ELSEVIER

Alzheimer's & Dementia ■ (2018) 1-4

Alzheimer's & Dementia

Editorial

New thinking about thinking, part two. Theoretical articles for Alzheimer's & Dementia

There is one question often asked during scientific meetings, business travel, or dinner parties that is just as easily and equally posed by members of the research community, the general public, or by friends and family: what's new in Alzheimer's research? Today, there is growing interest from readers into the insights derived from the development of new interventions, systems biology, and network modeling analytics. There is also increasing public health awareness for the translation and application of precision medicine, community-/population-level data, and big omics data into effective interventions, meaningful health policy, and robust technologies to better monitor, assess, and control disease progression. These varied expressions of Alzheimer's translational research perhaps represent the best examples of what is new.

The amplification of translational research and the resulting translational knowledge now presents an important publication challenge for new ideas and insights. Similar to many other journals, Alzheimer's & Dementia receives many manuscripts for review that include representation from multidisciplinary teams who push science forward, beyond siloed research domains. These reports often describe new technologies, different methodologies, or recalibrated analytical approaches. Along with the results, discussion, and conclusion, these papers comprise a large collection of the published literature and, in a unique and paradoxical sense, a new area of concern for the field.

In 2005, Carl R. Woese [1] highlighted this potentially looming problem in scholarly writing, "science is impelled by two main factors, technological advancement and a guiding vision (overview). Without a guiding vision, there is no road ahead; the science becomes an engineering discipline, concerned with temporal practical problems." He continued, "a society that permits biology to become an engineering discipline, that allows the science to slip into the role of changing the living world without trying to understand it, is a danger to itself."

The journal is enthusiastic about the exciting recent calls for a more pluralistic neuroscience [2]. This view encompasses a balanced consideration of both the theoretical and the experimental aspects of brain-behavior research, particularly in the aging individual. While there is no question about the importance of reporting novel data or new investigative techniques, there is now a growing imperative for authors to articulate their new insights, ideas, or hypotheses within the context of a summation of previous investigations and conceptual frameworks.

To support this aim, Alzheimer's & Dementia is describing the specifications, format, and layout for articles that present a theoretical perspective. The new format for theoretical articles will provide authors the option to submit manuscripts such as those that synthesize early or pilot data into new testable conceptual models. Manuscripts might also describe theoretical frameworks or hypotheses spanning any of the following generic areas including (but not limited to) biology, chemistry, clinical/medical interventions, behavior/neuropsychology, social sciences, nursing, health economics, health services research, ethics, and public policy. This editorial presents a new standard format for the theoretical article type and provides some guidelines for preparation of these types of manuscripts for publication in Alzheimer's & Dementia.

Theoretical articles, and specifically the abstract, should be written for a diverse audience, so that the central research question, the expression of the hypotheses, the important research challenges, and the linkages with existing ideas, conceptual frameworks, or theories are easily understood. Manuscripts should follow the format below and include each element and sub-element listed:

1. Structured abstract
2. Objective
3. Background
   a. Historical evolution
   b. Rationale
4. New or updated hypothesis
   a. Early experimental or observational data
   b. Future experiments and validation studies
5. Major challenges for the hypothesis
6. Linkage to other major theories

Each of these elements and sub-elements will be described in further detail below. In addition, the other required items include key words, references, acknowledgments, conflicts, and funding sources. Length may not

https://doi.org/10.1016/j.jalz.2018.05.002

exceed 3500 words (excluding the abstract, references, technical appendices, figures, and tables), a maximum of 50 references, no more than six figures, boxes, tables, or some combination of six figures, boxes and tables.

The following section provides an outline as a general guide for organizing the six elements for a theoretical article. To help illustrate, the example used below discusses the important elements for a future hypothesis on neuroinflammation. Please note that this general format comes with a strong caveat: individual topics may require some modification to this template.

1. Structured abstract for the theoretical article

The abstract should contain the elements presented previously for the theoretical article format including, the following headings: Objective, Background, New/Updated Hypothesis, Major Challenges for the Hypothesis, and Linkage to Other Major Theories. Each heading should have short sentences that summarize the individual elements as described below. The structured abstract should not exceed 350 words.

The main body of the paper contains the following sections:

2. Objective

In a brief paragraph orient the reader regarding the main purpose of the paper: what is the basic (specifically, the take-home) message or headline news for the proposed hypothesis.

For example: "This paper is a proposal for an update of the Hypothesis on Inflammatory Mechanism in Neurodegeneration-Dementia-Alzheimer syndrome (abbreviated hereafter as the Hypothesis) based on emerging novel evidence. The present draft intends to: (1) promote new thinking about the biological substrates and the origins of neurodegeneration; and (2) solicit input from other key leaders in the field to amend further and finalize the present version of the Hypothesis. This effort aims to reassess the role of inflammation in neurodegeneration and to identify potential disease-modifying interventions and/or risk-reducing therapeutic strategies that target the mechanistic relationships between inflammation and neuronal and/or glial cell functions/functioning."

3. Background

This element contains a brief narrative about the background, historical evolution, and rationale for the reevaluation of the present claims of the hypothesis, proposed revisions, and/or reformulation of the hypothesis. In presenting a brief history, there should be some discussion of how the historically postulated mechanisms may play a central role in neurodegeneration. Depending on the depth of the literature, a more extensive review of this discourse may be attached as an appendix. After the background and historical review, clearly state the theoretical rationale. Please note, in some instances, the construction of a robust and logical theoretical argument may require the use of several declarative sentences that then conclude with a single interrogative sentence.

The following example might be paraphrased to fit the proposed hypothesis: "The customary paradigms of therapy development, essentially derived from current ideas and existing models of etiology, have not yielded any effective treatments during the last 3 decades. In addition, the recent string of unsuccessful clinical trials has provided further credence to the growing recognition that there are major gaps in understanding the biology of Alzheimer's disease. This breakdown in treatment strategies, based on current ideas, indicates the need to examine the problem from a different perspective. It is very likely that the present notions on the pathogenesis of dementia Alzheimer's disease, which provide the mechanistic rationale for typical models of drug discovery-development, may be insufficient. Such a drastic transformation in thinking will need new conceptual models that integrate a wide range of biochemical mechanisms that underlie the pathogenesis of various forms/types of neurodegeneration, dementia, and Alzheimer's disease."

4. New or updated hypothesis

This element should provide a concise articulation of the major claims that the new or reformulated hypothesis need to address. This discussion should enumerate the key postulates and may include not only speculations about putative mechanisms but also strategies to confirm (i.e., crucial experiments) the predictions of the revised hypothesis. Authors should provide examples of experiments that could falsify the new hypothesis. Revisions to existing hypotheses may require a higher burden of proof to supplant an established idea.

In addition to this discussion, manuscripts will need to include two sub-elements (1) Early Experimental or Observational Data; and (2) Future Experiments and Validation Studies. For the sub-element, Early Experimental or Observational Data, manuscripts should review and describe early-, pilot-, simulated-, or meta-data derived from experimental or observational research. This section should follow the familiar, albeit condensed, format of a typical research paper's methods and results sections. If such data do not exist, the authors will need to explain why and provide some other basis for justification.

For the sub-element, Future Experiments and Validation Studies, manuscripts must explain the specific predictions that the updated hypothesis will offer along with a detailed outline of potential experiments necessary to test them.

5. Major challenges for the hypothesis

The aim of this section is a careful review of barriers that must be surmounted or the technical challenges necessary to