REVIEW ARTICLE

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Beyond Nutrition: Deciphering the Roles of Amino Acids as Molecular Regulators of Memory Mechanisms

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Memory formation is a complex process involving multiple neural and molecular mechanisms through synaptic plasticity, neurotransmission, and intracellular signaling pathways. While these processes are nutrient-sensitive, the specific mechanistic roles of dietary amino acids in memory pathways remain underexplored. This review analyzes evidence on how key amino acids (e.g. glutamate, tryptophan, and BCAAs) regulate molecular mechanisms of memory. Glutamate drives long-term potentiation (LTP) through NMDAR and mGLUR activation, although its activity requires tight regulation to avoid excitotoxicity. Tryptophan availability enhances serotonergic signaling, promoting LTP and memory consolidation through PKA/CREB and MAPK signaling pathways. Branched-chain amino acids (BCAAs) and large neutral amino acids (LNAAs) modulate central neurotransmitter synthesis through competitive transport at the blood-brain barrier, thereby influencing synaptic signaling. Additionally, amino acids availability regulates epigenetic processes via methyl donor metabolism and acetyl-CoA production, mechanisms that are closely linked to activity-dependent gene expression underlying synaptic plasticity and memory function. Amino acid modulates memory formation through molecular mechanisms in synaptic plasticity, neurotransmitters, and intracellular signaling pathways. Targeting amino acids intake offers promising strategies for cognitive health. Future research should prioritize human studies, personalized nutrition, and gut microbiome-amino acids interactions.

Keywords: amino acids, memory formation, neurotransmitters, synaptic plasticity

Introduction

Memory is a fundamental cognitive process that enables the acquisition, storage, and recall of information. Its maintenance and modulation allow us to learn, adapt, and make decisions in dynamic environments.[1,2] Aging, metabolic disorders, and suboptimal dietary patterns have been associated with cognitive decline, emphasizing the need to identify modifiable factors that support memory maintenance.

At the cellular level, current hypothesis proposes that memories are stored by preserving the synaptic connections between certain groups of neurons. These connections are not static, rendering memories to strengthening or weakening over time.[1] These synaptic modifications are governed by tightly regulated molecular mechanisms, including neurotransmitter signalling[3], activity-dependent protein synthesis and degradation[4], and gene expression control.[5,6] Collectively, these processes determine memory consolidation and persistence.

Emerging evidence suggests that memory formation is influenced not only by neuronal activity but also by systemic metabolic status. The brain is metabolically demanding, and cognitive function is inherently sensitive to nutrient availability. Among macronutrients, amino

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acids are of particular interest. They play a crucial role as building blocks of synaptic proteins[7], act directly as neurotransmitters or neurotransmitters precursors[8,9] and modulate intracellular signalling pathways involved in synaptic plasticity.[10] Despite this, most studies on memory mechanisms focus predominantly on intracellular neuronal processes, while nutritional influences are often examined at behavioural or epidemiological levels without sufficient mechanistic integration.

This disconnect represents a significant research gap. Although individual amino acids have been studied in isolation, there remains limited study in linking dietary amino acid intake to molecular mechanisms of memory pathways. Therefore, this review focuses on molecular and cellular mechanisms linking dietary amino acids to memory processes and aims to summarize molecular mechanisms underlying memory formation and consolidation, examine how dietary amino acids influence neurotransmission, synaptic plasticity, and gene expression relevant to memory function, and offering perspective for integrating molecular neuroscience with nutritional strategies to support cognitive health.

Results and Discussion

Phases of Memory Formation

Memory formation is a complex process involving multiple neural and molecular mechanisms that will lead to structural changes. There are three phases to memory formation: encoding, consolidation, and retrieval.[11] The initial phase of memory formation is encoding. This phase involves the transformation of various kinds of new information (sensory input) into a form that can be stored inside the brain. This phase requires the participation of various brain systems, especially cerebral cortex and the limbic system, especially the hippocampus and the amygdala.[12,13] During consolidation, encoded information is stabilized and stored as long-term memory. If memories are not consolidated, these newly formed memories will decay quickly. This process is highly dependent on sleep, particularly non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. They help memory consolidation through synaptic modification.[14,15] REM sleep is associated with the stabilization and enhancement of memory traces, while non-REM sleep is involved in the reactivation and redistribution of memories as well as synaptic normalization.[16,17] Consolidating memory in neurons requires changes in the connections between participating neurons, a process called synaptic plasticity. Synaptic plasticity is the dynamic regulation of preexisting connections between neurons or synapses to change in strength in response to neural activity.18 This synaptic communication is a fundamental mechanism of experience-dependent remodeling of nervous system during memory formation.[19–21] The final phase is retrieval, where stored information is accessed and used. Retrieval converts stored memories into conscious awareness through the reactivation of neural patterns.[22,23] However, this process is affected by various factors, including integration at encoding, synaptic plasticity, and stress.[24,25]

Synaptic Plasticity: The Molecular Basis of Memory Phases

While memory phases (encoding, consolidation, retrieval) define the temporal sequence of memory processing, synaptic plasticity provides the underlying biological mechanism for these stages. Synaptic plasticity is observed in many pathways of the brain, primarily the part that is crucial for learning and memory, the dentate gyrus and hippocampus.[26] The causal link between synaptic plasticity and memory was formalized by Morris and colleagues.[27] The role of synaptic plasticity in memory formation involves the activity-dependent change that modifies the strength or efficacy of synaptic transmission in response to synapses' activity. The changes of synaptic plasticity can be either an increase (long-term potentiation, LTP) or a decrease (long-term depression, LTD) of synaptic strength.[27–29]

LTP, as a primary cellular mechanism underlying memory, involves a high-frequency stimulation around those dendritic spines. This stimulation is crucial for initiating the process that leads to LTP as it transforms the silent synapses into functional ones.[30,31] Then, it is followed by a long-lasting increase of synaptic strength.[32,33] This LTP induction is centered around calcium signaling and protein kinase activation. It requires the activation of the ionotropic receptor, the N-methyl-D-Aspartate (NMDA) receptors, by glutamate as its primary agonist that binds to the GluN2 subunit as well as glycine or D-serine as the primary co-agonists that bind to the GluN1 subunit. The binding of these co-agonists is essential for the NMDARs' activation.[34–37] NMDA receptors are highly permeable to calcium ions, which allow those ions to enter the postsynaptic neurons, that will lead to the signaling cascade that will increase the strength of synaptic connections.[38,39] This increase of Ca^{2+} concentration in the postsynaptic membrane can activate protein kinases. The activation of calcium/calmodulin-dependent kinase II (CaMKII) is necessary to phosphorylate

various molecules. Once activated, CaMKII undergoes autophosphorylation at Thr286, which is crucial to maintain the induction of long-lasting synaptic plasticity.[40] While CamKII autophosphorylation at Thr286 was traditionally viewed as essential for LTP, recent studies propose that persistent CamKII binding to GluN2B subunits sustains synaptic strength independently of phosphorylation.[41–43]

Another form of LTP is NMDAR independent, where it relies on metabotropic glutamate receptors (mGluRs)[44] and calcium-permeable AMPA receptors (AMPARs).[45] The mGluRs are primarily activated by the neurotransmitter glutamate, one of the standard amino acids and the major excitatory neurotransmitter in the central nervous system (CNS). mGluRs are activated by the binding of glutamate to the extracellular domain of the receptor.[46] This binding will induce conformational changes that activate intracellular signaling pathway through G-proteins.[47,48] Group I mGluRs (mGluR1 and mGluR5) are involved in the process of neural plasticity, including LTP. According to studies by Naie et al. (2004) and Bikbaev et al. (2008), a prolonged pharmacological blockade of mGluR5 with its antagonist, 2-methyl-6-(phenyl-ethynyl) pyridine (MPEP), impaired the spatial memory through a reduction of mGluR1a-expression in dentate gyrus and suppressed the LTP in dentate gyrus.[44,49] Meanwhile, AMPARs are also heavily involved in synaptic plasticity. The induction of LTP leads to the incorporation of AMPARs into the postsynaptic membrane, while LTD causes the removal of AMPARs.[50] This insertion further enhances synaptic strength and results in dendritic spines structural changes. The plasticity that involves AMPARs is reversible. The application of its agonist, AMPA, after LTP can reverse the increase in synaptic strength, a process called depotentiation.[51,52]

Although it is less studied, LTD complements LTP by refining synaptic connections, preventing saturation, and enabling new memory encoding53. LTD induction involves a GluN2B-containing NMDAR as well as the ubiquitin-proteasome-mediated AMPAR internalization.[54–56] Together, LTP and LTD maintain synaptic homeostasis and plasticity. Unchecked potentiation may impair the acquisition of new memories, while synaptic strength reduction facilitates circuit optimization.[57]

Neurotransmitter Systems

Neurotransmitters are endogenous chemical messengers that facilitate communication among neurons. The primary role of neurotransmitters is to communicate sensory, motor, and integrative neural messages. Neurotransmitters are essential for brain function. As a result, fluctuations in neurotransmitter levels can affect normal brain function and neurotransmitter receptors, as well as molecules associated with their synthesis and modulation.[58]

As the primary excitatory neurotransmitter, glutamate plays a crucial role in various forms of synaptic plasticity, primarily acting through the NMDARs and AMPARs.[59,60] The activation of both receptors is directly linked to memory encoding and storage processes.[61,62] The primary sources of glutamate and glutamine for memory formations are intricately linked through the glutamate-glutamine cycle, which involves both neurons and astrocytes. Inside neurons glutamate is converted from glutamine by the phosphate-activated glutaminase. The glutamate released into the synaptic cleft is then taken up by astrocytes and converted back into glutamine by the enzyme glutamine synthetase. This glutamine will be transported back to neurons, completing the cycle.[63,64] Glutamate can be further metabolized into the inhibitory amino acid γ-aminobutyric acid (GABA) by glutamic decarboxylase.[65]

Acetylcholine plays a crucial role in various aspects of memory formation, where it influences both the excitatory and inhibitory neurons in the hippocampus and cortex. Acetylcholine acts through nicotinic (nAChRs) and muscarinic receptors (mAChRs).[66] In the presynaptic membranes, activation of nAChRs increases the probability of neurotransmitter release and facilitates Ca^{2+} influx, which is essential for neurotransmitter release and synaptic modulation.[67,68] In the postsynaptic membrane, nAChRs activation leads to membrane depolarization, which in turn triggers intracellular signaling pathways and gene transcription.[68] Meanwhile, activation of mAChRs enhances LTP by increasing the excitability of pyramidal neurons, facilitating Ca^{2+} ions influx, which is necessary for synaptic strengthening. Acetylcholine-mAChRs can also induces LTD, involving endocannabinoid signaling and modulation of glutamatergic synapses.[69–72]

Intracellular Signaling Pathways

Several key pathways and mechanisms connected to memory formation have been identified through various studies, including cAMP/PKA/CREB and MAPK/ERK pathway. The cAMP/PKA/CREB pathway is activated through external stimulation that increases the intracellular levels of cyclic adenosine monophosphate (cAMP), including neurotransmitters. The binding of neurotransmitters to

G-protein coupled receptor (GPCRs) (i.e. acetylcholine binding to metabolic acetylcholine receptors) will lead to the activation of adenylyl cyclase, which converts ATP to cAMP.[73,74] The increased level of cAMP activates protein kinase A (PKA) by dissociating its regulatory subunits from the catalytic subunits. Activated PKA further phosphorylates various target proteins, including the cAMP response element-binding protein (CREB). Phosphorylated CREB binds to cAMP response element (CRE) on the DNA, recruiting transcriptional coactivators to initiate gene transcription.[75–77]

CREB is a crucial transcription factor for synaptic plasticity and memory formation. Increasing CREB activity is linked to enhanced LTP in hippocampal neurons and its positive feedback loop sustains gene transcription necessary for memory consolidation.[78,79] A potent modulator of CRE-driven gene transcription in the brain, CREB-regulated transcription coactivator 1 (CRTC1), enhances dendritic growth, synaptic plasticity, and memory consolidation. Alteration in CREB activity is associated with impaired long-term plasticity and memory, while its dysregulation contributes to neurodegenerative diseases.[78,80–82]

The MAPK/ERK pathway is essential for the development of the nervous system and the regulation of synaptic plasticity as well as gene transcription.[83,84] The pathway is initiated when extracellular signals bind to the tyrosine kinase receptors (TRKs) on the cell surface.[85] The binding activates a series of proteins, which in turn activates ERK. ERK proteins (ERK1 and ERK2) are activated and translocated to the nucleus, where it can influence gene expression by phosphorylating various transcription factors, influencing cellular and synaptic plasticity.[85,86] The MAPK/ERK also triggers genomic responses leading to changes in protein synthesis, which are necessary for long-term memory consolidation (**Figure 1**).[87]

The mammalian target of rapamycin (mTOR) pathway is an important regulator of various cellular processes in the brain, including synaptic plasticity, memory formation, and neuronal development.[88–90] mTOR consists of two complexes, mTORC1 and mTORC2, where mTORC1 primarily regulates protein synthesis, while mTORC2 is involved in cytoskeletal organization and cell survival. The molecular basis of mTOR pathway includes regulating signaling inputs, recruiting substrates, localizing biological membranes, and activation. The mTOR pathway integrates signal from nutrients, including amino acids and glucose, growth factors, and cellular energy status to regulate its activity. Amino acid availability, for example, is sensed upstream of

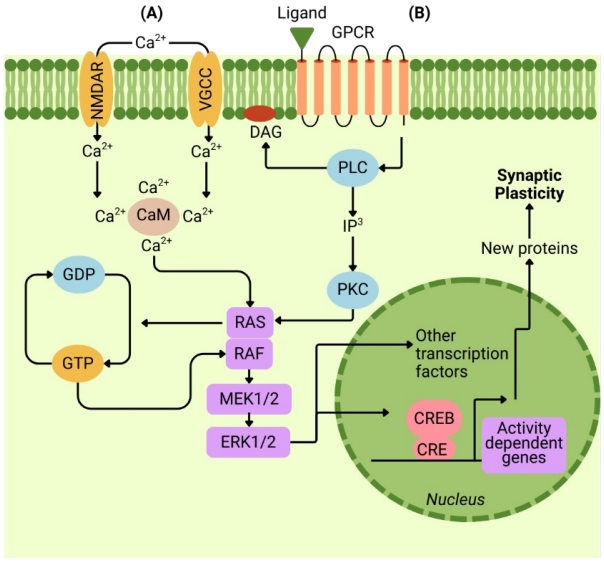


Figure 1. Schematic for the MAPK/ERK Metabolic Signaling Pathway[144].
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(A) The activation of N-methyl-D-aspartate (NMDA)-type glutamate receptors (NMDARs) or voltage-gated calcium channels (VGCCs) induces calcium (Ca2+) influx. Elevated intracellular Ca2+ activates Ras and increases Ras-GTP levels. The precise mechanism by which Ca2+-dependent Ras activation remains unclear. It is thought to involve the activation of Ras-guanyl nucleotide exchange factors (GEFs) and the inhibition of Ras-GTPase-activating proteins (GAPs). An increase in GTP levels activates the Raf-MAPK/ERK kinase (MEK)-ERK signaling cascade. This allows the phosphorylation of ERK and its nuclear and cytoplasmic targets. Among these targets, the transcription factor CREB induces the expression of genes involved in synaptic plasticity. The activation of CREB-dependent gene transcription promotes the protein synthesis required for long-term synaptic-remodeling. **(B)** Binding of ligands to GPCRs activates the phosphoinositide-specific phospholipase C (PLC), leading to the formation of diacylglycerol (DAG) and inositol 1,4,5-triphosphate (IP3). IP3 diffuses rapidly into the cytosol and binds to IP3 receptors on the endoplasmic reticulum membrane, inducing the release of Ca2+ from the internal stores. Together, the elevated intracellular Ca2+ and DAG activate protein kinase C (PKC), which subsequently engages the Ras-MEK-ERK signaling cascade.

Rheb, a small GTPase that activates mTORC1.[91–94] mTOR signaling is essential for synaptic plasticity by regulating the initial translation initiation at synapses, influencing long-term memory formation, thus its dysregulation may risk conditions such as Alzheimer's disease.[89,92]

Role of Amino Acids in Memory Formation Pathways

Glutamate, a non-essential amino acid, is the primary excitatory neurotransmitter in the mammalian CNS and a critical mediator of synaptic plasticity and memory formation. Glutamate is naturally present in many foods and food additive in the form of monosodium glutamate (MSG). Dietary glutamate undergoes an extensive first-pass metabolism in intestinal enterocytes that convert glutamate into other compounds, such as lactate and alanine. Consequently, very little glutamate reaches systemic circulation.[95,96] Dietary glutamate is not significantly transferred to the brain because of the blood-brain barrier (BBB) to prevent excitotoxicity, a state of excessive stimulation that could damage and kill neurons. Excitotoxicity has been linked to cognitive deficits, particularly in Alzheimer's disease, Parkinson's disease, and Huntington's disease.[97,98] Nevertheless, it is suggested that dietary glutamate may indirectly modulate memory pathways. Oral glutamate supplementation in rats increased hippocampal glutamate and gamma-amino butyric acid (GABA) level while enhancing spatial learning and memory performance.[99]

Applications in human subjects remain uncertain due to the tightly regulated nature of glutamate transport across the BBB. According to the evaluation of the European Food and Safety Authority (EFSA) panel on Food Additives and Nutrient Sources added to Food, the established acceptable daily intake (ADI) of glutamic acid and glutamates as food additives is 30 mg/kg body weight per day.[100] This ADI was derived using a safety margin from no observable adverse effect level (NOAEL) of 3,200 mg monosodium glutamate/kg body weight per day, at which no neurobehavioral effects were detected in vivo. These regulatory limits suggest that typical dietary exposure to glutamate additives is unlikely to induce neurotoxicity under normal physiological conditions. Under physiological conditions, glutamate transport at the BBB is predominantly directed towards efflux, therefore limiting extracellular accumulation and protecting against excitotoxicity.[8] However, in pathological states characterized by BBB dysfunction, such as epilepsy and chronic neurodegenerative disorders, this regulatory balance might be compromised.[101,102] Barrier disruption in these conditions is associated with endothelial damage, inflammatory activation, and altered expression or function of glutamate receptors.[103,104] Such changes may impair glutamate clearance and enhance NMDAR-mediated signaling, leading excessive Ca^{2+} influx and activation of downstream of enzymatic pathways, which induces excitotoxic neuronal death.[105] Additionally, excessive activation of endothelial NMDARs can disrupt tight junction proteins via the Rho/ROCK signaling pathway, further increasing barrier permeability. Collectively, these mechanisms suggest that BBB failure may amplify excitotoxic mechanism by diminishing glutamatergic homeostasis.

Tryptophan, an essential amino acid, has a significant role in memory formation primarily through its conversion to serotonin. Several studies have shown that ingested tryptophan increases brain tryptophan concentration, stimulating the synthesis and release of serotonin, which in turn promotes synaptic plasticity (LTP) and memory consolidation through the activation of PKA, PKC, and MAPK cascades in synaptic plasticity.[106–110] Consumption of tryptophan-rich foods has been associated with improved cognitive function and reduced cognitive decline in older adults.[111,112] Conversely, acute tryptophan depletion reduces serotonin levels, resulting in an impaired long-term memory and episodic memory consolidation.113–115

Besides functioning as serotonin precursor, gut-derived tryptophan metabolites are also involved in the microbiome-gut-brain axis. Alterations in gut microbiota have been linked to memory impairment, including Alzheimer's disease.[116–119] Gut microbiota regulates tryptophan metabolism by influencing the availability of tryptophan for serotonin and kynurenine pathways, affecting CNS function. The kynurenine pathway metabolizes tryptophan into kynurenic acid (KYNA) and quinolinic acid (QUIN). KYNA is an NMDAR antagonist, where it competes with glycine site of the receptor, reducing excitatory neurotransmission. KYNA has been shown to have neuroprotective properties against excitotoxicity and amyloid β peptide model of neurodegeneration.[120,121] However, high KYNA levels in the brain have also been linked to neurocognitive deficits, such as impaired spatial and contextual memory. This might happen because increased KYNA levels reduce extracellular glutamate, dopamine, and acetylcholine or due to the hypofunction of NMDAR and α7 nicotinic acetylcholine receptors.[122–125] QUIN is an excitotoxic agonist of NMDAR. It mimics the binding of glutamate to NMDAR, leading to the opening of the influx of Ca^{2+} ions

which induces excitotoxicity and neurodegeneration.[126,127]

In addition, targeting tryptophan metabolism through probiotics may influence memory-related outcomes. Oral administration of two *Lactococcus* strains (L. lactic WHH2078 and L. cremoris WHH2080) in aged mice significantly improved cognitive and depressive-and anxiety-like behaviors.128 This intervention promoted the secretion of gut 5-hydroxytrptophan, a precursor to serotonin, while reducing kynurenine, 3-hydroxykynurenine, and indole-3-lactic acid levels, suggesting a shift in tryptophan metabolism towards serotonergic pathways, away from neurotoxic kynurenine metabolites. Moreover, the probiotic treatment also restored hippocampal neuronal integrity and attenuated neuroinflammation in the hippocampus. These findings support a mechanistic link between microbial modulation of tryptophan metabolism and improved cognitive function in aging models.

Branched-chain amino acids (BCAAs) are essential amino acids that include leucine, isoleucine, and valine. They have a complex relationship with cognitive function, influencing brain activity through various mechanisms. BCAAs, particularly leucine, activate the mTORC1 complex, which is crucial for neuronal growth and protein synthesis.[129] This pathway is also modulated by NMDAR activation by affecting the transport of amino acids.[130] BCAAs are also crucial for the synthesis of glutamate and GABA, where they participate in the nitrogen cycle between astrocytes and neurons.[131,132] This shows the essential role of BCAAs in maintaining neurotransmitter levels.

However, BCAAs also possess potential risks. High level of BCAAs have been linked to neurotoxic effects, where their accumulation leads to cognitive deficits and neurological dysfunction.[133] Elevated serum leucine levels have been reported in individuals with Alzheimer's disease.[134] Higher circulating leucine concentrations were associated with reduced brain volume and poorer cognitive performance, suggesting a potential link between altered BCAA metabolism and neurodegenerative processes. BCAAs and other large neutral amino acids (LNAAs) including tryptophan, tyrosine, and phenylalanine share a common transport mechanism at the BBB, primarily mediated by the large neutral amino acid transporter 1 (LAT1). Because the two amino acids transport competitively, increased plasma concentrations of one LNAA can influence the cerebral uptake of others. Elevations in circulating tryptophan or tyrosine enhance their transport into the brain, whereas increased BCAA levels may lower tryptophan and tyrosine uptake by competitive inhibition.[135] Such shifts in amino acids uptake may subsequently affect central neurotransmitter synthesis, including serotonin and catecholamines.[135] Therefore, while BCAAs can enhance certain aspects of cognitive function, their impact on memory is not yet clear. Further research is needed to find the precise mechanisms and optimal conditions for BCAAs supplementation in cognitive health.

Amino Acids and Epigenetic Regulation of Memory

Epigenetic mechanisms which include DNA and post-translational histone proteins modifications are critical regulators for synaptic plasticity and memory formation. Activity-dependent changes in gene expression required for LTPs and memory consolidation are tightly controlled by chromatin remodeling process.[136] Dietary amino acids may influence these mechanisms both directly and indirectly through metabolic pathways.

Methionine, an essential amino acid, plays a central role in one-carbon metabolism, leading to the production of S-adenosylmethionine (SAM), the primary methyl donor for DNA and histone methylation. DNA methylation and post-translational histone modifications are essential regulators of activity-dependent gene expression required for synaptic plasticity and memory formation.[137] Consequently, alterations in SAM availability may influence cognitive process by modifying epigenetic regulation in the brain.

In addition to methylation, amino acids may influence histone acetylation through their effects on cellular metabolism. Histone acetylation depends on acetyl-CoA availability, a key substrate for histone acetyltransferases (HATs). Acetyl-CoA levels are tightly linked to nutrient-dependent metabolic pathways, including intermediates derived from amino acid catabolism that enter the tricarboxylic acid cycle.[138] Enzymes such as acetyl-CoA synthetase and ATP-citrate lyase contribute to the generation of nuclear acetyl-CoA from metabolic intermediates.[139] Therefore, fluctuation in acetyl-CoA availability can alter histone acetylation status and chromatin accessibility. Increased histone acetylation is generally associated with enhanced transcription of plasticity-related genes, while reduced acetylation may impair memory-associated gene expressions.[140,141]

Dysregulation of epigenetic processes has been reported in several neurodegenerative conditions. For example, altered DNA methylation and hydroxymethylation

patterns in the substantia nigra of Parkinson's disease patients have been observed, affecting genes related to neuronal differentiation and survival.[142] In Alzheimer's disease, abnormal DNA methylation patterns have been associated with genes regulating the amyloid production and β-amyloid clearance, processes central to the disease pathology.[143] These findings indicate that epigenetic alterations contribute to neurodegenerative progression and suggest that metabolic factors influencing methyl donor availability may represent additional pathway through which nutritional status could modulate cognitive function.

Conclusion

Memory formation involves dynamic molecular mechanisms that include synaptic plasticity (LTP/LTD), neurotransmission, and epigenetic regulation. This dynamic is profoundly modulated by dietary amino acids. Glutamate drives NMDAR-dependent LTP but requires strict metabolic control to prevent excitotoxicity. Tryptophan shows dual roles as a serotonin precursor enhancing hippocampal plasticity via PKA/CREB signaling and as a substrate for gut microbiome-derived metabolites (KYNA/QUIN) that can tip the balance between neuroprotection and excitotoxic neurodegeneration. Branched-chain amino acids (BCAAs) and other large neutral amino acids (LNAAs) influence central neurotransmitter synthesis through competitive transport at the blood-brain barrier, thereby modulating synaptic signaling dynamics. In addition, amino acids availability regulates epigenetic mechanisms via methyl donor metabolism and acetyl-CoA production, linking metabolic state to activity-dependent gene expression underlying synaptic plasticity and memory function. These findings emphasize the integrated role of amino acids metabolism in shaping neural plasticity and cognitive function. Consequently, amino acids bioavailability and their metabolic fate impacted cognitive health. Targeting amino acids pathways offers promising strategies against memory dysfunction. Future research must prioritize human trials, personalized nutrition, and microbiome-directed interventions to translate mechanistic insights into clinical applications.

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Authors' Contributions

RFH was responsible for the conception of paper ideas, literature research, writing, and manuscript revisions. NAS was involved in the writing of the manuscript and literature research. RO assisted with the proofreading and revision of the manuscript. Every author reviewed and accepted the final draft of the manuscript. Furthermore, all authors accepted full responsibility for the work, ensuring its integrity and precision.

Conflict of Interest

The authors declare no competing interests.

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