

Treatment Protocol for Preventing and Reversing Alzheimer's Disease (AD)

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ABSTRACT

A monograph presenting a comprehensive five-step AD treatment protocol has been published recently.^[1] The protocol is based on the following systemic medical principle: at the present time, removal of cause is a necessary, but not necessarily sufficient, condition for restorative treatment to be effective. Implementation of the five-step protocol offers the promise of 1) potentially preventing and reversing AD in selected cases, and 2) dramatically lowering AD healthcare costs. The present Research Note summarizes the findings of reference.^[1] For more details, references, and supplementary material, the reader is directed to reference.^[1]

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INTRODUCTION

Non-communicable diseases have overtaken communicable diseases as the leading cause of global mortality. The impacts of non-communicable disease expansion on healthcare and associated costs have been dramatic.

The mainstream medical approach emphasizes treatments over prevention for non-communicable diseases. Given the expansion of non-communicable diseases, the present treatment-dominant approach is insufficient. More balance between treatment and prevention is required. Eliminating the actionable foundational causes of these diseases is at least as important as applying new treatments, if there is to be any hope for full or partial reversal of non-communicable diseases.

Toward that end, I developed a systemic medical principle that would form the bedrock of a healing protocol for diseases: At the present time, removal of cause is a necessary, but not necessarily sufficient, condition for restorative treatment to be effective (where "removal" encompasses "neutralization" in those cases where actual "removal" is not possible, and "restoration" encompasses restoration of health to the organ/tissue as well as restoration of function). To prevent disease, the actionable foundational causes (tangible contributing factors over which one has some control) that underlie the disease symptoms need to be identified and removed as

comprehensively, thoroughly, and rapidly as possible. To reverse disease (if irreversible damage has not been done and genetic predisposition to the disease in question is not a dominant factor), the preventive steps above need to be implemented as well. If the preventive protocols alone are inadequate for reversing disease progression, they need to be augmented by treatments. The first step in either disease prevention or reversal is to identify the full spectrum of potential foundational causes/contributing factors for the disease(s) of interest.

In April 2017, we published a monograph entitled Prevention and Reversal of Alzheimer's Disease,^[2] which focused on identifying and eliminating the foundational causes of AD. The approach and findings of reference^[2] were based on two observations:

- much of the information required to identify and eliminate these foundational causes of AD is in the biomedical literature already, but is not being extracted and exploited adequately;
- The biomedical literatures for many chronic diseases such as AD are large, and extracting these AD foundational causes comprehensively from the literatures (without reading each paper) is a complex text mining problem.

Following publication of reference,^[2] we decided to extend our approach to the identification of AD treatments. The present monograph^[1] identifies a wide spectrum of AD treatments and the AD characteristics they impact (an AD characteristic is a measurable quantity associated with a test subject/patient whose changes in value may reflect changes in the progression or reversal of AD. The AD characteristics can be divided into five categories: 1) behaviors (e.g., aggression,

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agitation, delirium, etc); 2) performance (e.g., cognition, memory, learning, etc); 3) psychological states (e.g., apathy, anxiety, etc); 4) biomarker/metabolic function (e.g., oxidative stress, neuroinflammation, Abeta, tau phosphorylation, mitochondrial function, synaptic plasticity, etc); and 5) biomarker/metabolic metrics (e.g., acetylcholine, ABCA1, BCL-2, BDNF, ADAM10, GSK-3, homocysteine, BACE1, etc)). The identified AD treatments, characteristics, and contributing factors are integrated to generate an individually-tailored treatment protocol.^[1]

METHODOLOGY

Overview

There are two main goals of the study reported in reference:^[1] identify the full spectrum of treatments for AD, and develop an individually-tailored treatment protocol that could be used for prevention and reversal of AD. The operational objectives that contribute to these goals include

- comprehensive identification of the existing and potential AD treatments, characteristics, and contributing factors
- subsequent integration of
 - 1) the AD treatments and their impacts with
 - 2) the AD contributing factors and their impacts
- Generation of a treatment protocol that will prevent and reverse AD.

Assume the

- existing and potential AD treatments can be related to their effects on the AD characteristics identified above
- existing and potential AD contributing factors can be related to their effects on the same AD characteristics
- AD characteristics are amenable to measurement

Then, a treatment protocol can be generated that identifies

- the amount that measured AD characteristics deviate from the norm for each AD patient
- the contributing factors that have to be eliminated to restore the AD characteristic measurements back to the norm
- the treatments required to restore the AD characteristics back to the norm

Strategy

The overall strategy for identifying AD contributing factors, treatments, and characteristics was essentially the same. The strategy components are:

- Select source database (Medline/Pubmed was selected as the primary source database, although the Thomson-Reuters version was used when proximity searching was performed).
- Generate a core AD database (a Pubmed query was used to generate a core AD database).
- Retrieve records relevant to AD treatments (or AD contributing factors or AD characteristics) from the core AD database (a combination of MeSH-based, text-based, and visual examination approaches was used to retrieve records relevant to AD treatments, AD contributing factors, and AD characteristics, and to extract the desired AD treatments, AD contributing factors, and AD characteristics from these retrieved records).

Why was the above combination of approaches necessary? The MeSH-based approach by itself would have been far less time-consuming, since there are thousands of MeSH terms and millions of Abstract phrases to be analyzed. The text-based approach was developed and used because

- not all Medline records have MeSH terms assigned
- for those records with MeSH terms, the terms do not always form a comprehensive set
- for records with MeSH terms, the Qualifiers appended to the Heading are not always complete

Thus, the text-based approach complements (and overlaps) the MeSH-based approach.

Fundamentally, the text-based approach

- identified linking terms that were strongly associated with AD treatments and their consequences
- used these linking terms to search for the AD treatments and consequences of interest

These linking terms were obtained from reading the records retrieved with the MeSH-based approach, and selecting those terms strongly associated with AD treatments and their consequences. Some of the more useful linking terms identified included the following: treat*, therapy*, prevent*, protect*, improve*, reduce*, attenuate*, ameliorate*, enhance*, revers*, promote*, alleviate*, inhibit*, remove*, suppress*, mitigate*, restore*, lower*, preserve*, regenerate*, rescue*, slow*.

The text-based approach was

- used as part of the total AD Medline database query to retrieve records strongly associated with AD treatments
- applied to the parsed abstract phrases of the retrieved records imported into the text mining software to surgically extract the existing AD treatments and their consequences

- used to develop patterns of terms for searching the non-AD Medline literature to generate literature-based discovery of potential AD treatments

The main text mining advance in this study was development and demonstration of this AD treatment pattern filter for

- querying the Medline database
- extracting AD treatments and their consequences from the parsed abstract phrases
- discovering potential AD treatments from the non-AD biomedical literature

RESULTS

Treatments, Contributing Factors, Characteristics Identified

We have identified ~600–700 existing AD treatments (the exact number depending on how these treatments are aggregated). The number of AD treatments identified represents an order of magnitude more AD treatments than we have seen in any AD/dementia article in the published literature. As emphasized in the monograph, far more AD treatments could be identified in an expanded study using the advanced text mining techniques we have developed.

We have identified ~250 existing AD characteristics. This represents an order of magnitude more existing AD characteristics than we have seen in any AD/dementia article in the published literature. As emphasized in the monograph, far more AD characteristics could be identified in an expanded study.

We have identified ~400–600 existing foundational AD contributing factors (the exact number depending on how these contributing factors are aggregated), which represents an order of magnitude more existing foundational AD contributing factors than we have seen in any AD/dementia article in the published literature. As emphasized in the monograph, far more existing foundational AD contributing factors could be identified in an expanded study using the advanced text mining techniques we have developed.

In addition to the identification of voluminous numbers of existing AD treatments, characteristics, and contributing factors, we have developed literature-based discovery techniques that can identify far greater numbers of potential AD treatments, characteristics, and contributing factors. Some illustrative

examples of potential AD treatment discovery are provided in reference,^[1] but the method is easily adapted to characteristics and contributing factors.

Treatment Protocol

The five treatment protocol steps are as follows:

- **Step 1** – obtain a detailed medical and habit/exposure history from the patient;
- **Step 2** – administer written and clinical performance and behavioral tests to assess the severity of the higher-level symptoms and degradation of executive functions;
- **Step 3** – administer laboratory tests (blood, urine, imaging, etc.);
- **Step 4** – eliminate ongoing AD contributing factors;
- **Step 5** – implement AD treatments.

CONCLUSION

This individually-tailored AD treatment protocol can be implemented with the data available in the biomedical literature presently. Additionally, while the methodology developed for this study was applied to AD, it is general and applicable to any chronic disease that, like AD, has an associated substantial research literature. Thus, the protocol and methodology we have developed to prevent or reverse AD can be used to prevent or reverse any chronic disease (with the possible exceptions of individuals with strong genetic predispositions to the disease in question or who have suffered irreversible damage from the disease).

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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