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REGULAR ARTICLE

Impaired morphological processing: insights from multiple sclerosis

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ABSTRACT

Multiple Sclerosis (MS) is a neurological disease characterised by damage affecting large bundles of white matter fibres. Morphological segmentation of complex words (e.g. *walked*) into stems (*walk*) and suffixes (*~ed*) is thought to depend on intact white matter. We tested the hypothesis that Arabic speaking patients with MS may lose the ability to segment morphologically complex words in a primed lexical decision task using word pairs that shared either a root and a semantic relationship (+R + S, e.g. “AnzAl”–“nuzwl” *lowering-landing*), a root without semantics (+R–S, e.g. “rtAbp”–“trtyb” *monotony-tidying up*),a semantic relationship (–R + S, e.g. “xyr”–“nEmp” *good-grace*), or a phonological relationship (–R + Phon, e.g. “mEdn”–“mEAnd” *mineral-stubborn*). While healthy controls showed priming by root regardless of semantics and inhibition by phonology, the patients showed facilitation by semantics (+R + S and –R + S), and inhibition by phonology (–R + Phon). These findings are used to adjudicate three contending models of lexical processing.

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Morphological processing; white matter damage; auditory lexical decision; priming

Introduction

Multiple sclerosis (MS), a common neurodegenerative chronic disease of the central nervous system, causes various physical and intellectual changes (McFarlin & McFarland, 1982; Poser et al., 1983). From the neuropathological point of view, MS is characterised by inflammations varying in severity and affecting white matter fibre tracts in multiple regions of the brain (Correale et al., 2017; Dobson & Giovannoni, 2019; Pugnetti et al., 1993). Research into the neuropsychological deficits caused by MS faces Janus-like in two distinct directions. The first, more clinical direction, is mainly used in hospitals to aid the diagnosis and follow-up of patients with MS. Historically, the typical practice in this research tradition was the use of global measures of sensory (Kurtzke, 2015; Rae-Grant et al., 1999), motor (Finlayson & van Denend, 2003; Johansson et al., 2007), cognitive (Nortvedt et al., 1999; Rao et al., 1991), or linguistic functions (Arrondo et al., 2010) to inform intervention planning by quantifying the severity of impairment. Recent advances in neuroimaging techniques have significantly helped clinicians, allowing them to detect MS disease activities even when the patient did not show any abnormality on standard test batteries (Wattjes et al., 2015).

The second direction of MS research is theoretical and has specifically sought to ground our understanding of this condition in a general theory of cognitive processing and representation (Alali et al., 2018; Beatty & Monson, 1990; Friend et al., 1999; Gerald et al., 1987; Lethlean & Murdoch, 1994; Sonkaya & Bayazit, 2018). For example, Lethlean and Murdoch (1994) reported a naming task in which patients with MS produced naming errors that were semantically related to the target word (e.g. *cow* named as *horse*). The authors interpreted this pattern of behaviour as evidence of a lexical semantic access deficit in these patients and contended that naming disturbances in MS may result from disruption of the perceptual and semantic systems that depend on subcortical white matter structures. Beatty and Monson (1990) took issue with this characterisation of the lexical semantic deficit in patients with MS contending that such a deficit is better understood as a semantic retrieval failure than a breakdown in the structure of lexical semantic memory. Their claim was based on results from an untimed priming task in which patients with MS exhibited normal overall levels of semantic priming compared with matched normal participants, suggesting that impairments in naming tasks, and

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verbal fluency tests are examples of general difficulty in retrieving established verbal knowledge. In other words, since patients with MS process information slowly (Beatty et al., 1989; Lebkuecher et al., 2021; Litvan et al., 1988; Rao et al., 1991), they will be at a disadvantage in tasks that require a rapid response. Similarly, Friend et al. (1999) showed that both chronic-progressive and relapsing-remitting patients with MS performed worse than controls on naming, aural comprehension, letter fluency, category fluency, as well as other language-based cognitive measures. Other studies have shown that MS can be conducive to a wide variety of aphasias ranging from non-fluent aphasia (Demirkiran et al., 2006; Olmos-Lau et al., 1977), to conduction (Arnett et al. 1996), to global aphasia (Friedman et al., 1983), along with naming, fluency, and reading deficits (Blecher et al., 2019; Jónsdóttir et al., 1998; Zarei et al., 2003).

The existing research provides a broad picture of the general linguistic abilities that can be affected by MS, suggesting that impairments in this condition may affect different aspects of performance, such as verbal fluency, lexical access, and language comprehension. However, apart from investigations of semantic knowledge using naming (Barwood & Murdoch, 2013; Drake et al., 2002) and untimed priming (Beatty et al., 1989; Beatty & Monson, 1990), little is known about the potential deficits of specific linguistic domains such as syntax, phonology and morphology in patients with MS.

This is quite a surprising situation since neurocognitive research over the last 2 decades has established that the neural language system involves a left-lateralised, fronto-parieto-temporal network of grey matter regions that interact seamlessly via the white matter fibre tracts that demyelination in MS affects (Catani et al., 2005; Friederici, 2009; Hickok & Poeppel, 2004; Tyler & Marslen-Wilson, 2008). In this study, we explored the effects of diffuse demyelination and inflammation along axons in MS on morphology, the linguistic domain related to our knowledge of the internal structure of words. This ability is evidenced to depend on long-range white matter tracts (Catani et al., 2005; Hickok & Poeppel, 2004; López-Barroso & de Diego-Balaguer, 2017; Martino et al., 2010). If the integrity of the white matter is a prerequisite for the morphological decomposition of words into stems and affixes for language comprehension, diffuse white matter damage in MS, should lead to measurable disruptions in the processing of this linguistic domain. Before developing this general claim into a more specific prediction, and pitting it against other accounts, we briefly outline what morphological processing is and how it is underpinned by the neuro-cognitive system.

MS and morphological processing

There is ample evidence suggesting that operations of morphological disassembly such as parsing the past tense suffix ∼*ed* from forms like *walked* and *talked* or segmenting the plural suffix ∼s from complex words such as *cats* and *tables*, involves a well-defined fronto-temporal left-lateralized network that depends on intact white matter (Bozic et al., 2015; Meunier & Segui, 1999; Sahin et al., 2006; Tyler et al., 2004). Thus, unlike simple words such as *claim* and *trade*, which were found to activate both right and left fronto-temporal brain regions, including bilateral BA45 and -47, morphologically complex words (e.g. *walked, blamed*) engaged the STG and MTG bilaterally as well as the IFG specifically, BA45, (Bozic et al., 2010). When the white matter fibre tract connecting the posterior to anterior regions of the language network is damaged to different degrees, performance on various language comprehension and production tests is significantly affected (Rolheiser et al., 2011; Tyler et al., 2005). More specifically, Tyler et al. (2005) compared priming among morphologically (e.g. *walked-walk*) and phonologically related words (e.g. *tinsel-tin*) and found that facilitation for the former correlated significantly with signal intensity in brain regions that closely correspond to the classical Broca–Wernicke–Lichtheim model of language functions, where the white matter tract of the arcuate fasciculus connects the superior temporal and inferior frontal regions in the neural language system and to the dorsal route identified in more recent neural accounts of the language system (Friederici & Alter, 2004; Hickok & Poeppel, 2000; Ueno et al., 2011). In a more recent study, Rolheiser et al. (2011) used diffusion tensor imaging to directly examine the impact of white matter fibre tract damage on language performance in a group of participants with white matter damage. Whole-brain voxel-by-voxel correlations between white matter damage and scores in different linguistic tests revealed that the dorsal and ventral language pathways were differentially involved in processing the various linguistic domains, with morphology and syntax in particular engaging the dorsal and ventral processing pathways, while other linguistic domains (i.e. semantics and phonology) selectively engaged either one or the other pathway. One of the various theoretical views that have been developed on the basis of neuroimaging studies of patients and healthy controls is the bihemispheric language model, which makes the specific claim that morphological processing engages a temporo-parieto-frontal network connected by long range white matter fibres (Bozic et al., 2010; Tyler et al., 2005).

As relapsing remitting patients with MS typically show a higher susceptibility to pathological processes of long-range white matter fibre bundles than short range white matter connections (Au Duong et al., 2005; Cader et al., 2006), the bihemispheric view suggests that such patients should show evidence of little or no morphological priming if this priming is contingent on intact connections between distant language areas.

A second theoretical view based on more direct assessments of the behaviour of patients with MS, the conscious neuronal workspace (CNW) model leads to different expectations. This view emphasises the distinction between subconscious automatic processes supported by short to medium-range white matter connections between spatially contiguous areas, and integrative conscious processes thought to depend on long-distance connections among distant regions (Dehaene et al., 1998; Dehaene et al., 2003; Reuter et al., 2007). It further contends that processes relying on the integrity of short-range white matter fibres such as visual recognition, lexical processing and semantic processing can be fully preserved in relapsing-remitting patients with MS (Pijpers-Kooiman et al., 1995; Reuter et al., 2007; Reuter et al., 2009). Accordingly, if morphological parsing as gauged in an overt auditory-auditory priming timed task occurs at an automatic subconscious level, which we believe it does, the CNW predicts patients with MS will show preserved priming patterns among words sharing a morphological unit such as the English or Arabic roots.

A third view of the potential linguistic deficits in MS comes from the processing speed deficit account, according to which the primary cognitive deficit associated with such patients is a generalised slowing in information processing speed (Archibald & Fisk, 2000; Bergendal et al., 2007; Denney & Lynch, 2009). Many authors have consistently reported substantial differences in information processing speed between patients with MS and controls, in which patients with MS are systematically slower in various timed-tasks such as simple lexical decision, n-back tasks and rapid serial processing tasks (Bodling et al., 2010; de Sonneville et al., 2002; Hughes et al., 2011). Therefore, priming effects with a well-defined time window may or may not be found in patients with MS depending on their time course. In the remainder of this study, we first spell out this set of predictions from the perspective of Modern Standard Arabic (MSA), a Semitic language characterised by a rich morphological system (Boudelaa, 2014; Boudelaa & Marslen-Wilson, 2015), and then we describe an auditory-auditory priming experiment designed to adjudicate between the contending predictions.

Arabic morphological system

There are several reasons for using MSA as a testing ground for the possible effects of MS on morphological processing. First, in MSA morphological assembly and disassembly operations are obligatory, not only for inflectional morphemes, as is the case for English, but also for derivational morphemes (Boudelaa, 2014; Boudelaa & Marslen-Wilson, 2015). Second, MSA morphological effects are not only fully divorced from meaning-based and form-based effects, but also have differential time courses. Thus, for instance, MSA words sharing the three consonants of the root (e.g. {ktb} *writing*) prime each other significantly in overt and covert priming tasks regardless of whether they share a transparent semantic relationship (e.g. "mktb"–"kAtb"[1] *office-writer*) or not (e.g. "ktybh"–"kAtb" *squadron-writer*), (Boudelaa & Marslen-Wilson, 2004, 2005, 2015). At the same time prime and target pairs sharing only a semantic relationship (e.g. "mAl~f"–"kAtb" *author-writer*) or an orthographic/phonological relationship (e.g. "k*Ab"–"kAtb" *liar-writer*) show effects at later processing stages (Boudelaa et al., 2009; Boudelaa & Marslen-Wilson, 2005). Third, it is important to test neuropsychological claims about different linguistic domains in different patient populations in languages typologically unrelated to English (and other Indo-European languages) so that the resultant neuro-cognitive account of language that we build can be more viable in terms of specificity and generality.

Against this linguistic background, we can now elaborate on the predictions that follow from the three theoretical views described above. For the Bihemispheric view, language processing engages a left-lateralised frontotemporal subsystem, specialised for grammatical computations, and a bilateral subsystem, which underpins whole-word, stem-based lexical access processing of lexicalised and unpredictable complexity, present in derived words (Bozic et al., 2015). The left-lateralised frontotemporal subsystem in charge of parsing morphologically complex forms relies on the integrity of the dorsal and ventral white matter fibre bundles connecting the temporal and frontal regions. Since Arabic words have been repeatedly demonstrated to automatically engage operations of morphological disassembly, the bihemispheric view predicts that priming among Arabic words sharing a root and an opaque sematic relationship should be disrupted in patients with MS. On this view, disruption of the parsing route due to white matter damage should further lead Arabic patients with MS to rely on full-form processing and show evidence of priming among words sharing a root and a transparent semantic relationship as well as words sharing a transparent semantic relationship without sharing a root. For the phonologically related items, the bihemispheric account predicts that these should show evidence of competition among full forms indexed as inhibition or simply a lack of facilitation.

As for the CNW theory, a central claim is that in the early stages of MS, cognitive dysfunction is mainly focused on integrative processes requiring consciousness such as working memory, attention and executive function, while early complex processing such as object recognition or semantic processing is preserved (Reuter et al., 2007). Reuter et al., reported that patients with MS showed preserved priming behaviours in a masked task in which their ability to perform a number comparison on the prime was assessed. Since auditory-auditory priming taps into early effects that require neither conscious processing nor attentional resources, the CNW predicts that Arabic patients with early MS should show evidence of priming among words sharing a root and transparent semantics, as well as words sharing a root and an opaque semantic relationship. For word pairs that share only a semantic or a phonological relationship, the CNW model predicts an effect that may be facilitatory or inhibitory depending on the patient's language since the co-activation of such words does not depend on intact long-distance white matter fibres. In the present context, this model predicts facilitation among semantically related words and inhibition (or lack of facilitation) among phonologically related words because it is the standard result with normal participants in the language.

Finally, according to the processing speed deficit model, the hallmark of early MS is a general slowness processing speed. This suggests that early effects may be weaker or even non-existent in patients with MS, while long lasting effects should be observed. Early research on the effects of the root in Arabic and Hebrew strongly suggests that this unit has a durable effect. Specifically, Boudelaa and Marslen-Wilson (2005) showed that root priming effects are equally robust across four stimulus onset asynchronies of 32, 48, 64 and 80 ms. In contrast, semantic and phonological effects were much shorter lived, showing up only in the stimulus onset asynchronies of 80 ms. Similarly, Bentin and Feldman (1990) showed that while Hebrew words sharing a root and an opaque semantic relationship produced significant facilitation with as many as 15 intervening items between the prime and the target, words related by semantics alone showed facilitation only when there were no intervening items between the prime and target. If so, then the processing speed deficit view leads us to expect strong priming effects among words sharing a root regardless of semantic transparency, and no priming effects among words related by semantics or phonology.

Auditory-auditory priming experiment

In this study, we used auditory-auditory immediate repetition priming, a task that has previously been used to study morphological processing in different languages (Boudelaa & Marslen-Wilson, 2001; Emmorey, 1989; Marslen-Wilson & Xiaolin, 1999). In this task the participant hears a spoken prime (e.g. government) followed by an auditory probe (e.g. GOVERN) related in some way to the prime in some way. An interval of 50 ms is introduced between the prime and the target so that the two events are not conflated into a single perceptual event. The participant makes a lexical-decision response to the target, and response latency relative to a baseline condition is used to measure any priming effect. The baseline is the participants' response to the same target preceded by an unrelated spoken prime (e.g. careful). The participants are unaware of the relationships underlying the primes and targets because the proportion of relatedness is usually dissipated using of a large proportion of unrelated prime-target pairs. We chose to use this timed task for several reasons. First, auditory-auditory priming has typically revealed robust priming effects much stronger than those observed with other variants of this technique such as masked or cross-modal priming. For example, Boudelaa and Marslen-Wilson (2004) report a morphological facilitation effect of 22 ms in masked priming, but a much larger effect of 34 ms in auditory-auditory priming. We chose not to use cross-modal priming to avoid potential reading problems that patients with MS may have during reading. Second, auditory-auditory priming has been shown to be sensitive to different linguistic domains of knowledge such as morphology (Bacovcin et al., 2017; Boudelaa & Marslen-Wilson, 2004; Marslen-Wilson & Tyler, 1997; Post et al., 2008; Tyler et al., 2002), phonology (Dufour & Peereman, 2003; Radeau et al., 1989; Slowiaczek et al., 1987), and semantics (Daltrozzo et al., 2011; Guediche et al., 2020; Holcomb & Neville, 1991). Therefore, this task will allow us to capture priming effects in any of the preserved domains of knowledge in patients with MS.

Although the auditory-auditory priming paradigm undoubtedly provides an interesting methodological tool for studying various aspects of the language recognition system, some researchers have argued that priming in this paradigm originates at least in part from response biases (Norris et al., 2002). However, there is ample evidence that a substantial component of the priming process observed in this task is indeed automatic. For example, results from studies examining prime–target pairs sharing a phonological overlap have indicated that the size of the effect decreases when the inter-stimulus interval (ISI) increases (McQueen & Sereno, 2005; Radeau et al., 1995). If priming effects were purely based on bias, one would expect them to increase with longer ISIs. However, this was not the case, suggesting again that bias contamination were not the only factor at play in this task. Another way of establishing that priming in auditory-auditory priming is mostly automatic is the use of varying proportions of related prime–target pairs as did Slowiaczek et al. (2000), who found greater facilitation in the high (75%) than in the low (26%) relatedness proportion condition. Because a high proportion of related trials encourages the development of strategies, the effect observed in such a condition could be due in part to controlled processes. Slowiaczek et al. (2000) performed a time-ordered analysis of control trials and found that response times (RTs) became slower throughout the experiment in both the high and the low proportion-related trial conditions. The slowing down on control trials was, however, not reliable, thus indicating that strategies did not develop over the course of the experiment and that they did not play any substantial role in final overlap facilitation. In sum, it seems that a significant component of the auditory priming effect is nonstrategic, but due to automatic processing that operates before lexical access (Dufour, 2008; Norris et al., 2002, Slowiaczek et al., 2000). This makes the auditory priming paradigm particularly useful for the study of morphological facilitation.

Table 1. Patients' demographic information, lesion extent and EDSS scores.

Patient N	Gender	Age	Lesion vol. (mL)	N lesions	FS-score	Mobility-score
Patient 1	Male	51	68.39	20	2	4.5
Patient 4	Female	24	28.50	16	2	3.0
Patient 5	Male	53	22.80	40	2	4.0
Patient 7	Female	64	31.65	46	2	4.0
Patient 15	Male	55	46.74	28	2	4.5
Patient 16	Female	44	29.73	21	1	3.0
Patient 17	Male	66	39.90	24	1	3.5
Patient 18	Female	66	26.44	26	1	3.5

NB: Lesion vol (mL) = Lesion Volumes in millimetres, FS-score = functional systems score. The patients are numbered according to their order in a larger study, which included more patients. EDSS, expanded disability status scale.

Method

Participants

A group of eight patients (four females) with relapsing-remitting MS participated in the experiment. They were aged 41.87 years on average (standard deviation [SD] = 9.78), and the mean disease duration was 7.62 years (SD = 8.91). Their education in Arabic spanned an average period of 10.66 years (SD = 3.61). Participants with a history of alcohol or other drug abuse, optic neuritis, deficient visual acuity, and scotoma in the visual field were excluded. All patients fulfilled a multiple sclerosis diagnosis based on a locally adapted version of the Expanded Disability Status Scale (EDSS) (Kurtzke, 1983). For the present purposes two aspect of the EDSS score are particularly relevant. The first relates to the "ambulatory capacities" of the patient and consists of a score ranging from 0 (normal neurologic examination) to 10 (death by MS). The second pertains to the different "functional systems" (FS) of the patient and yields a score ranging from 0 (normal) to 5 (demented). On both aspects of the EDSS, our patients scored within the normal range with a mean of 3.75 (sd. 0.6) for ambulatory capacities, and a mean of 1.63 (sd. 0.52) for FS. Furthermore, a series of five structural magnetic resonance imaging (MRI) sequences were acquired for each patient, including 3-PL Loc, T2 FSE, T1 SPGR, and T1 FSPGR 3D. These were used to establish the existence and extent of white matter lesions. In Table 1, we provide the relevant information about the patients including their demographics, individual scores in the EDSS battery and the number of lesions they have and their lesion volumes in millimetres.[2] Finally, two patients were on solu-medrol (2 g/ 2 months) and one was on rubifen, but none had experienced a relapse or treatment with steroids in the 3 months preceding the experiment. None of the patients had any other co-existing neurological disorders.

A control group of 35 healthy participants (16 females) also participated in the experiment. They were age and educational level-matched to the patients. All participants (patients and healthy controls) were right-handed and none wore a hearing-aid. All participants provided informed consent to participate in this study, which was approved by the Peterborough and Fenland Ethical Committee, United Kingdom, and the local Ethics Committee of the University Hospital of Fez, Morocco.

Stimuli and design

The target list consisted of 160 words. They ranged between 4 and 8 letters in length (mean 6.12 letters)

Table 2. Sample stimuli in Arabic script with a transliteration and an English gloss.

Condition	Related Prime	Baseline Prime	Target
1. +R + S	مخلص "mxlS" loyal	عجيب "Ejyb" wonderful	إخلاص "AxlAS" loyalty
2. +R–S	مسكين "mskyn" poor	إجازة "AjAzap" vacation	سكون "skwn" haunted
3. –R + S	عروس "Erws" bride	فندق "fndq" hotel	زواج "zwAj" marriage
4. –R + Phon	مبادرة "mbAdrp" initiative	انفصال "AnfSAl" separation	مباراة "mbArAp" match

with an average acoustic duration of 744 ms (SD = 25.80). The overall average frequency was 15.36 per million (range: .01–234) in ARALEX (Boudelaa & Marslen-Wilson, 2010). These words were divided into 4 sets of 40 words each to construct the four experimental conditions as displayed in Table 2.

In the first condition, labelled + R + S, the target was paired with a prime word that shared the root and a transparent semantic relationship (e.g. "t$ryE"–"$ryEp", *legislation-law*). The second condition, +R–S, consisted of prime and target pairs sharing a root but an opaque semantic relationship (e.g. "tsbyH"–"sbAHp", *praising-swimming*). In the third condition, labelled –R + S, the prime and target shared a transparent semantic relationship without sharing a root (e.g. "nktp"–"fkAhp", *joke-humour*). The final condition, labelled –R + Phon, consisted of prime target pairs that shared a phonological relationship, without sharing a root (e.g. "SyAH"–"-SAHbp", *shouting-companion*). Each target was also paired with an unrelated baseline condition. The characteristics of the prime words are displayed in Table 2. The full list of the experimental materials along with the raw reaction times, error rates, and R code used to analyse the two data sets are accessible as R-Data frames and Jupyter notebooks here: https://osf.io/bj7mn/?view_only=bf374804c39d4b6e9eb978d1b7a8352c.

The first two variables in Table 3 are acoustic duration measured in ms from word onset to word offset, and frequency of occurrence, which refers to the surface frequency of the word defined in Aralex (Boudelaa & Marslen-Wilson, 2010). The third characteristic in Table 2, (Sem_Rel), is the semantic relatedness between the prime and target, as rated by 15 independent judges on a scale of 1–9 (1 = *semantically unrelated* and 9 = *semantically highly related*). This is followed by a more objective measure of semantic distance (Cos_Dist) between the prime and target in different conditions based on the Arabic word semantic vectors developed using the WORD2VEC approach, and accessible at https://fasttext.cc/docs/en/crawl-vectors.html (Mikolov et al., 2013). The final variable in Table 2, (Shared_Ph), refers to the average number of phonemes shared between the prime and the target. All variables were included in the statistical analyses to partial out any modulatory effects they may have across conditions.

For the purposes of lexical decision, we constructed a second set of 160 nonwords by changing one to two phonemes of existing words (e.g. "ktAj" from "ktAb", *book* or "*mnlfp" from "mnTqp" *area*). Overall these non-words matched the real targets in terms of the number of phonemes and acoustic duration. Half of them were paired with related prime words with which they shared phonological overlap (e.g. "ktA~n" *linen* paired with the nonword "ktA~j") whereas the other half were paired with unrelated words (e.g. "HSAr" *embargo* paired with the nonword "jmwq"). Additionally, 36 practice trials comprising 18 word and 18 non-word responses were constructed in such a way as to be representative of the experimental trials. Two experimental lists were constructed each containing 320 pairs of which 160 were word/word pairs and 160 word/pseudo-word.

Procedure

All the prime and target words were recorded by a native speaker of Arabic and digitised with a sampling rate of 44 kHz, down-sampled to 22 kHz using the Cool-Edit programme, and stored on a portable computer. The items were recorded over different sessions in a random sequence, but with members of prime/probe pairs well separated to avoid their having more similar voice qualities than any other two items chosen randomly from the set of material. Two portable computer monitors were used to test participants in a quiet room. They heard the stimuli at a comfortable level using HD 250 Sennheiser headphones. The sequence of stimulus events within each trial was as follows: the prime word was played and around 50 ms after its offset the target was presented. The time out period was 3 s, and the inter-trial interval was 2 s.

The timing and response collection were controlled by two laptops running the DMDX package (Forster & Forster, 2003). Latencies were measured from the acoustic onset of target words. The mean duration of the target words was 736 ms in the + R + S condition, 785 ms in the + R–S condition, 722 ms in the –R + S,

Table 3. Stimulus items characteristics.

		Prime		Prime and Target		
Condition	Relation	Duration	Frq	Sem-Rel	Cos_Dist	Shared-Ph
+R + S	Related	721 (4.58)	21.26 (1.94)	7.88 (0.05)	0.59551 (0.0067)	3.7 (0.04)
	Baseline	753 (5.06)	34.96 (2.84)	1.08 (0.01)	0.85993 (0.0035)	1.15 (0.03)
+R–S	Related	730 (4.95)	18.12 (2.16)	2.18 (0.05)	0.83263 (0.0054)	3.25 (0.02)
	Baseline	768 (5.12)	30.79 (3.92)	1.43 (0.04)	0.862082 (0.0048)	0.5 (0.03)
–R + S	Related	690 (6.65)	28.80 (3.58)	7.13 (0.05)	0.69692 (0.0106)	0.35 (0.03)
	Baseline	684 (5.47)	63.43 (8.69)	1.25 (0.02)	0.82936 (0.0053)	0.225 (0.02)
–R + Phon	Related	780 (5.71)	19.80 (3.68)	1.38 (0.03)	0.84436 (0.0033)	3.025 (0.04)
	Baseline	779 (5.45)	25.95 (3.58)	1.33 (0.03)	0.85137 (0.0044)	0.175 (0.02)

NB. Frq = surface frequency in ARALEX, Sem-Rel = semantic relatedness, Cos_Dist = cosine distance, Shared-Ph = shared number of phonemes between primes and targets.

and 736 in the –R + Phon conditions. Participants were instructed to make lexical decisions as quickly and accurately as possible by pressing a YES or NO key. The YES response was always made by the dominant hand. The experiment, which lasted approximately 30 and 45 min for the patients, and between 25 and 35 min for the normal controls started with the practice trials followed by the rest of the stimuli. As this is the standard in the literature, the patients were tested on both versions of the materials, with an interval of at least 24 h between each testing session (cf., Reuter et al., 2007; Tyler et al., 2005), while the normal participants took part in only one testing session. During each session, the patients were automatically prompted to take a break after every 16 trials to avoid fatigue. The normal participants were prompted to take a break after every 32 trials. After the break, participants had to press the "space bar" to continue. The order of stimulus presentation was pseudorandomised, and the items from the various conditions were evenly spread across the two versions of the experiment. Finally, for each patient, we acquired a series of structural magnetic resonance images either after the completion of the first or second experiment session.

Results

We begin by describing the results of the control participants to show that the typical morphological priming pattern in Arabic is replicated and we lay the ground for the discussion of the patients' performance and how it deviates from normal processing. For the normal participants, there were 5600 data points (35 participants with 160 data points each) from which response times (RTs) shorter than 200 ms or greater than 2000 ms were discarded (8.01%). For the patients

Table 4. Normal participants' mean response times in ms, standard errors (parentheses), percent accuracy and priming scores.

Condition	Relation	RT	%Error	Priming
+R + S	Related	794 (6.19)	3.57	61*
	Baseline	855 (6.94)	5.71	
+R–S	Related	855 (6.97)	6.14	36*
	Baseline	891 (6.95)	6.00	
–R + S	Related	780 (6.89)	4.43	28*
	Baseline	808 (7.26)	6.86	
–R + Phon	Related	868 (6.36)	6.71	–14
	Baseline	854 (7.31)	9.14	

Table 5. Patients' mean response times in ms, standard errors (parentheses), percent accuracy and priming scores.

Condition	Relation	RT	%Error	Priming
+R + S	Related	831 (10.65)	3.12	39.00*
	Baseline	870 (11.80)	5.00	
+R–S	Related	890 (12.61)	8.12	21.00
	Baseline	911 (13.58)	10.00	
–R + S	Related	811 (10.29)	5.31	36.00*
	Baseline	847 (11.49)	5.31	
–R + Phon	Related	882 (9.73)	8.12	–7.00
	Baseline	875 (13.04)	8.75	

with MS, there were 2560 data points (8 patients with 320 data points each) of which we removed RTs shorter than 200 ms, or greater than 2500 ms (7.81%). The overall mean RT of the normal participants (839.09 ms) was slightly but significantly ($p < 0.000$) faster than that of the patients (864.53 ms). The mean correct RTs, error rates and magnitudes of priming for targets in each experimental condition (+R + S, +R–S, –R + S, and –R + Phon) are displayed in Table 4 for controls and Table 5 for patients.

We used the lme4 package (version 1.1-27.1; Bates et al., 2012) within the R environment for statistical computing to run linear mixed models (LMMs). Condition (four levels: +R + S, +R–S, –R + S and –R + Phon) crossed with Relation (two levels: related, baseline) were the fixed factors for each model. Participants, primes and targets were treated as random variables. All models we ran, contained a full random structure (e.g. Barr et al., 2013) that included random slopes for the main effects and their interactions, as well as acoustic duration, frequency, semantic relatedness, cosine distance and the number of shared phonemes between primes and targets as nuisance variables. For error analyses, we used logistic generalised linear mixed models (GLMMs), starting with a full random structure model. If a model containing the full random structure failed to converge, it was systematically trimmed until it converged, first by removing correlations between random effects, and then, if necessary, by removing their interactions. Thus all findings reported here are from successfully converging models. Log transformation was performed on the RTs to reduce distribution skewing (Baayen et al., 2008).

Control participants: latency and accuracy data

The control participants' results showed significant effects for Condition [F (3, 75.34) = 6.87, $p < 0.000$] and Relation [F (1, 72.72) = 27.07, $p < 0.000$] as well as the interaction between them, [F (3, 65.20) = 9.20, $p < 0.000$]. Priming was significant in the + R + S [t (1319.8) = −6.6589, $p < 0.000$], the + R–S [t (1227.7) = 3.34, $p < 0.000$] and the –R + S [t (1306.8) = 2.83, $p < 0.004$] conditions. Pitting the magnitude of priming in the different conditions against each other reveals statistically reliable differences between + R + S and every other condition (all $p < 0.000$). The amount of priming was also significantly larger in the + R–S condition than in the –R + S ($p < 0.000$) and –R + Phon ($p < 0.000$) conditions. The magnitude of priming was significantly larger in the + R–S condition than the –R + S ($p < 0.000$) and–R + Phon ($p < 0.000$) condition. Finally, the error rates revealed no significant main effects or interactions.

Patients: latency and accuracy data

The results of the patients showed a significant effect for Condition [F (3, 158.85) = 5.04, $p < 0.002$], Relation [F (1, 146.69) = 4.64, $p < 0.032$], and their interaction [F (3,145.18) = 3.13, $p < 0.027$]. To unpack the interaction between Condition and Relation, we took a paired comparisons approach, correcting for multiple comparisons using the Holm p-value adjustment method. We first evaluated the priming effects in each condition separately, and then compared the magnitude of priming across conditions. Priming was significant only in the + R + S [t (599.22) = −2.2062, $p < 0.028$] and the + R–S [t (599.9) = −2.0461, $p < 0.041$] conditions. Furthermore, the magnitude of priming in the + R + S condition was significantly different from that in the + R–S ($p < 0.000$) and –R + Phon conditions ($p < 0.004$). Priming in the –R + S condition was also significantly different from that in the + R–S ($p < 0.000$) and the –R + Phon ($p < 0.000$) conditions. None of the other possible comparisons were significant.

Since the magnitude of priming in the + R–S condition was 21 ms, a numerically sizable amount in this type of study, and since our sample size was eight patients, we sought to determine whether the absence of significance of facilitation in this condition was not due to lack of statistical power. Accordingly, we conducted power analyses using the pwr package in R with power (1−β) set at 0.80 and α = 05, two-tailed. This revealed that our sample size would have to increase to N = 913 patients with MS in order for the 21 ms priming to reach statistical significance at the .05 level. Thus, it is unlikely that the lack of statistical significance of priming in the + R–S condition can be attributed to the limited sample size. Our analysis of the patients' accuracy data using a logit model revealed no significant results either for the main effects, or their interaction.

Patients: lesion volume and magnitude of priming

In order to establish if there is a relationship between the amount of white matter loss and the magnitude of priming overall for each patient (c.f., Rao et al., 1989; Zurita et al., 2018), we used the lesion prediction algorithm (Schmidt, 2017, Chapter 6.1) as implemented in the lesion segmentation toolbox version 3.0.0. (www.statistical-modelling.de/lst.html) for SPM. This algorithm consists of a binary classifier in the form of a logistic regression model trained on the data of 53 patients with MS with severe lesion patterns. We used the parameters of this model fit to segment white matter lesions in our T2 FLAIR images and obtain an estimate for the lesion probability for each voxel (the T2 FLAIR images are available at OSF: https://osf.io/6kce2). The output of the model consists of the estimated volume of the lesion in millimetres as well as the number of lesions, which we displayed in Table 1. In the correlation analysis we report the results with lesion volume rather than number of lesions because the former captures more accurately the extent of the damage in the sense that a patient may have a large volume of damage but a smaller number of lesions and vice versa. Accordingly, we correlated lesion volume with a *priming-proportion* for each patient obtained by dividing the difference between the unrelated and related prime reaction times (RTs) by the unrelated prime RT for each of the four conditions. This calculation minimised the effect of overall RT differences across the patients (cf. Tyler et al., 2005). The results of these analyses reveal negative correlation between priming-proportion averaged across all conditions and lesion volume ($r = -0.7$, $p < .05$) suggesting that the larger the volume of white matter lesion the smaller the priming effect. Correlations in different conditions when analysed individually, showed trends that failed to reach significance: +R + S ($r = -0.6$), +R–S ($r = -0.5$) and –R + Phon ($r = -0.6$), and a non-significant positive correlation in –R + S ($r = 0.5$).

Discussion

The purpose of this study was to explore the implications of early relapsing remitting MS for morphological decomposition processes in Arabic. The specific question we addressed was whether the typical damage to long distance white matter fibres linking temporal and frontal regions that support – among other processes – operations of morphological disassembly would adversely affect the standard root extraction processes that characterise Arabic word recognition processes. We investigated this issue using intra-modal immediate auditory priming, an overt task that has previously revealed robust root effects that were fully divorced from meaning- and form-based effects (Boudelaa & Marslen-Wilson, 2011, 2013). Accordingly, it is reassuring that the results of the normal participants tested here replicate the standard effects found in Arabic in previous research using overt and covert versions of the priming technique (Boudelaa & Marslen-Wilson, 2004, 2011, 2015). In particular, the control participants in the current study showed significant root facilitation effects regardless of whether the prime and target were semantically related (+R + S) or unrelated (+R–S), lending credence to the view that Arabic words undergo obligatory decomposition whereby the root and the word pattern are systematically extracted. The normal participants also showed a significant priming effect among words related only by semantics (–R + S), and a non-significant inhibitory effect for words related only by phonology (–R + Phon).

The pattern of results of patients with MS departs in one important way from the behaviour of standard normal participants. Specifically, the patients with MS showed a priming effect among words related by a root and a transparent semantic relationship (+R + S), but not those related by a root without semantics (+R–S). Where pure semantics (–R + S) and phonology (–R + Phon) are concerned, the patients results reflect those of the normal participants with significant priming among words sharing semantics and a non-significant tendency towards inhibition among phonologically related words. Therefore, what are the implications of these results for the three models discussed earlier?

On the bihemispheric view, the morphological operation of extracting a morpheme like the Arabic root is a morpho-grammatical operation that directly depends on intact white matter connections between fronto-temporal regions. If these white matter connections are damaged, there is no neuronal basis to support morphemic extraction, thus pure morphological effects such as priming among + R–S words in Arabic cannot be observed. This is exactly the pattern of results observed here: control participants showed reliable facilitation among words sharing a root without sharing a transparent semantic relationship (e.g. "blAgp"–"mblg", *eloquence-amount*), while the patients with MS showed no evidence of such priming, suggesting that the process of parsing Arabic words into their component morphemes is significantly affected in this population because of diffuse demyelination of the white matter fibre tracts that relay the temporo-frontal language network (López-Barroso & de Diego-Balaguer, 2017; Rolheiser et al., 2011;). A second outcome, also in keeping with the bihemispheric view, is the significant facilitation among words sharing a transparent semantic relationship without sharing a root (e.g. "Erws"–"zwAj", *bride-marriage*). Priming among such words does not depend on long-range white matter fibre tract connections, but arguably on links among full-form representations established within the same cortical lobe. Finally, phonologically related words (–R + Phon), which do not depend on long range white matter links, typically show a tendency towards inhibition but never any facilitation in auditory-auditory priming tasks in Arabic. This is what we found here with both the control participants and the patients presumably because such words share some random consonants that neither correspond to the same root nor map onto the same semantic representation, leading to some competition among them.

The second view we consider, the CNW, seems to be partly at variance with the present results. This theory explicitly claims that automatic processing, such as that tested here, can be preserved in patients with early MS. Since intra-modal priming is an automatic process, the CNW captures the priming results among + R + S words as well as priming among –R + S words, but falls short of accommodating the lack of priming among + R–S words. On this account, there should be significant priming in the + R–S because priming is not contingent on conscious or attentional resources in intra-modal auditory-auditory priming. In defense of the CNW one might argue that the patients tested here showed a strong trend towards priming in the + R–S condition with a 21 ms facilitation, and that the lack of statistical reliability in this condition stems from the fact that only eight patients were tested. However, this "statistical power argument" can be safely ruled out as we demonstrated above that the 21 ms priming in the + R–S condition would require testing as many as 913patients to reach statistical significance.

Finally, the Processing Speed Deficit asserts that a generalised slowing in information processing speed is the primary cognitive deficit associated with MS (Demaree et al., 1999; Hughes et al., 2011). At a global level this claim is supported here, since the patients with MS showed an overall RT response (864 ms) that was slightly but significantly slower ($p < 0.000$) than the controls' RT (837 ms). In addition, the error rates were numerically higher for the patients (6.72%) than those the controls (6.07%). The decreased speed of information processing in patients with MS predicts that long-lived effects should not be affected while short-lived effects may miss the window of opportunity and fail to show up. In the context of our study, the purely morphological root facilitation effects gauged by our + R–S condition are long-lived and are thus expected to show up. That this is not the case, poses the first problem to the Processing Speed Deficit account. A second problem for this account comes from the behaviour of purely semantic effects, as measured in the –R + S condition. These are typically short-lived in Arabic and were observed only at a stimulus onset asynchrony of 80 ms in Boudelaa and Marslen-Wilson's (2005) study. As semantic priming effects are short lived in Arabic they are not expected in patients with MS because of their generalised slower processing.

A final issue of interest here is the presence of a significant negative relationship between the volume of white matter lesion and the overall magnitude of priming shown by each participant. This result suggests that correlating lesion volume with continuous behavioural data is strikingly able to detect changes in the behaviour of the language processing system even with a relatively small number of participants. More significantly, this result suggests that a meaningful correlation between brain and behaviour may be found even with a limited number of observations, and without having to make a priori assumptions about the exact lesion location.

Beyond this, the outcome of the present study suggests that when the Arabic language processor incurs damage that affects the pathways linking fronto-temporal regions as is the case in patients with early MS, the backup strategy is to resort to full form processing (and storage) subserved by the bilateral subsystems.

Conclusion

A significant result of this research is the absence of priming in the + R–S condition in patients with MS. We have previously argued that Arabic language processing relies on an obligatory morphological decomposition process whereby each word –heard or read – is parsed into its component morphemes, that are its root and word pattern (Boudelaa, 2014; Boudelaa & Marslen-Wilson, 2015). The present data suggest that the obligatory morphological decomposition process may be dysfunctional in patients with MS. These patients had to resort to full form processing and representation. Thus, prime-target pairs which can be argued to share links at the level of word form and/or meaning such as those used in the + R + S and –R + S show evidence of facilitation while prime-target pairs that share links only at the morphemic level, like the + R–S pairs, cannot prime. The implication is that, although morphemic decomposition may be obligatory in normal Arabic word processing, if the system is noisy (due to neural damage), the decomposition route becomes non-viable and a full-form word-based route is used.

Notes

1. We use the Buckwalter Transliteration scheme: https://en.wikipedia.org/wiki/Buckwalter_transliteration
2. We describe in detail how number of lesions and lesion volumes were obtained in the data analysis section.

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No potential conflict of interest was reported by the author(s).

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Open practices statement

The data file and output of the statistical analysis from this study can be found in the Open Science Framework, at https://osf.io/bj7mn/?view_only = bf374804c39d4b6e9eb978d1b7a8352c. None of the experiments reported here were preregistered.

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