Beneficial Effects of Omega-3 Fatty Acid on Neurological Disorder and Macular Degeneration

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Abstract:

Omega-3 polyunsaturated fatty acids are essential nutrients as their advantageous effects in coronary and autoimmune diseases, as well as in diabetes, have been proven from literature. In addition, their role in maintaining normal physiology of the eyes has been extensively discussed. We will explain the important dietary sources, features, properties, metabolism, and bioavailability of omega-3 PUFAs and their effects on Autism, Alzheimer's, Huntington, Parkinson's, Attention Deficit Hyperactivity Disorder, Dementia, Depression and Visual Health in this review. Omega-3 polyunsaturated fatty acids and their mediators regulate several processes within the brain such as cell survival, neurotransmission, neuro-inflammation, mood and cognition. The diet having Omega-3 polyunsaturated fatty acids may contribute to new therapeutic conceptualization for the prevention and management of neurological disorders.

Key words:

Omega 3 fatty acids, Autism, EPA, DHA, Dementia, Alziemer, Parkinson's, Macular Degeneration

Introduction:

Omega-3 fatty acid are also known as the essential fatty acid for the functioning and growth development of brain. Omega-3 fatty acid is fused into cell layers. They are discharged from layer phospholipids and comprise substrates for eicosanoid combination, i.e. prostaglandins, prostacyclins, thromboxanes and leukotrienes. Omega-3 is polyunsaturated, has two or more double bound in chemical structure. It includes 2 major components; Dicosahexaenoic acid (DHA) and

Eicosapentaenoic acid(EPA).² EPA is 20 carbons long, with 5 double bonds. Forming Signaling is the main function called eicosanoids, which play many physiological roles.³ DHA is along chain of 22 carbons with 6 double bonds and essential component of skin, retina in the eye and leads to improve vision. DHA is important for functioning and development of brain and other mental disorders.⁴

Omega 3 fatty acids (DHA and EPA) revealed to be effective and beneficial for many diseases. They play an imperativepart in prevention and as well as the treatment of neurological disorders (such as Depression, ADHD, Autism, Alziemer and Parkinson's) and Macular degeneration. It helps to recover the mental illness through the sufficient intake. ^{5,6}

Risk factors of neurological disorder and Macular degeneration have been elucidated as genetic factors and environmental factors. Potential of environmental factor is more which includes modern lifestyle.⁷

The Dietary Guidelines and American Dietetic Association supports that one should take nutrients from food consumption as a prevention rather than having supplements or fortified food to meet suggested DHA and EPA levels from their regular diet customers who are looking for alternative sources should know the products contain ALA, EPA or DHA in order to receive full health benefits. For adults to prevent the deficiency of omega-3, minimal daily intake recommended is 0.35 to 0.40 g/day which is 0.5 percent of the total intake of fat. Whereas, EPA and DHA range is 0.25 and 2 g/day. 8

Several millions of individuals worldwide are influenced by neurological disorders. Due to Stroke every year above 6 million individual die;

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80% out of these deaths are from low and middle income countries. Above 50 million people are suffering from Epilepsy worldwide. Approximately 47.5 million individuals are of Dementia with 7.7 million fresh cases every year, and Dementia common cause is Alzheimer's disease which contributes to 60–70% of cases. Prevalence of migraine is more than 10% worldwide. Schizophrenia is chronic and more than 21 million people worldwide are affected from severe mental disorder. 10 1 in 160 children has an autism spectrum disorder (ASD). 11

According to the estimate that around 1.3 billon people suffers from vision impairment i.e, distance or near vision impairment. As for distance vision 188.5 million suffers mild impairment, 217 million suffer moderate to severe impairment and 36 millon are blind. Whereas for near distance, 826 million people are suffering.¹²

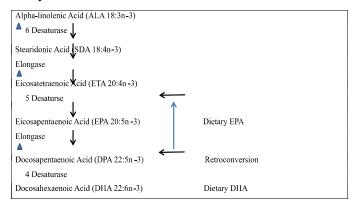
Green leaves are not good source of fats but have a significant amount of alpha linolenic acid. Significant proportion of alpha linolenic acid is also present in some nuts, seeds and seed oil. Flaxseeds oil has 45 to 55% and soybean oil have 5 to 10 percent of alpha linolenic acid. Some other such as Rapeseed oil, Corn oil, Walnuts, safflower oil and Sunflower oil have α -linolenic acid but in little amount. α -linolenic acid but in little amount.

Fish is considered a good source of omega 3 fatty acid. Ratio of fatty acid depends upon different types of fish i.e. cod can provide 0.3g of EPA and DHA where as salmon provide 1.5g or more. Marine fish predators are the richest food sources of DHA and EPA. There are many other types of sources such as Mackerel (4107 mg per serving), Salmon(per serving 4023 mg), Herring(per serving 3181 mg), Oysters (per serving 565 mg), Sardines (per serving 2205 mg) Anchovies (per Serving 951 mg), Caviar (per serving 1086 mg), Flaxseeds (per serving 2338 mg), Chia Seeds (per serving 4915 mg), Walnuts (per serving 2542 mg) and Soybeans (per serving 1241 mg).

Aim of the study was to review the existing literature on the importance of consumption of omega-3 FAs in our diet according to daily requirement to prevent mental disorders, macular degeneration and for proper functioning and development of brain.

Mechanism of Omega-3 Fatty Acids in the body: Alpha-linolenic acid being the simplest fatty acid (n-3) comes from linoleic acid through desaturation, catalyzed by $\Delta 15$ -desaturase. The process of synthesization takes place in the liver along with elongation and desaturation. $\Delta 6$ desaturase alpha-Linolenic acid convert's to stearidonic acid which is then converted to eicosatetraenoic acid Δ5-desaturase makes Ecosapentanoic acid. Same enzymes convert Alpha-linolenic acid into Ecosapentanoic and linoleic acid to arachidonic acid. Further conversion of Ecosapentanoic via Docosapentaenoic to Docosahexaenoic is possible. Δ6-Desaturase participation ensures partial Beta-oxidation. Conversion of Alpha-Linolenic acid into Ecosapentanoic, Docosapentaenoic, and Docosahexaenoic proves that this alteration is poor where DHA seems to be especially limited as an end product. Stearidonic acid is converted to Ecosapentanoic is superior to that of α -linolenic acid, probably due to conversion of stearidonic acid does not need the activity of the rate-limiting $\Delta 6$ desaturase enzyme. Limited peroxisomal βoxidation of Docosahexaenoic can generate Ecosapentanoicand Docosapentaenoic, a process termed retro-conversion. Ecosapentanoic, Docosapentaenoic, and Docosahexaenoic are often collectively referred to as very long-chain (n-3) PUFA.¹⁸

Fig 1;- Metabolic Pathway of Dietary Omega-3 Fatty Acid



Autism:

In 2014, a study was conducted in which they discuss importance of omega 3 fatty acid in our regular diet. It plays a very important function in our body and lack of fatty acid in body may cause many diseases which also include many brain related disease and one of them is known as Autism.¹⁹ Autism spectrum disease is a brain related disease in which a person is unable to develop proper communications skills or thinking skills like a normal person and this disease usually happens in children and adults.²⁰ This disease can be inherited or it may be caused due to any unknown environmental factor.21 Study conducted in 2014 in United States which showed that autism effects one in sixty eight children.22

In 2015 a study was conducted to check the efficacy of omega 3 fatty acid among children suffering from Autism Spectrum Disorder. That was based on twelve weeks supplementation between age group of 7 to 18 years old children with ASD was taken as a sample. Majority was of boys (36 boys and 5 girls). Result was positive on all scales of social and attention problems. Significant improvements were showed without causing any other side effect.²³

In 2015, a comparison study was conducted by Sarah A. Brigandi between two groups, autistic patients and non-autistic to check the level of omega 3 fatty acid compositions of red blood cells. To compare the fatty acid content, 121 autistic and 110 non-autistic participants were selected aged between three to seventeen years. Result of analysis of participants showed lower level of omega-3 fatty acid component; DHA in autistic group as compared to other group. Study demonstrated the importance of balanced level of Omega-3 fatty acid in autism patients.²⁴

A randomized trial was conducted in 2018 by Hajar Mazahery that indicated omega-3 reduces irritability and hypertension in children suffering from Autism Spectrum Disorder. Randomised children of ASD in New Zealand aged 2.5 to 8 years were given 722mg per day of DHA; major component of omega-3 fatty acid for

12 month. Out of 111 children who completed the data collection, sixty six percent showed positive outcome of reduction in irritability and Hypertensive symptoms in children with ASD.²⁵ In 2014, an internet based trail was conducted to check the efficacy of evidence that suggested omega-3 fatty acid play an important role in children suffering from Autism Spectrum Disorder for hypertension reduction. Designed interventions sent by e-mail to parents of Patients (children suffering from autism) aged five to eight years. Targeted 28 states, 57 participants were given 1.3 grams of omega fatty acid for 6 weeks obtained outcomes were positive all 57 children had reduction in hypertension.²⁶

Attention Deficit/Hyperactivity Disorder (ADHD)

In 2016, an experimental study was held among school children of age between 9-10 years. Some randomized participants were given omega-3 capsule twice a day and other were treated with other medicines for three months. Out of 154 children, 122 completed three months trail and among these participants children with ADHD showed beneficial improvement in reading ability specifically visual analysis and phonologic decoding.²⁷

In 2014, a study conducted among 95 children age between 6-12 years diagnosed with ADHD. Supplements of omega 3 fatty acid (EPA and DHA) were given to them under the supervision of their parents, teachers and investigators. By using questionnaire their behavior was assessed. Out of 95, 81 participants were examined before and after the trial improvement was shown in memory functioning and in other measures of attentions.²⁸

A study was conducted in 2016 by Ken Yonezawa. Aim of the study was to treat ADHD through daily intake instead of medicines. 28 ADHD patients between age nine to eighteen were selected to investigate. From their medical reports of poly unsaturated fatty acid level of EPA, DHA, AA and other drug treatments were investigated that showed lower level of both

EPA and DHA and higher level of AA classified as omega. ADHD can be improved with the balance of omega-3 and omega-6.²⁹

A study was held in 2013 to investigate the difference of omega-3 fatty acid plasma level between two groups of ADHD children and non-ADHD children whereas ADHD participants were 31 and non-ADHD participants were 32. By the comparison of their plasma omega-3 level result, it was observed that children with ADHD had lower level of omega-3 instead of non-ADHD children.³⁰

In 2014, two analysis based studies were conducted by Elizabeth. Study 1 overviewed 9 previous studies related examination of blood levels of omega 3 in ADHD patients and observed 586 individuals had lower level of omega-3 in ADHD patients. Study 2 overviewed 16 studies to find result of omega-3 supplements on patient with ADHD and it was observed that 1408 individuals showed improvement in symptoms of ADHD. It was evident from both studies that omega-3 fatty acid showed beneficial effects in ADHD patients.³¹

Alzheimer's Disease:

Main reason of dementia and most occurring neurodegenerative disease in old age is Alzeimer.³² In 2013, an interventional study was conducted in old adults to assess the intake of seafood or fish oil sources of omega 3 aged between 50 to75 years. 65 individuals with healthy mental state were selected for the experiment, 30 were female individuals. Experiment continued for 26 weeks. Individuals were kept on either seafood or fish oil. Result showed positive impacts as working of brain were improved than before.³³

A study was held in 2015 which stated that higher intake of fish will decrease the risk of Alzheimer's disease. Results were identified by overview of relevant studies that compared the intake of omega 3 fatty acids with the consumption of fish. After a couple of tests they concluded that by adding 100 grams of fish in diet per week can lower the risks of Alzheimer's disease to 11%.³⁴

A study was conducted in 2016 by Kulzow Nadine. Aim of study was to introduce strategies to prevent Alzheimer's Disease through omega-3 supplementation. 44 participants were selected for the experiment aged between 50 to 75 years. 20 were female individuals. Supplements were given on daily basis for 26 weeks. Memory performance of individuals were tested before and after the intervention. Outcome showed positive result and strategy suggested to maintain cognitive functions in older age.³⁵

In 2016, a study was done to check the relationship of omega 3 fatty acids and chances of mental degeneration in older age. Six studies were reviewed that were continued for three to forty month. The portion of omega 3 fatty acid was kept in between 400-1800mg. Result of analysis showed that omega 3 fatty acids lowers mental degeneration and helps in avoiding mental degeneration in old age.³⁶

A study was conducted in 2016 based on the management of Alzheimer's disease. Review of different interventional studies on fish oil and important role in prevention of Alzheimer's disease was discussed. Fish oil contained both EPA and DHA. According to reviews of previous studies, both can reduce symptoms of Alzheimer's disease such as dementia, mood disorders and maintain brain functions.³⁷

Parkinson's Disease:

A disease in which the nervous system and specially the neurons in the brain degenerate. It is caused by many factors that are environmental and genetic, both.³⁸

In 2018 Ibrahim NA and his fellows evaluated the preventive and curative effect of omega-3fatty acid on motor damage and mental biochemical disturbances in mice model to which Parkinson's disease was caused by rotenone. They divided 60 mice in 6 groups containing 10 each. 1st group of mice were used as controls. They were injected under the skin with the (fifty μ l dimethylsulfoxide + 950 μ l sunflower oil per kg body weight for 30 days. The 2nd group of mice were injected with rotenone three mg/kg for thirty days. The 3rd

group of mice were given rotenone for thirty days. The fourth protection group mice were given omega-3 oil 300 mg/kg daily by mouth an hour before every rotenone injection for thirty days. In the fifth and sixth groups, therapeutic groups, mice were given Omega-3 oil everyday by mouth for seven and fifteen days after the promotion of Parkinson disease mice model. Hence, it was concluded that omega-3 fatty acid consumption potentially reverses motor and neurochemical changes caused by rotenone.³⁹

In 2015, K. M. Denny Joseph and his fellow led a research to see outcome of fish oil and quercitin supplements to patients with Parkinson's disease orally. Fish oil contains omega 3 fatty acids which are already recognized for regulating the nervous system. The experimental study was done on male rats which were given either fish oil or quercitin or both for twenty eight days. It was found that the combination of both, fish oil and quercitin showed a higher degree of protection from neurodegeneration. Hence, it was concluded that supplementation of fish oil with any antioxidant provides increased protection from neurodegenerative diseases such as Parkinson's disease.⁴⁰

In 2018, Paula Perez-Pardo and his collegues led a research to study the role of diet containing uridine and fish oil that has decosahexanoic acid on Parkinson's disease. Dietary changes were made in rats and after 1 week, Parkinson's disease was induced in them by giving rotenone orally or through injections. It was found that dietary changes like uridine and decosahexanoic acid played a role in preventing from motor and non motor symptoms of Parkinson's disease. 41

Schizophrenia:

Schizophrenia is a long-lasting psychiatric condition with a genetic and neurobiological experience that effects initial brain development, and is a amalgamation of psychotic indicators such as hallucinations, delusions and disorganization and motivational and cognitive dysfunctions.⁴²

In 2014, Hamidreza Jamilian and his collegues led a study to see the result of Omega 3

supplements as an addition in treating Schizophrenia. Sixty patients of Schizophrenia were separated in two groups. One group was given Omega 3 fatty acid supplements along with tranquilizers for eight weeks whereas the other group was not given any omega 3 supplements. As a result, it was founded that Omega 3 supplements may increase the effect of old tranquilizers that are used to reduce the mental symptoms of schezopherania.⁴³

In 2015, G Paul Amminger with his fellows studied the long term outcome by Omega 3 fatty acids on Schizophrenia. Schizophrenic sufferers were kept under observation for 6.7 years. It was concluded that most of the patients who were given Omega 3 supplements did not suffer from any functional defects and reduced mental symptoms at following check ups. 44

In 2015, Pawełczyk T and his peers investigated the effect of thirteen hundred and twenty milligram per day Ecosapentanoic acid and eighty eight milligram per day Decosahexanoic acid or Olive oil on eighty two schizophrenic patients aged between sixteen and thirty five for twenty six weeks. The patients were randomly allocated to these interventions. Later, it was concluded that it improved the mental health of those schizophrenic patients.⁴⁵

In 2016, Messamore E with his fellows studied outcome of treating Omega 3 fatty acid deficiency in mental disorders including Schizophrenia. The blood samples of one hundred and thirty patients were analyzed and it was concluded that treatment of such patients with products that have fish oil in it led to improvements in mental symptoms and the side effects of it were not even noticeable. 46

Huntington Disease:

It is shattering to patients and their families with autosomal inheritance, starts usually in the adult life and consists of combination of motor, cognitive and behavior features. The Huntington's infection is an innate neurological confusion in which oxidative pressure initiated by free radicals is a critical harm. Essential unsaturated fats importantly affect oxidative

stress.47

In 2017 Morales A and et al investigated if olive oiland fish oil rich food inhibited oxidative harm in mice. Mice were nourished with olive oil and fish oil diet for twenty days. Results revealed that fish oil reduced rotating behavior and prevented oxidative harm in striatal tissue.⁴⁸

In 2018 Htami A and et al investigated the result of polyunsaturated fatty acid treatment in a thump in mouse model of Huntington disease which consisted of motor impairment, neuropathology and cognitive decline. Mice were given a diet having either deuterated polyunsaturated fatty acids or hydrogenated polyunsaturated fatty acids for five months starting at the age of 1 month. Deuterated polyunsaturated fatty acids management significantly performance improved In novel object recognition tests.⁴⁹

Depression:

In 2014, an investigation was conducted to conclude the relationship between the intake of omega 3 fatty acids and depression. More than 6000 people in different regions of the world participated in the trial and every region had different set of results according to the epidemics of their region. The results indicated that the lifestyle of the participants had a direct relation with the results. Recurring episodes of depression lessened for high omega 3 and omega 6 consumers then low consumers of omega 3 and 6.50

A study in 2014 was conducted in which metaanalysis was performed on people with different clinical symptoms of depression but with the same Omega 3 fatty acid treatment. RCT's were done in order to compile the meta-analysis. Treatment in addition to the primary treatment was given to the participants to reach the ultimate goal. EPA, DHA and omega 3 as mono were used as well. EMBASE, MEDLINE and PsychInfo was performed in the study. The conclusion supported positive effects of Omega 3 on depression patients with major depression disorders as well as on patients without it.⁵¹

A latest study in 2017 compiled all the trial

studies that took place between 1980-2014 relating to the affinity of Omega 3 with depression. RCT's were performed in order to eliminate the discrepant findings and to adhere to a more solid result. A total of 11,000 participants were taken for the study with more than 60% on the RCT and less than 40% on placebo. EPA formulations affected more than 50% of the study showing its dominance over DHA which was even less than 40%. ⁵²

Amyotrophic Lateral Sclerosis:

A study in 2014 was especially designed to study the association between -3 intake & the progression of ALS. Panel Analysis based on more than 1 million participants (47% women and 52% men) with the cohort study reaching up-to 5 in number prospectively. Each cohort study was examined on the base of food frequency surveys with different clinical settings. Modifications were made in each cohort.

Participants were categorized on the bases of the nutrient energy intake and dietary intake. The results showed low death rate and high ALS prevention rate in direct relation to omega 3 fatty acids intake.⁵³

In 2017, a controlled trial with DHA of -3 as the star against the progression of ALS was performed. Oral treatment was given to the patients in the experimental group of 14. 1g of DHA daily for the experimental group. The other group was given 1gram of olive instead (the placebo group). This continued to a 1 year trial with blood samples taken at the end of every 3 months from each group to measure the fat level. Weight loss pre-diagnosis, Forced Vital Capacity (FVC) and ALS Functional Rate Scale (ALSFRS) as clinical strictures were observed and recorded. The fat level didn't have the expected change which led to the conclusion that the disease was evolving and that larger quantities of dosage was required to have a proper conducive result.54

A recent study in 2017 concluded that omega 3 fatty acids delayed onset of ALS for a short time but if only used moderately. It can only sustain

minor motor neuron functions. This happens when people retort to self-omega 3 treatment with no proper dosage. The effect of omega-3 and omega 6, on motor neuron work in rats articulating mutant human superoxide dismutase 1 which predominantly gives familial ALS and instigates a comparative grouping of motor neuron decay and possible passing when articulated in mice. Mice got standard eating regimens enhanced with proportionate measures of omega 3 and omega 6 or a 10 times increment in omega 6 with no change in omega 3 initiating at about a month of age. Motor neuron function and biochemical/histological parameters were examined by standard strictures.55

Macular Degeneration:

In 2014 Merle BM studied about omega 3 fatty acids and macular degeneration. The examination evaluated the relationship of red blood cell membranes, serum and dietary long chain with macular deficiency. The study involved 290 patients of the age related macular deficiency in one eye and early age related macular degeneration lesions in the other eye, and 144 normal vision controls without age related macular degeneration. Intake of oily fish,

seafood were significantly lower in macular degeneration patients than in controls. Confirmation from animal models and human studies suggested that there was an inverse association between omega 3 long-chain polyunsaturated fatty acids and age-related macular degeneration.⁵⁶ In 2013, Bharghva et al., studied the outcome of omega 3 fatty acids on dry eye syndrome. Two eye centers were choose from which 264 patients with dry eye were given 1 dose of omega-3 500mg two times each day and 175mg DHA for 3 months. The omega-3 group was contrasted with a group of patients who got a placebo.65% of patients in 1st group and 33% of patients in other group had improvement in 3 months. There were outstanding changes in the two groups. Subsequently, it was inferred that Omega-3 unsaturated fats have a particular role in dry eye disorder.⁵⁷ In 2014 Georgiou T et al., conducted studies in patients with dry age related macular degeneration using high amount of omega 3 fatty acids that is 3.4 g of eicosapentaenoic acid and 1.6 g of decosahexanoic acid for 6 months regularly. After omega-3 supplementation momentous improvement in patients with dry AMD within four and half months was observed.⁵⁸

Intervention element	No of subjects	Duration of intervention	Effect of intervention	Reference
Omega 3 fatty acids supplementation	41 children and adolescents diagnosed with Autism Spectrum Disorder age between 7–18 years (5 girls, 36 boys)		Significant improvement in Autism patients	Ooi YP et al., (2015) ²²
Decosahexanoic acid supplementation = 722mg per day Vitamin D=2000IU/ day	Children from 2.5 to 8 years diagnosed with Autism Spectrum	12 months	Vitamin D and Omega 3 fatty acids intake reduced irritability symptoms in children with ASD	Mazahery H et al., (2018) ²⁴

omega-3 fatty acid (EPA and DHA) Supplements.	95 children diagnosed ADHD aged 6 to 12 years	16 weeks	ADHD was improved by increased DHA, EPA and decreased arachidonic acid.	Widenhorn- Müller K <i>et al.,</i> (2014) ²⁸
omega-3 supplementation =2,200mg/day	44 participants aged between 50 to 75 years. 20 were female	26 weeks	Outcome showed positive result and strategy in	Külzow N et al., (2016) ³⁵
Fish oil (2 mL/kg bw) or Quercetin (25 mg/kg bw)	Rotenone model of neurotoxicity in rats diagnosed with Parkinson's disease	28 days	Fish oil with any antioxidant provides increased protection from Parkinson's disease	Joseph KD, (2015) ⁴⁰
omega-3 (1000 mg/day)	60 patients diagnosed with documented schizophrenia	8 weeks	Reduced the mental symptoms of schezopherania	Jamilian H <i>et al.,</i> (2014) ⁴³
Fish and oil rich diet 15% QUIN (240nmol/µl)	Rats diagnosed with Huntington Disease	20 days	Reduced rotating behavior and prevented oxidative harm in striatal tissue	Morales-Martínez A <i>et al.,</i> (2017) ⁴⁸
omega-3= 500mg two times a day DHA=175mg / day	264 patients diagnosed with dry eye syndrome	3 months	Omega 3 fatty acids have played a specific part in improving dry eye syndrome	Bhargava R et al., (2013) ⁵⁷
Eicosapentaenoic acid=3.4g Decosahexanoic acid=1.6g daily	Patients with dry AMD	6 months	omega-3 supplementatio n momentous improvement in patients with	Georgiou T <i>et al.,</i> (2014) ⁵⁸
Intake of omega-3 LC-PUFAs (0.11% of total Energy or 240mg of (EPA+DHA)	1837 people aged 55-80 years	who were enrolled in the 12 year	AMD is reduced by increased intake of omega-3 LC- PUFAs	Jooste M <i>et al.,</i> (2016) ⁵⁹

Conclusions:

Omega 3 Fatty Acid plays a dynamic role in prevention and management of neurological disorders such as Autism, ADHD, Alzheimer's disease, Schezophrenia, Parkinson's disease, Hutington's Disease, Depression, Amyotrophic Lateral Sclerosis and Macular Degeneration. The positive affect of Omega 3 fatty Acid on neurological disorders and macular degeneration is proven by many clinical trials and analysis based studies. In the light of such examinations, the capability of utilizing omega 3 unsaturated fats in the treatment of neurological issue and macular degeneration is high and it ought to be additionally researched, particularly as far as progressively clinical preliminaries with larger sample sizes.

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