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CAN MINDFULNESS BEAT ALZHEIMER'S DISEASE?

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Abstract The purpose of this paper is to identify to what extent the development of Alzheimer's disease can be delayed or prevented through the use of mindfulness-based interventions. Alzheimer's disease (AD) is a progressive neurodegenerative disease in which accumulation of amyloid plaques and neurofibrillary tangles (NFTs) play an important role. This leads to neuronal cell death and synaptic degeneration, especially in the default-mode network (DMN). No current effective treatment is available. Mindfulness has been related to an increase in volume and connectivity of the exact brain areas affected in AD. Therefore, mindfulness-based interventions (MBIs) such as mindfulness-based stress reduction (MBSR), meditation and yoga have been tested in people with mild cognitive impairment (MCI). MCI is seen as a transitional state between healthy age-related cognitive decline and AD pathology, hence an open window for early intervention. In this paper it is found that mindfulness has great potential to prevent AD-related pathology of the DMN, hence decreasing cognitive decline in people with MCI.
Keywords: Alzheimer's disease (AD), mindfulness-based interventions (MBIs), mild cognitive impairment (MCI), cognitive decline, default-mode network (DMN)

1 Introduction

With progressing age, people are often afraid of losing their mind due to the well-known fact that with aging comes a decline in cognitive functioning. Unfortunately, the brain´s aging process can advance even more rapidly than it should, causing significant problems in daily life. In these cases people are said to have *dementia*, which is caused by damage to brain cells (Dementia, n.d.). The most common form of dementia is the progressive neurodegenerative disease called *Alzheimer's disease* (AD), accounting for 60-70% of all dementia cases (Wong, Hassed, Chambers & Coles, 2016). People with Alzheimer's generally have characteristic symptoms, including problems with memory, thinking and planning, language and communication, and eventually lose the ability to respond to the environment or take care of themselves (Stages of Alzheimer's & Symptoms | Alzheimer's Association, 2017). These symptoms of Alzheimer's can become very severe. Therefore, research is being done to highlight the pathological hallmarks of AD and find a cure or treatment to slow down or prevent the development of the disease. Wong et al. (2016) proposed *mindfulness* as a possible non-pharmacological intervention to improve cognitive abilities and therefore prevent the development of AD. Mindfulness can be considered as non-judgemental awareness that arises from training your attention to be in the present moment (Creswell, 2017). At the moment, there is no cure or treatment that can slow down or stop the progression of AD. The only existing medical treatment consists of several types of drugs that are used to temporarily alleviate the symptoms of the disease. However, there is no conclusive evidence that this treatment actually improves cognition or delays the progression of the disease (Wong et al., 2016). As AD is the most common form of dementia, tackling this disease would have a great impact on the problems that come along with dementia. Around the world, 47.5 million people have some form of dementia, and this is estimated to increase with 7.7 million new cases each year (Latest Alzheimer's Facts and Figures, 2016). To make matters worse, AD is the sixth leading cause of death in the United States (Innes, Selfe, Khalsa & Kandati, 2016) and poses a huge burden on family and the economy. Thus, it is of great importance to find effective new forms of treatment for AD, as there is no current cure. Mindfulness-based interventions show great promise as an affordable non-pharmacological treatment option for AD. Growing evidence has linked mindfulness to changes in the structure of the brain (Luders, 2014), demonstrating that practicing mindfulness can increase grey matter volume and strengthen brain functional connectivity (Luders, 2014; Wong et al., 2016), the exact problems present in AD. Nevertheless, the scientific investigation of mindfulness is still in its infancy,

with only a limited number of completed studies and randomized trials (Luders, 2014). Consequently, the exact positive effects of mindfulness on cognitive decline have not yet been elucidated and should be further examined.

Therefore, this paper addresses the research question: To what extent can the development of Alzheimer's disease be delayed or prevented through mindfulness-based interventions? In the paper, it is argued that mindfulness-based interventions (MBI) have great potential to delay or prevent the development of Alzheimer's disease, as studies consistently show that mindfulness counteracts age-related grey matter atrophy and increases brain connectivity and brain volume in the exact brain areas that are affected in Alzheimer's. Firstly, the cause and progression of Alzheimer's disease is examined. Thereafter, the neurobiological effects of mindfulness in relation to AD are highlighted, after which the effectiveness of mindfulness training in individuals with mild cognitive impairment (MCI) is discussed. The paper ends with a conclusion of the findings in relation to the research question, the possible implications these findings have, and a discussion of present limitations.

2 The Cause and Progression of Alzheimer's Disease

Not everything is known about the cause of Alzheimer's disease; however, several neuropathological hallmarks have been found. These include brain atrophy due to synaptic degeneration and neuronal cell death at the macroscopic level, which are thought to be caused by amyloid plaques and neurofibrillary tangles (NFTs) at the microscopic level (Lista & Hampel, 2016). Brain atrophy essentially means that the brain shrinks dramatically in size due to the loss of neurons (see figure 1) (Dennis & Thompson, 2013). Consequently, the cerebral cortex, the outer layer of the brain, is mostly damaged. The cortex consists mainly of neuron cell bodies, and is called the grey matter (due to its greyish colour). Within the cortex are all the main areas that play a key role in most of our cognitive abilities. These include memory, attention, perception, awareness, thinking, language and consciousness. Shrinkage of the cortex due to cell death consequently means a loss of these cognitive abilities. Thus, brain atrophy leads to the characteristic progressive cognitive deterioration seen in all Alzheimer's disease patients. Some degree of cerebral shrinkage is part of the natural process of aging; however, in Alzheimer's disease this decline is rapidly accelerated, with specific brain areas hit hardest (Dennis & Thompson, 2013). A critical step in developing interventions to delay or prevent the rapid decline in AD is to determine how the course of decline differs from that of the normal aging process. One important

research focus has been the association between Alzheimer's disease and the formation and accumulation of amyloid plaques in the brain's extracellular space. These plaques are abnormal clumps of the amyloid beta (ab) peptide, originating from a larger amyloid precursor protein found in the membrane surrounding brain cells. Some 'misfolded' forms of these ab molecules can aggregate into soluble oligomers (Lista & Hampel, 2016), which build up in plaques. These plaques are thought to be toxic to nerve cells, resulting in synaptic dysfunction and loss (Lista & Hampel, 2016). In this way, the formation of misfolded forms of the amyloid beta peptide molecules are thought to play a crucial role in the pathology of Alzheimer's disease. In addition to these plaques, so-called neurofibrillary tangles (NFTs) play a crucial role in AD pathology (as exemplified in figure 2 and 3). These NFTs are made up of another protein: tau. All healthy cells have a transport system made of proteins, which is organized in orderly parallel strands (like railroad tracks). The tau protein helps the strands remain straight so that vital molecules can travel along them within the cell (Brain tour, 2017). In AD, tau dissociates from the strands and self-aggregates into twisted strands called tangles (NFTs) (Lista & Hampel, 2016). As a consequence, the strands of the transport system cannot stay straight and the system collapses (see figure 2) (Lista & Hampel, 2016). Essential molecules like nutrients can no longer travel through the cells, eventually leading to cell death (Brain tour, 2017) and, consequently, contributing to the onset of Alzheimer's disease. By using various brain imaging techniques scientist have been able to identify which brain areas are most affected by plaques and NFTs. The default-mode network (DMN) has been consistently linked to Alzheimer's disease. The DMN is thought to represent a brain system made up of several anatomically connected and interactive brain areas (Dennis & Thompson, 2013; Buckner et al., 2008). The system is deactivated when a person is not focused on an external task, such as visual attention, or during cognitive working memory tasks. It becomes active the moment someone goes into wakeful rest during, for example, daydreaming or mind-wandering (Dennis & Thompson, 2013). Mind-wandering often involves thinking about oneself or others, remembering the past or envisioning the future. These are all examples of internally directed or self-generated thoughts, which include autobiographical or episodic memory retrieval (Buckner et al., 2008). The activity during internally oriented tasks is thought to be necessary for memory consolidation (Dennis & Thompson, 2013). As memory is exactly the cognitive domain which is highly impaired in Alzheimer patients, there appears to be a convincing link between AD and the default-mode network. Consistent with the clinical manifestation of Alzheimer's disease that impaired memory is one of the first symptoms, cortical structures linked to memory are the first areas to be affected in the dis-

ease (Buckner et al., 2008; Serra et al., 2015). Amongst others, the hippocampus, which is part of the DMN, is often already damaged by plaques and NFTs before symptoms emerge and AD is diagnosed (Serra et al., 2015). The hippocampus is involved in the storage of information into long-term memory and the retrieval of memories. As the disease progresses, the plaques and NFTs spread through the cortex in a pattern that is remarkably similar to the anatomy of the default-mode network (see fig.3) (Buckner et al., 2005; Dennis & Thompson, 2013; Serra et al., 2015), leading to overall functional disconnection within the network. Thus, plaques and NFTs seem to accumulate in the DMN, affecting this network even before symptoms emerge. The question is why specifically these regions are most affected. Several theories have been proposed to explain why the default-mode network is particularly vulnerable to AD pathology. Buckner and colleagues (2005) found that there is a striking correlation in the brain areas involved in DMN activity in young adults and the brain regions affected by amyloid deposition in AD. This finding led Buckner and colleagues to the idea that the continuous activity of the network, and with that the high metabolic rate, directly relates to - or even causes - AD pathology. They called this idea the *metabolism hypothesis*. The preferential use of the default network throughout life may lead to increased accumulation of ab protein and the pathological consequences. This theory explains why memory systems may be preferentially affected in patients with AD, as these systems play a central role in resting brain activity as part of the DMN. The theory is supported by the finding that formation of the amyloid precursor protein (APP) is dependent on neuron activity (Simic, Babic, Borovecki, & Hof, 2014). Since regional increases in neuronal activity are linked to regional increases in the concentration of APP, it may be possible that due to their constant activity, DMN neurons produce and release more APP than occur elsewhere in the neocortex. This, in turn, leads to an increase in production, oligomerization, and aggregation of the ab protein as well as formation of NFTs. Formation of NFTs is presumably caused by the released ab oligomers (Simic et al., 2014). In short, brain areas involved in the default-mode network (DMN) are the most affected in Alzheimer's disease, which can be seen from the accumulation of amyloid plaques and NFTs in these areas. This can be explained by the metabolism hypothesis that states that the almost continuous activity of the DMN leads to increased production of the ab protein. The DMN regions are highly involved in memory, hence disruption leads to memory problems characteristic in Alzheimer's disease. What becomes apparent is that an effective treatment for AD would encompass either the preservation or regeneration of areas affected in AD. To what extent this is possible with mindfulness based interventions will be analysed in the following section.

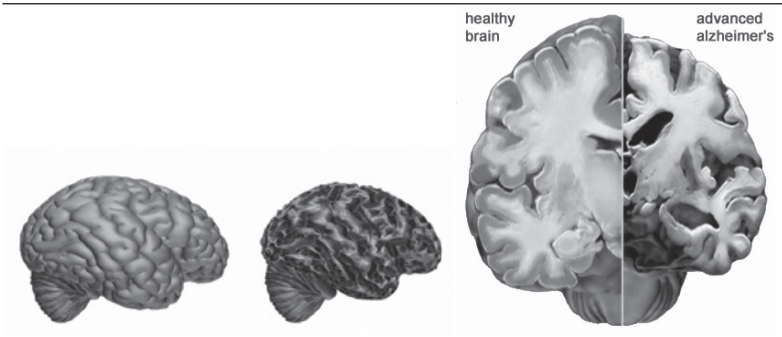

Figure 1 *Brain atrophy; shrinkage of the cortex due to neuron loss in AD (Brain tour,2017).*

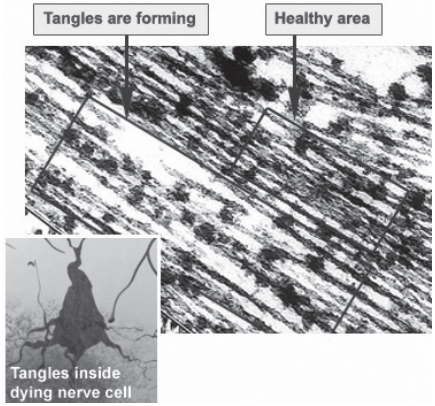

Figure 2 *The difference in transport system between healthy and dying brain cells (Brain tour, 2017).*

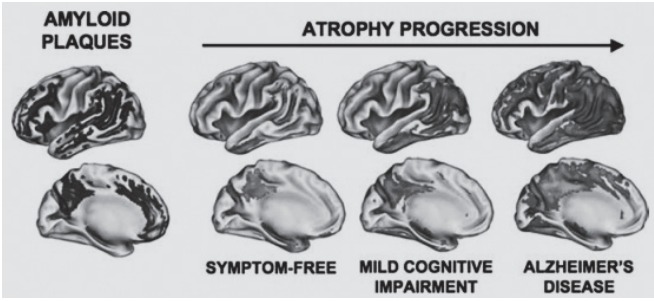

Figure 3 *Plaques and NFTs spread through the cerebral cortex in a predictable pattern in AD (Buckner et al., 2008)*

3 Mindfulness and the brain

Mindfulness can be defined in several ways; however, in this paper mindfulness is defined as a way of training attention and fostering awareness with a non-judgemental attitude (Wong et al., 2016). Mindfulness or mindful meditation has been taught in different ways, both in private settings as well as in clinical or research settings. Examples of clinical or research forms are mindfulness-based interventions (MBIs), such as mindfulness-based stress reduction (MBSR), or mindfulness-based cognitive therapy (MBCT) (Brewer et al., 2011). In this section, the physical and mental health effects of these programs are studied to discover how mindfulness affects us and our brains. Although mindfulness research is still in its infancy, there are already several studies that have explored the use of mindfulness-based interventions. Research indicates that mindfulness training is associated with positive cognitive, behavioural and neural changes in both healthy and clinical populations (Larouche et al., 2014; Luders, 2014). Some studies even suggest that sustained mindfulness practice may have a neuroprotective effect against age-related decline (Larouche et al., 2014; Luders, 2014). Based on growing evidence it is therefore thought that mindfulness training may potentially be a feasible and affordable, effective, non-pharmacological treatment approach to improve cognitive function in patients with neurodegenerative diseases, such as AD (Wong et al., 2016). The interesting question remains then, how does mindfulness training enhance cognition and possibly prevent neurodegenerative diseases? Several pathways have been proposed through which mindfulness training can have beneficial effects on cognition. Of these pathways, one is particularly interesting in relation to Alzheimer's disease. Research shows that the hippocampus and other regions of the default-mode network (DMN) are typical areas involved in the practice of meditation or mindfulness exercises (Holzel et al., 2008; Luders et al., 2013). Moreover, studies have shown that mindfulness practice has positive effects on brain volume, gray matter concentration, and brain functional connectivity (Luders, 2014). These findings combined suggest that mindfulness training can prevent the pathological characteristic of AD, namely tissue loss in the hippocampus, progressive loss of gray matter, and decreased functional connectivity in the DMN (Wong et al., 2016). For this reason, it is interesting to look at how mindfulness accomplishes its positive effects on the default-mode network. As mentioned above, when we are distracted or inattentive our brain switches to default mode. Our mind wanders. This can also be seen as being unmindful, since mindfulness is defined as being attentive and aware of the present moment. Mindfulness has been found to switch off the DMN. Brewer et al. (2011) investigated brain activity in experienced meditators

and meditation-naive controls during several kinds of mediations. Results show that across all meditation types, the main regions of the DMN were deactivated in experienced meditators, which was not the case in the controls. Moreover, functional connectivity analysis revealed stronger connections between the main regions of the DMN both at rest and during meditation (Brewer et al., 2011). Greater connectivity within the DMN of meditation practitioners has also been found by Jang et al. (2010) and Taylor et al. (2012), confirming that mindfulness practice strengthens present-moment awareness. These findings show that mindfulness can decrease DMN activity, thus preventing amyloid accumulation and thereby increasing resistance to the disruption in functional connectivity of the DMN as seen in Alzheimer's disease. This idea is supported by studies that show differences in the atrophy of DMN regions between people practicing mindfulness and controls. The foremost used method to investigate the effect of mindfulness in relation to Alzheimer's disease is to either compare the brains of (experienced) meditators to those of healthy mindfulness-naïve controls, or compare the brains of healthy participants who have been given a mindfulness training and healthy controls. In this way, it has been consistently found that the hippocampus differs between meditators and non-meditators (Luders et al., 2013). Two different structural studies both detected significant larger grey matter concentration in the right hippocampus (Holzel et al., 2008), and greater right and left hippocampal volume (Luders et al., 2009; Luders et al., 2013).These findings were complemented by functional imaging studies using positron emission tomography (PET) scans or functional magnetic resonance imaging (fMRI), which show that, in both novice and expert meditators, there is increased brain activity in the left and right hippocampus during meditation or mindfulness exercises (Engström, Pihlsgård, Lundberg & Söderfeldt, 2010; Luders et al., 2013). Furthermore, investigations of pre-post changes in brain gray matter concentration and volume in participants of mindfulness-based interventions show promising results in other areas besides the hippocampus as well. For instance, Lazar et al. (2005) examined the link between age and cortical thickness, as shrinkage of the cortex (brain atrophy) is a characteristic symptom of aging, aggravated in those with Alzheimer's disease. The authors compared meditators and controls with respect to their cortical thickness, which revealed significant group differences between both groups. The average cortical thickness of the 40- to 50-year-old meditators was similar to the average thickness of 20- to 30-year old meditation and control participants. Additionally, the results showed that in the control group cortical thickness decreased significantly with age, whereas the decrease was nonsignificant in the meditation group, explaining why meditator´s cortical thickness is similar to that of younger participants (Lazar et al., 2005). Similar

results have been replicated in other studies (e.g., Pagnoni & Cekic, 2007) and thereby provide strong evidence for the argument that mindfulness practices could prevent or delay the age-related neuronal changes seen in Alzheimer's disease. One might object here that it is not clear what causes the difference in brain anatomy between mindfulness practitioners and non-practitioners. It has been suggested that people that practice mindfulness may have innate unique cerebral differences that attract them toward mindfulness in the first place or help them continue ongoing practice (Luders, 2014). Moreover, the anatomical changes could be due to confounding variables, such as diet or a difference proneness to cognitive and neural aging between the subjects (Pagnoni & Cekic, 2007). However, there is more scientific support for the possibility that the actual practice changes brain anatomy. Recent brain imaging studies provide direct evidence for meditation-induced anatomical changes, such as increased gray matter volume and density. Based on this research, two underlying mechanisms have been proposed to explain the anatomical changes found in the brains of mindfulness practitioners. On the one hand, the less significant loss in gray matter in meditators can possibly be explained by a link between meditation, or other mindfulness practices, and neuroprotection. The neuroprotective effect of meditation possibly slows down the rate of age-related neurodegeneration (Lazar et al, 2005; Luders, 2014). There are several studies supporting this idea with evidence. Luders, Cherbuin and Kurth (2015), for example, studied the link between age and whole-brain gray matter in meditators and healthy controls. They found that, in both groups, age-related gray matter decline was present, however the slope the regression line was significantly steeper in controls than in meditators. This indicated that in meditators, the age-related loss of gray matter is less profound than in non-meditators (Luders et al., 2015). On the other hand, it is thought that engaging in mindfulness practices can possibly induce changes as a result of neuroplasticity. This includes mainly neurogenesis and synaptogenesis (Luders, 2014). This idea is supported by research. For example, Hölzel et al. (2011) found that participation in an eight-week MBSR course is associated with increases in grey matter concentration in brain areas involved in learning and memory processes, emotion regulation and self-referential processing. Moreover, Pagnoni and Cekic (2007) found that in meditators total gray matter increased over time, suggesting that there are mechanisms that not only preserve (neuroprotection) gray matter, but also induce growth (neuroplasticity). These results show that mindfulness practices can indeed prevent neurodegeneration and even induce the growth of new brain cells, leading to an increase in gray matter volume. Finally, there is even evidence for a genetic effect of mindfulness, resulting in physiological changes, such as neuronal growth and slowed age-related decline. Dusek et

al. (2008) assessed healthy, long-term practitioners of daily mind-body practices (group M), healthy individuals who completed 8 weeks of training in those practices (group N2), and controls (group N1). They found that 2209 genes were differently expressed in daily mindfulness practitioners group compared to group the healthy individuals who received training group, and 1561 genes in the latter groupcompared to the control group. Moreover, the mindfulness group and the mindful training group shared 1561 differentially expressed genes, indicating that even in novice meditators (after only 8 weeks of practice) genes were already affected. Gene analyses showed that the affected genes play significant roles in biological processes important for preventing cellular damage (Dusek et al., 2008). All these studies support the suggestion that mindfulness-based intervention may be an effective non-pharmacological treatment approach to improve cognitive function and potentially delay or prevent the development of Alzheimer's disease by counteracting the characteristic pathological brain atrophy of the default-mode network regions.

4 Effectiveness of MBI in people at risk for AD

In general, Alzheimer's disease develops rather slowly, and is often preceded by preclinical forms of cognitive decline. This preclinical condition is called *mild cognitive impairment* (MCI), and is characterized by a wide range of cognitive deficits similar to those present in AD (Larouche, Hudon & Goulet, 2014). Mild cognitive impairment is, therefore, often seen as a transitional state between healthy age-related cognitive decline and dementia (Innes et al., 2016). Risk of development into Alzheimer's in individuals with MCI is very high; 5-15% of people with MCI convert to AD each year (Innes et al., 2016), which is 2.5 times higher risk than in healthy aging (Eyre et al., 2016). Those with *amnestic mild cognitive impairment* (aMCI), primarily affecting memory, are most at risk. Their memory deficits are caused by AD-related pathology - plaques and NFTs - starting in the same memory-related brain areas involved in the DMN as in Alzheimer's (Larouche et al., 2014). The idea that mild cognitive impairment could possibly be a transitional state in the development towards Alzheimer's disease is evident from studies showing the connection between their pathologies. Serra et al. (2015) found that people with MCI show a more severe pattern of regional gray matter atrophy and default-mode network disconnection, similar to AD. Additionally, decline in the hippocampus has been found to be a biomarker of MCI and a good predictor of progression towards AD (Larouche et al., 2014; Innes et al., 2016). There is growing evidence that premature interventions in people with MCI can restore

cognition, and possibly postpone the onset of AD by interrupting the neuropathological progression leading to the disease (Larouche et al., 2014). The slow development of AD together with the occurrence of the preclinical phase MCI, caused by AD-related pathology, offers an opportunity for early intervention. To date, there are no approved treatments for people with MCI, but mindfulness-based interventions may offer a form of treatment that specifically addresses the risk factors for conversion to AD. As seen in the previous section, mindfulness holds promise for slowing down or possibly preventing cognitive decline. However, it is questionable whether people experiencing cognitive problems can be asked to follow mindfulness programs. Innes and colleagues (2016) tested this by asking participants to follow a home-based relaxation program daily for 12 weeks, and afterwards as often as they liked for the following three months. They found that practice adherence was excellent with 93% of the sessions completed in the first 12 weeks, and 71% during the following three months (Innes et al., 2016). Moreover, questionnaires revealed a high satisfaction with the program. Therefore, the study concluded that mindfulness programs are feasible in adults with early memory loss (Innes et al., 2016). This conclusion is supported by the findings of Wells et al. (2013a), who assessed safety and feasibility of MBSR in the form of eight, two-hour weekly sessions of meditation and yoga, plus one mindfulness retreat day in individuals with MCI (n=14). The authors systematically recorded class attendance and used questionnaires and qualitative interviews to assess well-being of the participants. Average class attendance was 7.9 out of 9.0. The interviews showed that most participants enjoyed the MBSR program, leading to the conclusion that adults with MCI can safely participate in such a program. Overall, these two studies show that experiencing cognitive problems does not reduce one's capability to follow a mindfulness program. Next to mindfulness-based interventions being feasible, scientist recently have started to test whether these interventions lead to the expected outcomes in people with MCI or other forms of early cognitive decline. While several studies have shown differences in brain structure between meditators and non-meditators (see previous section), it is relevant to examine whether such changes also occur in older adults with less extensive training. Although this field of research is in its early stages, several studies have found positive results. Smart et al. (2016) tested the effect of mindfulness training (MT) specifically in older adults. The training involved cultivation of moment-to-moment attention regulation as well as development of mindful attitudes (non-judgemental awareness and nonreactivity). The training consisted of several different practices, such as gentle yoga and sitting meditation. The results show a robust change in the percentage of brain volume of participants receiving MT, compared to the control group.

This shows that structural neuroplasticity (lasting change) does occur in older adults exposed to shorter periods of mindfulness training. Several other studies have found promising results of mindfulness-based stress reduction (MBSR) interventions as well. For instance, the study by Wells et al. (2013a) showed a trend towards reduced hippocampal atrophy in the MBSR group. This trend was not found in the group receiving usual care for MCI. Additionally, the authors found increased functional connectivity post-MBSR between the hippocampus and the posterior cingulate cortex (PCC) and the medial prefrontal cortex (Wells et al., 2013a; Wells et al., 2013b). These areas are three core areas of the default-mode network involved in memory, and the exact areas that are affected early in MCI or AD pathology. Thus, MBSR interventions may influence connectivity within the default-mode network in people with MCI, possibly improving memory function. Other types of mindfulness-based interventions have also been tested on people with mild cognitive impairment. An example is the study by Eyre et al. (2016), which examined changes in neural connectivity and memory following a yoga intervention. Yoga is believed to enhance neuroplasticity processes, such as the production of brain derived neurotrophic factor, a protein that encourages neuronal growth (Eyre et al., 2016). The yoga group (n=14) showed brain activity changes related to memory improvement, mainly increased connectivity within the default-mode network. This suggests that yoga might be an effective form of mindfulness intervention to enhance memory recall. Overall, research shows that mindfulness based-interventions may be effective treatment options to prevent or delay Alzheimer's disease, as mindfulness counteracts the neuropathological process leading to cerebral and cognitive decline. Lastly, it is important to examine whether the effect of mindfulness programs are comparable to those of existing therapies for people who may have Alzheimer's disease. To do this, Quintana-Hernández and colleagues (2014) designed a study in which they compared mindfulness-based Alzheimer's stimulation (MBAS) to the most used non-pharmacological therapies. These include cognitive stimulation therapy (CST) and progressive muscle relaxation (PMR), as well as to a control group (caretaking-at-home). In all cases, the therapy was combined with the use of medication (donepezil), except the control group who only received medication. The intervention consisted of weekly 90-minute group session and lasted two years for all groups (n=8). The results revealed that all cognitive abilities assessed were maintained for two years within the MBAS group. In contrast, the scores on assessment in the group receiving medication alone or in combination with PMR began to decrease from six months onwards (Quintana-Hernández et al., 2014). The results were equivalent to those in the CST group. Thus, mindfulness appears to be a very good option for non-pharmacological treatment, as it is

equal to CST and has greater long-term efficiency compared to other treatments. This study also provides preliminary evidence for possible long-term effects of mindfulness in AD.

5 Conclusion and Discussion

This paper found a strong link between mindfulness and Alzheimer´s disease, which answers the research question: to what extent can the development of Alzheimer's disease be delayed or prevented through mindfulness-based interventions. Based on the findings discussed in this paper, it can be concluded that mindfulness-based interventions (MBIs) have great potential to delay or prevent the development of Alzheimer's disease. This is based on the fact that mindfulness and meditation have been consistently associated with specific brain areas that are affected by AD (Brewer et al., 2011, Wong et al., 2016). Evidence can be found in studies that show that mindfulness counteracts age-related grey matter atrophy and increases brain connectivity and brain volume in the hippocampus and other regions of the DMN (Luders et al., 2013, Holzel et al., 2008, Holzel et al., 2011). Furthermore, several studies have shown that mindfulness-based interventions have positive outcomes for people with mild cognitive impairment (MCI), who are at greater risk to develop Alzheimer's disease (Wells et al., 2013a, Wells et al., 2013b, Eyre et al., 2016). All these results show that mindfulness may be a feasible non-pharmacological treatment approach for improving cognitive function and preventing the development of Alzheimer's disease. Mindfulness' positive effect on cognition indicates possible usefulness in other neurodegenerative diseases, for instance Parkinson's disease. Moreover, several other interesting applications are possible, for example in dementia due to brain injury or another disease. These could be interesting avenues for future research. It is important to keep in mind, though, that the exact mechanisms behind the effect of mindfulness on neuroplasticity and cognition are not fully understood. Although current research is on the right track considering the positive effects found, there is still a lot to be examined in this field of research. For instance, the combination between mindfulness and medication shows great potential (Quintana-Hernández et al., 2016). Exploring this further might help to increase the effectiveness of mindfulness-based interventions. Consistent findings support the usefulness of mindfulness-based interventions in Alzheimer's disease; however, caution has to be taken when drawing conclusions. Research into mindfulness and AD is in its infancy. The extent to which mindfulness is effective as a treatment approach is not yet clear, as several limitations are present in the methodology of the studies that pro-

vide evidence. First of all, most studies reviewed in this paper included small sample sizes. Hence, results should be interpreted as preliminary. Moreover, mindfulness-based interventions involve factors other than mindfulness that could have positive influence on people at risk for AD and are often not controlled for. These include social and intellectual engagement, a weekly commitment, and instructor attention. Lastly, most studies used a mindfulness program of eight weeks, and the long-term effects of mindfulness-based interventions are yet to be discovered. Follow-up studies with larger sample sizes are needed to improve the reliability of the current findings, as well as studies using long-term interventions to examine whether mindfulness will actually prevent Alzheimer's in people at risk. Despite these limitations, this paper has shown that mindfulness-based interventions hold great promise to delay or prevent the onset of Alzheimer's disease, giving new and important insight into the prevention and management of this disease.

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