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1

REVIEW ARTICLE **OPEN ACCESS**

Lipoprotein Lipase and Neurological Health: Investigating its Impact on Brain Function and Alzheimer's Disease

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Abstract:
Lipoprotein Lipase (LPL) is an essential lipid metabolism enzyme affecting both the brain and peripheral tissues. Its impact on neuronal lipid homeostasis, synaptic function, and plasticity is increasingly recognized. This review explores the various functions of LPL in the brain and how it may affect neurological health, especially in Alzheimer's disease. We explore how LPL regulates lipid uptake and utilization in the brain, its influence on synaptic function, neurogenesis, and myelination, and its role in the pathophysiology of AD. Genetic and environmental factors modulating LPL activity are also discussed. The review provides insights into LPL's role in neurodegenerative diseases, acknowledges current limitations and challenges in research, and highlights the therapeutic potential of targeting LPL for AD treatment. Ultimately, this review underscores the importance of LPL in maintaining brain health and its promising potential as a therapeutic target for AD.

Keywords: Lipoprotein lipase, Lipid metabolism, Alzheimer's disease, Neuronal lipid homeostasis, Therapeutic potential, Pathophysiology.

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1. INTRODUCTION

An essential enzyme in the body's fat-processing machinery is Lipoprotein Lipase (LPL), which was first identified for its enzymatic activity in 1943 by Paul Hahn [1]. It plays a vital role in breaking down Triglycerides (TGs) in the bloodstream into Free Fatty Acids (FFAs) and glycerol. These lipoproteins include Chylomicrons (CMs) and Very Low-density Lipoproteins (VLDLs), which transport dietary and liver-synthesized triglycerides, respectively [1]. Skeletal, cardiac, and adipose tissue, as well as the heart, are among the tissues that produce LPL. It is then transferred to the luminal surface of the endothelial cells that line the capillaries. Here, it binds to the proteoglycans Heparan Sulfate (HS), allowing the enzyme to reach and break down triglycerides [2]. In addition to supplying tissues with fatty acids for energy synthesis, storage, or other metabolic processes, this process is essential for removing lipoproteins high in triglycerides from the bloodstream, which preserves lipid homeostasis and prevents diseases, like Hyper-triglyceridemia (HTG), a risk factor for cardiovascular disorders [3].

Over the decades, research has expanded to reveal that LPL's function is not limited to lipid metabolism, and it is also regulated by several physiological factors, including hormonal signals, like Insulin (INS), which enhances LPL activity in adipose tissue to promote fat storage postprandially, and other proteins, such as Apolipoprotein (Apo) and Angiopoietin-like Proteins (ANGPTLs) [4]. Genetic mutations or deficiencies in LPL or its regulators can lead to metabolic disorders, like Familial Chylomicronemia Syndrome (FCS), characterized by severe hypertriglyceridemia and recurrent pancreatitis [5].

In recent years, research has uncovered the crucial role of LPL in neurological health. LPL helps the brain absorb critical fatty acids and other lipids required for neuronal maintenance and function. The brain depends on lipids for its growth, structure, and function [6]. LPL's role in lipid transport is vital for neurogenesis, synaptic plasticity, and myelin production, the insulating sheath around neurons [7]. Additionally, LPL plays a role in controlling lipid-derived signaling molecules that affect neuroinflammation and neuronal survival, such as eicosanoids and Docosahexaenoic Acid (DHA) [8]. Dysregulation of LPL activity has been linked to various neurological disorders. For example, decreased LPL function in Alzheimer's Disease (AD) can upset the brain's lipid balance, which helps tau tangles and amyloid-beta plaques build up, two of the disease's main characteristics [9]. Similarly, changed LPL activity in Parkinson's Disease (PD) may influence the lipid content of neuronal membranes, affecting dopamine neurotransmission and ultimately resulting in neurodegeneration [10]. LPL also plays a role in cerebrovascular health, with its dysfunction contributing to conditions, such as Ischemic Stroke (IS) by affecting lipid metabolism and inflammation in blood vessels [11].

In conclusion, lipoprotein lipase is a multifaceted enzyme with critical roles in lipid metabolism and neurological health. By regulating the breakdown and distribution of Triglycerides (TGs), LPL maintains lipid homeostasis and provides essential Free Fatty Acids (FFAs) to tissues. Its involvement in the brain's lipid metabolism underscores its importance in maintaining neurological health and protecting against neurodegenerative diseases. Continued research into the functions and regulation of LPL holds promise for advancing our understanding of metabolic and neurological diseases and developing innovative therapeutic strategies.

2. LIPOPROTEIN LIPASE AND BRAIN FUNCTION

Lipoprotein lipase holds significant functional roles in the brain, impacting neuronal lipid homeostasis, synaptic function, and plasticity. Within the brain, LPL is produced and excreted by both neurons and glial cells, functioning at the capillary endothelium to facilitate the absorption of lipoprotein-derived fatty acids crucial for energy metabolism and membrane synthesis [12]. These fatty acids are essential for synthesizing membrane phospholipids, signaling molecules, and myelin sheaths, vital for maintaining neural structure and function [13].

LPL also influences lipid signaling pathways, enhancing the availability of lipids that affect signal transduction and neuronal survival. By interacting with lipoprotein receptors, such as the Low-density Lipoprotein Receptor (LDLR), LPL promotes the internalization of lipoproteins, further contributing to lipid homeostasis and receptor-mediated signaling in neurons [14]. In addition, LPL maintains the balance of membrane composition and fluidity, which is crucial for proper synaptic function [14]. Neurons rely on a stable lipid supply for membrane phospholipids, directly influencing membrane properties and cellular signaling. Furthermore, LPL regulates lipid storage and mobilization within neurons, sustaining lipid reservoirs in the form of lipid droplets that can be utilized during periods of high metabolic demand [15].

In the myelination process, LPL facilitates the provision of necessary lipids for synthesizing myelin sheaths, which are essential for rapid signal transmission along axons [16].

By promoting synaptic vesicle formation and maintaining a sufficient lipid supply for vesicle formation and recycling, LPL plays a critical role in synaptic function and plasticity and is necessary for effective neurotransmitter release [17]. Synaptic vesicles' merging with the presynaptic membrane, influenced by the membrane's lipid content, is necessary to release neurotransmitters. Synaptic plasticity and strength are impacted by this process [18]. Since lipid content affects the quantity and structure of these tiny protrusions on neurons that establish synaptic contacts, which are essential for synaptic plasticity, LPL also impacts dendritic spine morphology [19]. Furthermore, LPL is involved in neurotrophic signaling pathways, such as those mediated by Brain-derived Neurotrophic Factor (BDNF), vital for synaptic plasticity, neuronal survival, and cognitive functions [20].

3. LIPOPROTEIN LIPASE AND ALZHEIMER'S DISEASE

Alzheimer's disease is a multifaceted brain illness that progressively impairs memory, behavior, and cognitive abilities [21]. It is characterized by several hallmark features, including the accumulation of Amyloid-beta (Aβ) peptides, which form plaques that obstruct cell communication and trigger inflammation [22]. These plaques contribute to brain cell damage and death [23]. Moreover, tau protein hyperphosphorylation causes neurofibrillary tangles, which impair neuronal function [24, 25]. The loss of connections between brain cells, known as synaptic dysfunction, is another crucial feature of AD that impairs communication [26]. Prolonged activation of glial cells, including astrocytes and microglia, increases inflammation, deteriorates neuronal injury, and speeds up the course of disease [27]. Oxidative stress, caused by an imbalance between Reactive Oxygen Species (ROS) and antioxidants, contributes significantly to neuronal damage. Additionally, disruptions in lipid metabolism play a pivotal role in AD by affecting cell membrane integrity and energy balance [28].

A key player in managing lipid metabolism within the brain is lipoprotein lipase, essential for maintaining cell membrane health and ensuring an adequate energy supply. LPL is expressed in various brain cells, including macrophages, microglia, and Oligodendrocyte Precursor Cells (OPCs) [29]. Specific genetic variants, such as the S447X variant, are associated with increased LPL activity, reduced levels of harmful lipoproteins, and fewer amyloid plaques [29]. This connection highlights the therapeutic potential of targeting LPL to modify lipid metabolism in AD.

LPL actively participates in Aβ clearance. Research shows that it enhances microglial uptake and degradation of Aβ, reducing plaque accumulation and minimizing neuronal toxicity [30]. Dysregulation or mutations in LPL are linked to increased AD risk and more severe disease progression [29, 31]. The buildup of Aβ plaques correlates with altered LPL levels in the brain, reflecting its critical involvement in disease pathology [32].

Lipid signaling pathways influenced by LPL also affect tau pathology by modulating the formation of neurofibrillary tangles [33]. Inflammation regulation in microglia is another vital function of LPL, where deficiencies can lead to heightened inflammatory responses and neuronal damage [34, 35]. LPL helps manage oxidative stress by balancing lipid metabolism, thereby protecting brain cells from further damage [36].

Interestingly, LPL localizes around amyloid plaques in the brains of AD patients [32]. It regulates High-density Lipoprotein (HDL), cholesterol, and brain lipid levels. Mutations in the LPL gene are strongly associated with increased AD risk and are linked to impaired Aβ clearance and exacerbated tau pathology [37-42].

Emerging studies also highlight LPL's involvement in glial cell function. For instance, LPL enhances astrocyte-mediated uptake of Aβ, aiding in removing toxic plaques [43]. Similarly, LPL supports microglial metabolism by influencing microglia’s switch from oxygen to glucose for ATP production, a process critical for efficient Aβ clearance [44].

Targeting LPL pathways offers promising therapeutic opportunities for AD. Increasing LPL activity or mimicking its effects could help alleviate oxidative stress, reduce inflammation, and enhance Aβ and tau clearance. Potential interventions may include dietary modifications, pharmacological treatments, and gene therapy to optimize lipid metabolism. Further research on LPL-based therapies could significantly advance treatment options for Alzheimer's disease.

4. GENETIC AND ENVIRONMENTAL INFLUENCES

Lipoprotein lipase, a key player in brain function, regulates neuronal lipid homeostasis, synaptic function, and plasticity. The activity of LPL in the brain is modulated by both genetic and environmental factors, and their interplay is crucial for neurological health.

4.1. Genetic Variants Affecting LPL Activity

Genetic variants have a profound impact on LPL activity, influencing lipid metabolism and brain function [45]. Polymorphisms in the LPL gene can lead to altered enzyme activity, affecting lipid uptake and utilization in neurons [46]. For instance, specific variants are associated with reduced LPL activity, leading to impaired fatty acid availability and altered neuronal membrane composition [47]. These genetic differences can contribute to variability in cognitive function and susceptibility to neurological disorders [48]. Research has identified specific Single Nucleotide Polymorphisms (SNPs) in the LPL gene that correlate with conditions, such as Alzheimer's disease [29], highlighting the profound impact of genetic influences on LPL function in the brain.

4.2. Environmental Factors Modulating LPL Expression

Environmental factors play a crucial role in controlling brain activity and expression of LPL. The function and levels of LPL can be significantly influenced by exposure to pollutants, physical activity, and diet. A diet high in fats can increase LPL expression to facilitate lipid metabolism. At the same time, physical exercise has been shown to enhance LPL activity, promoting efficient lipid utilization and energy production in neurons [49]. Conversely, exposure to environmental toxins, such as heavy metals or pollutants, can impair LPL function, disrupting lipid homeostasis and neuronal health. Chronic stress is another environmental factor that can negatively affect LPL activity, potentially exacerbating neurological conditions by disrupting lipid metabolism [50].

4.3. Interaction between Genetics and Environment in Neurological Health

The intricate interplay of hereditary and environmental factors significantly determines neurological health. Genetic predispositions can modulate the impact of environmental factors on LPL activity and brain function [51]. For instance, individuals with genetic variants that reduce LPL activity may be more susceptible to the adverse effects of a high-fat diet or environmental toxins. Conversely, favorable genetic variants may enhance the protective effects of beneficial environmental factors, like physical exercise. This connection also involves epigenetic alterations, like DNA methylation and histone acetylation, which can change the expression of the LPL gene in response to environmental cues [52]. Comprehending the complex interaction between heredity and the environment is essential for creating customized strategies to preserve and enhance neurological well-being.

To summarize, genetic and environmental variables influence lipoprotein lipase activity in the brain, which has significant consequences for synapse function, neuronal lipid homeostasis, and plasticity. The intricate relationship between these variables emphasizes how crucial it is to consider environmental exposures and genetic predispositions when assessing brain health.

5. EXPERIMENTAL MODELS AND CLINICAL STUDIES

Research into the role of lipoprotein lipase in neurological disorders, using experimental models and clinical studies, is not only aimed at elucidating its mechanisms, but also at identifying potential therapeutic targets that could bring hope to patients.

Animal models, particularly rodents, have played a pivotal role in advancing our understanding of lipoprotein lipase functions in the brain and its implications for neurological disorders. Transgenic mice with targeted deletions or overexpression of the LPL gene in specific

brain regions have been instrumental in uncovering the enzyme's role in neuronal lipid metabolism and synaptic function. Studies using these models have demonstrated that altering LPL expression impacts lipid homeostasis, synaptic plasticity, and cognitive performance [53].

To achieve precise modifications in gene expression, researchers commonly employ advanced techniques, such as CRISPR/Cas9 for gene editing, Cre-loxP systems for conditional knockouts, and RNA interference (RNAi) for gene silencing [54]. These approaches enable the creation of animal models tailored to study the neurological consequences of altered LPL function. Additionally, these models help link LPL dysregulation to conditions, like Alzheimer's disease and other neurodegenerative disorders, providing insights that inform potential therapeutic strategies.

For instance, LPL knockout mice have shown deficits in learning and memory, shedding light on the enzyme's involvement in cognitive processes. These models have been instrumental in understanding the effects of LPL deficiency on brain development and function, and in assessing potential therapeutic interventions targeting LPL activity. Electrophysiological assays (*e.g.*, patch-clamp recordings) and optogenetics are commonly used to examine neuronal signaling, while MRI and PET scans provide non-invasive means to observe structural and functional changes in the brain [55].

Table 1. Studies involving animal models investigating the role of lipoprotein lipase in neurological disorders.

Animal Models	Findings	Ref.
Genetically modified mice with neuron-specific Lipoprotein Lipase (LPL) deficiency	Impaired cognitive functions, altered neuronal signaling, disrupted lipid profiles, and glucose homeostasis	[6]
Double-transgenic mice involving lipoprotein lipase and Amyloid Precursor Protein (APP)	Reduced amyloid-beta burden and improved memory function	[60]
LPL knockout mice	Decreased AMPA receptor phosphorylation, impaired synaptic function, and neurobehavioral abnormalities	[61]
LPL knockout mouse model	Aggregation of α-synuclein and a decrease in ubiquitin C-terminal hydrolase L1 disrupting protein homeostasis and neuronal function, potentially leading to neurodegenerative conditions	[62]

Table **1** shows some studies that collectively highlight the critical roles of lipoprotein lipase in neuronal function, lipid metabolism, and the potential development of neurodegenerative conditions. Genetic modifications in animal models have provided insights into how LPL deficiency or overexpression can impact cognitive functions, synaptic health, and susceptibility to diseases, like Alzheimer's and Parkinson's. These studies often use biochemical assays measuring changes in lipid profiles, lipidomic analyses, and enzyme activity. Furthermore, western blot analysis, immunohistochemistry, and mass spectrometry are employed to assess molecular and protein alterations linked to LPL function in the brain [56].

On the other hand, clinical studies have explored the association between LPL activity and Alzheimer's disease, a prevalent neurodegenerative disorder. Reduced LPL activity has been observed in the brains of AD patients, suggesting a link between impaired lipid metabolism and disease pathology. A study conducted by Gong *et al*. [57] showed that LPL is significantly associated with neurite pathology in Alzheimer's disease, with its levels being markedly reduced in the dentate gyrus of affected brains. This reduction in LPL may contribute to the neurodegenerative processes and cognitive decline observed in AD. Imaging techniques, such as PET scans and Cerebrospinal Fluid (CSF) biomarker analysis, are often employed in clinical settings to track LPL levels and correlate them with disease progression. Genetic studies have identified polymorphisms in the LPL gene that may increase the risk of developing AD, highlighting the enzyme's potential as a biomarker for early diagnosis and as a target for therapeutic strategies [6, 58, 59].

Previous studies have provided valuable insights into the role of lipoprotein lipase in neurological disorders, such as its effects on cognitive function, neuronal signaling, and lipid metabolism. However, several critical gaps still need to be addressed, including a limited focus on LPL regulation in neurodegeneration, a narrow exploration of lipid-related signaling pathways, and a lack of investigation into its effects on neurogenesis and synaptic plasticity. While past research has concentrated on specific aspects, like amyloid-beta accumulation and synaptic dysfunction, it has not thoroughly examined LPL's involvement in broader lipid-derived signaling molecules, neuroinflammation, or myelin production. Our study has addressed these gaps by examining how LPL regulation influences a broader range of lipid signaling pathways, neuroinflammation, and synaptic plasticity, offering new insights into the enzyme's role in neurodegenerative diseases and suggesting potential therapeutic strategies. This novel approach may contribute to an understanding of LPL's multifaceted role in neurological health.

6. LIMITATIONS AND CHALLENGES IN CURRENT RESEARCH

Despite the progress in understanding LPL's role in the brain, several limitations and challenges persist in current research. One significant drawback is the difficulty in identifying the precise effects of LPL on the brain due to its intricate regulation and wide range of actions in various tissues [63]. Additionally, animal models, while informative, do not fully replicate the human condition, and findings may only sometimes translate to clinical outcomes. Human studies are often constrained by genetic background variability, environmental exposure, and lifestyle factors, which can confound results. Furthermore, the mechanisms by which LPL influences neurodegenerative processes remain incompletely understood, necessitating further research to unravel these complex pathways. The development of advanced

models and methodologies, along with interdisciplinary approaches, is essential to overcome these challenges and advance our understanding of LPL's role in neurological health.

In summary, experimental models and clinical studies provide valuable insights into the role of lipoprotein lipase in neurological disorders, particularly Alzheimer's disease. Although there has been considerable progress, more study is still required to address the obstacles and restrictions, which could eventually lead to improved methods for treating and preventing neurodegenerative disorders.

7. THERAPEUTIC POTENTIAL AND STRATEGIES TARGETING LPL FOR ALZHEIMER'S DISEASE TREATMENT

7.1. Targeting LPL for Alzheimer's Disease Treatment

Because of lipoprotein lipase's complex roles in inflammation, lipid metabolism, and Amyloid-beta (Aβ) clearance, all of which are essential to AD pathology, targeting LPL for AD treatment has attracted much attention [6, 8]. To preserve the health and function of neurons, LPL plays a critical role in removing circulating triglycerides and controlling the distribution of lipids in the brain. The characteristic of Alzheimer's disease is dysregulation of lipid metabolism, which is associated with reduced LPL activity and can cause neuronal damage and cognitive loss.

LPL, expressed in neurons and microglia, is a key player in controlling inflammatory responses and is a significant factor in AD development. Research has shown that increased LPL activity can effectively reduce neuroinflammation, thereby slowing the progression of the disease [8, 64]. Furthermore, LPL aids glial cells in binding, absorbing, and degrading Aβ peptides, thereby reducing their accumulation in the brain, a critical step in AD development [9].

LPL is critical for maintaining cholesterol and fat metabolism, preventing lipid droplet formation, and promoting energy production in microglia, in addition to its function in the clearance of Aβ. The survival of neurons and the integrity of the central nervous system depend on these processes [65]. In addition, LPL provides neuroprotection and promotes CNS repair by activating the Peroxisome Proliferator-activated Receptor (PPAR). The dual function of LPL in inflammation and lipid metabolism suggests that it may be a valuable target for treating neurodegenerative illnesses, like Alzheimer's. Promising approaches for slowing AD and improving cognitive results may come from emerging treatments that increase LPL activity or combine it with PPAR isomers [8].

7.2. Current Therapeutic Approaches and Clinical Trials

Multiple strategies for treating Alzheimer's disease include pharmacological manipulation of lipoprotein lipase. One such approach uses LPL activators, biologics, or small molecules to improve lipid metabolism, counteract inflammation, and promote Amyloid-beta (Aβ) clearance. However, it is difficult to develop targeted and effective LPL activators because lipid metabolism is complex, high selectivity is needed to avoid off-target effects, and there are many difficulties in crossing the blood-brain barrier [66].

In the future, gene therapy using state-of-the-art technology may provide new possibilities for treating disease. Viral vectors or CRISPR/Cas9 gene editing techniques may change AD treatment by directly enhancing LPL expression in the brain [67].

Lipid-modifying drugs that indirectly affect LPL function have been studied because of clinical trials done on them for Alzheimer's disease, especially those targeting Peroxisome Proliferator-activated Receptors (PPARs) [68]. This progress should boost confidence in ongoing efforts for Alzheimer's disease research.

According to Tobeh and Bruce [69], researchers are working on identifying the individual LPL modulators, determining their effectiveness, and screening and assessing their safety in respective preclinical animal models. The goal is the development of promising candidates for clinical trials. These are enough and very promising boreholes as far as the future of AD treatment is concerned.

Moreover, LPL is stimulated by thyroid hormone, and equally, LPL is essential for fat metabolism. Evidence shows that elevating blood fat levels due to decreased thyroid activity may enhance the possibility of a person having Alzheimer's disease. Aerobic exercise enhances the activity of LPL, which promotes the decomposition of fats and protects an individual from low thyroid activity, hence protecting an individual from Alzheimer's disease [70]. There is, however, another close link to this disease, which is obesity. Researchers have recently discovered a natural compound called scopolin that is essential in breaking down fat by inhibiting the formation of fat cells, a process regulated by LPL. By preventing weight gain and hindering the process of fat cell formation, scopolin may help protect against Alzheimer's disease [71].

7.3. Future Directions in LPL-based Therapies

Advancing lipoprotein lipase targeting for Alzheimer's disease holds significant promise. Understanding the molecular mechanisms that regulate LPL expression and activity in the brain is a crucial step toward designing effective therapies [32]. The identification of biomarkers for LPL activity could revolutionize patient stratification and treatment monitoring. The potential synergy of LPL modulators with other therapies, such as anti-inflammatory agents, Aβ-targeting antibodies, or lipid-lowering drugs, offers hope for enhanced treatment efficacy. Personalized medicine approaches tailored to individual genetic and metabolic profiles could significantly improve outcomes [72].

Advanced drug delivery systems, including nanotechnology for targeted brain distribution and

techniques to improve blood-brain barrier penetration, are essential for enhancing bioavailability and minimizing side effects [73]. Long-term research is necessary to evaluate the safety and effectiveness of LPL-targeted treatments, focusing on their impact on biochemical markers, imaging outcomes, and cognitive function.

LPL is also recognized as a protective agent against brain injury in AD by modulating synaptic loss and restructuring. Additionally, LPL binds to Amyloid-beta (Aβ) protein and promotes its uptake, making it a significant target for drug therapy [74]. Emerging therapeutic strategies include gene therapy to substitute the LPL gene and compounds that elevate LPL mRNA, protecting LPL from inhibition by Angiopoietin-like 4 (ANGPTL4), such as the N-phenylphthalimide derivative 50F10 [70].

In summary, LPL targeting represents a promising therapeutic approach for AD. Although still in the early stages, the need for continued research and innovative strategies is paramount. This commitment may eventually lead to effective treatments for this debilitating disease.

CONCLUSION

Lipoprotein lipase plays a pivotal role in maintaining brain health, with its dysregulation being implicated in Alzheimer's disease due to disrupted lipid homeostasis, increased neuroinflammation, and inadequate clearance of Amyloid-beta (Aβ). Enhancing LPL activity could potentially address these underlying issues. Current therapeutic strategies focus on pharmacological approaches and gene therapies aimed at activating LPL, with ongoing clinical trials evaluating lipid-modifying agents. Future research will be crucial in unraveling the molecular regulation of LPL, developing targeted activators, and optimizing clinical trial designs. These efforts, particularly through multi-modal treatment approaches, hold promise for personalized therapeutic options that could significantly improve AD management and patient outcomes.

AUTHORS' CONTRIBUTION

A.R.A: Study conception and design; A.R.A, R. S.A: Writing drafting of the manuscript. Both authors have reviewed the results and approved the final version of the manuscript.

LIST OF ABBREVIATIONS

LPL	=	Lipoprotein Lipase
FFAs	=	Free Fatty Acids
CMs	=	Chylomicrons
VLDLs	=	Very Low-density Lipoproteins
HTG	=	Hypertriglyceridemia
Apo	=	Apolipoprotein
FCS	=	Familial Chylomicronemia Syndrome
INS	=	Insulin
HS	=	Heparan Sulfate
DHA	=	Docosahexaenoic Acid
PD	=	Parkinson's Disease
TGs	=	Triglycerides
FFAs	=	Free Fatty Acids
LDLR	=	Low-density Lipoprotein Receptor
BDNF	=	Brain-derived Neurotrophic Factor
Aβ	=	Amyloid-beta
OPCs	=	Oligodendrocyte Precursor Cells
SNPs	=	Single Nucleotide Polymorphisms
RNAi	=	RNA interference
APP	=	Amyloid Precursor Protein
CSF	=	Cerebrospinal Fluid
PPAR	=	Peroxisome Proliferator-activated Receptor
ANGPTL4	=	Angiopoietin-like 4

CONSENT FOR PUBLICATION

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the publication of this work.

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