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REVIEW ARTICLE

Navigating the Labyrinth: Understanding Dementia's Effect on the Brain and the Role of Educational Therapy-Based Interventions in Dementia Treatment

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ABSTRACT

Dementia presents a profound challenge to cognitive function, impacting various regions of the brain, including the frontal, parietal, temporal, and occipital lobes, as well as the hippocampus. This article explores the specific effects of dementia on these brain regions, the interplay of acetylcholine (ACh) and brain-derived neurotrophic factor (BDNF), and the implications for cognitive decline and memory loss. Current research suggests that dementia-related changes in the brain involve cortical thinning, neuronal loss, and alterations in synaptic connectivity, leading to impairments in memory, executive function, spatial awareness, and visual processing. Of particular significance is the role of the hippocampus in memory formation and retrieval, which is often one of the earliest brain regions affected by dementia pathology. In addition, educational therapy is also mentioned as a promising approach to dementia treatment by providing tailored interventions to address cognitive deficits and enhance remaining cognitive abilities. By incorporating strategies such as cognitive stimulation, memory training, problem-solving exercises, and multisensory learning techniques, educational therapy aims to optimize brain function and improve overall quality of life for individuals living with dementia. Moreover, educational therapy interventions can be adapted to suit the specific needs and preferences of each individual, promoting personalized care and maximizing therapeutic benefits.

***Keywords:** Acetylcholine, Brain-derived neurotrophic factor, Cortical lobes, Dementia, Educational therapy-based intervention, Hippocampus*

1. INTRODUCTION

Millions of people worldwide suffer from dementia, which is a condition marked by rapidly progressive neurological decline (Geschwind, 2016; Geschwind et al., 2008; Josephs et al., 2009) in a person's mental capability severe enough to interfere with the activities of his/her daily living (Mattson, 2004). It is not a specific disease but rather a group of symptoms (Webster, 2021) associated with a decline in memory (especially in remembering, storing and recalling), reasoning (or impairment in judgment), and other cognitive skills (e.g., language difficulties) as well as changes in behavior.

As a neurological disorder, dementia can affect different parts of the brain (Brand & Markowitsch, 2008; Sandilyan & Dening, 2014) involved in memory, language, reasoning, and decision-making: hippocampus, frontal lobe, temporal lobe, parietal lobe and occipital lobe. Depending on which parts of the brain are affected, different types of dementia can result. Alzheimer's disease, which "accounts for 60-80% of dementia cases" (Alzheimer's Association, 2024, para. 2), is the most common type of dementia, but there are other types such as vascular dementia, Lewy body dementia, and frontotemporal dementia (see Bolla, Filley, & Palmer, 2000, for detail) in the nosology of dementia. According to Chiu (2005), "the current classification is very limited in its structure to assist in further understanding the concept, clinical features, neuropathology and therapeutics of dementia" (p. S17).

Each of the four types of dementia (Bolla et al., 2000; Carr, 2017; Chiu et al., 2006) as mentioned above has its own set of symptoms and causes:

1. **Alzheimer's disease** (Keith et al., 2023; Scheltens et al., 2021): The symptoms include the following: memory loss (especially recent memories), difficulty with problem-solving and planning, confusion about time or place, challenges with language, e.g., finding the right words), and changes in mood and personality. The exact cause of Alzheimer's disease is not fully understood yet, but it is believed to involve a combination of genetic, environmental, and lifestyle factors. Abnormal protein deposits in the brain (amyloid plaques and tau tangles) are characteristic features (see Morishima-Kawashima & Ihara, 2002, for detail).

2. **Vascular dementia** (Korczyn, Vakhapova, & Grinberg, 2012; Lee, 2011; O'Brien & Thomas, 2015): The symptoms include the following: problems with reasoning, planning and judgment, slowed thinking, difficulty concentrating, memory loss (though often less pronounced than in Alzheimer's disease, and mood swings and depression. This type of dementia can be caused by conditions like high blood pressure, high cholesterol, diabetes, smoking, and obesity, which damage blood vessels in the brain, leading to strokes or small vessel disease (Iadecola, 2013).

3. **Lewy body dementia** (Sanford, 2018; Walker et al., 2015): The symptoms include the following: visual hallucinations, fluctuations in alertness and attention, Parkinson's-like symptoms (e.g., rigid muscles and tremors), REM sleep behavior disorder (acting out dreams), and memory loss and cognitive decline. The exact cause of this type of dementia is unknown. However, it is characterized by the presence of abnormal protein deposits (Lewy bodies) in the brain (Mayo & Bordelon, 2014). Genetic factors and environmental influences may contribute to its cause, too (Sanghvi et al., 2020).

4. **Frontotemporal dementia** (Antonioni et al., 2023; Ulugut & Pijnenburg, 2023): The symptoms include the following: changes in personality and behavior (e.g., apathy or disinhibition), difficulty with language (which includes speaking, understanding, reading, or writing), impaired judgment and reasoning, and memory loss may not be as prominent in the early stages. This type of dementia is caused by progressive nerve cell loss in frontal and/or temporal lobes of the brain (Sivasathiaseelan et al., 2019). Genetics also plays a significant role in some cases, while in others, the cause is idiopathic or unknown (see Fenoglio et al., 2018, for more detail).

As briefly described above, the symptoms of dementia can vary in severity and may overlap between different types of dementia. Other conditions affecting brain function and structure can have diverse

causes, including genetic predisposition, environmental factors, infections, autoimmune reactions, and neurodegenerative processes. Each condition requires specific diagnostic evaluation and appropriate management.

2. HIPPOCAMPUS

The hippocampus is located in the medial temporal lobe of the brain. It is a crucial structure in the brain that is involved in memory formation and consolidation as well as spatial navigation (Kitamura & Inokuchi, 2014; Kühn & Gallinat, 2014) and emotional regulation (Zhu et al., 2019). It plays a crucial role in converting short-term memory into long-term memory and is involved in various aspects of learning and memory consolidation (Eichenbaum, 2017). Understanding how the hippocampus is impacted by dementia (Bettio, Rajendran, & Gil-Mohapel, 2017) is crucial because the hippocampus plays a key role in memory formation and retrieval (Teyler & DiScenna, 1985). Dementia often leads to cognitive decline, including memory loss, and the hippocampus is one of the brain regions most affected by conditions like Alzheimer's disease (Rao et al., 2022), which is the most common cause of dementia. By understanding how dementia affects the hippocampus, researchers and therapists can develop better strategies for early detection, treatment, and management of the condition.

In Alzheimer's disease, abnormal protein deposits, such as beta-amyloid plaques and tau tangles, accumulate in the hippocampus (Rajmohan & Reddy, 2017). These deposits interfere with neuronal communication and disrupt synaptic function, impairing the hippocampus's ability to encode new memories and retrieve existing ones. Consequently, individuals with Alzheimer's often experience difficulty in learning new information and recalling past events.

The progressive neurodegeneration seen in dementia leads to the loss of neurons and synaptic connections within the hippocampus (Arendt, 2009). As neurons degenerate, the volume of the hippocampus decreases, which can be observed through neuroimaging techniques like MRI scans. This shrinkage further impairs memory function and contributes to the cognitive decline characteristic of dementia.

Additionally, inflammation in the hippocampus is common in dementia (Stefaniak & O'Brien, 2015). Chronic inflammation exacerbates neuronal damage and accelerates cognitive decline. Immune cells in the brain release inflammatory molecules in response to the presence of abnormal proteins and cellular damage, contributing to ongoing neurodegeneration.

Furthermore, vascular dementia, another common form of dementia, can also affect the hippocampus (Du et al., 2002; Nishio et al., 2010). Reduced blood flow to the brain due to conditions like strokes or small vessel disease can damage hippocampal neurons, leading to cognitive impairment.

In summary, the hippocampus is profoundly affected by dementia through various mechanisms including protein deposition, neurodegeneration, inflammation, and vascular damage. These pathological changes disrupt the crucial role of hippocampus in memory formation and spatial navigation (Kitamura & Inokuchi, 2014; Kühn & Gallinat, 2014), contributing to the cognitive decline observed in individuals with dementia.

3. THE FOUR LOBES OF THE BRAIN

Dementia impacts the four lobes of the brain; each cortical lobe is responsible for various functions critical to our cognitive and emotional well-being. Understanding how dementia manifests in these lobes provides insight into the complexity of the condition and aids in developing targeted interventions and support strategies.

The brain consists of four main lobes (Casillo, Luy, & Goldschmidt, 2020): the frontal lobe, parietal lobe, temporal lobe, and occipital lobe. Each lobe serves distinct purposes and houses specialized regions responsible for different aspects of cognition and behavior. In dementia, these lobes undergo progressive deterioration, leading to a decline in cognitive abilities and behavioral changes.

All the four cortical lobes work together in complex ways to facilitate cognitive functions, sensory processing, and motor control (Casillo, Luy, & Goldschmidt, 2020). Damage or dysfunction in any of these areas can lead to specific cognitive, sensory, or motor deficits, highlighting the importance of each lobe's specialized functions in overall brain function and behavior (Gaetz, 2004).

3.1 Frontal Lobe

The frontal lobe is located at the front of the brain. It plays a crucial role in executive functions such as decision-making, problem-solving, planning, and emotional regulation (Chayer & Freedman, 2001). It also houses the primary motor cortex, responsible for voluntary muscle movement. This cortical lobe plays a crucial role in executive functions, including decision-making, problem-solving, and impulse control (Chayer & Freedman, 2001). In dementia, particularly in conditions like frontotemporal dementia (FTD), degeneration of the frontal lobe results in alterations in personality, disinhibition, apathy, and impaired judgment (Snowden, Neary, & Mann, 2002). Individuals may exhibit socially inappropriate behaviors and struggle with planning and organizing tasks.

Frontal lobe dysfunction is a hallmark feature of various types of dementia (Neary et al., 1988), including Alzheimer's disease, frontotemporal dementia, and vascular dementia. The frontal lobes play a crucial role in executive functions, such as decision-making, problem-solving, planning, impulse control, and social behavior regulation. When affected by dementia, these functions deteriorate, leading to significant cognitive and behavioral changes. One prominent effect is impairment in executive functions (Voss & Bullock, 2004). Individuals may struggle with planning and organizing daily tasks, initiating activities, and maintaining attention on tasks. Decision-making becomes compromised, leading to poor judgment and difficulty adapting to new situations. This can result in a decline in overall independence and functional abilities. Furthermore, changes in personality and behavior are common manifestations of frontal lobe dysfunction in dementia (Chow, 2000). Patients may exhibit disinhibition, impulsivity, apathy, or socially inappropriate behaviors. They may also experience mood disturbances, such as depression or irritability. These alterations can strain interpersonal relationships and impact the individual's quality of life. Additionally, language difficulties can arise from frontal lobe involvement, although they are more pronounced in frontotemporal dementia (Hardy et al., 2016; Peelle & Grossman, 2008). This can manifest as reduced verbal fluency, difficulty finding the right words, or comprehension deficits.

As dementia progresses, the frontal lobe atrophy worsens, exacerbating cognitive and behavioral symptoms (Broe et al., 2003; Neary et al., 1988). Care strategies often focus on compensatory techniques and behavioral interventions to support individuals in maintaining their independence and managing their symptoms (Sörensen et al., 2006). While treatments may alleviate some symptoms temporarily, there is currently no cure for dementia (Grand, Casper, & MacDonald, 2011), highlighting the urgent need for continued research and improved interventions to address frontal lobe dysfunction and its impact on individuals with dementia and their caregivers.

3.2 Parietal Lobe

The parietal lobe, positioned at the top and back of the brain, integrates sensory information from various modalities, including touch, pressure, temperature, and pain (Fogassi & Luppino, 2005). It

houses the primary somatosensory cortex, which receives and processes tactile information, as well as the association areas responsible for spatial awareness and attention. This cortical lobe is involved in processing sensory information, spatial awareness, and perception (Fogassi & Luppino, 2005). Dementia affecting this lobe, such as in Alzheimer's disease or posterior cortical atrophy (PCA), leads to difficulties in spatial orientation, navigation, and recognizing objects or faces. Individuals may experience challenges in understanding spatial relationships and may struggle with activities requiring hand-eye coordination.

The parietal lobe plays a crucial role in various cognitive functions, including spatial awareness, perception of stimuli, interpretation of sensory information, and integration of sensory input with memory and language (Fogassi & Luppino, 2005; Valler & Coslett, 2018). In dementia, particularly in conditions like Alzheimer's disease and frontotemporal dementia, the parietal lobe undergoes significant structural and functional changes. One of the hallmark features of parietal involvement in dementia is spatial disorientation (Valler & Coslett, 2018). Patients may have difficulty navigating familiar environments, getting lost easily, or misjudging distances. This impairment stems from the role of parietal lobe in processing spatial information and integrating it with sensory input. Additionally, individuals with parietal involvement in dementia may experience deficits in attention and concentration (Neufang et al., 2011). They may struggle to maintain focus or shift attention between tasks due to disruptions in the parietal networks responsible for attentional control. Furthermore, sensory processing abnormalities (Özata Değerli & Altuntaş, 2023) can occur, leading to sensory misperceptions or difficulty distinguishing between different sensory modalities. For instance, patients may have trouble recognizing objects by touch or interpreting visual information accurately. Language disturbances can also manifest, particularly in the comprehension and production of complex sentences (Kirshner et al., 1984; Potkins et al., 2003). This difficulty arises from the parietal lobe's involvement in higher-order language processing and semantic integration.

On the whole, dementia-related changes in the parietal lobe result in a myriad of cognitive impairments, including spatial disorientation, attention deficits, sensory processing abnormalities, and language disturbances. These impairments significantly impact an individual's daily functioning and quality of life, highlighting the importance of understanding and addressing the parietal involvement in dementia management and care strategies.

3.3 Temporal Lobe

The temporal lobe, situated on the sides of the brain, is primarily involved in auditory processing, language comprehension, memory formation, and emotion regulation (see Wong & Gallate, 2012, for detail). It contains the hippocampus, critical for memory consolidation (Pronier, Morici, & Girardeau, 2023), and the auditory cortex, responsible for processing sound. This cortical lobe is vital for memory formation, language processing and comprehension (Bi et al., 2011; Meyer et al., 2005), emotion regulation (Brockway et al., 1998) and some aspects of visual perception. In dementia, particularly in Alzheimer's disease and frontotemporal dementia, degeneration of the temporal lobe is so significant that it leads to various cognitive and behavioral changes (Bozeat et al., 2000; Silveri, 2007) as a result of memory loss, language difficulties, and emotional disturbances (Chan et al., 2001). Individuals may have trouble recalling recent events, finding the right words, and regulating their emotions.

One primary significant impact is on memory function. The hippocampus, a structure within the temporal lobe, is responsible for forming and consolidating memories (Eichenbaum, 2017). In dementia, this area is often one of the first to deteriorate, leading to deficits in short-term memory and difficulty in forming new memories. As the disease progresses, long-term memories may also be affected, impacting an individual's ability to recall past events and information. Language processing is another significant function of the temporal lobe (Bi et al., 2011; Meyer et al., 2005), particularly in the left hemisphere, that is impacted in dementia. Damage to this area can result in language difficulties, such as aphasia, where individuals struggle to find the right words, comprehend language, or express themselves coherently.

Emotional changes are commonly noted in patients with dementia, partly due to the involvement of the temporal lobe (Kumfor et al., 2014). As the disease advances, individuals may experience mood swings, apathy, or heightened emotional responses. This can significantly impact their quality of life and relationships with others. Additionally, visual perception may be affected (see Mori et al., 2000, for more detail), particularly in cases where the disease progresses to involve areas responsible for processing visual information within the temporal lobe. This can lead to problems with object recognition, spatial awareness, and visual-spatial navigation.

In general, the involvement of the temporal lobe in dementia leads to a wide range of cognitive and behavioral symptoms, profoundly impacting an individual's daily functioning and quality of life as the disease progresses. Early detection and appropriate interventions are crucial in managing these symptoms and improving the patient's overall well-being.

3.4 Occipital Lobe

The occipital lobe, located at the back of the brain, plays a crucial role in processing visual information. It contains the primary visual cortex, which receives and interprets visual stimuli from the eyes, and higher-order visual association areas responsible for object recognition, spatial processing, and motion perception. This cortical lobe is primarily responsible for processing visual information. While dementia primarily affects other lobes, visual disturbances can occur in conditions like dementia with Lewy bodies (DLB) or posterior cortical atrophy (PCA) (Metzler-Baddeley et al., 2010). Individuals may experience visual hallucinations, difficulty recognizing objects or faces, and problems with depth perception (Renouf et al., 2018).

While dementia primarily affects cognition, memory, and behavior, it can also impact the occipital lobe, leading to various visual disturbances and impairments (Armstrong & Kergoat, 2015; Fymat, 2019). For instance, as dementia progresses, structural changes occur in the brain, including the occipital lobe. These changes can manifest as visual impairments such as difficulties with depth perception, contrast sensitivity, color perception, and motion detection. As a result, patients with dementia may experience visual hallucinations or misinterpretations of what they see due to disruptions in the function of the occipital lobe. Additionally, changes in this occipital region can influence mood and behavior. Visual disturbances and difficulties (e.g., visuospatial dysgnosia) may lead to frustration, stress, anxiety and/or depression (known as SAD Syndrome; see Xie & Wang, 2021, for detail) in individuals with dementia. Furthermore, damage to the occipital lobe can exacerbate other cognitive symptoms of dementia. For example, impaired visual processing can hinder a person's ability to recognize faces or objects (known as **prosopagnosia)**, which may contribute to confusion and disorientation (i.e., perceptual distortion and thought disorder) (Warren et al., 2024). It can also affect visuospatial awareness (i.e., visuospatial dysgnosia), making it challenging for individuals to navigate their surroundings safely (Davous et al., 1996; Ricker, Keenan, & Jacobson, 1994). Moreover, because the occipital lobe is interconnected with other brain regions involved in memory and executive function, its dysfunction can further exacerbate cognitive decline in dementia patients.

In summary, dementia can affect the occipital lobe, leading to a range of visual impairments and disturbances, which in turn can impact cognitive function, behavior, and emotional well-being. Understanding these effects is crucial for developing interventions to improve the quality of life for individuals living with dementia.

4. INTERPLAY OF ACETYLCHOLINE AND BDNF IN DEMENTIA: UNRAVELING THE NEUROLOGICAL NEXUS

The interplay between acetylcholine (ACh) and brain-derived neurotrophic factor (BDNF) is crucial for maintaining cognitive function (Girotra et al., 2022; Hachisu et al., 2015). ACh is a neurotransmitter

involved in various cognitive processes, including memory and learning, while BDNF is a protein that operates within the synapses, facilitating communication between nerve cells, and supports the growth, survival, and function of neurons.

In dementia, particularly in conditions like Alzheimer's disease, there is a disruption in this interplay. Reduced levels of ACh are observed due to the degeneration of cholinergic neurons, which are responsible for releasing ACh. This reduction in ACh leads to impaired neurotransmission, contributing to cognitive decline. Additionally, BDNF plays a role in synaptic plasticity and neuroprotection. Reduced BDNF levels are also observed in dementia, potentially due to decreased production or impaired signaling (Ng et al., 2019). This decrease in BDNF further exacerbates neuronal damage and impairs synaptic function, worsening cognitive deficits as noted in patients with dementia. Therefore, the dysregulation of both ACh and BDNF, either individually or through their interplay, contributes to the pathophysiology of dementia, leading to cognitive decline and other symptoms associated with the condition.

Although the precise causes of dementia remain not fully understood or largely are yet unknown, several elements, such as abnormalities in neurotransmitters and deficiencies in neurotrophic function, have been found to be involved in the neurodegenerative condition. Acetylcholine (ACh) (Mseulam, 2013; see Figure 1) and brain-derived neurotrophic factor (BDNF) (Gao et al., 2022) stand out among them as important participating culprits that may provide insights into and avenues for intervening in the tale of dementia.

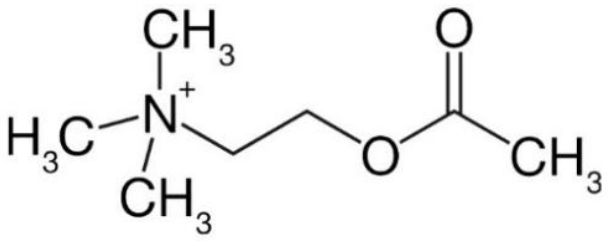

Figure 1: Chemical structure of acetylcholine

4.1 ACh: The Neurotransmitter that Supports Cognitive Functions

According to Hasselmo and Sarter (2011), the neurotransmitter ACh, a chemical messenger excitatory in nature that transmits signals between neurons in the brain, is essential for cognitive functions such as *memory, thinking, learning and attention*. ACh is mainly synthesized within *cholinergic neurons* from *choline* and *acetyl coenzyme A (*which comes from the sugar molecule glucose). These cholinergic neurons are highly concentrated in the *basal forebrain.* The basal forebrain houses the major cholinergic output of the central nervous system (see Figure 2). Within the basal forebrain, the *nucleus basalis of Meynert* (NBM) is a significant source of ACh (Koulousakis et al., 2019).

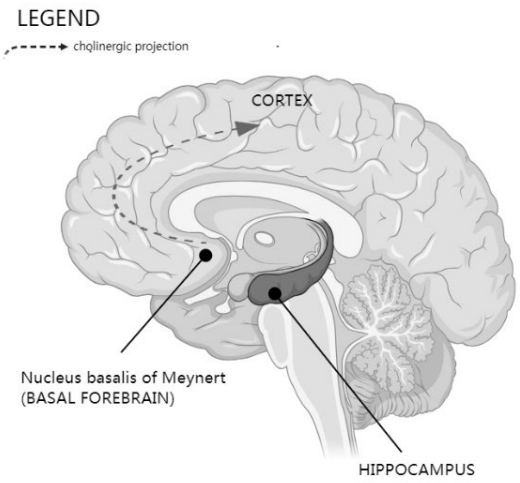

Figure 2: The cholinergic projection from basal forebrain

These cholinergic neurons project extensively into hippocampus and almost all layers of the cerebral cortex, influencing cortical activation during wakefulness and rapid eye movement (REM) sleep (Hasselmo & Sarter, 2011). Following neuronal activation, acetylcholine is subsequently encapsulated into vesicles and released into the synaptic cleft (see Figure 3), where it attaches to cholinergic receptors on postsynaptic neurons to transmit signals linked to memory and learning (Gasnier, 2000).

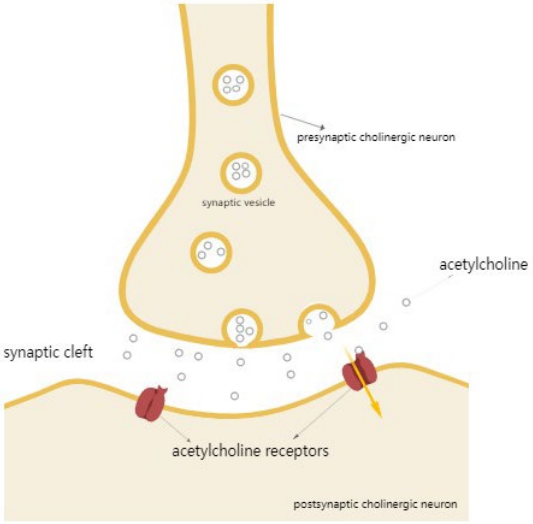

Figure 3: Acetylcholine in synaptic vesicles released into synaptic cleft

Postmortem studies of AD brains have consistently revealed a significant loss and dysfunction of cholinergic neurons at the basal forebrain (Gratwicke et al., 2013). It contributes to the cognitive decline observed in the disease.

Other widespread consequences of ACh deficiency in dementia include the following:

a) Memory impairment: ACh is intricately involved in hippocampus-dependent learning. Cholinergic neurons densely innervate the hippocampus, influencing both episodic and semantic memory. According to Hasselmo and Sarter (2011), disrupted ACh signaling impairs the hippocampus, a crucial memory area, making it harder to encode, consolidate, and retrieve information.
b) Executive dysfunction: Planning, thinking, and decision-making abilities are impacted by ACh decrease, which impacts frontal lobe function (Logue & Gould, 2014).
c) Attention deficits: Lower levels of ACh make it harder to focus and block out distractions, which makes it harder to multitask and causes cognitive fatigue (Parikh & Bangasser, 2020).

4.2 BDNF: The Architect of Neurogenesis, Neuroplasticity and Neuronal Survival

Another important participant is brain-derived neurotrophic factor (BDNF), a protein functioning as a 'nerve nourishment' to stimulate neurogenesis, neuronal repair and synaptic plasticity (Wurzelmann et al., 2017). BDNF is also implicated in mood regulation which low levels have been linked to depression, suggesting a potential role in mental health.

According to Allen et al. (2013), BDNF is primarily produced by neurons themselves, with the highest levels found in the hippocampus, cortex, cerebellum, and brainstem. BDNF is widely expressed throughout the brain, with particularly high levels in regions implicated in learning and memory, such as the hippocampus and cerebral cortex. It plays a crucial role in synaptic plasticity, the ability of synapses to strengthen or weaken in response to experience (Schindowski, Belarbi, & Buée, 2008). This neurotrophin promotes the formation of new synapses, enhances synaptic transmission, and increases neuronal excitability, thereby facilitating learning and memory processes. Importantly, BDNF levels are tightly regulated by neuronal activity, with synaptic stimulation leading to increased BDNF expression and release.

Deficiencies in BDNF, even if not the initial trigger for disease onset, can escalate neurodegeneration, synaptic dysfunction, neuronal loss, cell demise, and cognitive decline, leading to symptoms of neurological disorders like dementia and AD (Giacobbo et al., 2019). Multiple mechanisms, including oxidative stress, inflammation, and neurodegeneration, contribute to this decline (Zuccarini & Cattaneo, 2009). Reduced BDNF levels, as noted by Bekinschtein et al. (2014), correspond to diminished neuroplasticity, impairing cognitive function and memory by limiting the brain's adaptability and learning capacity. Wurzelmann et al. (2017) have further highlighted that decreased BDNF levels correlate with reduced neurogenesis in the hippocampus, inhibiting the brain's ability to replace damaged cells and promote healing. Additionally, insufficient BDNF increases neuronal susceptibility to damage and death, intensifying neuronal vulnerability (Zuccarini & Cattaneo, 2009), and are associated with both normal and pathological aging as well as psychiatric disease such as dementia (Miranda et al., 2019).

4.3 The Intertwined Relationship of ACh and BDNF in Dementia

ACh and BDNF have a complex feedback loop that results from their nuanced interaction. This goes beyond a simple parallel relationship. Research (e.g., Glowacka et al., 2022; Hachisu et al., 2015; Yoon et al., 2022) indicates that ACh increases the expression of BDNF genes, which raises BDNF levels and improves neuronal health. This process is known as *ACh-stimulated BDNF production* (Pang & Lu, 2004). However, cholinergic neurons are supported in their survival and function by BDNF, which subsequently indirectly raises ACh levels (Niewiadomska et al., 2011). In other words, this implies that dementia is a vicious cycle. On the contrary, cholinergic projection decline which reduces ACh cause a fall in BDNF levels (Pang & Lu, 2004). Memory and cognitive functions are impacted by such decreased ACh resulting from neurodegeneration while neurons at the hippocampus as neurogenesis will be reduced (Wurzelmann et al., 2017). Heightened susceptibility to injury hastens the deterioration of neurons and exacerbates cognitive ageing.

4.4 The Interplay between Educational Therapy, BDNF and Acetylcholine

Pharmacological therapeutic approaches, such as acetylcholinesterase inhibitors like donepezil, are known to increase BDNF levels and promote synaptic plasticity (Korabecny et al., 2019). However, the focus of this paper is on non-pharmacological intervention strategies like physical exercise, cognitive training, and social engagement, which fall under the umbrella of educational therapy (ET) in dementia treatment. According to Chua and Chia (2023), "[U]nder the purview of the World Health Organization (WHO), ET has been officially recognized and classified under the diagnostic code 93.82 since 1986 in

the International Classification of Diseases, Clinical Modifications-Ninth Edition-Clinical Modification, Volume 3 (ICD-9-CM, Vol. 3) (World Health Organization, 1986)" (p. 5). ET involves personalized strategies addressing cognitive and emotional challenges. It can be adapted to help individuals maintain cognitive function through tailored exercises, memory aids, and communication techniques, thereby improving their quality of life and potentially slowing cognitive decline.

These educational therapy-based interventions (ETbI), including physical exercise, cognitive training, and social engagement, have been shown to enhance cholinergic function and improve cognitive outcomes in dementia patients (Del Arco et al., 2007). Several fMRI studies (e.g., Lima et al., 2014; Nguyen et al., 2019; van Praag et al., 2000) have shown that enriched environments with these activities activate brain regions associated with the cholinergic system, promoting cognitive skills, memory, learning, attention, synaptic plasticity, and neural connectivity.

Activities such as participating in educational programs, learning new skills, solving puzzles, and regular aerobic exercise also increase BDNF expression and enhance cholinergic function (Cotman & Berchtold, 2002; Novkovic et al., 2015; van Praag et al., 2000). Additionally, social support and engagement contribute to increased BDNF expression and improved neuronal health (Cao et al., 2017).

These non-pharmacological ETbI activities are integral parts of dementia treatment programs, playing a significant role in increasing cholinergic transmission and BDNF levels (Fabel et al., 2009) by promoting neuronal survival and synaptic plasticity (Cotman & Berchtold, 2002). By understanding the cognitive roles of different brain regions affected by dementia, educational therapists working with these patients can develop targeted interventions to optimize learning and cognitive functioning. These interventions include enhancing memory encoding and retrieval, improving executive functions, enhancing sensory integration and spatial reasoning abilities, providing memory aids and language therapy techniques, and offering visual support and rehabilitation.

In addition, there are five other examples (see Marim et al., 2013; Thinnes & Padilla, 2011, for additional information) of how ETbI activities can be applied in dementia treatment focusing on different parts of the brain as follows:

1. The hippocampus plays a crucial role in memory consolidation (Pronier, Morici, & Girardeau, 2023). The ETbI activities aim at enhancing memory encoding and retrieval can be beneficial.
2. Frontal lobe impairment may affect executive functions (e.g., planning and decision-making) (Hodges et al., 1999). The ETbI strategies focus on improving organization and problem-solving skills.
3. Parietal lobe involvement can lead to difficulties with spatial awareness and sensory processing (Jacobs et al., 2011; Zhang et al., 2023). Hence, the EBtI activities aim to enhance sensory integration and spatial reasoning abilities.
4. Temporal lobe damage can impact memory formation and language processing (Hodges et al., 1999). Therefore, memory aids and language therapy techniques are incorporated in ETbI activities.
5. Occipital lobe dysfunction (see Uhlhaas et al., 2008) may result in visuospatial disturbances (e.g., visuospatial dysgnosia) and impairments in visual processing (Pal et al., 2016), indicating the need for visual support and rehabilitation to be included as ETbI activities in the dementia treatment program.

By understanding the interplay between BDNF and ACh, the cognitive roles of the different regions of the brain and how dementia affects them, implementing ETbI activities in dementia treatment can help to optimize learning and cognitive functioning for such patients.

5. LIMITATIONS OF EDUCATIONAL THERAPY IN DEMENTIA TREATMENT

However, non-pharmacological approaches such as educational therapy-based interventions (ETbI) for dementia treatment (Marim et al., 2013; Thinnes & Padilla, 2011), while beneficial, have their limitations, too. Here are just five examples to explain the limited application of ETbI activities as follows:

1. Hippocampus Damage (see Gulyaeva, 2019): Dementia often involves hippocampal damage, affecting memory formation and retrieval. ETbI activities may struggle to address memory deficits caused by hippocampal dysfunction.

2. Temporal Lobe Deficits (see Snowden et al., 2018): The temporal lobes, including the hippocampus, play a crucial role in memory and learning. Damage to these areas can hinder the effectiveness of ETbI activities aimed at cognitive enhancement.

3. Frontal Lobe Dysfunction (see Neary et al., 1988): Dementia frequently involves frontal lobe dysfunction, impacting executive functions like planning, organizing, and decision-making. ETbI activities may not fully address these deficits, limiting its effectiveness in improving daily functioning.

4. Parietal and Occipital Lobe Involvement (Brand & Markowitsch, 2008): Dementia can also affect the parietal and occipital lobes, impairing sensory processing, spatial awareness, and visual perception. ETbI activities may struggle to address these impairments adequately.

5. Progressive Nature of Dementia (Geschwind, 2016; Geschwind et al., 2008): Dementia is often progressive, leading to ongoing decline in cognitive function. While ETbI activities can provide short-term benefits, its long-term efficacy may be limited as the disease advances.

In summary, while educational therapy-based interventions can offer some benefits for individuals with dementia, its effectiveness may be constrained by the specific deficits associated with hippocampal and lobar dysfunction, as well as the progressive nature of the disease. Complementary approaches, such as pharmacological interventions and support for caregivers, may be necessary to provide comprehensive care for individuals with dementia.

6. CONCLUSION

In summary, dementia presents a multifaceted challenge involving the interplay of neurotransmitter dysfunction, neurotrophic support deficits, and regional brain degeneration. From the vulnerability of cholinergic neurons in the basal forebrain to the diverse manifestations across the four lobes of the brain, the complexity of dementia underscores the importance of comprehensive understanding and targeted educational therapy-based interventions. By elucidating the roles of acetylcholine, BDNF, and lobar involvement, researchers and healthcare professionals are better equipped to develop innovative treatments and personalized care strategies. Through collaborative efforts focused on preserving cognitive function, addressing behavioral symptoms, and providing tailored support, we can strive towards enhancing the quality of life for individuals affected by dementia as well as the psychosomatic wellness of their caregivers.

7. ACKNOWLEDGEMENT

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8. COMPETING INTERESTS

Authors have declared that no competing interests exist.

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