

Nutritional Neurosciences

Senthilkumar Rajagopal
Saravanan Ramachandran
Geethalakshmi Sundararaman
Swarnalatha Gadde Venkata *Editors*

Role of Nutrients in Neurological Disorders

 Springer

Part II Specific Food and Nutritional Qualities on Neurological Disorders

- 8 **Best Foods for Repair of Brain Damage** 161
Geethalakshmi Sundararaman and Ashok Ganapathy
- 9 **Role of Micronutrients in Neurological Development** 177
 Neenu Ravikumar, Madhubalaji Chegukrishnamurthi,
 and Swarnalatha Gadde Venkata
- 10 **Algae as a Potential Vegetative Source of PUFA for the Prevention of Neurological Disorders** 201
 C. K. Madhubalaji, Neenu Ravikumar, Swarnalatha Gadde Venkata,
 and E. C. Surendranatha Reddy
- 11 **Natural Foods for Suppressing Dementia** 223
 N. Nirmala Devi and C. Viswanathan
- 12 **Nutrients' Role in the Treatment of Parkinson's and Alzheimer's Diseases** 237
 A. Thabitha, N. Vignesh, and R. Saravanan
- 13 **Novel Marine-Derived Natural Products for the Treatment of Depressive Disorder** 247
 K. Kamala, P. Sivaperumal, G. Dharani, Saravanan Ramachandran,
 and Dhanraj G
- 14 **Nanoceticals as Theranostics Against Neurodegenerative Diseases** 263
 Prabhakar Mishra and Santosh Anand
- 15 **Role of Antioxidant Nutraceuticals in Neurodegenerative Diseases** 281
 Rajadurai Murugan, Anand Paramasivam,
 and Lokesh Adhappa Chandrashekar
- ## Part III Herbal Remedies for Neurological Disorders
- 16 **Herbal Drugs: Its Mechanism to Prevent Alzheimer's Disease with Special Reference to Non-phenolic Secondary Metabolites** 303
 Kamsala Venkata Ratnam, Lepakshi Md. Bhakshu, and Rudraraju Reddy Venkata Raju
- 17 **Preventive Role and Mechanism of Herbal Medicine in Alzheimer's Disease with Special Reference to Phenolic Compounds** 319
 Lepakshi Md. Bhakshu, Kamsala Venkata Ratnam,
 and Rudraraju Reddy Venkata Raju
- 18 **Herbal Remedies for Autism** 333
 Mukundan Chilambath and Geethalakshmi Sundararaman

Chapter 8

Best Foods for Repair of Brain Damage

Geethalakshmi Sundararaman and Ashok Ganapathy

Abstract Brain is the vital organ of human body which is kept safely placed inside the skull surrounded by cerebrospinal fluid. But injuries happening in brain sometimes go undetected. OCD is one common brain damage that occurs in the current day scenario. Treatment and cure protocols are available for this but they have their own disadvantages. Medicines used for treatment will only suppress the symptoms which also produces unwanted side effects. Psychological methods cannot be applied to all categories of patients and takes a longer time of recovery. Hence, a natural curing method which does not require any additional protocol is needed. Medical field is focusing its direction in dietary supplements for curing several complications. This chapter also focuses on the nutritional supplements that can be provided to the brain damage patients. It also describes the action of the components on the brain and their positive impact on brain damage. Also, it explains the role of exercise during recovery.

Keywords Brain injury · OCD · Nutrition · BDNF · Exercise

8.1 Introduction

Brain is the most vital organ in the human system and is the central organ of nervous system. It regulates the abundant quantity of information that the body needs for functioning properly. This includes realizing pain levels, regulating blood pressure, scheming nervous response, creating and secreting hormones, helping in digestion, along with organizing countless other signals the body transmits to the brain to enable our body to function without any deficiency. Thus, supplying brain with vital nutrients is essential for effective functioning of the body (Dimond 2013).

G. Sundararaman (✉) · A. Ganapathy
Department of Biotechnology, Sree Narayana Guru College, Coimbatore, Tamil Nadu, India

8.1.1 Brain Damage and Its Types

An injury that causes damage to the brain cells is called **Brain Injury**. It is caused by any type of injury in the head but all head injuries need not be brain injury. It is of two types:

- **Traumatic Brain Injury (TBI):** It is caused by an external force like a blow to the head. It causes the brain to move inside the skull and/or damages the skull which in turn damages the brain (Ghajar 2000).
- **Acquired Brain Injury (ABI):** It occurs at the cellular level. It is linked with pressure developed on the brain which could come from a tumor, neurological illness, or other brain related complications (Greenwald et al. 2003).

These injuries are not degenerative and usually occur after birth. But some brain injuries occur during the birth which may be due to genetic defect or birth trauma. They are called as congenital brain damage.

Localized brain damage or focal brain damage is the injury that is restricted to a small area of the brain. Diffused brain damage causes damage to several parts of the brain on the whole. The rigorousness of brain damage varies with the type of brain injury.

- Mild injury—Causes headache, memory problems, confusion, and nausea and last only for few minutes to few hours.
- Moderate injury—Symptoms will be prominent and last longer, may be for few weeks to few months. In both the cases, recovery is possible.
- Severe injury—Results in cognitive, behavioral, and physical disabilities. Recovery is almost impossible (Woodward et al. 1984).

8.1.2 Causes of Brain Damage

Brain damage occurs due to many types of injuries or illnesses. It can also happen when the enough oxygen is not supplied to the brain for a long time. Male individuals in the age group of 15–24, young children of age below 10 years, and elderly people who are above 65 years are more prone to this damage compared to female due to their high-risk behaviors.

Traumatic brain injury may be caused by accidents, blows on the head, injuries caused during sports, falling down from heights or by physical aggression. Acquired brain injury may be caused by poisoning or exposure to toxic substances, infection, strangulation, choking, drowning, stroke, heart attack, tumors, aneurysms, neurological illnesses or by drugs (Lishman 1968).

8.1.3 Symptoms of Brain Damage

Symptoms of brain damage are categorized cognitive, perceptual, physical, and behavioral/emotional symptoms.

Cognitive symptoms of brain damage consist of difficulty in processing information, expressing thoughts, understanding others, short attention span, inability to understand concepts, impaired decision-making ability, and finally memory loss.

Perceptual symptoms of brain damage include change in sensing, spatial disorientation, balance issues, and increased sense toward pain.

Persistent headaches, extreme physical and mental fatigue, tremors and seizures, sleep disorders, indistinct speech, loss of conscious, and paralysis are the symptoms of physical damage.

Aggressiveness/sluggishness, decrease in stress tolerance, emotions, and reactions and increase in irritability include the behavioral/emotional symptoms of brain damage (Schulman 1965).

8.2 Obsessive Compulsive Disorder (OCD)

Obsessions are unwanted disturbing thoughts, images or instinct that occurs repeatedly inside the brain that induce stress and cannot be controlled. Persons affected by obsessions will not want these thoughts to happen and finds them disturbing. These obsessions usually go with uncomfortable feelings such as fear, doubt, and aversion. These feelings interfere with a person's day-to-day activities and are time consuming. Ultimately, it affects a person's values and morality.

The individual affected by obsessions may try to get rid of/reduce these feelings by engaging in certain procedures/habits which are called as **compulsions**. But compulsions like avoiding or escaping from the situation only provide a temporary relief. All recurring behaviors are not compulsions. This concept has to be seen in the context of brain functioning. For example, learning new skills, daily routines, and other day-to-day practices are repetitive activities but involve active and functional brain. Such disorder arising in the brain is called **obsessive compulsive disorder (OCD)**. All people experience such conditions in their lifetime and that does not mean they are affected by OCD (Leckman et al. 1997; Obsessive Compulsive Cognitions Working Group 1997). The onset of the disorder can be confirmed only when these obsession and compulsion cycles repeat and at one stage, they become extreme. At this point, diagnosis and proper treatment is essential; else, the individual will experience a severe brain damage which may be fatal (Fig. 8.1).

Several studies have analyzed the process involved in OCD and found that it involves decrease/loss of communication between the front part and interior of the brain. The neurotransmitter **Serotonin** is (Fig. 8.2) is responsible for this communication between body and brain (Baumgarten and Grozdanovic 1998). The normal level of this neurotransmitter is 101–283 ng/ml in the blood. During OCD

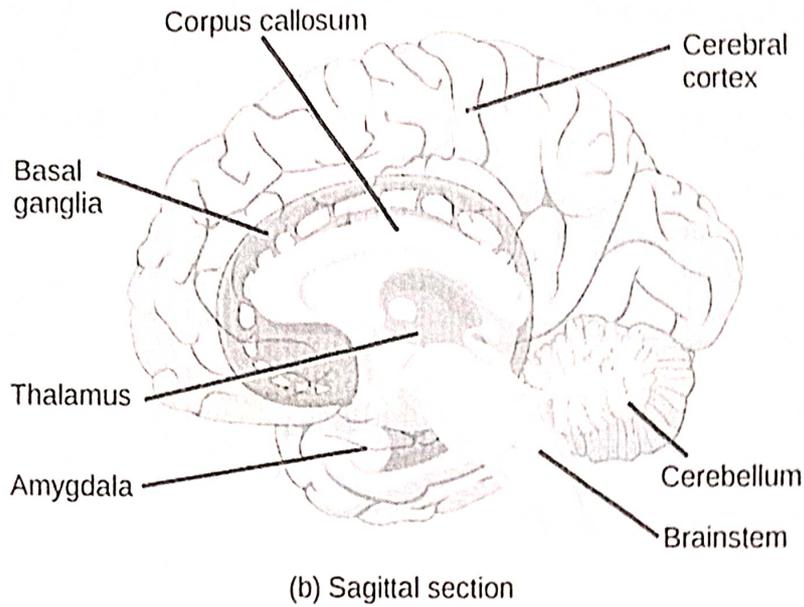


Fig. 8.1 Anatomy of human brain

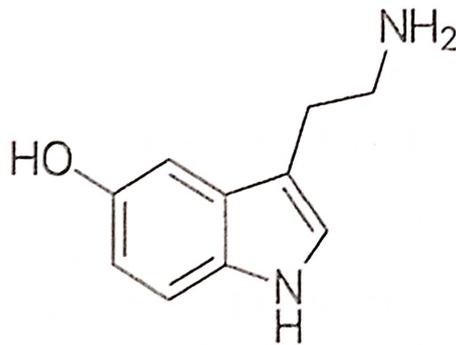


Fig. 8.2 Structure of serotonin

conditions, the level of serotonin is found to decrease. Hence, symptoms such as depression, anxiety, nausea occurs. If left untreated in the initial stages, these symptoms lead to the onset of OCD. If left untreated, OCD leads to brain damage, which ultimately end up in paralysis, stroke, coma, and brain death (Van Dijk 2008).

8.3 Treating OCD and Brain Damage

8.3.1 Antidepressant Drugs

The initial stages of the brain damage where the serotonin levels are less can be treated with antidepressant drugs. They are medications that help to relieve anxiety disorders and depressions. These drugs work by balancing the neurotransmitters and

their transmission to brain (Zafonte et al. 2002). There are several types of these drugs:

- Serotonin and noradrenaline reuptake inhibitors (SNRIs).
- Selective Serotonin reuptake inhibitors (SSRIs).
- Tricyclic antidepressants (TCAs).
- Monoamine oxidase inhibitors (MAOIs).
- Noradrenaline and specific serotonergic antidepressants (NASSAs).

But these drugs cause various side effects on prolonged usage. Constipation, dry mouth, weight gain, drowsiness and sedation, blurred vision, hypertension, edema, tremors, and hypoglycemia are some of the side effects of these antidepressant drugs (Elmorsy et al. 2017).

8.3.2 Rehabilitation Therapies

Rehabilitation therapies are therapies given to brain damage patients under controlled environment to help the body heal, relearn skills and new ways to do activities without any difficulty. There are three types of rehabilitation therapies: occupational, physical, and speech.

Occupational therapies help patients who require assistance to execute their day to day activities like eating, brushing, sleeping, etc. Physical therapies are given to patients who experience pain in functioning of their body parts. Such therapies help people to relieve pain, improve the movement of body parts, and recover from injuries and strengthen the cardiovascular operations. Speech therapy is given to patients who have difficulty in speech and communication especially in Parkinson's disease, Huntington's disease, etc. (Soo and Tate 2007; Williams et al. 2003).

8.3.3 Psychological Support

Some basic management skills such as controlling stress, anger, and unwanted thoughts can be done using psychological treatment along with some medications.

Though there are enough number of treatments, drugs, and support mechanisms for handling brain damage, these methods have their own disadvantages such as:

- Wrong diagnosis;
- Non-cooperation from the patients;
- Time duration;
- Theorizing on brain damage;
- Optimizing the treatment methods depending on the patients' age, gender, damage vigor, potency of the patient, etc.;

- Side effects of the drugs;
- Allotment of specific time duration for the treatment;
- Cost;
- Requires experts.

Thus, alternative methods of treating brain damage are required. The novel method must be natural, without causing/causing minimal side effects, applicable to patients of all categories, must not require specific time duration, expertise, and must be easily available and cost effective. One such method is devising treatment using natural food supplements (Jenike 2001).

8.4 Nutrition for Brain Damage

As conventional treatment methods have their own disadvantage and are not suitable for all people and situations, natural and convenient methods of treating brain injuries are devised. During normal working condition, the human brain needs lot of energy and this is drastically increased when it sustains injury and damage. Hence, proper diet must be designed which is rich in nutrients and energy boosters which will rejuvenate the brain and make it function effectively. Thus, certain essential elements such as protein, magnesium, zinc, antioxidants, and minerals must be present in the diet on a daily basis to boost up the brain function (Gomez-Pinilla and Kostenkova 2008). There are also certain elements that have to be avoided during brain damage because poor diet affects the function, behavior, and mood of the brain. Essential elements in the food help in enhancing proper biochemical reactions in the nerves and brain and also maintain the level of neurotransmitters. Thus, healthy diet is very essential for effective and speedy recovery from brain damage. The diet must include vegetables, fruits, and grains, low fat foods such as fish, beans, and lean meat. The quantity of salt, sugar, and alcohol must be reduced and quantity of water intake must be increased. Recent research indicates choline, creatine, omega-3 fatty acids, and zinc are useful for recovery (Gomez-Pinilla 2011).

8.4.1 *Essential Vitamins*

Different foods have different vitamins in them and each has their own role to play regarding the brain health. Table 8.1 gives the consolidated purpose of each type of vitamins (Aquilani et al. 2011; Spector and Johanson 2007).

Table 8.1 Vitamins and their role in brain health

S. No.	Vitamin	Source	Role in brain health	Deficiency
1.	B1 (thiamine)	Grains, legumes, pork, nuts, and seeds	Metabolism of glucose which promotes muscle growth and as energy source	Beri-Beri
2.	B12 (cobalamin)	Eggs, meat, and milk	Maintains the myelin sheath	Impaired brain function and nerve damage
3.	B9 (folic acid)	Yeast, beans, wheat, nuts, and broccoli	Effective function of neurotransmitters and brain	Nervous disorders and anemia
4.	B3 (niacin)	Wheat bran, meat, fish, peanuts, and milk	Effective function of neurotransmitters and brain	Pellagra, psychosis, and loss of memory
5.	A (retinol)	Spinach, eggs, carrot, fish, and meat	For functioning of eyes and protection against infection	Vision impairment
6.	E (tocopherol)	Greens, cereals, and plant oils	Oxygen supply to brain	Peripheral neuropathy
7.	B6 (pyridoxine)	Fish, pork, chicken, wheat, fruits, and vegetables	Supports nervous system functioning	Mental depression, confusion, convulsions, and anemia

Table 8.2 Minerals and their role in brain health

S. No.	Minerals	Source	Role in brain health
1.	Iron	Fish, poultry, and meat	Formation of hemoglobin to carry oxygen throughout the body
2.	Manganese	Grains, nut, fruits, and vegetables	Helps in brain functioning
3.	Selenium	Liver, eggs, and sea foods	Synthesis of hormones and protection from cell damage
4.	Zinc	Liver, eggs, red meat, dairy products, and vegetables	Protection from cell damage
5.	Magnesium	Grains, butts, green leafy vegetables, and seeds	Transmission of nerve impulse
6.	Copper	Seeds, nuts, sea food, cereals, and dark chocolates	Maintains immune response and brain function

8.4.2 Essential Minerals

Minerals, like vitamins, play an important role in maintaining the brain health. Table 8.2 lists the essential minerals that must be supplied to brain (Hasan et al. 2011).

Considering these parameters, the best food that must be taken by patients affected by brain damage is consolidated as follows.

8.5 Best Food for Brain Injury

In order to recover from brain damage naturally with minimal side effects and complications, dietary supplements are formulated. Some of the required diet components are discussed in the following.

8.5.1 *Omega-3 Fatty Acids*

Omega 3 fatty acids are very essential for nerve and brain functioning, signal transmission, neurotransmitters functioning, and all operations related to brain and nervous system. Human brain consists of 60% fat and most of these fat molecules belong to Omega-3 FA category: α -linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA) (Bourre 2004). There are many studies done recently on polyunsaturated fatty acids (PUFA) and monounsaturated fatty acids (MUFA) and there is increasing evidence that these fatty acids play an important role in maintain the brain health. They help in rejuvenating the damaged brain and nerve cells. It also helps in maintaining the neuroplasticity (Avallone et al. 2019). Omega-3 and Omega-6 FA which comprises linoleic acid (LA) and arachidonic acid (ARA) comes under PUFA and Omega-9 FA under MUFA. Of these FAs, Omega-3 determines several cerebral functions and DHA plays an important role in facilitating the functioning of the brain. Figure 8.3 shows the structure of PUFA. These PUFAs are present adequately in fish such as sardines, salmon, and trout. They contain 0.6–1.24 g/portion of DHA. These fish varieties must be baked or broiled to get the maximum effect of PUFA. PUFA is also present in walnuts, pumpkin seeds, flax seeds, soybeans, and dark leafy vegetables like spinach (Dyall 2015; Healy-Stoffel and Levant 2018).

DHA is presents in esterified form in food. When consumed, in the intestine, lipases convert esterified DHA into unesterified form and transfer it to small intestine. In the small intestine, it under goes metabolism and is converted to free DHA. These free DHA molecules pass through the blood–brain barrier (BBB) with the help of fatty acid-binding proteins (FABP) and endothelial lipases and get distributed within the central nervous system (Medina and Tabernero 2002; Song et al. 2019).

8.5.2 *Dark Chocolate*

Dark chocolates contain high level of magnesium and antioxidants. These two nutrients are essential for recovery of the brain from TBI. Especially the variety of dark chocolate which contains more than 60% cocoa is the most preferred type of chocolate to be given to the brain damage patients (Toker et al. 2018).

Omega-3 fatty acids

ALA: α -Linolenic acid

C18:3 n-3



EPA: Eicosapentanoic acid

C20:5 n-3



DHA: Docosahexanoic acid

C22:6 n-3

Omega-6 fatty acids



LA: Linoleic acid

C18:2 n-6



AA: Arachidonic acid

C20:4 n-6



DPA: Docosapentanoic acid

C22:5 n-6

Fig. 8.3 Structure of PUFA

Magnesium acts as a neuroprotective agent and is found to reduce the infarct zone and neurodeficiency. It actually reduces the mortality rate of the brain cells and also exhibits antioxidant effect on damaged tissues. It acts as a protective agent of blood-brain barrier (BBB); if administered as magnesium sulfate, its effect show many fold increase on the brain and nerve cells. The antioxidative protection mechanism of magnesium can be understood in two steps: one is inhibiting the lipid peroxidation which is catalyzed by Fe ions and the other is restoring the glutathione level in the cells thereby increasing the level of GSH in the blood. There are evidences which indicate the direct correlation between the concentration of Mg^{2+} and GSH. GSH

along with α -tocopherol, β -carotene, and ascorbic acid scavenges the free radicals generated due to the damage of brain cells, thereby stimulation adequate oxygen supply, which helps in rejuvenating the damaged cells. Mg^{2+} also plays an important role in activating neurotransmitter function (Zheltova et al. 2016; Shadman et al. 2019).

8.5.3 Berries

Berries are rich in antioxidants, which are very helpful in protecting the brain from damage and reducing inflammation. Strawberries and blueberries are essential for improving memory, learning, and other cognitive functions. They promote brain derived neurotrophic factor (BDNF) which plays an essential role in neuronal survival and growth, modulates neurotransmitters, maintains neuronal plasticity, and helps in learning and improving memory power (Choi 1993; Arteaga et al. 2017).

8.5.4 Meat

Another nutrient that gets depleted due to brain damage is zinc. Zinc (Zn) helps to modulate responses of neurotransmitters to their receptors (Pillsbury et al. 2011). It also has neuroprotective properties. Zn occurs in two forms inside the brain cells: (1) Tightly bound to proteins and (2) As a free ion in the cytoplasm or extracellularly in presynaptic vesicles. Under normal conditions, Zn released from the synaptic vesicles modulates both ionotropic and metabotropic post-synaptic receptors. Numerous specific transport mechanisms are required to transport Zn across the cell membrane (Cuajungco and Lees 1997). Deficiency of Zn affects the secretion and activity of serum thymulin, a thymic hormone, which is essential for maturation and differentiation of T helper (Th) cells (Mezzaroba et al. 2019).

Red meat, legumes, soybeans, squash, and flax seeds are rich in Zinc. However, large consumption of red meat can cause other health issues such as heart disease, diabetes, and cancer.

8.5.5 Turmeric Root or Powder

Turmeric is one of the well-known Indian spice which is a rich source of curcumin. Curcumin has high benefits for TBI patients, being an antioxidant and stimulating the production of BDNF. BDNF induces neurogenesis, a process in which new nerve cells are formed and damaged cells are rejuvenated (Bathina and Das 2015; Bath et al. 2012). The mechanism of BDNF in inducing neurogenesis is as follows.

BDNF affects the synaptic and neuronal plasticity via a mechanism in which CREB protein (cyclic AMP response element binding protein) and GAP-43 (growth associated protein 43, also known as Synapsin-I) has vital roles. Synapsin-I belongs to the family of proteins called nerve terminal specific phosphoproteins which inhibits the release of neurotransmitters, elongation of axons and maintaining the synaptic associations. Synapsin-I synthesis and its phosphorylation is controlled by BDNF and hence there will be an increase in the synthesis and release of neurotransmitters (Rossi et al. 2006; Bath et al. 2012).

Similarly, GAP-43 located in the terminal region of axons stimulates the growth of axons and release of neurotransmitters which is helpful in memory and learning. One of the transcription factors in brain, called cAMP response element binding protein (CREB), in association with BDNF regulates the gene expression involved in neuronal resistance. Thus, BDNF has a vital role in neurogenesis (Habtemariam 2018).

The curcumin present in turmeric is essential for synthesis of BDNF, thereby indirectly helps in revitalization of brain cells. Being a spice, turmeric can be added to any type of food. Even if boiled, its properties do not change. Also, turmeric powder increases the immunity of the entire system (Sangiovanni et al. 2017).

8.5.6 *Eggs and Avocados*

One of the important sources of choline (2-hydroxyethyl-trimethyl-ammonium) is eggs. Choline in brain helps to improve the cognitive functions of the brain. It also has many important physiological functions in brain like:

1. Choline is responsible for synthesis of acetyl choline, an essential neurotransmitter in brain.
2. It regulates cholinergic neurotransmission in specific brain regions that are involved in the cognitive behavior.
3. It acts as a precursor for the synthesis of several phospholipids such as phosphatidylcholine (PC), phosphatidylethanolamine (PE), and sphingomyelin (SM). These phospholipids mediate cell signaling, myelin sheath formation, cell division, lipid transport, membrane biogenesis and help in development and functioning of the brain.
4. Choline is an effective methyl group donor. With the help of S-adenosine methyl transferase (SAM), choline transfers methyl group which plays a vital role in nerve rejuvenation, plasticity and development of cognitive skills (Bekdash 2018; English et al. 2009).

Another important component essential for normal brain functioning is oleic acid (OA). It is a monounsaturated fatty acid present in oils, fats, and avocados. Oleic acid is the major component of phospholipids and is present abundantly in myelin. OA is also needed for axonal and dendritic growth, in synapse formation, neuronal

aggregation and also act as a neurotrophic factor. OA reduced nerve cell death by decreasing the toxic effects of lipid peroxidation cycles.

Combining choline and oleic acid helps to boost the neurotransmission and helps in reformation of brain and nerve cells (Canty and Zeisel 1994; Tayebati and Amenta 2013).

8.5.7 Foods to Avoid During Brain Injury

Though many nutrients help in restoring from brain damage, there are some food which should be avoided during brain damage conditions because these foods interfere with the supplements thereby affecting the role of essential components like BDNF, choline hence decreasing the signaling and plasticity of the brain. Also, to break down certain nutrients, the body utilizes vitamins and minerals, like the case of alcohol and caffeine. Hence nutrient deficiency occurs, which leads to decrease in ATP level. As a result, the brain cells starve for energy which alleviates the damage (Selhub 2015). Hence, certain food has to be avoided like:

1. Saturated fats and processed sugar,
2. Alcohol, caffeine,
3. Other drugs,
4. Butter, cream, milk, cheese,
5. Processed meat.

8.6 Role of Exercise During Recovery

Physical exercise, much like the diet is beneficial to the neurons facilitating increase in BDNF levels and decreasing the stress. Specifically, exercise induces axon or dendrite growth and development, maintaining the synaptic structure and for the formation of new neurons (neurogenesis) (Matsuda et al. 2010). There are research studies which indicate continuous exercise helps the brain to be stronger in cognitive point of view. Also, it helps in reducing infarction and induced prophylactic effect on brain damage (Leddy et al. 2016).

In conditions like Parkinson's disease (PD), exercise seems to increase the motor ability of the patients but the time duration, period, and time of exercise is still controversial. One of the most effective forms of exercise for brain damage is cardiovascular exercise. Swimming and treadmill have a visible effect during the recovery process. Along with these activities, running and walking is also found to have effect on nerve regeneration. It also increases neuroplasticity and increases the cellular expression of neurotransmitters. Drastic increase in the coordination of

sensory motor cortex, increases hippocampal volume and spatial memory were observed in animals.

The primary growth factors that mediate the effects of physical exercise on brain are BDNF, VEGF (vascular endothelial derived growth factor), and IGF-1 (insulin-like growth factor-1). These three factors function together to regulate the plasticity, function, and health in the brain, thereby producing functional effects. IGF-1 and BDNF combine together to regulate the cognitive skills and stress relief, while VEGF and IGF-1 combine to stimulate neurogenesis and angiogenesis. During angiogenesis, IGF-1 helps in the increase of VEGF protein level, which in turn is involved in the increase of mitotic activity specific to vascular endothelial cells. This helps in proliferation of blood vessels, capillary tube formation, adhesion, and survival (Cotman et al. 2007).

8.7 Combined Effects of Diet and Exercise

Neuronal plasticity and effective functioning of the brain is enhanced by the combined effects of diet and exercise. Among many nutrients that can improve the brain function, omega-3 fatty acids, saturated fats and polyphenols work well when combined with physical exercise (Gomez-Pinilla 2011).

The effects of DHA are enhanced by exercise; they combine to influence the hippocampal plasticity and stimulate the cognitive function. It is found that DHA is retained on the plasma membrane of the brain cells which in turn enhances the signal transmission. This is due to the fact that the receptors on the plasma membrane for DHA are activated by BDNF, whose secretion is increased by physical strain thereby preserving the DHA on the cell surface. Similarly, flavanoid-rich diet in combination with exercise has been shown to enhance the gene expression that is directly related to plasticity simultaneously, decreasing the negative gene expression causing inflammation and cell death. Also, the energy homeostasis in hypothalamus and hippocampus was boosted up with the combined effects (Gómez-Pinilla et al. 2002; Grande et al. 2010).

It was also found that combination of curcumin and DHA has an enormous effect on the mechanism of neuronal repair in comparison with their individual effects. Energy generating metabolic pathways are directly associated with pathways that govern neuronal plasticity. Thus, the rate of energy generation can influence the learning and behavioral capacity of the brain. Hence, exercise has a direct effect on molecular systems such as IGF-1, AMPK, ubiquitous mitochondrial creatine kinase (uMtCK), UPC-2 (uncoupling protein-2) which are the critical mediators of energy metabolism. Thus, dietary therapy which boosts the energy of the patient, in combination with exercise can help in faster recovery of brain damage (Gomez-Pinilla 2011).

8.8 Conclusion

Brain damage and neurological disorders are not caused by single factors but are the combinations of malfunctioning of various targets. Thus, pharmacological studies are quite complicated and do not provide reliable results. Hence, a multi-targeted treatment methodology is mandatory in this regard. Dietary supplements and exercise influence molecular systems which afford resistance to cell damage, enhance synaptic transmission and increase cognitive skills. In particular, DHA and curcumin are shown to improve the membrane physiology and signal transduction. Certain other supplements like omega-3 fatty acids have the capacity to store energy and in combination with exercise can stimulate restoration of brain function (Yu et al. 2018). An extensive research is needed in this aspect which highlights the application of these concepts to a majority of the population and also that will be able to explain in detail the action of all the components of diet in restoration of brain and nerve functioning after damage. In conclusion, it can be understood that recovery from brain damage can be faster using natural food supplements compared with synthetic drugs and pharmaceutical products.

References

- Aquilani R, Sessarego P, Iadarola P, Barbieri A, Boschi F (2011) Nutrition for brain recovery after ischemic stroke: an added value to rehabilitation. *Nutr Clin Pract* 26(3):339–345
- Arteaga O, Álvarez A, Revuelta M, Santaolalla F, Urtasun A, Hilario E (2017) Role of antioxidants in neonatal hypoxic–ischemic brain injury: new therapeutic approaches. *Int J Mol Sci* 18(2):265
- Avallone R, Vitale G, Bertolotti M (2019) Omega-3 fatty acids and neurodegenerative diseases: new evidence in clinical trials. *Int J Mol Sci* 20(17):4256
- Bath KG, Akins MR, Lee FS (2012) BDNF control of adult SVZ neurogenesis. *Dev Psychobiol* 54(6):578–589
- Bathina S, Das UN (2015) Brain-derived neurotrophic factor and its clinical implications. *Arch Med Sci* 11(6):1164
- Baumgarten HG, Grozdanovic Z (1998) Role of serotonin in obsessive-compulsive disorder. *Br J Psychiatry* 173(S35):13–20
- Bekdash RA (2018) Choline, the brain and neurodegeneration: insights from epigenetics. *Front Biosci* 23:1113–1143
- Bourre JM (2004) Roles of unsaturated fatty acids (especially omega-3 fatty acids) in the brain at various ages and during ageing. *J Nutr* 8:163–174
- Canty DJ, Zeisel SH (1994) Lecithin and choline in human health and disease. *Nutr Rev* 52(10):327–339
- Choi BH (1993) Oxygen, antioxidants and brain dysfunction. *Yonsei Med J* 34(1):1–10
- Cotman CW, Berchtold NC, Christie LA (2007) Exercise builds brain health: key roles of growth factor cascades and inflammation. *Trends Neurosci* 30(9):464–472
- Cuajungco MP, Lees GJ (1997) Zinc metabolism in the brain: relevance to human neurodegenerative disorders. *Neurobiol Dis* 4(3–4):137–169
- Dimond SJ (2013) *Neuropsychology: a textbook of systems and psychological functions of the human brain*. Butterworth-Heinemann
- Dyall SC (2015) Long-chain omega-3 fatty acids and the brain: a review of the independent and shared effects of EPA, DPA and DHA. *Front Aging Neurosci* 7:52

- Elmorsy E, Al-Ghafari A, Almutairi FM, Aggour AM, Carter WG (2017) Antidepressants are cytotoxic to rat primary blood brain barrier endothelial cells at high therapeutic concentrations. *Toxicol In Vitro* 44:154–163
- English BA, Hahn MK, Gizer IR, Mazci-Robison M, Steele A, Kurnik DM, Stein MA, Waldman ID, Blakely RD (2009) Choline transporter gene variation is associated with attention-deficit hyperactivity disorder. *J Neurodev Disord* 1(4):252–263
- Giljajar J (2000) Traumatic brain injury. *Lancet* 356(9233):923–929
- Gomez-Pinilla F (2011) The combined effects of exercise and foods in preventing neurological and cognitive disorders. *Prev Med* 52:S75–S80
- Gomez-Pinilla F, Kostenkova K (2008) The influence of diet and physical activity on brain repair and neurosurgical outcome. *Surg Neurol* 70(4):333
- Gómez-Pinilla F, Ying Z, Roy RR, Molteni R, Edgerton VR (2002) Voluntary exercise induces a BDNF-mediated mechanism that promotes neuroplasticity. *J Neurophysiol* 88(5):2187–2195
- Grande I, Fries GR, Kunz M, Kapczinski F (2010) The role of BDNF as a mediator of neuroplasticity in bipolar disorder. *Psychiatry Investig* 7(4):243
- Greenwald BD, Burnett DM, Miller MA (2003) Congenital and acquired brain injury. 1. Brain injury: epidemiology and pathophysiology. *Arch Phys Med Rehabil* 84(3 Suppl 1):S3–S7
- Habtemariam S (2018) The brain-derived neurotrophic factor in neuronal plasticity and neuroregeneration: new pharmacological concepts for old and new drugs. *Neural Regen Res* 13(6):983
- Hasan S, Bilal N, Naqvi S, Ashraf GM, Suhail N, Sharma S, Banu N (2011) Multivitamin–mineral and vitamins (E+ C) supplementation modulate chronic unpredictable stress-induced oxidative damage in brain and heart of mice. *Biol Trace Elem Res* 142(3):589–597
- Healy-Stoffel M, Levant B (2018) N-3 (Omega-3) fatty acids: effects on brain dopamine systems and potential role in the etiology and treatment of neuropsychiatric disorders. *CNS Neurol Disord Drug Targets* 17(3):216–232
- Jenike MA (2001) An update on obsessive-compulsive disorder. *Bull Menninger Clin* 65(1: Special issue):4–25
- Leckman JF, Grice DE, Boardman J, Zhang H, Vitale A, Bondi C, Alsobrook J, Peterson BS, Cohen DJ, Rasmussen SA, Goodman WK (1997) Symptoms of obsessive-compulsive disorder. *Am J Psychiatr* 154(7):911–917
- Leddy J, Hinds A, Sirica D, Willer B (2016) The role of controlled exercise in concussion management. *PM&R* 8(3):S91–S100
- Lishman WA (1968) Brain damage in relation to psychiatric disability after head injury. *Br J Psychiatry* 114(509):373–410
- Matsuda F, Sakakima H, Yoshida Y (2010) The effects of early exercise on brain damage and recovery after focal cerebral infarction in rats. *Acta Physiol* 201(2):275–287
- Medina JM, Taberero A (2002) Astrocyte-synthesized oleic acid behaves as a neurotrophic factor for neurons. *J Physiol Paris* 96(3–4):265–271
- Mezzaroba L, Alfieri DF, Simão ANC, Reiche EMV (2019) The role of zinc, copper, manganese and iron in neurodegenerative diseases. *Neurotoxicology* 74:230–241
- Obsessive Compulsive Cognitions Working Group (1997) Cognitive assessment of obsessive-compulsive disorder. *Behav Res Ther* 35(7):667–681
- Pillsbury L, Oria M, Erdman J (eds) (2011) Nutrition and traumatic brain injury: improving acute and subacute health outcomes in military personnel. National Academies Press, Washington, DC
- Rossi C, Angelucci A, Costantin L, Braschi C, Mazzantini M, Babbini F, Fabbri ME, Tessarollo L, Maffei L, Berardi N, Caleo M (2006) Brain-derived neurotrophic factor (BDNF) is required for the enhancement of hippocampal neurogenesis following environmental enrichment. *Eur J Neurosci* 24(7):1850–1856

- Sangiovanni E, Brivio P, Dell'Agli M, Calabrese F (2017) Botanicals as modulators of neuroplasticity: focus on BDNF. *Neural Plast* 2017
- Schulman JL (1965) Brain damage and behavior, a clinical-experimental study
- Selhub E (2015) Nutritional psychiatry: your brain on food. *Harvard Health Blog* 16(11):2015
- Shadman J, Sadeghian N, Moradi A, Bohllooli S, Panahpour H (2019) Magnesium sulfate protects blood-brain barrier integrity and reduces brain edema after acute ischemic stroke in rats. *Metab Brain Dis* 34(4):1221–1229
- Song J, Kim YS, Lee DH, Lee SH, Park HJ, Lee D, Kim H (2019) Neuroprotective effects of oleic acid in rodent models of cerebral ischaemia. *Sci Rep* 9(1):1–13
- Soo C, Tate RL (2007) Psychological treatment for anxiety in people with traumatic brain injury. *Cochrane Database Syst Rev* 3
- Spector R, Johanson CE (2007) Vitamin transport and homeostasis in mammalian brain: focus on vitamins B and E. *J Neurochem* 103(2):425–438
- Tayebati SK, Amenta F (2013) Choline-containing phospholipids: relevance to brain functional pathways. *Clin Chem Lab Med* 51(3):513–521
- Toker OS, Konar N, Palabiyik I, Pirouzian HR, Oba S, Polat DG, Poyrazoglu ES, Sagdic O (2018) Formulation of dark chocolate as a carrier to deliver eicosapentaenoic and docosahexaenoic acids: effects on product quality. *Food Chem* 254:224–231
- Van Dijk TA (2008) Discourse and power. Macmillan International Higher Education
- Williams WH, Evans JJ, Fleminger S (2003) Neurorehabilitation and cognitive-behaviour therapy of anxiety disorders after brain injury: an overview and a case illustration of obsessive-compulsive disorder. *Neuropsychol Rehabil* 13(1–2):133–148
- Woodward JA, Bisbee CT, Bennett JE (1984) MMPI correlates of relatively localized brain damage. *J Clin Psychol* 40(4):961–969
- Yu J, Zhu H, Taheri S, Mondy W, Perry S, Kindy MS (2018) Impact of nutrition on inflammation, tauopathy, and behavioral outcomes from chronic traumatic encephalopathy. *J Neuroinflammation* 15(1):1–16
- Zafonte RD, Cullen N, Lexell J (2002) Serotonin agents in the treatment of acquired brain injury. *J Head Trauma Rehabil* 17(4):322–334
- Zheltova AA, Kharitonova MV, Iezhitsa IN, Spasov AA (2016) Magnesium deficiency and oxidative stress: an update. *Biomedicine* 6(4):1–7

Editors

Senthilkumar Rajagopal 
Department of Biotechnology, School of
Applied Science
REVA University
Bengaluru, Karnataka, India

Saravanan Ramachandran
Faculty of Allied Health Sciences
Chettinad Academy of Research and Education
Kelambakkam, Tamil Nadu, India

Geethalakshmi Sundararaman
Department of Biotechnology
Sree Narayana Guru College
Coimbatore, Tamil Nadu, India

Swarnalatha Gadde Venkata
Department of Biochemistry
Rayalaseema University
Kurnool, Andhra Pradesh, India

ISSN 2730-6712

ISSN 2730-6720 (electronic)

Nutritional Neurosciences

ISBN 978-981-16-8157-8

ISBN 978-981-16-8158-5 (eBook)

<https://doi.org/10.1007/978-981-16-8158-5>

© The Editor(s) (if applicable) and The Author(s), under exclusive licence to Springer Nature Singapore Pte Ltd. 2022

This work is subject to copyright. All rights are solely and exclusively licensed by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, expressed or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

This Springer imprint is published by the registered company Springer Nature Singapore Pte Ltd.
The registered company address is: 152 Beach Road, #21-01/04 Gateway East, Singapore 189721, Singapore