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Case Report

Alzheimer's Disease Is A Fiction

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Abstract

Purpose: This article is a summary of my previous publications in 2016 [1] and 2017 [2, 3], in an attempt to tighten the fact that Alzheimer's Disease is indeed a fiction, as there are other nonvascular disorders in Auguste's autopsied materials revealed by Perusini. The objective is to help the general public as well as the professional neuroscientists understand that the meaning of AD has changed many folds over the past half a century. Its main semantic focus is now popularly but erroneously regarded as equivalent to "dementia" as a disease; it is then claimed to be cured or prevented by deleting Amyloid Beta, so-called Amyloid Beta Hypothesis, which is a substance of protein in the brain as debris. The method of deleting amyloid beta as debris from the brain is claimed to be sleeping or drinking a commercialized liquid product advocated by specialists on AD, thereby having nothing to do with the two "hallmarks" originally advocated by Alzheimer and his associates.

Method: Since this is a summary of previously published articles and books of mine, the method taken is a standard literature review which may include publications other than mine.

Results: AD was invented by Kraepelin in 1910 [4], alluding only to fabrillary patterns in three illustrations taken from Perusini's microscopic preparations of Auguste's autopsied materials. Its diagnosis varies from senile dementia to senium praecox to MCI leading to AD as the most feared form of dementia. The guidelines of DSM-IV even indicate the elimination of any vascular disorder in patients with dementia to automatically come up with the diagnosis of AD, unaware that Auguste had an evenly atrophic brain with four vascular disorders, among others; the evenly atrophied brain was most likely caused by the disorders of neuroglial cells and neurovascular arteriorsclerosis; the causes of both were completely missed by Perusini and all subsequent investigators However, AD has been traditionally kept alive for contrast with other forms of dementia in several ways: (1) **debate** on a one-to-one cause-effect relationship, like Amyloid-Beta Hypothesis; and now with tauopathy; (2) **arguments** on intervention or prevention of AD, by confusing dementia as AD; (3) **using animal models** to mimic AD; (4) **assignment of lesion** in the hippocampus as AD, or (5) **using AD as a contrast** to create new terms for neurological disorders. Worse, AD is now even commercialized for a drink and advertized to be the direct result of Amyloid Beta, one-to-one advocated in a TV Show, called Gotten, by NHK.

Conclusion: This summary takes issue with this development of such traditions as a serious error as well as with the commercialization on false claims, because Alzheimer did NOT discover plaques, least of all a new disease. Consequently, AD is a fiction not worth keeping in clinical practice and its pursuance has become a wild-goose chase, with worsening consequences, which must be stopped for the sake of restoring the credibility of the medical sciences in general and the neurosciences in particular.

INTRODUCTION

In 2008, I published a booklet [5], going through the historical facts in time and space regarding Alzheimer's career at Frankfurt, Heidelberg, and Munich, as well as Perusini's work on Auguste and Bonfiglio's parroting of Alzheimer's two unique findings in 1906 at a meeting of German psychiatrists in Tübingen for his oral presentation which was met with a big yawn; Bonfiglio did not even attend the meeting but believed along with Alzheimer and Perusini that Alzheimer discovered a new disease which Alzheimer, Perusini, and Bonfiglio could not classify according to the then ruling paradigm of Kraepelin's Dementia Praecox. For this historical make-believe discovery of a new disease, the false

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two unique findings of Alzheimer's oral presentation in 1906 have come down to this date to become known as the two hallmarks of AD.

Having sensed this unscientific make-believe story of two unique findings, I started more carefully the literature review and discovered that Perusini changed his mind later by rejecting his support, published in Italian this time, of Alzheimer's publication in 1907 and called senile plaques he found in Auguste's autopsied materials Fischer Plaques [6] along with Vedrani [7]. Later, Simchowicz, who had also worked under Alzheimer, confessed in 1924 [8] and joined forces to decline the support of the two unique findings of a new disease allegedly discovered by Alzheimer.

In addition to those false claims, I should add that plaques in fact had been described by Blocq and Marinesco [9] in a patient who also had epilepsy and by Redlich [10] in two patients. Alzheimer and Bonfiglio were not even aware of these publications, although Oskar Fischer dug deep to take issue with Redlich's findings. However, their differences can be resolved as suggested in Peng [5] and I reiterate the resolution again in Peng [2].

The most serious, damaging and unscholarly fabrication of AD is Alzheimer's own claim in 1911 of three supporting cases, after Kraepelin's false proclamation of "This Alzheimer's disease of the most serious form of senile dementia" [4]. Kraepelin therefore gave Alzheimer a wrong sense of confidence, as Alzheimer [11] then cited Bonfiglio's case [12] and one of Perusini's four cases [13], which was the same patient, as well as Perusini's detailed description of Auguste as "three new cases" in support of his discovery of a new disease. Most practitioners in the medical field are not aware of such fabrications; some even claim "Alzheimer's Disease re-discovered" [14]. For this reason, my first booklet [5] was published to correct this serious historical mistake, because I began to suspect whether Alzheimer's Disease really exists or not.

However, in 2012, a couple of neuropsychologists, unhappy with the claim of two hallmarks of AD in humans, started to use specially engineered mice in an attempt to mimic human AD. Such an attempt prompted me to publish a second booklet [15] in which I voice my strong objection on the ground that dementia in humans pertains to language disorders and family history of genetic background and that dementia is not synonymous to AD which, I was convinced then in 2012, does not even exist.

DISCUSSION

From these historical backgrounds, I should now proceed to the summary of my publications in 2016 and 2017 to discuss two things: (1) what are the evidence I have to prove that Alzheimer's Disease is a fiction. And (2) why, unaware of the fiction, most practitioners in the medical sciences continue to pursue AD in a wild goose chase, by neglecting Oskar Fischer's important contributions on dementia and his valuable insight that "There were no cases with tangles without plaques".

The Evidence

There are several pieces of evidence which have actually been in existence for more than a century. They require a careful and scientific probing and a detailed anatomo-physiological understanding of brain functions coupled with the environmental and disciplinary advances in neuroscience with which to grapple. Otherwise, they would have remained hidden for more wild goose chase.

Auguste's Medical Conditions While still Living

I have pointed out [5] that Alzheimer never treated her when she was admitted to the Asylum in Frankfurt at the age of 51 in 1901 until she died in 1906; she was assigned to Gaetano Perusini from the beginning by its Director, Sioli. However, Perusini lost interest on her for a period of more than one year, but resumed observation for a short period, during which time valuable clinical reports were recorded. But Perusini could not make any sense out of them; namely, (1) her strange behaviors in bed by pulling her legs to her chest, (2) her blindness, and (3) her serious language disorders.

Her strange behaviors: Her strange behaviors in bed gave me the insight that she had decubitus angina which is a periodic cardiac pain while lying down. By pulling her legs to her chest, to raise the stomach in order to push the diaphragm against the heart, she could somehow reduce the cardiac pain periodically. Without knowing her medical conditions, he simply brushed aside her behaviors as "strange". I then pointed out that her decubitus angina was the direct cause of her death, an important insight of her serious medical condition that must have shocked contemporary researchers on AD. Of course, Perusini could not make any sense then, other than saying "strange behavior".

Her medical condition of blindness: Her medical condition of blindness was equally missed by Perusini whom actually could not be blamed when he simply called it "psychic blindness". In the early twentieth century – 1900's—nobody knew anything about DM (diabetes mellitus). However, her autopsy reveals that she had abnormal growths of veins in her lower extremities which did not make any anatomo-physiological sense of vascular pathology to Perusini but gave me immediately a valuable pathological insight that she had DM and that it must have started long before she was admitted to the Asylum, to result in total blindness before Perusini could have realized that her legs would have to be amputated had she lived longer. But I am certain that she could no longer get up to walk while still living, a pathological sign that would have given Perusini a clue that she might have had something serious, which was related to her total blindness. But Perusini could not have had that insight because the overall medical knowledge of DM at that time was not yet available.

Her serious language disorders: Her serious language disorders were detected by Perusini who also tested her erroneous readings

which were obviously compounded by her worsening eyesight. But he could not be blamed for neglecting her serious language disorders as an important symptom of her deteriorating brain functions of memory and cognition, even though she was obviously seriously demented when judged by today's clinical standards. However, even so, many researchers today, as evidenced by the neuropsychologists working on animal models to mimic human dementia, would not have the knowledge either of language disorders in connection with the onset or progression of deteriorating brain functions of memory and cognition in dementia. They would not have been able to test language disorders in their specially engineered mice, any way, nor to check the family history of those mice, because they have no idea of what language is and have no way of checking the family history of their specially engineered mice. The neuropsychologists were just too eager to beat the status quo of AD having two hallmarks by getting into more nonsense without awareness of the worse pitfall they dug for themselves.

Even today, the brain functions of memory and cognition are grossly misconceived by psychologists and neuroscientists, because memory and cognition are **heads and tails of the same coin**, a brand-new concept that differs distinctly from the tradition that cognition subsumes thinking, learning, and memory. Language in the brain in humans is behavior which is memory governed, meaning-centered, and multifaceted, because sign language is now a bona-fide human language in its true sense.

Be that as it may, Perusini discovered her vascular disorders only at autopsy and could not have suspected such vascular disorders while she was still living. But her vascular disorders alone, in connection with her DM and blindness coupled with her decubitus angina, would totally disqualify the claim that Alzheimer discovered a new disease; they would also simply nullify Bonfiglio's parroting that Alzheimer's oral presentation in 1906 had two unique findings – leading erroneously to the two hallmarks – which could not be nosologically classified by him and Alzheimer himself. Hence, in Peng [1] I adamantly point out that there are NO two hallmarks of AD because it is a fiction.

Auguste's Pathologies at Autopsy as Revealed by Perusini After Her Death

Perusini's autopsied materials of Auguste after her death in 1906 also revealed four very important pathological findings: (1) an evenly atrophied brain, (2) arteriosclerosis of the major vessels in her brain, (3) internal and external hydrocephaly, and (4) of course the abnormal growths of veins in her lower extremities. All four findings have been totally ignored by contemporary researchers on AD, and most importantly overlooked or even ignored by people working for the Alzheimer's Association. Instead, they prefer to hold annual conferences, as in July 2016 held in Toronto, with 5000 participants taking part, according to Dr. Amos Korczyn who attended, for a more wild goose chase by replacing the Amyloid Beta Hypothesis with tauopathy.

Her evenly atrophied brain – from cortical to subcortical structures or even: The cerebellum – would most certainly disqualify all subsequent claims of researchers on AD by changing the pathogenesis of AD as they please: For instance: {a) Dementia of any form is AD; (b) Dementia without any vascular disorder is AD (in contrast with vascular dementia); (c) Dementia caused by lesions in the hippocampus is AD; (d) Dementia with atrophy other than in frontal-temporal lobes is AD; (e) Dementia caused by amygdaloid beta to form plaques is AD, the so-called Amyloid Beta Hypothesis that has dominated for more than two decades; and (f) Dementia with plaques and tangles of whatever origin is AD (the so-called two hallmarks). Now tau is added as another cause of AD.

On top of these self-claimed ADs, some researchers on AD even attempted to fabricate histopathological slides of plaques and tangles, using modern technology for staining in histopathology to claim that Alzheimer made them in 1906 at his oral presentation or in 1907 for his barely two-page long case report on Auguste. Alzheimer did nothing of that sort.

For instance, my open letter of 2006 to *Science* [2] reveals in great detail the false statement and fake slides of the two hallmarks reported by the authors for the centennial commemoration of Alzheimer's "discovery" of the two hallmarks. In 2013, as another example at the international congress held in Taipei, Taiwan, two neuroscientists--one from Australia and the other from Singapore--- argued whether Newt Gingrich's naïve "ultimatum" in 2000, "we would eliminate and cure AD by 2015", could be accomplished or not. In so doing, each one of them fabricated their histopathological slides made in their own labs, using modern staining technology to make them look like Alzheimer had made them in 1906. There was no such staining method at that time. For this reason, all histopathological illustrations published by Fischer in 1906 and 1910 were either microscoptic preparations or hand-drawn. Alzheimer did the same thing in 1911. Kraepelin's three illustrations in 1910, taken from Perusini's autopsied results, were also microscopic illustrations.

Arteriosclerosis of the major brain vessels: Arteriosclerosis of the major brain vessels should have given Perusini more insights of pathologies of all vessels, especially cardiovascular and neurovascular arteriosclerosis which caused her arteriosclerosis throughout her body as well as her decubitus angina and stupor. But he missed all these vascular pathologies. As a result, DSM-IV brushes them aside and all subsequent researchers on AD have ignored them to the detriment of inventing new terms to suit the purpose of their own meanings of AD, including Amyloid Beta Hypothesis and now tauopathy to seek a one-to-one cause-effect correlation with AD. I have therefore done my part to describe in some details her cardiovascular and neurovascular pathologies [1], in order to add to my proof that there are no two hallmarks of AD because it is a fiction. Nor has amyloid beta or tau got to do

with AD; they may result in causing dementia, if accumulated as a part of the ongoing process of wear and tear, but dementia is not a disease nor is it equivalent to or synonymous with AD as AD is a fiction.

Her internal and external hydrocephaly: Her internal and external hydrocephaly could only be discovered at autopsy in 1906, which could not have been treated while she was still living, as there was no VP-Shunt neurosurgery available in 1906. These two pathologies were the only non-vascular disorders Auguste had, suggesting that she also had ependymal disorders stemming from the overall pathology of her glial cells. Note that neuroglial or simply glial cells out-number neuronal cells in the brain 3 to 1 and exist throughout the brain, but are more so in the mid-brain. Therefore, I claim that her evenly atrophic brain ensued from the overall pathology of glial cells in her brain. The evidence is her internal and external hydrocephaly.

Ependymal cells, as they are known today, constitute an important part of neuroglial cells. They form the extremely thin membrane that lines the ventricles of the brain and choroid plexuses. But I should add that internal hydrocephaly alone or both cause very serious neurological disorders in behaviors, thereby jeopardizing brain functions of memory and cognition.

The abnormal growths of veins: The abnormal growths of veins in her lower limbs have already been described in relation to her DM. They should have been taken into account by contemporary "experts" on AD, instead of suggesting Amyloid Beta Hypothesis or tauopathy, not to mention the creation of new terms, such as MCI (Mild Cognitive Impairment) which is a poor reinvention of Oskar Fischer's dichotomy of simple dementia (without glandular necrosis) and presbyophrenic dementia (with glandular necrosis). I have described the importance and value of his dichotomy in Peng [2, 3], especially in relation to a misdiagnosed case of AD reported by Caron Leid [15] regarding her mother's death which is better attributed to Fischer's Disease as I have vividly pointed out [3].

Conclusion

Having summarized the essence of my point that Alzheimer's Disease Is A Fiction, I should conclude that, such being the fact, neuroscientists working on dementia and AD should abandon two things which are interrelated: (1) inventing more new terms and (2) creating their own meanings of AD. Both points are deep-rooted in the age-long erroneous notion that dementia is a disease, when it is not; in so doing, they only perpetuate the wild goose chase by translating erroneously Kranckheit in German into English as "disease", a serious linguistic error that inevitably hinders the understanding that human dementia is not a disease, although it exists due to aging, as aging is the ongoing process of wear and tear, a process that can be delayed somewhat, depending on each individual's life style, but cannot be stopped nor cured. Thus, it is time to face the fact that Alzheimer's Disease does not exist because it is a fiction.

For this reason, my two other publications [2, 3] point out that (1) when wear and tear triggers apoptosis in the central nervous systems, it leads to dementia gradually, regardless of where in the brain apoptosis starts. Thus, epilepsy, PD, SCA, HD, FD (Fischer's Disease), PiD (Pick's Disease) and what not, will all produce/ensue in dementia eventually on account of metabesity, an important new concept that will be described briefly below. At the same time, (2) I should add, as in [2, 3], that the nervous systems are structurally interrelated and functionally interdependent. Therefore, any brain disease is not an isolated incidence of neurological disorders.

The new concept, called Metabesity, was started by a small group of neuroscientists in London and elsewhere; there will now be the first International Congress Targeting Metabesity on October 30-31, 2017. They claim that it expresses the links among diverse major diseases and conditions to shared metabolic roots; even the aging process itself shares such metabolic and inflammatory provenances.

I am glad that I finally have people whose view is exactly what I mean by structural interrelation and functional interdependency of the nervous systems. I shall therefore submit a manuscript, entitled "Dementia in Epilepsy: A Clinical Contribution to the Metabesity of Epileptology, Geriatrics and Gerontology", to a journal for publication in order to help promote the new concept for the good of neuroscience and much-needed understanding of what human life is all about.

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