Review

A Scoping Review of Alzheimer's Disease Hypotheses: An Array of Uni- and Multi-Factorial Theories

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Abstract.
Background: There is a common agreement that Alzheimer's disease (AD) is inherently complex; otherwise, a general disagreement remains on its etiological underpinning, with numerous alternative hypotheses having been proposed.
Objective: To perform a scoping review of original manuscripts describing hypotheses and theories of AD published in the past decades.
Methods: We reviewed 131 original manuscripts that fulfilled our inclusion criteria out of more than 13,807 references extracted from open databases. Each entry was characterized as having a single or multifactorial focus and assigned to one of 15 theoretical groupings. Impact was tracked using open citation tools.
Results: Three stages can be discerned in terms of hypotheses generation, with three quarter of studies proposing a hypothesis characterized as being single-focus. The most important theoretical groupings were the Amyloid group, followed by Metabolism and Mitochondrial dysfunction, then Infections and Cerebrovascular. Lately, evidence towards Genetics and especially Gut/Brain interactions came to the fore.
Conclusions: When viewed together, these multi-faceted reports reinforce the notion that AD affects multiple sub-cellular, cellular, anatomical, and physiological systems at the same time but at varying degree between individuals. The challenge of providing a comprehensive view of all systems and their interactions remains, alongside ways to manage this inherent complexity.

Keywords: Alzheimer's disease, amyloid, cerebrovascular disease, hypothesis, metabolism, mitochondrial dysfunction, scoping review, theory

INTRODUCTION

After more than a century of research, Alzheimer's disease (AD) remains perplexing, a thorn in the side of modern medical science. Its etiological underpinning remains under debate, with numerous alternative hypotheses having been proposed. None were confirmed to a level sufficient for its operationalization into a therapeutic approach unequivocally proven effective and efficient in a clinical setting. Surveying this landscape of ideas—some vibrantly pursued, others nearly forgotten—should

provide insights as to future general directions for research.

One aspect commonly agreed upon is that AD is inherently complex. Its most common form is primarily associated with aging, and hence overlaps exist between the wide variability in anatomical and physiological changes that accompany the latter with those of the former, early in the disease process at the very least. Beyond aging but related to it, multiple risk factors have been identified from epidemiological studies, ranging from education in early life; hearing loss, traumatic brain injury, hypertension, alcohol consumption, and obesity at mid-life; to smoking, depression, social isolation, physical inactivity, air pollution, and diabetes, in later years [1]. Yet, the compounding factor of time renders difficult the determination of whether some of these factors are early disease markers, etiological agents, catalysts, or a combination of these roles. The sheer breadth of these identified risk constructs, with impacts at scales ranging from proteins to behaviors, further points to the complexity of uncovering disease pathways at the most fundamental levels—and therefore amenable to therapeutic approaches, pharmacological or otherwise—that compound into the observed pathological cognitive and behavioral presentations.

A common agreement on what constitutes AD seems therefore a first and necessary step to address this complexity and work together towards a solution. In fact, the discordance between the clinical presentation of AD and some of its most accepted biomarkers (e.g., amyloid-β (Aβ), present in AD but also prevalent at all ages without necessarily affecting cognition [2], and histopathological findings (e.g., similar lesions being associated with dementia or not [3]), means that the very definition of the disease remains a question as much of viewpoints as one of evidence. Thus, one could argue that there are three effective, overlapping yet still irreconciled definitions of AD: one arising from a clinical/cognitive viewpoint; a second, informed by *in vivo* biomarkers; and a third, defined by histopathological evidence.

An important aspect of this debate was introduced by Alois Alzheimer himself, when he first described the disease in his seminal paper [4], relating his observations on one patient, who had first come to the clinic at 51 years of age with clear clinical dementia. Based on the age of this patient and her rapid decline, it has been argued that this was a form of autosomal dominant AD. For the first time, Aβ plaques were observed and reported. Yet, this seminal observation has set the parameters of a major argument that still rages more than a century later: are Aβ plaques fundamental or accessory to the *pseudo-sporadic (pseudo-*, as some would argue that AD is determined by gene combinations and therefore not sporadic *per se*) form of the disease, form that is by far the most prevalent? Is AD an amyloidosis, first and foremost, in all cases—not only early in life, but in older patients as well? This amyloid hypothesis [5], which has been at the center of research for the past few decades, is the field's major attempt at a "great unifying theory". It also oriented minds into a paradigm often seen in medical research, the search for a single etiological cause, regardless of the complexities inherent to human biology. Consequently, this singular view of the disease set in motion a quest, so far with limited positive results, for a similarly singular cure. Yet, the amyloid hypothesis is now seriously under siege. While it never made unanimity, as theories are initially wont to be, significant drawbacks in the past few years have led many to look anew for alternatives. First is the high prevalence of amyloid deposition in otherwise cognitively healthy individuals [6] and the lack of association between amyloid deposition and transverse and longitudinal cognitive status in otherwise cognitively healthy individuals [7]. Next we can find the highly combinatorial nature of pathologies present (especially cerebrovascular lesions) when one looks at large post-mortem samples [8], meaning that amyloid is likely not the only etiology driving decline. Finally, the accumulated failures of tens of phase III trials focused on Aβ removal to reach meaningful clinical changes [9], even when compared to those few that succeeded with modest (but, to be fair, statistically significant) success [10]. While many see these last trials as vindication of the hypothesis, others notice how the equivocal results cast further doubts on its centrality, given significant levels of side effects [9] and lack of response in many sub-groups [11]. Given their efficacy at removing amyloid but restrained clinical outcomes, combinatorial approaches will likely be necessary [12], circling back to the same issue: what exactly constitutes AD?

Thus, to solve this riddle, a theoretical framework must be sufficiently complex and detailed to be able to explain these multiple events. Many have attempted to do so in the past. It is their work which is reviewed here (using the "Scoping Review" frame), in an attempt first to enumerate, then to assess the relative importance of the diversity of hypotheses and theories that have been proposed in the past decades. We aimed to survey this wide array of

ideas, listing all hypotheses, and reporting on their meta-characteristics. The sheer size of the literature precludes us from offering but the most cursory overview of each theoretical grouping, as well as delving into the evidence propose to rank, qualitatively or quantitatively, any one theory. Indeed, assessing the quality of evidence of even a single theory adequately deserves an entire manuscript. This being so, we draw some general conclusions to orient the field.

METHODS

Literature search strategy and sources

This review followed the PRISMA guidelines [13] and was conducted using the Web of Science, Embase, Medline, and PsycInfo databases for articles published from their inception through to 14 September 2023. Keywords referred to the variables of interest (AD theory). The search strategy is presented in Supplementary Table 1. Due to the sheer volume of work that has been published on AD, we limited the number of databases and search terms/synonyms. This qualifies our work as a scoping rather than systematic review.

Study selection process

Inclusion criteria were established as follows: (a) must be a peer-reviewed, scientific article; (b) must be written in either English or French; (c) must describe a hypothesis or theory related to AD; and (d) must not report solely on a pre-clinical model of AD.

Article selection was performed using the Covidence systematic review software (Veritas Health Innovation). After the initial search (L.S.R., S.D.), duplicates were removed. Next, a first sort was performed based on article titles and abstracts, followed by a second sort based on the full-text articles. All articles were evaluated against the inclusion and exclusion criteria, and some articles were excluded accordingly. The screening was made by independent reviewers (L.S.R.; F.B.; L.A.W.; B.C.; M.A.; V.L.; S.D.; S.M.P.). Articles that were not included by reviewers were reevaluated by a third and included or excluded by common agreement.

Study selection

On 14 September 2023, 13,807 studies were uploaded to Covidence from Embase ($n = 4,787$), Medline ($n = 1,159$), Web of Science ($n = 4,240$),

and PsycInfo ($n = 1,321$) databases. Of these studies, 4,784 duplicates were removed. Three reviewers (L.S.R.; F.B.; S.D.) screened the remaining 9,022 titles and abstracts according to the inclusion and exclusion criteria. The intervention of a third independent reviewer was not required. A total of 8,398 references were excluded. Full-text screening of the 609 articles led to the exclusion of 466 articles after review by seven reviewers (L.S.R., L.A.W., B.C., M.A., S.D., S.M.P., V.L.). The excluded articles were either not describing a model (172), duplicates (86), described a non-etiological model (71), were proceedings (38) or non-peer reviewed articles (30), were in another language than English or French (23), were not applicable to AD (24), were inaccessible (12), were only concerned with the familial form of AD or Down syndrome (3), were not relevant for clinical (i.e. in humans) applications (6), or retracted (1) (see Fig. 1).

A final streamlining review of the 143 remaining articles was completed (S.D.) to remove papers from an author or group of authors that published the same hypothesis/theory more than once. We included only the earliest paper for each group in our review, as it was felt to represent the original inception of the idea. It is acknowledged that the latest manuscript, on the other hand, might have proposed the most up to date version of the hypothesis/theory under consideration. Four additional papers were added through the review process.

Following these steps yielded a final tally of 130 papers that were included in this review (Supplementary Table 2).

It must be stated unequivocally that this process, while rigorous, is more likely than not to have missed important papers, published decades ago or contemporary to us. Overall, the selection of manuscripts should be seen as representative of their categories, rather than seminal in the absolute. The emphasis is on identifying ideas within large categories, and not to initiate a subordinate debate on improper attribution of accolades. Thus, we apologize in advance to the authors of any other work that is not listed here and yet deserves to be shown.

Data extraction and classification

Characteristics of the included studies were extracted and are reported in Supplementary Table 2: lead author; country of lead author; whether there were other authors; title; year of publication; study design; and abstract.

Identification

References from databases/registers **(n = 13807)**
(as **n = 13806** studies)
    Embase (n = 1645)
    PubMed (n = 1139)
    Unspecified (n = 11023)

References from other sources **(n =)**
    Citation searching (n =)
    Grey literature (n =)

References removed **(n = 4784)**
    Duplicates identified manually (n = 0)
    Duplicates identified by Covidence (n = 4784)
    Marked as ineligible by automation tools (n = 0)
    Other reasons (n =)

Screening

Studies screened **(n = 9022)**

Studies excluded **(n = 8398)**

Studies sought for retrieval **(n = 609)**

Studies not retrieved **(n = 0)**

Studies assessed for eligibility **(n = 609)**

Studies excluded **(n = 482)**
    Double-entry or second entry for same group (n = 102)
    Retracted article (n = 1)
    Inaccessible article (n = 12)
    Non-scientific article (n = 30)
    Does not describe a model(n = 172)
    Proceeding (n = 38)
    Does not apply to human (n = 6)
    Does not describe an etiological model (n = 71)
    Neither in English nor French (n = 23)
    Does not apply to Alzheimer's disease (n = 24)
    Seoncd

Included

Studies added during the review process (**n = 4**)
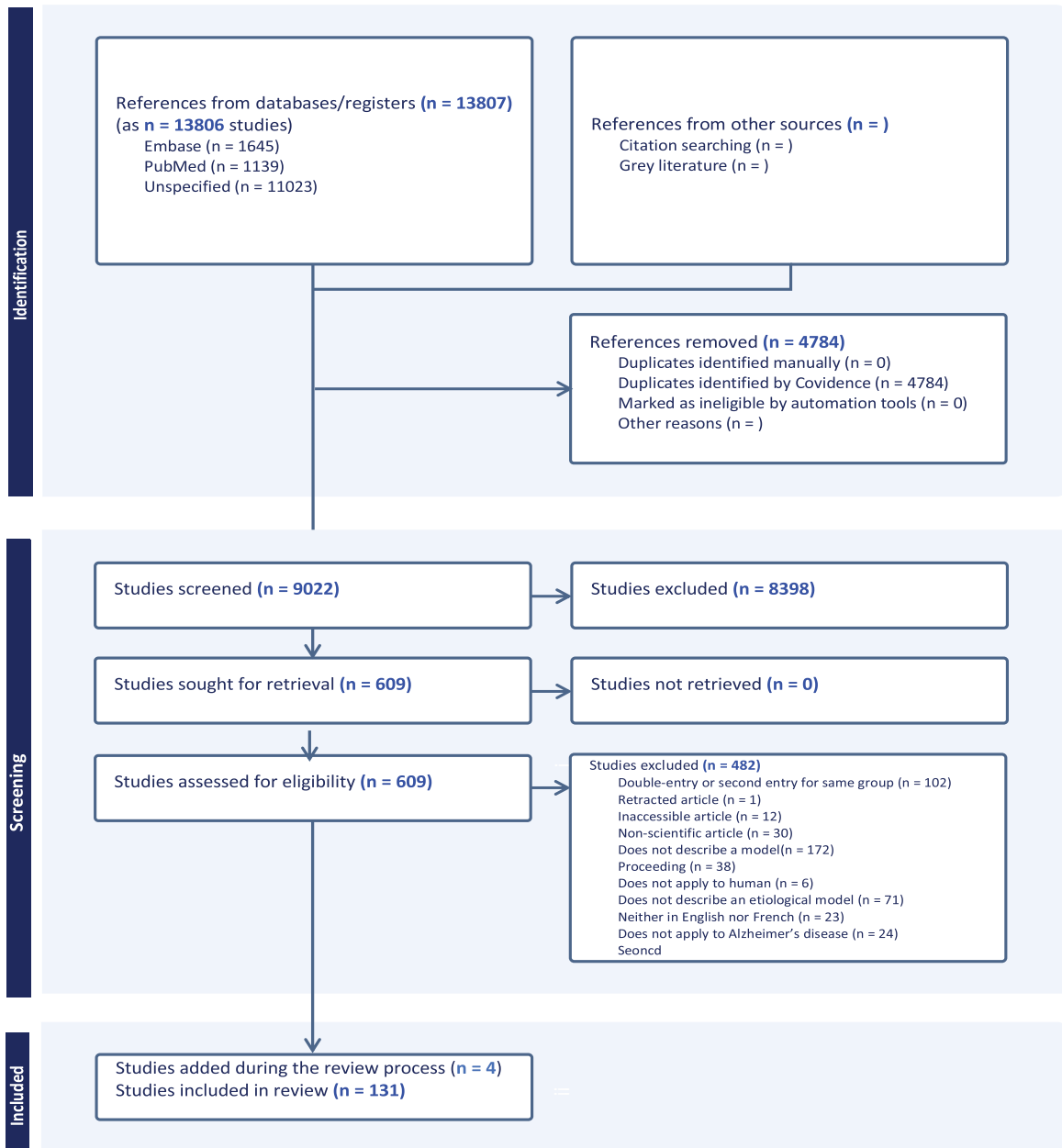Studies included in review **(n = 131)**

Fig. 1. PRISMA flowchart. Following the search strategy, 13,807 abstracts were extracted from the Embase, Web of Science, Medline, and Psycinfo databases. After removing duplicates and irrelevant studies, applying exclusion criteria and streamlining to keep only seminal and original articles, a total of 131 studies were included in this scoping review.

Citations count for each paper as of 22 December 2023 were obtained via the Google Scholar search engine. While it is known that this count may include self-citations, it was the only count that could be reliably obtained for each paper across publishers and other citation engines.

Studies were then classified (S.D.) according to two epistemological dimensions. First was whether the hypothesis/theory being proposed was *unifactorial* (e.g., Aβ over-production initiates a cascade of downstream effects leading to neuronal death and dementia) or *multifactorial* (e.g., the co-existence and interactions between amyloid, tau, and inflammation lead to neuronal death and dementia). Secondly, studies were grouped according to the primary factor that was pushed forward in the article, according to the

Table 1
Theoretical groupings (Modified from Ambrose 2015)

Grouping	Description	Studies
Amyloid	Abnormal production, accumulation, or removal of Aβ n-meric species and/or plaques	[5, 14–26]
Cerebrovascular and BBB	Vascular abnormalities affecting blood flow and perfusion, cerebrovascular lesions (infarcts, microbleeds, white matter hyperintensities), and BBB permeability	[27–38]
Genetics	Inherited genetic mutation(s), including *APOE*	[39–41]
Gut/brain axis	Dysbiosis in the gut microbiome	[42–45]
Infection	Protein misfolding in cells following infection by transmissible agents such as prion, subviral entities, HSV type 1	[46–56]
Inflammation/Immunological response	Autoimmune response and inflammation	[57–63]
Metabolism	Cortical glucose utilization and transport across the BBB	[64–72]
Metals	Neurotoxicity (e.g., Al, Hg) or deficiency in trace elements (e.g., Fe, Cu, Se)	[73–80]
Mitochondrial dysfunction	Dysfunction in brain mitochondria leading to energy deficits and oxidative stress	[81–88]
Neurotransmitter	Deficits in cholinergic, noradrenergic, and other neurotransmitters	[89–93]
Oxidative stress	Accumulation of oxidative damage in the brain from free radicals	[94–101]
Proteinopathy	Tau, TDP43, and/or other proteins dysregulation	[102–105]
White matter disease	Degeneration and disruption of white matter connections	[106, 107]
Others	Calcium channel blockers; nerve growth factors; autophagy, neuronal cell cycle abnormalities	[108–141]

BBB, blood-brain barrier.

modified theoretical grouping of Ambrose 2015 (see Table 1).

RESULTS

Studies overview

Out of 131 papers, a majority (76/131) was written by multiple, as opposed to a single, authors. First authors were mainly from the United States (60), the UK (9), Canada (8), or continental Europe (37) (see Table 2).

Study categories and impact

Nearly two third of studies proposed a hypothesis characterized as being single-focus (100/131), with the most important theoretical grouping being, unsurprisingly, the Amyloid group (14/131), followed by Metabolism (10/131) (18/131 when joined to Mitochondrial dysfunction articles), Infection (11/131), and Cerebrovascular and BBB (10/131) (Table 3).

Impact, as measured by total citations count, followed a similar pattern. Out of a total of 20,209 citations for the 131 papers, the most cited single-focused grouping was Amyloid (52%), followed by Mitochondrial dysfunction (6%, reaching 10.0% when adding Metabolism articles), then Cerebrovascular and BBB (8.6%) and Oxidative Stress (4%).

Evolution

The number of articles proposing, repositioning, or actualizing individual hypotheses and theories across time is shown in Fig. 2, from the very first (King et al.'s aluminum toxicity hypothesis in 1981) [79] to the latest entries in 2023. Likewise, a similar timeline but this time showing the impact (i.e., citation count) for each one of these articles is shown in Fig. 3.

DISCUSSION

Summary of findings

We have conducted a scoping review of AD-related hypothesis or theories in the literature dating from the early 1980 s to the current era. We selected 131 representative papers for review, written mostly by authors based in North America and Europe, and spanning a wide range of conceptual groupings.
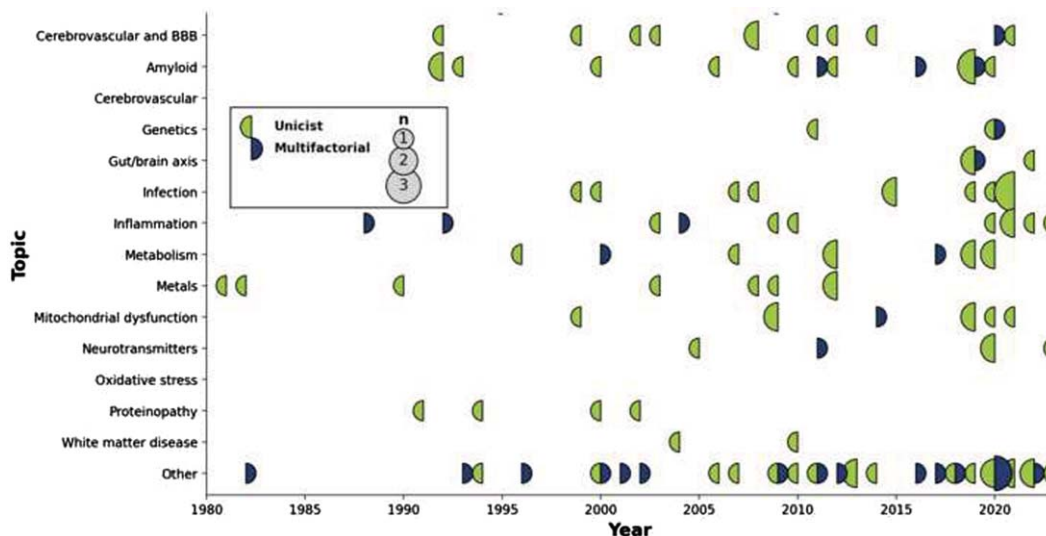
Fig. 2. Display of articles by topic through time. Circles are sized according to the number of publications that year, with a color code indicating whether the published articles were unifactorial (left circle hemisphere) or multifactorial (right circle hemisphere).
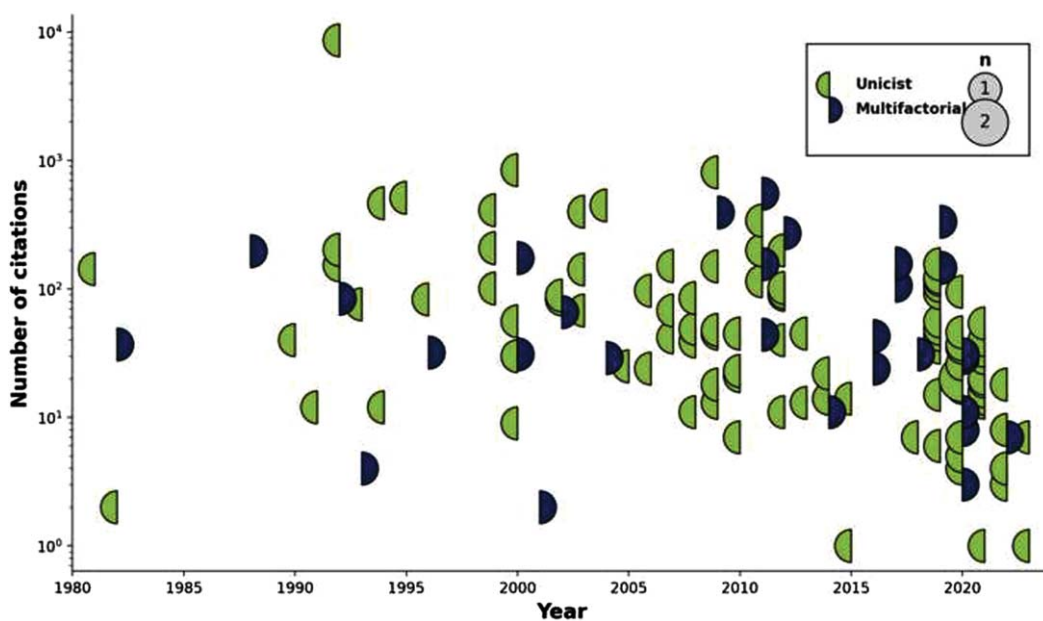

Fig. 3. Display of articles' citation count by topic through time. Circles are sized according to the number of citations that the articles achieved that year, with a color code indicating whether the published articles were unifactorial (left circle hemisphere) or multifactorial (right circle hemisphere).

Uni- or multi-factorial?

The idea that failure of a single pathway is responsible for the ensuing cascade of anatomical and physiological aberrations has been espoused not only for those hypothesizing about the role of Aβ, but all others as well, be they molecular, proteinic, cellular, or tissular entities, with nearly two-thirds of all theories being unifactorial (*cf.* Table 3). Given the massive increase in neuroscientific knowledge of the last few decades, clearly adding to our previous understanding of the intricate complexity of the brain, and the lack of any clinically meaningful results in therapeutic pursuits when targeting individual pathways, it remains puzzling why there remains such an emphasis on unifactorial hypotheses. This includes

Table 2
First author provenance

Country	N papers
United States	60
Canada	8
UK	9
France	7
Italy	6
Australia	5
Germany	4
Spain	4
Israel	3
Brazil	2
China	2
India	2
Poland	2
Singapore	2
The Netherlands	2
Turkey	2
Chile	1
Czech Republic	1
Hong-Kong	1
Iran	1
Japan	1
Malaysia	1
Portugal	1
Russia	1
Saudi Arabia	1
Slovenia	1
Switzerland	1
Total	131

the Amyloid hypothesis subgroup, the most studied of them all, for which unifactoriality was *de rigueur* until 2011; since then, *more* unifactorial point of view articles have been published than those espousing a multifactorial framework in which Aβ is a strong contributor. In essence, the field seems to have doubled down on the amyloid cascade hypothesis, albeit in a slightly modified form, regardless of disproving evidence as to its *centrality*. The existence of possible non-scientific reasons as to why this situation has been self-perpetuating is a possibility; a single theory does offer a direct promise of a high reward if proven correct.

Novelty and endurance of hypotheses

Three stages can be discerned in terms of hypotheses generation. The first phase (∼1980–1995) included the establishment of the main thrusts that have endured to this day. Its most prevalent entry was the Amyloid hypothesis, with the field-defining work of Hardy et al. (cited 8,633 times) [5], before the separation into clear autosomal dominant and pseudo-sporadic cases (often conflated or confounded with Early and Late Onset AD designa-

tions). In the same period were also introduced initial reports for the Glial [18], Infection [50], Inflammation [97], Metabolism [69], Oxidative stress [97], and Proteinopathies [102] hypotheses; the concept of interdependence across all scales, central to multifactorality [122]; as well as the by now marginal notion of neurotoxicity of trace elements [79]. The importance of BBB integrity was also recognized [28]. In the second phase (1995–2005), the importance of the Cerebrovasculature [35, 37, 38], Mitochondrial dysfunction [84], and Neurotransmitters [91] took center stage. Lately (2005–2020), evidence towards Genetics (outside of the autosomal dominant form) [41], and especially Gut/Brain interactions [42] came to the fore. The latter category has seen a rapid increase in impact when compared to others, with the paper from Angelucci et al. receiving a rate of 66.8 citations/year since its publication in 2019 (second only to the seminal Hardy et al. paper, with 269.8 citations/year since publication).

Biases

There are obvious biases in the impact statistics that must temper any interpretation. First, citation counts from Google Scholar often include self-citations; real numbers will therefore be smaller than recorded. Secondly, articles may be cited for positive (e.g., new evidence corroborating the hypothesis), negative (e.g., new evidence against the hypothesis), or even neutral (e.g., overview of the field) reasons, including positioning of one's hypothesis against the leading one (which, in the case of AD, would favor the citation rates attached to the Amyloid group). Raw citation count therefore may not reflect actual acceptance of any idea. Finally, the field is heavily biased towards ground-breaking, first-in-field articles; while seminal, they may not represent the best or most up to date version of a particular hypothesis. In particular, the article of Hardy et al. [5], already mentioned, established the amyloid cascade hypothesis, and represents 43.2% of *all* citations from the 131 papers in this scoping review. The power law of distributions is evidently quite at work here as elsewhere; the 10-most cited papers (Amyloid: 2; Cerebrovascular: 2; general theories around aging: 2; and Mitochondrial dysfunction, Oxidative stress, Neurotransmitters, and Glial disease: 1 each) are responsible for 67.0% of all citations.

Finally, we refrained from providing an assessment of the relative merit of each theory, as any such assessment would have been biased. First, since the

quality and quantity of evidence for each theory is demonstratively related to its preponderance in the literature (e.g., evidence on amyloid far outweighs that on the impact of gut microbiota). Next, since no theory, including the amyloid hypothesis, has overwhelmingly been demonstrated to explain all aspects of pseudo-sporadic AD, then it implies that either insufficient evidence has been gathered to arrive at a conclusion, or a sufficiently complete theory has yet to be formulated to fit the available evidence. Hence, we felt that any assessment would have been fraught without a clear epistemological direction.

Future considerations

Which hypotheses or theory have notable evidence?

We posit that to answer this question successfully a theory would need to fulfill three criteria: 1) unequivocal clinical benefit from a therapeutic intervention, with 2) unambiguous disease-modifying results confirming a 3) global theoretical framework of the etiology.

As of now, only three classes of interventions have achieved results. First are anti-cholinesterase inhibitors, approved in the late 1990 s [142] following clinical trials that demonstrated a statistically significant yet weak improvement in cognition for a limited time period. Acting on the principle that they enhance the availability of important neurotransmitters, they appear to provide but a temporary respite to clinical disease progression, while not influencing biomarkers of neurodegeneration. They remain seen as symptoms-, rather than disease-, modifiers [143]. Hence, while our first criterion seems met, the latter two are not.

A second class of intervention has gained traction in the past few years. Three Aβ antibodies have been approved by the Food and Drugs Agency in the United States following successful clinical trials, for which the primary outcome was biomarker defined, rather than clinical [144]. While the aptitude of both compounds at Aβ plaque removal is not in question (criterion 2), they had no effect on anatomy or physiology (e.g., neurodegeneration, neuroinflammation, neurometabolism) as well as limited clinically-observable effects (criterion 1), the latter remaining in doubt [9, 145], especially in the face of severe side-effects that point to an incomplete understanding of the role of Aβ [146]. Such antibodies are not the only compounds that have attempted to reduce production, block aggregation, or remove Aβ

plaques; as a general rule, these few successes are not strong indicators of the centrality of the amyloid hypothesis in any general theory of AD (criterion 3).

Finally, non-pharmaceutical combinatory approaches targeting lifestyle interventions, nutrition, physical exercise, and aggressive management of co-morbidities (e.g., hypertension, diabetes) have had also significant successes, with effect sizes that are actually equal to pharmacological approaches such as Aβ antibodies [147] (criterion 1). The difficulty here is to understand which one, or many, etiological pathways are affected and with which efficiency (criterion 2). It does however provide strong evidence that *multi-scale targeting* stands a better chance than other, single-pathway focused interventions (criterion 3).

Theory versus practice: pharmaceutical trials

Hypothesis-driven research, relatively free from the pressure of providing immediate returns to its largely state funders in terms of success or failure, has therefore kept on exploring avenues, new and old, with what can be seem at times steadfastness. Witness to this effect the 33% *increase* in Aβ-centric theoretical works that have been proposed in the 2010–2020 interval.

On the contrary, the field of pharmaceutical trials seems to have already integrated the notion of multifactoriality, exploring a host of different avenues, often in combination. This can be seen for example in the 54% *decrease* (41 versus 19) in the number of Aβ-centric clinical trials between 2010 and 2022 [148, 149].

Single versus multiple factors

On the face of the evidence presented it is therefore hard to refute completely any one of the hypotheses that have been proposed. While many concepts can be proven as extremely unlikely and rejected on this basis, most articles present compelling evidence to this or that effect that is either borne out in a clinical population, either via epidemiological studies or randomized clinical trials, or from translational work in animal models. Viewed differently, they reinforce the notion in fact that AD affects multiple sub-cellular, cellular, anatomical, and physiological systems at the same time but at varying degree between individuals. The simple fact of the existence of the incredible variety of etiological factors itself should makes one realize that we are dealing with a complex multi-

factorial problem; this is further evidenced by the correlation of dementia with all other health problems [150]. The biggest hurdle to overcome seems rather to provide a comprehensive overview of all these systems at the same time, and their interactions.

Further, any theory being proposed would need to explain a significant body of epidemiological evidence pointing to, for example, sex imbalance in the prevalence of AD [151], as well as in trajectories and therapeutic response in other ethno-centric and socio-economic factors [11].

The emphasis on unifactorial viewpoints is possibly an artefact of research, including the well-known bias towards positive research reporting [152]. The necessity to provide results that have reached statistical significance will naturally be easier to achieve in limited experimental settings, given statistical power considerations, and thus favor the study of individual effects over the logistically much more difficult task of deciphering interactions in a system; complexity increasing factorially with each new factor and parameter being considered.

CONCLUSION

Hence, while new frontiers keep being opened, it could be argued that most of the anatomical and physiological systems that impact or are impacted by AD, at various time and spatial scales, have already been well surveyed. A corollary of this observation is endurance. Indeed, some hypotheses have been proposed and therefore tested for over 30 years. The fact that we are still discussing whether AD is primarily an amyloidopathy, what is the importance of metabolism, or what role plays the cerebrovasculature, attests to both the complexity of the matter and the need for a holistic framework that could reframe the debate in simpler lines. Geometry provides an analogy: problems that are arduous in cartesian space become simpler when expressed in polar coordinates. Such a transformation might be necessary for the field to reach clarity.

AUTHOR CONTRIBUTIONS

Simon Duchesne (Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing – original draft; Writing – review & editing); Louis-Simon Rousseau (Conceptualiza-tion; Data curation; Formal analysis; Methodology; Validation; Writing – original draft); Florence Belzile (Data curation; Writing – review & editing); Laurie-Ann Welch (Data curation; Writing – review & editing); Beatrice Cournoyer (Writing – review & editing); Marianne Arseneau (Data curation; Writing – review & editing); Véronick Lapierre (Data curation; Writing – review & editing); Sara-Maude Poulin (Data curation; Writing – review & editing); Olivier Potvin (Data curation; Formal analysis; Visualization; Writing – original draft; Writing – review & editing); Carol Hudon (Conceptualization; Funding acquisition; Investigation; Methodology; Project administration; Resources; Supervision; Validation; Writing – original draft; Writing – review & editing).

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CONFLICT OF INTEREST

The authors have no conflict of interest to report.

DATA AVAILABILITY

The final list of articles selected for this scoping review is available upon request in tabular format.

SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: https://dx.doi.org/10.3233/JAD-230772.

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