenesis of each condition doors will be opened to new treatments, preventative measures and potentially a cure one day.

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Benfotiamine and Cognitive Decline

By Chantal Ann Dumas, ND

Cognition is a combination of processes in the brain, which include the ability to learn, remember, and make judgments. Subjective Cognitive Decline (SCD) is a form of cognitive impairment and considered one of the earliest noticeable symptoms of Alzheimer's disease (AD) and related dementias.[1] According to the Center for Disease Control (CDC), SCD is a public health issue with a prevalence of 11.1%, or 1 in 9 adults in the US population.[2] Cognitive decline can range from mild cognitive impairment to dementia, and it can have a profound impact on an individual's overall health and well-being.[3] SCD can have implications on performing everyday activities such as cleaning and cooking, or living with and managing chronic disease. Everybody's cognitive ability declines with age but it does not have to be our fate. There are several ways we can optimize our brain health!

Nutrition, the Brain and Cognitive Decline

Optimal brain function results from highly complex interactions between numerous genetic and environmental factors, including food intake, physical activity, age and stress.[4] Advances in epigenetics are increasing understanding of the underlying mechanisms involved.[5] Several studies have established links between numerous dietary patterns, foods and nutrients with both beneficial and detrimental effects on brain function, cognition and dementia. For example, a protective role has been reported for the popular Mediterranean diet, optimal energy status, fish, fruits, vegetables, flavonoids, polyunsaturated omega-3 fatty acids, zinc, copper and vitamins A, B, C, D and E.[6]

The Impact of Oxidative Stress

Oxidative stress produced by free radicals plays a key role in age-associated diseases. Studies show that the accumulation of damage inside our cells due to reactive oxygen species (a type of free radicals) may be involved in the functional impairment of aged tissues and contribute to the development of AD.[7] This contributes to explaining why a diet rich in antioxidants and supplementing the diet with antioxidants can have a positive impact on protective brain function.

The Impact of Blood Sugar

Over the years, numerous studies have established a link between high blood sugar levels over a long period of time and cognitive decline. A new study performed by a team from Imperial College London is one of the largest to establish the direct relationship between HbA1c (levels of glycated hemoglobin, a measure of overall blood sugar control) and subsequent risk of cognitive decline. The study involved more than 5,000 people aged over 50 who had their cognitive abilities measured over 10 years and showed that those with high blood sugar levels were more likely to fare worse on tests of memory and concentration. Significantly, the rate of cognitive decline was directly linked to a person's HbA1c status (with higher HbA1c meaning higher rate of cognitive decline), whether or not they were diabetic according to their HbA1c status at baseline.[8]

Cerebral Glucose Metabolism and Alzheimer's Disease

Besides the plaque, tangles and cognitive decline, several changes affect the brain of people diagnosed with AD. These changes include inflammation, oxidative stress and metabolic dysregulation. Cerebral glucose metabolism changes are observed decades before AD is diagnosed and reductions in glucose utilization correlate highly with cognitive decline in AD patients.[9] Because of this close connection between the effects of chronically elevated blood-sugar levels and AD, it is now often referred to as "type III diabetes".[10] Recognizing the impact of excessive blood sugar on dementia offers an entirely new approach to prevention.

Advanced Glycation End-products

One of the most damaging effects of chronic elevated blood glucose is the formation of advanced glycation end-products (AGEs). AGEs occur when sugar molecules chemically react with proteins and other critical biomolecules, altering their structure and impairing their function.[11]

Studies have shown that AGEs bind to specialized cell-surface receptors called RAGE for receptors for AGE. The AGE/RAGE interaction induces oxidative stress, activates inflammatory reactions, and promotes deposition of the toxic beta-amyloid proteins associated with AD.[12] A form of RAGE, called soluble RAGE (sRAGE), on the other hand, acts as a decoy, trapping AGEs and preventing them from activating the cell-bound RAGE. A recent study demonstrated that people with mild cognitive impairment had higher AGE, and lower sRAGE levels, than those without the condition.[13] Balancing blood sugar level through a proper diet and the use of natural supplements can shield the body from the harmful effects of AGEs and prevent the harm they could do to the blood vessels and the brain.

Benefits of Caloric Restrictions

Restriction of energy intake is a highly effective intervention for age-related functional decline.[14] One of the mechanisms by which dietary energy restriction may exert a neuroprotective effect on the ageing brain is its effects on decreasing oxidative stress and reducing apoptosis. Although effective, caloric restriction is not always easy or practical to implement and targeted nutritional supplements can support our on-going efforts.

Benfotiamine and Cognitive Decline

Thiamine (vitamin B1) is one such supplement profoundly involved in maintaining healthy brain function. A deficiency in this precious vitamin impacts most organs in the body, but it is especially damaging to the brain. There, it triggers a cascade of events that lead to oxidative stress and inflammation, which are major contributors to Alzheimer's, Parkinson's, and other dementia-producing disorders.[15]

Benfotiamine is a highly bioavailable form of thiamine which has a known track record of safety and effectiveness in metabolic disorders. In addition to its known importance in brain function, benfotiamine has the dual ability to support sugar metabolism while also helping protect against the damage caused by elevated blood sugar.[16] Benfotiamine has the ability to prevent AGEs from forming and also to neutralize oxidative stress.[17] This unique combination powerfully protects against blood vessel and tissue damage. At the same time, it reduces their impact on inflammatory processes that contribute to dementia.[18]

In a groundbreaking clinical study, supplementation with 300 mg/day of benfotiamine was found to produce significant cognitive improvement in individuals with mild-to-moderate Alzheimer's over 18 months.[19]

Conclusion

We can definitely optimize and protect our cognition as we age. Ideally, the focus needs to be on optimal energy status in relation to food intake, activity, body composition and a balanced Mediterranean diet. However, if it is impossible to improve food intake and activity, as may be the case particularly in elderly people, then the focus should be on key nutrients. Current evidence suggests that benfotiamine is a key nutrient for optimal cognition and that it belongs on the short list of supplements recommended for maintaining brain health well into old age.

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