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Research Article

Functional Foods for Cognitive Development and Memory in People with Down Syndrome

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Abstract

Down syndrome or trisomy of par 21 is a genetically determined human condition that promotes intellectual disability and functional changes interfering in development. Food can combat free radicals by attenuating brain aging in people with Down Syndrome. This article aimed to present information about functional foods that can contribute to cognitive improvement and brain development in people with Down Syndrome. There is evidence that foods that are sources of choline, phosphatadilcholine and phosphatadilserine, such as green tea and turmeric, through supplementation can contribute to brain function. This is due to the neuroprotective compounds present in turmeric and choline being the precursor of neurotransmitters.

Keywords: Trisomy; Alzheimer 'S; Green Tea

Introduction

Down Syndrome (SD) or Trisomy of peer 21 is a genetically determined human condition. The presence of the extra chromosome on par 21 determines specific physical characteristics and developmental delay [1].

People with DS have intellectual disabilities, anxiety, binge eating [2,3]. Due to excess genetic material, the brain of a person with DS is similar to that of a person with Alzheimer's with oxidized plaques. Premature brain aging is another feature in People's DS, so they need choline foods and supplements and phosphatadilcholine or lecithin [4,5,6]. Food sources of phosphatidylserine, green tea and curcumin are also important [7,8,9].

People with DS have early dementia typical of Alzheimer's disease, including degeneration of neurons and, for this reason, have impaired memory and attention. Therefore, choline supplementation already in pregnancy of a fetus with DS suggests benefits to the memory of this population. Choline source foods are important for neurotransmission and memory [10,11].

Foods sources lecithin or phosphatadilcholine such as soy, vegetable oils, eggs, meats, milk, peanuts, help in memory. Thus, the aim of this research is to report through a literature review the relationship of functional foods with memory improvement and cognition in people with Down syndrome [12].

Methodology

This article is a systematic literature review. The research of the articles was carried out from the databases, NCBI, academic google, CAPES Journal.

Having as indexer term: "epigallocatechin-3-gallate down syndrome", "curcumin Alzheimer's", "choline Down Syndrome", "maternal choline supplementation", "lecithin down syndrome", "Phosphatyl-choline Down Syndrome", "feeding and D syndrome itself"," Alzheimer Down Syndrome", "Down Syndrome brain", "Memory Down Syndrome", "memantine alzheimer's". The publications were pre-selected by the titles, these should contain as the first criterion the complete term on the importance of feeding for Down Syndrome, the relationship between the supply mentation of Green Tea EGCG for people with Down Syndrome, the benefits of Turmeric for memory and Alzheimer's. As well as the importance of supplementation and feeding with choline, phosphatadilcholine and phosphatarylcholine to the cognitive process of people with Down Syndrome and their dietary sources.

From the research, it was observed the occurrence of 15,000 articles in total. Only the articles that the title was related to the indexed words were included. Accompanied by reading the available abstracts. In the google academic database, 3000 articles on Down Syndrome were found, of which 2500 were excluded after initial analysis (phase 1 = reading the title, abstract and keywords),500 were for the evaluation of phase 2, after reading 480 articles were excluded for not meeting the inclusion criteria and then were selected, 30 articles. In the CAPES journal, an article was found that met the inclusion criteria and was therefore included in the study. In the NCBI database, 1199 articles were identified, 1100 excluded in phase 1 after reading the title and abstract, were for phase 2, 99 articles, of these were selected 69 articles.

Results and Discussion

Down syndrome

The term Down Syndrome (DS) originates from the pediatric physician John Langdon Down who classified the syndrome for the first time [13].

The triplication of the genetic material referring to chromosome 21 can occur in three different ways. In 96% of cases trisomy occurs by a total chromosomal non-disjunction, i.e., all cells of a developing fetus assume an extra chromosome 21. Only 4% of people with DS do not have all the cells affected by chromosome 21 extra, being termed as mosaicism. Gene translocation may also occur, in which part or all of the extra chromosome 21 binds to another chromosome, usually chromosome 14 or 22 [14,15].

The factors that contribute to DS are associated with maternal age, because the woman is already born with the amount of eggs that age along with her; male gametes age as well [16].

Clinical data from the medical records of 85 people with Down Syndrome were summarized. Of these, 75.3% were diagnosed with dementia. DS is associated with dementia, abnormal cognitive development, learning and language problems [17,18].

People with DS have mental retardation and develop neuropathological changes and Alzheimer's characteristics [19].

A postmortem brain study was conducted by Dr. George Jervis in the period 1750-1770 in 100 patients with DS. In 15 of these, aged over 30 years, dementia with Alzheimer's characteristics was detected [20].

The relationship between DS and Alzheimer's disease has been documented since (1986), where brain necropsy was performed in 12 patients with DS aged 31-65 years. Of these, only 1 patient did not have beta-amyloid plaques: alzheimer's characteristics [21].

In dogs with dementia, the presence of beta-amyloid plaques was verified in the brain of these animals. They had memory deficits, learning and problems in spatial learning [22].

Alzheimer's and chromosome 21

Alzheimer's disease has been described by German physician Alois Alzheimer after doing the autopsy on the brain of a patient who died of early dementia. Autopsy revealed cerebral cortex atrophy, loss of cells and numerous plaques throughout the cortex [23].

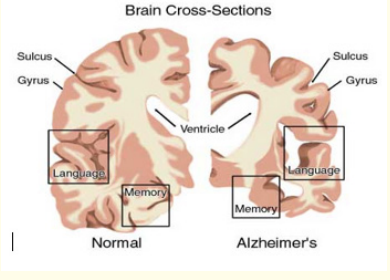

Figure 1: A brain without Alzheimer's and a brain with Alzheimer's.

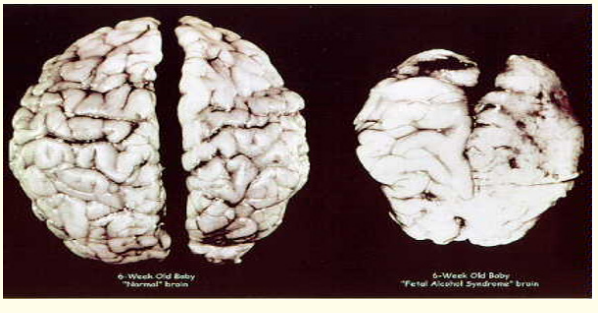

Figure 2: Brain without SD and brain with SD.

The symptoms of Alzheimer's disease are problems in memory, language, and there is the loss of cognitive functions [24].

The Alzheimer's gene is on chromosome 21. Chromosome 21 contains 233 genes encoding 299 non-coding long RNAs and 29

microRNA. One of these genes is responsible for the development of Alzheimer's. People with Down Syndrome have a third copy of the beta-amyloid precursor protein gene. This protein accumulates in the brain and causes Alzheimer's [25-27].

The beta-amyloid precursor protein, in rat models with SD characteristics, causes cholinergic neuron dysfunction in the forebrain and synapathic and this contributes to the cognitive dysfunction of Alzheimer's disease in Down syndrome [28].

Alzheimer's disease is a neurodegenerative taupathy, because the phosphotau protein of axons is hyperphosphorylade and this causes destabilization of microtubules and degeneration of neurons [29].

Several studies have been conducted on the cognition of people with Down Syndrome. A mouse model called the Ts65Dn model was developed with characteristics similar to those of SD. These rats have a trisomy in the distal region of the murine chromosome 16 to which they have 60% of the homologous genes of the rats contained in chromosome 21 of humans [30].

Memory

The region of the brain responsible for memory is the hippocampus. People with DS have cognitive impairment, impaired memory, and intellectual disability. The rat model with DS presents deficiency in the hippocampus and impaired cognition, gaba signaling of Ts65Dn rats is increased in the toothed gyre of the brain of these rats [31].

They conducted a double-blind study, clinical trial with 42 patients with Alzheimer's for 16 weeks with placebo and the memory medicine The group that received the drug had improved learning and memory, as this drug acts in the hippocampus [32].

People with DS have an extra copy of the DSCR1gene (Critical Region of Down Syndrome1). This gene encodes a protein that inhibits calcineurin. It is suggested that the drug for Alzheimer's, memantine, improves the memory and learning of this population because calcineurin modulates the activation of the N-Methyl-D--Aspartate receptor and memantine mimetizes the effect of calcineurin that is impaired in people with DS [33].

Using the Ts65Dn rat model with Down Syndrome treated with the drug Alzheimer's Memantina resulted in improvement in the memory of the guinea pigs [34].

In a study with two groups of people with Down Syndrome, from two different schools: a regular school and another a special school. Each school received a group of 9 members who performed recall tasks and cognitive tests. They concluded that the educational environment of people with DS has an influence on learning, memory, speech and cognition [35].

Functional foods: tea-green

Green tea is the aqueous extract of the dried leaves of the *plant Camellia Sinensis*. It contains a mixture of polyphenols such as flavonols, flavadiols, flavonoids and phenolic acids. Most of the tea polyphenols are flavonols, especially catechins [36].

The green tea catechins are the epicaequina, epigallocatechin and 3 epigallocatechin gallate, 3-gallate of epicatequina. Camellia Sinensis leaf tea does not undergo fermentation during processing [37,38].

In a randomized, phase 2 placebo-controlled double-blind trial, 43 young people aged 16-34 years with DS ingested green tea supplement (600 to 800 mg by weight) containing 45% of the active tea compound (Epigalocatequina gallate) for one year. During this period, cognitive training related to visual memory participated. The other 41 study participants received placebo and the same cognitive training. The results of this study showed that participants who received green tea had an improvement in clinically relevant memory in the brain neuroplasticity of individuals with DS [39].

The Ts65Dn mouse model that mimics the SD where the dosage of (EGCG: 326.25 mg/ml, 29.79 mg per day, 32.59 mg/kg per day) of green tea was administered. There was an improvement in the learning of rats [40].

A cohort study was conducted with 2,845 elderly people aged 60 years or older in Nakajima City, Japan to evaluate the consumption of green tea, black tea and coffee and its influence on the cognitive process and incidence of dementia in the elderly. The research result proved that the consumption of green tea every day is associated with a lower incidence of dementia [41].

The mouse model with SD called The Ts65Dn, these mice are deficient in memory and learning. 20 mg/kg/day of epigallocatechin-3-gallate (EGCG) was added to the water of these rats. There was no improvement in cognitive function when compared to rats that did not receive EGCG. They did not come to a conclusion of the dose to be used in humans, but low doses of EGCG have no effect on memory [42].

D was administered (10 mg to 360 mg) of de-caffeineted green tea extract for one month in Ts65Dn rats. These rats contain cognitive changes due to an increase in the expression of DYRK1A serine-threoin kinase in Hsa21, as in people with DS. Treatment with EGCG reverts to molecular changes in the brains of rats, improving the memory process of these rats [43].

In research in the rat model with DS that green tea EGCG can be used for the treatment of cognitive disorders in patients with DS [44].

Turmeric

Turmeric is a polyphenolic compound of Turmeric. It has anti-inflammatory and antioxidant properties. It also has neuroprotective properties. Curcumin at low concentrations (less than 0.2 mg/kg) stimulates neuronal cell proliferation. Curcumin improves neurogenesis in the hippocampus of adult rats and stimulates hippocampus neuroplasticity [45,46].

It was concluded that Turmeric's turmeric protects the brain from stress neurotoxicity [47].

It is known that the brains of people with DS have beta-amyloid plaques. In research using *in vitro* model it was found that turmeric reduces beta-amyloidplaques indicate an effect of curcumin on the reduction of amyloid plaques in animal models [48].

Turmeric is an excellent antioxidant and anti-inflammatory. Curcumin decreases the precursor protein of amyloid-β. This study suggests that in the future turmeric may be used as an adjunct pharmacological agent in the treatment of Alzheimer's disease [49,50].

One study revealed that curcumin-derived enol binds to amyloid beta aggregates [51].

Choline, phosphatadilcholine and phosphadilserine

Choline is an essential nutrient for the synthesis of neurotransmitters such as acetylcholine. It is necessary for cell membrane signaling, lipid transport and reduces homocysteine. When choline is oxidized it constitutes betaine as a donor of the methyl group for the conversion of homocysteine to methionine [53,54].

Choline is a precursor to phosphatadilcholine, lysophatidysphosphonadilchoand sphingomyelin phospholipids from all cell membranes. Eggs are a good source of choline (300 mg of choline), mainly in the form of phosphatidylcholine. Other food choline sources are presented in table 1 [55].

Foods	Amount of choline	Homemade measurement
Chicken liver	247 mg	100g
Soy flour	201 mg	1 cup
Raw quinoa	60 mg	1/2 cup
Milk	38 mg	260g
Baked cauliflower	24 mg	1/2 cup
Pea	22 mg	1/2 cup
Cooked broccoli	15 mg	1/2 cup
Black oatmeal	15 mg	1/2 cup
Whole egg	238,4 mg	50g
Egg yolk	238 mg	17g
Egg white	0,46 mg	33g

Table 1: Choline Source Foods.

Source: United States Department of Agriculture (USDA) [56].

Suplementaram hill in pregnant rats. This study suggests that choline supplementation induces cognitive benefits of offspring throughout the life of the Ts65Dn rat model [58].

In research on choline supplementation in rat pregnancy the benefits it makes in the spatial memory of these animals. Likewise in other research on the same subject as supplementation improves the memory of rats until adulthood. These results suggest that choline supplementation in pregnant women with a fetus with DS has a possible neuroprotective effect. Similar results were found in a study where choline supplementation in the gestation of Ts65Dn murines improves neuropathology associated with DS [59-61].

Phosphatadilcholine (lecithin) is an essential phospholipid in mammalian cells, through the choline pathway. Phospholipids are distributed in the cell membrane asymmetrically. Choline, sphingomyelin and phosphatadilcho are arranged in the outer layer of the membrane. Amystolipids such as phosphatadilserine and phosphatidyldilletanomine are in the inner layer of the membrane [62,63].

Phosphatadilserin in the plasma membrane is located in the cytoplasmic leaflet. In synapses, phospha tadilserin facilitates the activation of signaling proteins and receptors for synaptic differentiation and neurotransmission [64,65].

In a randomized double-blind placebo-controlled study evaluated the result of ingestion of 3 capsules of phosphadilserine and placebo to assess its effect on the cognition and memory of people with Alzheimer's and dementia. After, tests were performed, improvement scans of the memory of the health people with dementia and Alzheimer's were contacted. Cellular oxidative stress causes adverse consequences on the whole organism [66].

Thes cells of the person with DS have increased inflammatory process, higher occurrence of apoptosis and cell death and reduction in DNA repair. People with DS have an overexpression of protein kinase (DYRK1A) that can activate stat 3 route and this causes overexpression of lecithin [67,68].

Studies in animal models with Alzheimer's using phosphatadilserine dietary supplements have reduced the loss of choline acetyltransferase and rna messenger acetylcholine esterase transporter in the hippocampus of guinea pigs. The food sources of phosphatadilserine are meat, fish, legumes such as soy lecithin.

Conclusion

A person with DS has premature aging due to the third extra chromosome on par 21. They have Alzheimer's disease from the age of 40, have cognitive and memory deficits that can be attenuated through adequate nutrient nutrition, especially choline, phosphatadilcholine, phosphatadilserine, curcumin and Green tea EGCG.

Several studies have been done over the years in relation to the feeding of this population since 1960 worldwide.

The environment in which the person with DS is also inserted influence in this process of learning, memory and cognition. The stimulus, the multidisciplinary care, in addition to an adequate diet, are fundamental for the patient with DS to develop well.

It is justified to carry this out due to the fact that feeding can attenuate the brain aging of people with Down Syndrome and fight free radicals. However, more research is needed in humans with DS in relation to green tea EGCG and foods related to memory and cognition.

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