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Recent Research and Updates on Alzheimer's Disease

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Abstract

This research article seeks to compile current research work that has been done regardingthe origin, progress, and treatment of Alzheimer's disease (AD) in the year 2014. Much research has been carried out by university departments and medical centres in North America, Europe, the Middle East and Far East. However, a cure for AD is yet to be found. This assessment further emphasizes the reality that policy changes are necessary for patients and their families as they manage, and cope with the disease. Additionally, more funding and amenities for research are necessary to enhance all aspects of the disease and if possible to find a cure for AD.

Keywords: Alzheimer's disease, current research, policy recommendations

1. Introduction

"Alzheimer's disease (AD) has affected about 13% of the world's population over the age of 60" (World Alzheimer Report, 2013, p. 1). Between 2010 and 2050, the number is projected to increase from 101 million to 277 million worldwide (World Alzheimer Report, 2013); yet no current cure has yet been found for the disease (Parra-Damas et al., 2014). Alzheimer's is a disease that has a gradual, and on-going debilitating effect on memory and reasoning abilities of an individual. A conventional form of dementia, AD affects 64% of all dementias in Canada (Alzheimer.ca, 2014). "One in 3 seniors dies of the disease and more than 15 million family and friends serve as caregivers in the US alone"(Karlawish, 2014, p. 514).

Alzheimer's disease was first identified by Dr. Alois Alzheimer in 1906 (Alzheimer.ca, 2014).

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Two characteristics of the disease are increases in the protein 'amyloid-beta plaques' (tiny, dense deposits in the brain) and 'tangles' or obstructions in crucial processes causing a contraction of the brain (Alzheimer.ca., 2014). Risk factors relating to AD are the aging process, genetics, and pre-existing conditions brought about by toxins, infections, drug-use, and the environment (Alzheimer.ca, 2014). The progress of the disease is incapacitating and moves from one stage to another, affecting motor skills and behavior resulting finally in death.

The Global Deterioration Scale, also called the Reisberg Scale (Reisberg et al., 1982) has apportioned seven stages that occur in the growth and progress of the disease. In the first stage there is no cognitive regression, and the patient lives a normal life. In the second stage AD is mild and cognitive decline is in the area of forgetting common words relating to objects, or names. The third stage is characterized by mild cognitive decline when the patient has trouble travelling to familiar locations and struggles to perform satisfactorily at work. In the fourth stage, cognitive abilities deteriorate further and the individual has difficulty managing complex functions such as planning, and shopping. The fifth stage is characterized by moderately severe cognitive decline when the patient is unable to select clothing and has to be reminded to take a bath. During the sixth stage, severe cognitive regression sets in and the individual experiences a lack of memory of recent occurrences, needing help to bathe, and use of toilet. The seventh and final phase is typified by deficiencies in speech, movement and, food intake (Reisberg et al., 1982).

Neuroscientists, patients, and caregivers are interested to know about the recent developments of AD. Specifically, neuroscientists are exploring both pharmaceutical and non-pharmaceutical ways of slowing the onset, progress, and treatment of the disease. This review is a compilation of some of the current studies in the year 2014on Alzheimer's disease conducted by world-renowned researchers, mostly in North America, Europe and the Middle and Far East. While examining current literature (2014), themes that emerged were on a) the origins of AD, b) the progress of the disease c) treatment procedures, and d) policy changes.

2. Review of Current Research

2.1 Origin of Alzheimer's Disease

Current research on the *origins* of Alzheimer's disease has focused on a new imaging tool based on the operation of a sewing machine has been conceived to give new image and awareness of Alzheimer's and Parkinson's diseases. These two diseases have had their origins in minute toxic proteins, too miniscule to be viewed under conventional electron or optical microscopes. Developed by Physicist Tinker-Mill and colleagues (2014) of Lancaster University, this tool focuses on oligomers, which are a macromolecular complex of proteins that are chemically bound to form a small number of manomers or multicomplex proteins. This new pulsating scanner which possesses a high resolution image will now be used to assess the influences of pathways or inhibitors of oligomer formation, a new management of AD.Again, research has indicated that a new blood test can estimate the inception of AD (Crandall, 2014). This makes the process of detecting the origin of the disease in potential patients simple, and easy.

Further,Temple University researchers (Di Meco et al., 2014) have conducted an original pre-clinical study on a group of mice that revealed that chronic sleep disorders could initiate the inception of Alzheimer's disease. "The group of rodents that were sleep deprived demonstrated significant impairment in their working and retention memory, as well as in their learning ability" (Di Meco et al., 2014, p. 1). As well, certain functioning molecules have been discovered to prevent the inception of AD. Wang et al., (2014) at the University of Valencia (UV) in the Unit of Medicine Design and Molecular Topology have found eight functioning molecules against AD, through the molecular topology method. These new molecules prevent the buildup of beta-amyloid protein oligomers, initiated during the onset, and progress of the disease.

Based on a sample of 1.1 million young men, researchers at Gothenburg University, Sweden, have shown a correlation between cardiovascular fitnessand a lower IQ, with an early onset of dementia.A lower IQ entailed 4 times greater risk of the disease and combined with poor cardiovascular health, individuals are 7 times at greater risk of early onset dementia (Nyberg et al., 2014).

Stanford Medical Centre researchers (Altman et al., 2014) have come up with the finding that a variant in gene formation places women at higher risk of AD. Women tend to live longer than men and are more susceptible to the disease. Female ApoE4 carriers are more at risk for AD than male carriers due to the difference in molecular mechanisms that underlie the variant. However, adolescents carrying the APoE e4 allele, are not at risk of AD with no significant differences in plasma levels (Simmons et al., 2014). In adolescents, there is no difference in plasma concentrations of amyloid-B peptides in both carriers and non-carriers.

Researchers from the University of Toronto have linked sleep behaviour disorder (SBD) to brains diseases such as AD. Peever et al. (2014) have discovered that rapid-eye-movement (REM) is a vital cautionary mark of neurodegeneration that could result in some form of brain disease. Interestingly, about 80-90% of individuals with sleep behaviour disorders are likely to develop some form of brain disorder.

2.2 Progress of Alzheimer's Disease

Regarding the *progress* of AD, Duke medicine (2014) with a 36-month follow-up study has shown that PET scanscan predict cognitive decline. This type of imaging uses a radioactive tracerto look for chemical signs of disease in specific tissues. The radioactive dye used was Amyvid to estimate beta-amyloid plaque density. As well, the University of Michigan scientists(Joshi et al., 2014) "have discoveredthe molecular process behind Golgi fragmentation to delay or slow down the AD development. Amyloid B-peptide was found to be the main ingredient that facilitated forming plaques that kills cells in the brain of AD patients. It triggers Golgi fragmentation by activating an enzyme called cdk5 that modifies Golgi structural proteins" (Sciencedaily.com)

A group of researchers from the Sander-Brown Center for Aging at the University of Kentucky (Powell et al., 2014) have developed biomarkers connected with the development of AD. Using MRIs, this team has discovered that compromised white matter connections in the brain are closely associated with declining cognitive health. This particular study was conducted on patients with dementia and Down syndrome who were at risk of developing AD later on in life.

In reference to racial groups, Barnes and Bennett (2014) at Rush University Medical Center, suggest that African Americans may be at a greater risk of developing Alzheimer's disease than non-Hispanic whites. This study highlights the view that AD progresses differently in certain ethnic and racial groups relating to biological, and cultural factors. Cognitive tests need to be done periodically on the African American participants to study the onset and progression of the disease. There is a dire need for more participants to enlist in these studies.

"The National Neuroscience Institute (NNI) in Singapore (2014) has linked a novel function of protein to AD. The Amyloid Precursor Protein (APP), which controls the growth and maturation of brain cells, is one of the root causes in the development of AD" (Sciencedaily releases, 2014). APP has been discovered to regulate microRNA-574-5p which are tiny molecules found in human genes. Unregulated MicroRNA-574-5p therefore could result in the cause of brain disorders. Categorizing APP as a biomarker of AD is an exciting finding and the prospects are stimulating to future research in pharmaceutical drug production.

2.3. Treatment of Alzheimer's Disease

Treatment on AD has focused on improving memory functions, neuron repopulation through stem cells, diet, education, and exercise. Neuroscientists Crystal and Alford (2014) have validated the existence of *source memory* in rodents and suggest that this type of memory is a vital constituent of episodic memory. Source memory relates to the manner in which individuals obtain a piece of information. It refers to the mechanism that helps individuals remember people who narrate jokes or have told stories about certain relatives or events. This outcome will enable researchers to progress to new mediations of memory failure in Alzheimer's disease.

Scientists from the San Diego School of Medicine (2014) report that cathespin B gene blockade or its reduction by an enzyme inhibitor, E64d, deters the creation of key neurotoxic pGlu-AB peptides that are linked to AD. An important key finding was that E64d, the enzyme inhibitor, and the cathespin B gene blockade resulted in bringing about improved memory deficits in a mouse model of AD. Additionally, Shuster and Offen et al. (2014) of Tel Aviv University "discovered that introducing *stem cells* in brain tissues reduced symptoms of AD. The gene (Wnt3a) was introduced in mice brain and the results showed diminished symptoms as a result of this new

neuron repopulation" (Sciencedaily.com). Again, Nieznanski et al. (2014) have found that prion protein binds strongly to clumps of amyloid-beta peptides, but does not break them down further, as was determined earlier. This has contributed to an up-to-date approach in treating AD, which relates to using prion-based amalgams to prevent these minor toxic amyloid-beta fragments from developing.

Researchers at the Institute of Neuroscience of the University of Barcelona have ascertained "the cellular mechanism involved in memory consolidation" (Saito, 2014, p. 1) and that memory loss can be reversed through gene therapy during the initial stages of AD. When the protein Crtc 1 is injected into the hippocampus, memory signals are activated and this process strengthens long-term memory functions. A novel rodent representation can transform research in AD. Saito et al. (2014) in Japan have come up with a new model to expose the mechanism of Abeta deposition. The second model explicates neurodegeneration by examining Abeta-40 and 42 such as tauopathy. These models can help in drug developments as biomarkers for treating AD. According to Dr. Saito, "We have social responsibility to make Alzheimer's disease preventable and curable. The generation of appropriate mouse models will be a major breakthrough for understanding the mechanisms of the disease, which will lead to the establishment of presymtomatic diagnosis, prevention, and treatment of the disease" (2014, p. 2).

Researchers in Columbia University Medical Centre (Mecozzi et al., 2014) "have detected a novel group of compounds, namely pharmacologic chaperones that can stabilize the AD activating retromer protein complex of neurons. Retromer steers away APP, causing the toxic by-product amyloid-beta that elicits the growth of AD. Using virtual screening techniques, researchers have uncovered a new group of compounds called pharmologic chaperones that can increase retromer proteinlevels and decrease amyloid-beta levels in brain cells" (Mecozzi et al., 2014, p. 1).

UC Irving neurobiologists (Blurton-Jones et al., 2014) have "discovered that genetically modified neural stem cells can produce positive results in the brain of patients suffering with AD. Mice models injected with neprisyln-expressed genetically modified neural stem cells produced results that indicated a reduction in amyoid-beta pathology. Before this treatment can be clinically used in humans, more research needs to be done in the area" (Sciencedaily.com).

A German-French team (Laurent et al., 2014) has ascertained that caffeine causes a favourable impact on the tau deposits in AD. Tau deposits, together with beta-amyloid plaques, are characteristic features of AD degeneration. This could result in a new class of drugs to be acquired in the treatment of AD.

Healthy *dietary choices* in midlife may prevent dementia and AD in later years."The University of Eastern Finland, in a 14 year follow up study, have shown that a healthy diet with fruits, vegetables, berries, fish, and unsaturated fats from milk products, had a 90% chance of delaying or preventing the onset of dementia and AD" (Sciencedaily.com). As well the International Institute of Applied Systems Analysis has found that people who attended school for longer periods performed better in cognitive functioning.Schneeweis et al. (2014) at Linz University, Austria, have discovered that more *education* slows cognitive decline.

The University of Maryland researchers (Smith et al., 2014) have shown in their research that moderate *physical activity* can reduce the risk of AD onset. Adequate exercise may protect the neurodegeneration of the brain by preserving its capacity. Also regular workouts can prevent cognitive decline for those who have a genetic risk of AD. Individuals who carry the APOE-e4 allele on chromosome 19 are particularly at risk. Smith and colleagues from the Cleveland Clinic conducted the study on four groups of healthy adults between 65-89 for 18 months. The hippocampal volume by magnetic resonance imaging (MRI) was used as an indicator to determine the level of normal cognitive abilities.

2.4 Policy Recommendations

Policy changes are imperative to improve the lifestyle of AD patients and their families. Karlawish (2014) of the Penn Memory Centre in the US proposes the following policy changes:

a) "Prepare legal, banking and financial service providers to be able to competently assess an individual's decision-making ability.
b) Caregivers of Alzheimer's patients should be offered or even prescribed to attend caregiver training
c) Electronic Medical Records (EMRs) should be modified to provide access to caregivers and record their roles

d) Hospice care should be aligned with goals of care for patients with advanced dementia, rather than waiting until the last 6-months of life as currently required for insurance coverage
e) Prediction models and treatment alogrithms will need to be developed as 'biomarker positive' people are identified to have a brain at risk before symptoms emerge.
f) Legal reforms should be sought to minimize discrimination in employment and insurability as people are deemed at risk in pre-clinical stages." (Karlawish, 2014, 541-6)

The question that needs to be answered is "How should we live with it?" The Geisel school of Medicine at Dartmouth has reiterated the following strategies that could have significant implications on the AD community. There needs to be more funding for research, payment policy and regulatory functions in Medicare, long-term services and supports, public health, housing and community services, adequately trained caregivers, and justice and law enforcement to provide protection from exploitation, abuse, and neglect (Bynum, 2014).

3. Conclusion

This review of published current research work in the year 2014 indicates that much work is being done in North America, Europe and the Middle and Far East on various aspects of Alzheimer's disease. However, a cure is yet to be found and hence on-going research work is imperative, and necessary. To achieve this goal to a certain extent, an innovative project has been set up to strive to overcome hurdles in cost and time connected with clinical trials (http:www.brainregistry.org/). This project will also enable researchers to recruit volunteers to participate in projects related to brain diseases. Furthermore, the process will fast-track research and enable patients to be informed about the latest trends in AD treatment. Patients and families need to be informed about new developments in the treatment of the disease. Hence this new online registry to enhance research on brain diseases has been has been put together by researchers at UC San Francisco at the Memory and Aging Centre (http:www.brainregistry.org/).

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