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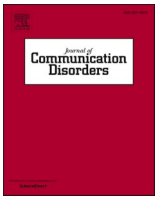

Language impairments in people with autoimmune neurological diseases: A scoping review

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ABSTRACT

Introduction: Autoimmune neurological diseases (ANDs) are a specific type of autoimmune disease that affect cells within the central and peripheral nervous system. ANDs trigger various physical/neuropsychiatric symptoms. However, language impairments in people with ANDs are not well characterized. Here we aimed to determine the kinds of language impairment that most commonly emerge in 10 ANDs, the characteristics of the patients (demographic, neurological damage), and the assessment methods used.

Methods: We followed the PRISMA Extension for Scoping Reviews (PRISMA-ScR). PubMed and Google Scholar were searched. We used a list of search terms containing 10 types of ANDs (e.g., multiple sclerosis, acute disseminated encephalomyelitis) in combination with the terms aphasia, dysphasia, fluency, language, listening, morphology, phonology, pragmatics, reading, semantics, speaking, syntax, writing. The reference lists and citations of the relevant papers were also investigated. The type of AND, patient characteristics, neurological damage and examination technique, language tests administered, and main findings were noted for each study meeting the inclusion criteria.

Results: We found 171 studies meeting our inclusion criteria. These comprised group studies and case studies. Language impairments differed largely among types of ANDs. Neurological findings were mentioned in most of the papers, but specific language tests were rarely used.

Conclusions: Language symptoms in people with ANDs are commonly reported. These are often not full descriptions or only focus on specific time points in the course of the disease. Future research needs to assess specific language functions in people with ANDs and relate their language impairments to brain damage at different stages of disease evolution.

1. Introduction

The prevalence of autoimmune diseases ranges between 3-5% in Western countries (Wang et al., 2015). The origin of autoimmune diseases is hypothesized to be a combination of genetic components and environmental factors (e.g., diet, smoking) (Davidson & Diamond, 2014). Furthermore, sex hormones and sex chromosomes (Gold et al., 2019; Ngo et al., 2014; Voskuhl, 2020), infectious

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processes (Armangue et al., 2018; Berger, 2020; Bjornevik et al., 2022; Dalakas, 2020; Lopez et al., 2021), and less frequently cancer can play a role in the emergence of these diseases (Lancaster, 2017). There are more than a hundred known types of autoimmune diseases (The American Autoimmune Related Diseases Association, 2018). Some autoimmune diseases are unique in that they affect the cells within the central and peripheral nervous system – these are called autoimmune neurological diseases (ANDs) and will be the focus of this review.

ANDs are the result of an overactive immune system attacking healthy central nervous system cells (e.g., Lerner et al., 2015). The immune system is a network of organs (e.g., adenoids, bone marrow, lymph nodes, thymus), cells, humoral factors, and proteins that defend our body against infection from bacteria, viruses, fungi, and toxins (Parkin & Cohen, 2001). The immune system communicates with the central nervous system, by modulating body temperature, sleep, and feeding behaviour, among others (Steinman, 2004). The symptoms that people with ANDs experience usually develop over several days or weeks after the acute phase and vary depending on the specific disease (Scolding & Fuller, 2004). Patients can develop neuropsychiatric problems, cognitive impairment, epilepsy, or movement disorders, among others (Liu & Tang, 2018, Tjaden et al., 2013, Tobin & Pittock, 2017).

To the best of our knowledge, a general review on language impairments in people with ANDs does not yet exist. It is important to characterize the language impairments that people with ANDs may have. This review is relevant to enhance the current awareness of clinicians, researchers, and the general public about language impairments in ANDs. Ultimately, this work could stress the need to assess and treat language impairments in this population. Therefore, here we report a scoping review of the current literature on language impairments in people with ANDs. The main goal is to determine the kinds of language impairment that most commonly appear in 10 ANDs, the characteristics of patients (demographic, neurological damage), and the assessment methods used. Given the vast number of ANDs and their heterogeneity (e.g. Bhagavati, 2021), we will not provide the reader with an exhaustive overview of all studies describing language impairments in people with different ANDs. Some of the ANDs we will discuss are objectively rare and by definition not frequently observed. Yet, the goal of this review is to provide a general picture of language impairments in this population, paving the way for systematic reviews and original research studies investigating language impairments in people with specific kinds of ANDs.

2. Methods

We followed the PRISMA Extension for Scoping Reviews (PRISMA-ScR), as described in Tricco et al. (2018). PubMed and Google Scholar were searched for peer-reviewed articles of ANDs and language impairments. No timeframe was used for the search because we did not expect a large number of articles and because we were unaware of classic references or a time when this topic was more heavily discussed in the literature. We searched for 10 ANDs based on a list generated by the Icahn School of Medicine at Mount Sinai (2021). This list was chosen as our source for ANDs because the Icahn School of Medicine at Mount Sinai is a leading institution in ANDs. As far as we know, no ANDs predominantly damage language circuits, but language impairments can be related to the presence of lesions or more diffuse neurological damage affecting brain connections (see Llufriu et al., 2016, for an example of Multiple Sclerosis (MS)).

We used 28 search items for our literature search (see Table 1). A search term related to the ANDs under investigation (left column) was searched for in combination with a linguistic term (right column). We used a PubMed search string (Table 2) to search for relevant literature. Additionally, the reference list and the citations of the included papers were examined to find more relevant papers.

Each paper was evaluated as follows: two independent reviewers (J.R., A.R) evaluated the titles and abstracts of all articles based on the exclusion criteria listed in the next paragraph. Based on this evaluation, a series of full texts were chosen to review. The full texts were evaluated according to the same exclusion criteria as earlier (see next paragraph). If the texts met the inclusion criteria, they were fully read by J.R. and A.R. and specific aspects of the papers were entered into a table: type of AND investigated (e.g., multiple sclerosis), number and characteristics of patients (i.e., age, gender, language background), neurological damage and neurological examination technique (e.g., electroencephalography [EEG] showed general slowing), and language tests administered (e.g., Boston Naming Test (Kaplan et al., 1983)). Moreover, the main findings of each study relating to language impairments were noted and

Table 1
Search terms used in this review.

ANDs	Language
Acute disseminated encephalomyelitis	aphasia
Anti-gamma-amino butyric acid antibody-associated diseases	dysphasia
Anti-$GABA_B$ receptor antibody-associated diseases	fluency
Anti-myelin oligodendrocyte glycoprotein antibody disease	language
Anti-MOG antibody disease	listening
Autoimmune encephalitis	morphology
Anti-NMDAr encephalitis	phonology
Anti-N-methyl-D-aspartate receptor encephalitis	pragmatics
Hashimoto's encephalitis	reading
Steroid responsive encephalopathy associated with autoimmune thyroiditis	semantics
Multiple sclerosis	speaking
N-type calcium channel antibody-mediated autoimmune encephalitis	syntax
Neuromyelitis optica	writing
Optic neuritis	
Transverse myelitis	

Table 2
PubMed search string used.

("Autoimmune Diseases of the Nervous System"[Mesh] OR "Hashimoto's encephalitis" [Supplementary Concept] OR "Thyroiditis, Autoimmune"[Mesh] OR "Optic Neuritis"[Mesh] OR anti-GABAB receptor antibody-associated disease*[tiab] OR anti-myelin oligodendrocyte glycoprotein antibody disease*[tiab] OR anti-MOG antibody disease*[tiab] OR autoimmune encephalitis[tiab] OR anti-NMDAR encephalitis[tiab] OR steroid responsive encephalopathy associated with autoimmune thyroiditis[tiab] OR multiple sclerosis[tiab] OR neuromyelitis optica[tiab]) AND ("Language"[Mesh] OR "Aphasia"[Mesh] OR aphasia*[tiab] OR dysphasia*[tiab] OR fluency[tiab] OR listen*[tiab] OR morpholog*[tiab] OR phonolog*[tiab] OR pragmatic*[tiab] OR reading[tiab] OR semantic*[tiab] OR speak*[ti] OR syntax[ti] OR writ*[ti]) NOT ("Articulation Disorders"[Mesh] OR articulation disorder*[ti] OR speech[ti] OR slurred[ti] OR dysarthria[ti] OR dysphonia[ti])

included in the table.

We excluded papers that reported: (1) ANDs other than the ANDs mentioned in Table 1 (left column); (2) impairments other than the language impairments stated in Table 1 (right column); (3) people with simultaneous ANDs; (4) comparisons between people with ANDs and people with other (neurological) diseases; (5) language impairments in people with ANDs that could have been affected by medical treatment or improved after speech-language therapy. We also excluded papers that (6) were written in languages other than English; (7) were not peer-reviewed; or (8) included no original data.

To clarify our exclusion criteria: (1) and (2) were implemented to limit the scope of the article, that is, to focus on 10 commonly reported ANDs and to only report on lexico-semantic and morpho-syntactic difficulties. Therefore, we excluded papers only reporting speech/voice impairments (e.g., slurred speech, dysarthria, dysphonia) or only cognitive impairments; (3) was implemented because when someone is diagnosed with two ANDs, it is hard to discern which AND is causing the language impairments. For example, this was the case for a person with acute disseminated encephalomyelitis (ADEM) and with autoimmune encephalitis (Aoe et al., 2019); (4) was implemented because these studies may not stress the main underlying impairments that people with ANDs have, rather, they tend to stress specific language/cognitive aspects that could be useful in distinguishing ANDs from other diseases (e.g., Clark et al., 1997; Covey et al., 2012; Roy et al., 2018); finally, the reason for exclusion criteria (5) is that the language impairments found in these studies can be biased by treatment/therapy instead of being due to AND pathology (e.g., Darestani et al. 2020; Sandyk, 1994).

Exclusion criteria did not extend to (1) studies examining people with an AND after central nervous system infections, because ANDs can be triggered by an infection (Bjornevik et al., 2022; Getts et al., 2014; Niederschweiberer et al., 2020); and (2) studies covering general language impairments (e.g., production, comprehension, aphasia) without mentioning which language tests were administered. The latter studies were included because they are able to provide evidence regarding the frequency of language impairments in people with specific ANDs, ensuring the detection of a sufficient number of articles to determine the types of language impairment that most commonly appear in this population.

The percentages mentioned in the results are based on the total number of papers found. In this way, we avoided one study dominating the percentage calculation due to having a bigger sample size. To calculate the percentages, the number of occasions an investigated aspect (e.g., language impairments mentioned, characteristics of patients [i.e., language background], neurological damage found, neurological examination technique used and language tests administered) was found were counted and divided by the total number of papers identified. Age and gender characteristics were only calculated for case studies and case series. We did not calculate the percentages related to age groups or gender ratios for group studies or for all included studies, to avoid studies with bigger sample sizes dominating the percentage calculation. We treated multiple case series as describing only one case when calculating the language impairments, language modalities, brain examination techniques and timing of language impairments. This means that, for example, if we found a case series that described two patients suffering from naming problems, we only counted this language impairment once. Due to the fact that in some papers multiple language impairments, language modalities, brain examination techniques, language tests or multiple patients are assessed, some of the percentages in the Results section do not sum to a 100% (e.g., the report of neurological damage and the nature of the language impairments found). Ratios were also provided to facilitate the transparency of the calculation process.

3. Results

A total of 3238 papers were identified by searching the electronic databases and reviewing article references. To this number, 11 articles were removed as they were duplicates. Based on the title and the abstract, 3014 articles were not considered eligible following our exclusion criteria. The remaining 213 articles were assessed for eligibility based on the full-text. Of these, 81 were excluded. Namely, twenty-seven correlational studies between cognitive impairments and brain pathology, 11 papers that did not discuss language, 11 papers showing no new data, 10 papers which reported ANDs and impairments after treatment, 7 papers that could not be retrieved, 5 papers which had an unclear AND diagnosis (e.g., two ANDs simultaneously), 4 papers discussing types of ANDs that we were not interested in or no AND at all, 3 validation/development papers for new test tools and 3 papers comparing ANDs to other diseases. The remaining 132 papers met the inclusion criteria and were considered eligible for this scoping review. To these articles, 39 papers were added by looking at the reference list of the aforementioned included 132 papers and the 3 review papers, resulting in 171 papers to be reviewed. See Fig. 1 for a flow diagram of this process.

In the supplementary material we have included a table with information for each paper regarding the type of AND, bibliographical reference, number and demographic information of the patients, neurological damage, language tests used, and main findings (Table A1). These papers were published between 1987 and 2022. Half of the reports were group studies (86/171, 50%), followed by single case studies (62/171, 36%), and multiple case studies reported in a single paper (14/171, 14%, i.e., case series).

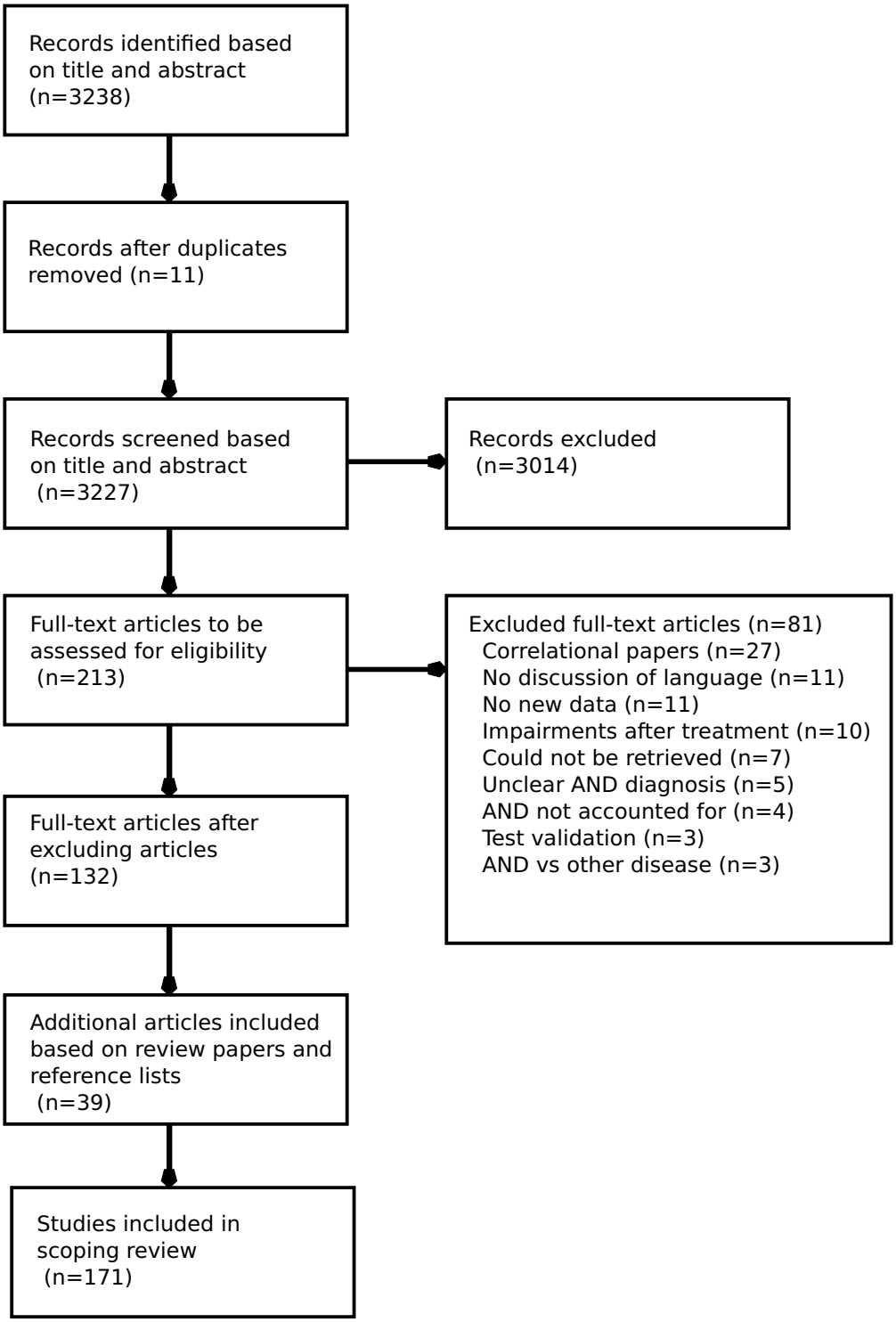

Fig. 1. Scoping review flow diagram.

Regarding type of AND, MS was most often found (98/171, 57%), followed by other types of ANDs, namely, Anti-N-methyl-D-aspartate receptor (anti-NMDAr) encephalitis (22/171, 13%), ADEM (21/171, 12%), steroid responsive encephalopathy associated with autoimmune thyroiditis (SREAT, Hashimoto's encephalitis) (14/171, 8%), neuromyelitis optica (5/171, 3%), Anti-myelin oligodendrocyte glycoprotein (anti-MOG) antibody-associated encephalitis (5/171, 3%), N-type calcium channel antibody-mediated autoimmune encephalitis (2/171, 1%), limbic paraneoplastic encephalitis (2/171, 1%), anti-voltage-gated potassium

channel encephalitis (1/171, 1%), and Anti-gamma-amino butyric acid (anti-$GABA_B$) antibody-associated disease (1/171, 1%). Studies of people with MS were most commonly reported as group studies (76/86, 88%) as opposed to other ANDs (10/86, 12%).

With regard to patient characteristics in the case studies and case series (106 patients in total), females were more frequently reported than males [68 females, (68/106, 64%), 38 males (38/106, 36%)], and adults were more often examined than children [80 adults (80/106, 75%), 26 children (26/106, 25%)]. The languages the patients spoke were explicitly mentioned in only 5 case studies (5/171, 3%) and in 22 group studies (22/171, 13%). These included: Chinese, Dutch, English, Finnish, French, German, Greek, Italian, Persian, Romanian, Russian, Spanish, and Swedish.

Regarding neurological damage, we found no mention of neurological damage or report of neurological damage specifically relating to the reported language impairments in 78 papers (78/171, 46%). Most of these studies (70/78, 90%) were of people with MS. Ninety-five papers (95/171, 56%) reported some details of a neurological examination. From these, in 12 papers (12/95, 13%) we found reports of patients without neurological damage, whereas in 87 papers (87/95, 92%) we found reports of neurological damage. Two papers (2/171, 1%) mentioned neurological damage without mentioning the neurological examination technique used.

Papers differed in the inclusion of brain examinations and in the types of neuroimaging and electrophysiological monitoring techniques used. Brain examination techniques were reported in 92 papers (92/171, 54%): 35 of these papers (35/92, 38%) used only one technique, while 57 of the papers (57/92, 62%) used 2 or more techniques. More specifically, 83 (83/92, 90%) of the papers mentioning brain examination techniques used a form of magnetic resonance imaging (MRI), 44 (44/92, 48%) electroencephalography (EEG), 25 (25/92, 27%) computed tomography (CT), 10 (10/92, 11%) positron emission tomography (PET), 8 (8/92, 9%) single photon emission computed tomography (SPECT), 2 (2/92, 2%) magnetic resonance (MR) spectroscopy, 1 (1/92, 1%) MR angiography, 1 (1/92, 1%) CT angiography, and 1 (1/92, 1%) magnetoencephalography (MEG). Only 2 papers (2/171, 1%) mentioned brain damage without citing the brain examination technique used.

The language impairments, as mentioned in the papers, are summarized in Table 3. Language impairments included different types of "aphasia/dysphasia" (63/171, 37%), "verbal fluency problems" (52/171, 30%), "naming difficulties" (26/171, 15%), "word-finding difficulties" (18/171, 11%), "impaired reading" (13/171, 8%), "paraphasias" (13/171, 8%), "repetition problems" (11/171, 6%), "writing difficulties" (9/171, 5%), "anomia" (5/17, 3%), "dysnomia" (2/171, 1%), "dyslexia" (2/171, 1%), "pragmatic comprehension problems" (1/171, 1%) and "logorrhoea" (1/171, 1%). Some papers mentioned concomitant language impairments.

Relative to the assessments, language production was more often assessed than language comprehension: 114 studies (114/171, 67%) assessed spoken language production, 13 studies (13/171, 8%) written language production, 35 studies (35/171, 20%) spoken language comprehension, and 17 studies (17/171, 10%) written language comprehension. Some studies mentioned multiple language modalities. In contrast, 49 studies (49/171, 29%) mentioned only general language impairments without stating whether production, comprehension or both were investigated (e.g., aphasia, global aphasia).

Relative to the language impairments, 100 studies (100/114, 88%) reported spoken production to be impaired, as opposed to 33 studies (33/114, 29%) which mentioned preserved spoken production skills. Note that the percentages do not add up to a 100%, since studies could mention multiple AND cases, of whom one shows preserved spoken production and another shows impaired spoken production. The same principle holds for the percentages mentioned for the other language modalities described below. Written production was reported to be impaired in 10 studies (10/13, 77%) and preserved in 3 studies (3/13, 23%). In 25 studies (25/35, 71%) spoken language comprehension was reported to be impaired and in 12 studies (12/35, 34%) preserved. Regarding written comprehension, impairments were reported in 15 studies (15/17, 88%) whereas preservation was reported in 3 studies (3/17, 18%).

Regarding the timing of impairments, we found language impairments at disease onset or as one of the first symptoms of the disease (12/171, 7%). Additionally, 71 studies (71/171, 42%) indicated language disturbances during disease progression, after hospitalization, or over several days or weeks after hospitalization. Moreover, 9 studies (9/171, 5%) reported language issues during disease relapse. In contrast, 87 papers (87/171, 51%) did not clearly define the timing relative to disease onset in which language impairments were assessed. In these studies, language impairments were mentioned relative to hospitalization or examination instead of relative to disease onset. Therefore, we could not trace back to when these symptoms started exactly. When language impairments developed during hospitalization, we interpreted them as symptoms developed over a period of a few days or weeks since these symptoms were not present at disease onset and were not part of the symptoms for which the patient was admitted to the hospital (e.g., Bernhardt et al.,

Table 3
Raw number and percentage of papers reporting language impairments in the ANDs under investigation.

Aphasia/dysphasia	63 (37%)
Verbal fluency problems	52 (30%)
Naming difficulties	26 (15%)
Impaired reading	13 (8%)
Paraphasias	13 (8%)
Repetition problems	11 (6%)
Writing problems	9 (5%)
Anomia	5 (3%)
Dysnomia	2 (1%)
Dyslexia	2 (1%)
Pragmatic comprehension problems	1 (1%)
Logorrhea	1 (1%)

Percentages based on 171 papers.

2017).

Language tests were only reported in 91 of the papers (53%). Most of these studies were on people with MS (79/91, 87%). The most frequently used language tests were verbal fluency tests, which were reported 93 times (93/171, 54%). Note that this number is higher than 91, because one paper could show reports of different types of (standardized) verbal fluency tests. In 54 of these cases (54, 54/93, 58%) a standardized version of a fluency task was mentioned. In 24 of the reports (24/93, 26%) a specific version of a fluency task was used, namely the Controlled Oral Word Association Test (COWAT) (COWAT; e.g., Benton & Hamsher, 1976; [13/24, 54%]), Word List Generation (e.g., Bever et al., 1995; [6/24, 25%]), the verbal fluency subset of Delis-Kaplan Executive Function System (Delis et al., 2001; [5/24, 21%]) and the Supermarket Test (e.g., Mattis, 1976; [2/24, 8%]). In 67 of the reports (67/93, 74%) no specific fluency task was indicated; rather, category fluency tests (38/67, 57%) and letter fluency tests (25/67, 37%) were mentioned (not mentioned: [4/67, 6%]). After the verbal fluency tests, the Boston Naming Test (BNT, e.g., Kaplan et al., 1983) was most frequently used (22/171, 13%). Other tests mentioned more than once, were the Token Test (e.g., Luzzatti et al., 1999) (5/171, 3%), Peabody Picture Vocabulary Task (e.g., Dunn & Dunn, 1981) (2/171, 1%), and Boston Diagnostic Aphasia Examination (BDAE-SF; (Goodglass & Kaplan, 1972) (2/171, 1%)).

4. Discussion

The present study examined language impairments in 10 ANDs. Of all detected papers, 171 papers met our inclusion criteria. These papers spanned over a period of 35 years (i.e., 1987 to 2022). The language impairments and neurological damage described varied across studies. This section discusses MS separately, as it is the AND that is most studied. After that, we describe the rest of ANDs we entered in this review combined, while giving a short explanation of the pathology and the language symptoms frequently seen. Thereafter, the general picture of what language impairments are in people with ANDs is discussed. For an overview of the papers found, the reader may refer the reader to Table A1 in the supplementary materials.

4.1. Multiple sclerosis (MS)

MS is an inflammatory demyelinating and neurodegenerative disease affecting both white and grey matter in the central nervous system (Dunham & Mahajan, 2021; Wootla et al., 2012). It is the most common autoimmune demyelinating disease, as it affects over 2.8 million people worldwide (Walton et al., 2020). MS is more prevalent in women compared to men, and its onset is often between 20 and 40 years (Rogers & MacDonald, 2015). The cause of MS remains elusive, but Epstein-Barr virus infection, genetic susceptibility and environmental factors (e.g., smoking and vitamin D deficiency) seem to be involved (Ascherio, 2013; Bjornevik et al., 2022; Hartung et al., 2016; Wootla et al., 2012). There are different clinical phenotypes: relapsing-remitting, secondary progressive, and primary progressive MS (Ford, 2020; Lublin et al., 2014).

With regard to brain damage, a general pattern was found: EEGs scans were often found to be abnormal with different symptoms, such as sharp wave activity (e.g., Trinka et al., 2001) or slowing (e.g., Sener et al., 2017). MRI frequently showed small lesions in white matter structures, such as the internal capsule (e.g., Rosso et al., 2006). In the papers included in this review, lesions were relatively more common in the left hemisphere. This is not unusual, since left hemisphere damage is common in MS (Llufriu et al., 2016; Preziosa et al., 2017).

In the majority of the articles found in this review, language difficulties were described from a rather general perspective, albeit with a certain variability. Severe impairments were described under labels such as global aphasia (Erdem et al., 2001) and aphasia (e.g., Ashtari et al., 2020; Katsuki et al., 1998). In other papers, the authors hinted to more specific difficulties, for example, by indicating that people with MS had issues with language production (expressive aphasia, Nicholas et al., 2016), with language comprehension (Wernicke's aphasia), or with both production and comprehension (mixed aphasia, Hamed, 2015). Unfortunately, these studies did not indicate the tasks used, so it is hard to pinpoint the specific linguistic aspects that could have been impaired (e.g., lexico-semantic, morpho-syntactic, pragmatic).

In other studies, spoken language production problems were indicated by stating that people with MS had word-finding difficulties or that they made grammatical errors while speaking (e.g., Bakker et al., 2004; Chanial et al., 2020; Spatt et al., 1994). Difficulties with language production were also found, for example, during naming (e.g., Day et al., 1987; Devere et al., 2000), verbal fluency (e.g., Cerezo García et al., 2015; Storm-Van's Gravesande et al., 2019), word and sentence repetition (Devere et al., 2000; Spatt et al., 1994), and during word reading (Jennekens-Schinkel, Laboyrie, et al., 1990). Naming, however, was not always impaired (Feuillet et al., 2007; Jakimovski et al., 2019), especially, when phonological or semantic cues were given (Joly et al., 2014; Joly et al., 2019). Such pattern of errors during naming has been interpreted from the perspective that people with MS have impairments with lexical access, also showing a relation between naming and subjective complaints (Brandstadter et al., 2020). During naming, patients are required to recognize a graphic representation of an object, retrieve the meaning the object from the semantic system, access the specific word that represents the object (i.e., lexical access), and articulate the phonemes corresponding to the word. Therefore, when the responses of patients are aided by cues (particularly phonological), this indicates difficulties with lexical access, as opposed to recognition, semantics, or articulation (Whitworth et al., 2014).

The most widely assessed language production domain was verbal fluency. In studies examining verbal fluency, category and letter fluency tended to be impaired compared to healthy controls (e.g., Cerezo García et al., 2015). However, in two studies there was no difference between healthy controls and people with MS on category fluency tasks (Storm-Van 's Gravesande et al., 2019; Tong et al., 2002). Furthermore, some studies reported differences in verbal fluency between people with different subtypes of MS, but no consistent pattern was found (Brissart et al., 2013; Gois et al., 2021; Huijbregts et al., 2004; Kraus et al., 2005; Rodrigues et al., 2011;

Wachowius et al., 2005). This inconsistency might have to do with other patient characteristics, such as the number of years a patient has already been living with the disease, as category fluency for example seems to continuously decline along the disease course (Lopez-Soley et al., 2021). Also, this inconsistency could be due to the fact that some people with MS can have other cognitive problems, for example, in executive functions (Renauld et al., 2016). This is particularly problematic for fluency tasks, since these tasks do not only tap into linguistic abilities but also into other cognitive domains, including executive functions (Rofes et al., 2021a; Shao et al., 2014).

While spoken language production was shown to be impaired in the majority of the papers included in this paper, reports of written language production difficulties were inconsistent. Some articles mentioned writing problems (Day et al., 1987; Gil Moreno et al., 2013), while others reported preservation of writing skills (Kujala et al., 1996).

Language comprehension problems were not mentioned as often as language production problems. However, when comprehension was assessed, people with MS frequently showed impairments, such as difficulties with discrimination of spoken language in background noise (Iva et al., 2020, 2021; Valadbeigi et al., 2014), or non-specified impairment of comprehension (Friend et al., 1999; Trinka et al., 2001). Again, some studies reported no oral comprehension difficulties (Rao et al., 1991). Written language comprehension issues were partly detected. In some studies forms of alexia were reported (Gil Moreno et al., 2013; Jónsdóttir et al., 1998) whereas other studies found no difficulties (Kujala et al., 1996). Further on language comprehension, some studies indicated difficulties at the sentence level during the Token Test (Filippi et al., 1993; Friend et al., 1999) and in sentence completion (Fyndanis et al., 2020; Matotek et al., 2001). Finally, two studies mentioned difficulties with pragmatics, namely, worse comprehension of humour and figurative items (Ehrlé et al., 2020, 2021; Lehtlean & Murdoch, 1997).

Overall, the level of detail reported in most studies was not sufficient to describe language impairments in a more exhaustive framework or to report on the specific linguistic nature of the disorder. In agreement with the systematic review of Renauld et al. (2016), we will argue that it is unclear whether the difficulties we reported are due to issues with language processing or if they also encapsulate issues with other cognitive domains (e.g., executive functions). Despite that, there are indications that people with MS may have difficulties with lexical access (Brandstadter et al., 2020; Joly et al., 2014, 2019). Therefore, the study of language abilities in people with MS seems relevant, also because some of these difficulties are reported by the patients themselves (Brandstadter et al., 2020; El-Wahshet al., 2021a, 2021b; Johansson et al. 2021).

4.2. Other ANDs

The following ANDs are not as common as MS. In the studies we reviewed, the term "aphasia" was commonly mentioned, indicating that people with other ANDs can have language impairments. In what follows, we provide a summary of general language difficulties (if possible, by mentioning the specific linguistic tasks involved) that people with other ANDs can have. In a similar way to the case of people with MS, these difficulties need to be further scrutinized to assess whether they are unique to language processing or if they occupy other cognitive domains.

Autoimmune encephalitis is an umbrella term for inflammation of the brain caused by an autoimmune reaction to different body-self cells (Gurrera, 2019). We reported five types of autoimmune encephalitis, some of which show anatomical and functional (e.g., EEG) differences predominantly in the left hemisphere (e.g., Barry et al., 2011; Biancheri et al., 2010; Finke et al., 2014; Hacohen et al., 2016). In our search, reports on people with anti-NMDAr encephalitis were more detailed regarding language than the other types of autoimmune encephalitis. People with anti-NMDAr encephalitis had production difficulties, for example, during naming (e.g., Iadisernia et al., 2012) and verbal fluency (Loughan et al., 2016; Wilkinson-Smith et al., 2022). Comprehension skills were not often studied, but if they were, they showed an inconsistent pattern (Deiva et al., 2014, Hacohen et al., 2016). Most of the studies we found did not make use of language tests. In the other types of autoimmune encephalitis (i.e., N-type calcium channel antibody-mediated autoimmune encephalitis, limbic paraneoplastic encephalitis, anti-GABABr encephalitis, anti-voltage-gated potassium channel encephalitis) we also found issues with language production and comprehension (e.g., Ohta et al., 2011), albeit the specific tasks or specific language levels that are most commonly impaired were normally not mentioned (e.g., Finkel & Koh, 2013; Ibrahim et al., 2017; Kornitzer et al., 2019).

Another type of AND is acute disseminated encephalomyelitis (ADEM). In our search, ADEM was reported to affect white matter tracts and to present with lesions in the left hemisphere, slightly more often in frontal areas (e.g., Aktas et al., 2020; Brinar et al., 2004; Niederschweiberer et al., 2020), the basal ganglia, and cerebellum (e.g., Shintani et al., 2001). Word-finding problems were mentioned in some studies (e.g., Brito et al., 2007; Degirmenci et al., 2013; Koshihara et al., 2014), but other studies found word-finding to be preserved (Adamec et al., 2013). Similarly to autoimmune encephalitis, when comprehension was examined, the reports were contradictory (Parrish et al., 2010 vs Takata et al., 1999). Most of the studies did not use standardized language tests to examine the language impairments seen.

Less commonly reported ANDs are: Steroid responsive encephalopathy associated with autoimmune thyroiditis (SREAT), Anti-MOG antibody-associated encephalitis, and Neuromyelitis optica (NMO). Reports of these diseases commonly indicate "aphasia" but specific tasks or more details on the type of language impairment are typically not mentioned. People with SREAT present with many different clinical symptoms, including cognitive and psychiatric impairments (Laurent et al., 2016). People with SREAT show variable results regarding brain damage, with some studies indicating no brain damage (e.g., Ryan et al., 2012; Yong et al., 2014) and others specific damage to the hippocampus or the temporal lobes (Sabbah-Talasazan & Piryatinski, 2018; Wang et al., 2013). Again, word-finding difficulties were reported (e.g., de Holanda et al., 2011) and these included phonemic paraphasias (Galluzzi et al., 2002) which may indicate a post-semantic deficit. Anti-MOG antibody-associated encephalitis is a demyelinating disease affecting different locations of the left hemisphere (Budhram et al., 2019; Katsuse et al., 2019; Ogawa et al., 2017; Patterson et al., 2019), or both the left

and right hemisphere (Sa et al., 2019). Language reports for anti-MOG antibody-associated encephalitis indicate "aphasia" as one of the symptoms of the disease (Budhram et al., 2019; Patterson et al., 2019). However, these reports do not provide further specification. Finally, in people with NMO, language impairments coexist with lesions in different parts of the brain, including the superior/middle frontal gyrus, thalamic region, and left temporal lobe (Lotze et al., 2008). Reports show difficulties in language production, particularly with semantic fluency (Vanotti et al., 2013; Zhang et al., 2015).

4.3. General discussion: language impairments in people with ANDs

The review indicates that language impairments can be found in people with ANDs and that, therefore, language impairments are relevant to consider upon examination of people with these diseases. Given the relative lack of scope on the study of language impairments in these populations, we would like the raise the following points in the current literature. These points are not ranked by importance and do not represent demands on how the field can be improved. Rather, the points represent recurrent issues in the study of language in ANDs. These points can provide motivation for future work in people with ANDs and also extend to other brain etiologies.

(i) The language tests used to assess people with ANDs and differed among the studies. When language tests were reported, we found that the types of tests used were quite diverse. The language tests used varied, for example, from test batteries examining aphasia after a stroke (e.g., Boston Diagnostic Aphasia examination in Constantinides et al., 2018) to specific language tasks (e.g. Boston Naming Test in Galluzzi et al., 2002). Furthermore, in many papers we could not find the version of the language task administered, which may be problematic in case of potential replication studies or studies comparing language assessments between different populations. Fluency tasks were commonly administered in people with ANDs. However, such tasks are also common in assessments of healthy individuals (Gaspers et al., 2012; Troyer et al., 1997) as well as people different aetiologies, including cardiovascular diseases (Levine et al., 2015), neurodegeneration (Vonk et al., 2020), brain infections (Rofes et al., 2022), brain tumours (Rofes et al., 2017), etc. Difficulties with fluency tasks can therefore not only be attributed to people with ANDs. However, this does not make the inclusion of such tasks uninteresting in people with ANDs. In fact, because fluency tasks not only require language processes but also executive functions (Rofes et al., 2021a; Shao et al., 2014), it is unclear whether the impairments reported in ANDs are unique to language and/or also embrace executive functions. In fact, in ANDs and especially in people with MS, difficulties with processing speed are commonly reported (Brandstadter et al., 2020).

(ii) Many papers indicated general language disturbances, such as aphasia (e.g., Budhram et al., 2019), but did not provide a detailed description of the patient demographic characteristics, what exact language difficulties were seen and how they were discovered. This is of course reasonable, if the goal of the study was not to characterize the specific nature of the language impairment. However, from a language perspective, this could be seen as being too general and raise a concern over validity. For example, it remains possible that what was reported to be a language problem, could actually be a motor speech or another type of cognitive issue (e.g., memory problems misconstrued as language issues). Related to this, oftentimes papers mentioned word-finding difficulties but it was unclear whether these difficulties were occurring during naming tasks or other tasks that also require word production, such as fluency tasks, or spontaneous speech. At the same time, difficulties with object naming are not always necessarily triggered by word finding difficulties, but could occur due to problems with visual recognition or access to the semantic system (Whitworth et al., 2014). Studying language impairments with a specific framework in mind (e.g., Whitworth et al., 2014) seems necessary, as from the current descriptions, it is unclear whether phonological, lexical, or semantic issues are impaired in people with MS or other ANDs.

(iii) Not all language skills are assessed to the same extent. Our findings show a general preference to report language production disturbances over language comprehension problems and to report spoken language over written language problems. This does not necessarily indicate that language comprehension or written difficulties are not present in people with ANDs but rather reflects a general tendency in language assessments where oral language production is favored over other language modalities. This same pattern has also been shown in assessments of people with other neurological disorders, such as stroke, brain tumors, or brain infections (Hula et al., 2010; Rofes et al., 2017, 2021b; Sevcik, 2006). Furthermore, studies often did not mention explicitly which language modality was examined and to which modality the language impairments belonged. Therefore, categorizing the language impairments mentioned in the papers was complicated (see Table 3).

(iv) Assessment times are not always mentioned, and if mentioned, these considerably vary across studies. Some studies report acute language impairments at disease onset (Degirmenci et al., 2013) and some studies as a symptom that develops over several days or weeks (Niederschweiberer et al., 2020; Ohta et al., 2011). This inconsistency in timing complicates comparing studies to each other. In some studies, it was hard to distinguish between acute and non-acute impairments because language impairments were often related to the admission of the patient in the hospital instead of to the onset of symptoms. Therefore, the exact timing of the language impairment in relation to the onset of the AND could be unclear. Furthermore, acute language impairments can be caused by other mechanisms than non-acute language impairments: acute language impairments can, for example, be a side effect of fever or delirium caused by the AND instead of being a symptom of the AND itself (Green et al., 2018). Due to the inconsistency in timing, the findings of the studies were hardly comparable to one another. Incomplete information on chronicity is one of the limitations of our current scoping review. Future work in the form of systematic reviews for individual ANDs may facilitate such comparisons.

(v) A few studies specifically investigated self-reported language/communication difficulties in people with MS. El-Wahsh et al. (2021b), for example, asked 260 people with MS to report their communication difficulties. They found 76% of the participants

to suffer from communication changes, which were found to affect psychological wellbeing and relationships. Johansson et al. (2021) indicated that one third of their MS patient pool reported speech/communication problems. Because of these problems, one in three people experienced issues in professional and social life. Finally, Brandstadter et al. (2020) reported that the only subjective cognitive complaint that people with MS reported more often than healthy controls was word-finding difficulty. These subjective reports may be indicative of mild language and communication impairments in people with MS. It is possible that these impairments may affect processes that are not commonly assessed or that may only be visible when reaction times or specific item comparisons/tasks are administered (e.g., Brandstadter et al., 2020 for a rapid naming task). Therefore, these results seem to grant further examination of language impairments in people with MS (and other ANDs).

(vi) Neurological damage was regularly reported in the literature, but no consistency was found regarding the brain examination techniques used and the time in which they were administered. Some studies, for example, made use only of MRI (e.g., Ashtari et al., 2020), whereas others did not take MRI into account (e.g., Hammoud et al., 2009). Next to that, the exact timing of the neurological examination differed among the studies and was not always precisely reported in relation to the onset of language impairments or disease progression. As a result of these inconsistencies in brain examination techniques and timing, sometimes contradictory results regarding neurological damage can be seen in people with ANDs. Indeed, regional predominance of damage and neurological manifestations of each AND are diverse, and the clinical picture can vary from one patient to another, even in a given disease. Therefore, based on the current literature reviewed, it is very difficult to relate the language impairments found to specific lesion characteristics.

In future research, we envisage studies in which language impairments in people with ANDs are examined in more detail. Studying language in more detail, possibly under a consistent framework (e.g., Whitworth et al., 2014), will provide a detailed picture of language impairments in people with ANDs in general and in specific types of ANDs. Also, such studies will help to relate this information to the type of neurological damage found in these individuals and to establish stronger links between language impairments in this population and people with other types of brain damage (e.g., stroke, dementias, brain infections). In addition, a review on speech/voice impairments could also be relevant as we found many studies that mentioned issues such as dysarthria, absence/inability of spontaneous speech or mutism, slurred speech, prosodic problems, foreign accent syndrome, dysphonia, and paucity of speech. Note that adding this latter information was outside the scope of this review as the goal of this paper was to provide an overview of the language impairments seen in ANDs. Next to reviewing speech impairments in future research, systematic reviews and original research on language impairments seen in specific ANDs (e.g., aphasia in ADEM) are warranted. In this way, we could come up with statistically relevant information about the language pathologies seen in specific ANDs, which was beyond the scope of the current scoping review.

Following this review, future studies may pay attention to the following two points. First, administering language protocols that look at the underlying deficit. For example, it seems relevant to understand for single words, if the problem is segmental, lexical or semantic; for sentences, whether it affects morphology or argument structure; and for longer pieces of language, such as spontaneous speech, whether there are issues with pragmatics. Also, the version of the language task as well as the specific timing of the examination may be mentioned. Second, to provide a more specific overview of neurological damage in each type of AND, and to connect language impairments to neurological damage in each type of AND, brain and language examination techniques may be administered at specific moments during the disease, such as symptom onset, six months after symptom onset, one year, etc. We would suggest to make use of a test battery that is able to identify mild language difficulties (e.g., Dutch Diagnostic Instrument for Mild Aphasia, Satoer et al., 2022). This test battery should have different versions so that language impairments can be evaluated over disease progression. With regard to timing, we would suggest that the initial evaluation, including both language and cognitive assessments, ideally would be performed at the acute phase of the AND. Evaluation should then be repeated in the non-acute phase to track progression and to detect residual deficits. We suggest language and cognitive assessment (e.g., assessments of cognitive status) to be performed at disease onset. Re-evaluation should take place every few years or when a clinical decline is being detected, for example, in a relapse. Brain examination should ideally take place at the same moments as the language and cognitive assessments.

5. Conclusions

This paper reviewed 171 articles spanning over more than 30 years. In studies of 10 commonly reported ANDs, a tendency towards reporting no consistent information of patient characteristics (e.g., language background), neurological damage (e.g., techniques used, time of administration), and language assessment practices (e.g., standardized tests, functions, time of assessment) was found. Major takeaways of this review are that people with ANDs can have language impairments in production and comprehension. Also, that these impairments can be elucidated with specific language tasks (e.g., naming, fluency), perhaps pointing to specific lexico-semantic, morpho-syntactic or pragmatic difficulties. Further emphasis on reporting the language tasks used is relevant to provide a clearer picture of the common/underlying language impairments in this population. Detailed studies of language processing, along with the administration of comprehensive language batteries and brain examination protocols at specific time points in the progression of each disease may be of great help to achieve such purposes.

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Janine Rook: Conceptualization, Methodology, Formal analysis, Software, Data curation, Writing – original draft, Writing – review & editing. **Sara Llufriu:** Conceptualization, Writing – review & editing. **Dörte de Kok:** Writing – review & editing. **Adrià Rofes:** Conceptualization, Validation, Supervision, Data curation, Writing – review & editing.

Declaration of Competing Interest

The authors declare no conflict of interest.

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Supplementary materials

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