Impaired mental simulation of specific past and future personal events in non-depressed multiple sclerosis patients

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ABSTRACT

The aims of the present study were (i) to explore autobiographical memory and episodic future thought in multiple sclerosis (MS), using Levine's Autobiographical Interview; (ii) to investigate the influence of the Interview's high retrieval support condition (the specific probe phase) on MS patients' past and future simulations and (iii) to obtain the patients' estimations of their own difficulties, during the test, and in everyday life.

To that end, we examined 39 non-depressed relapsing–remitting MS patients and 34 healthy subjects matched for gender, age and education level. The 73 participants underwent an adapted version of the Autobiographical Interview in two conditions: remembering and imagining personal events. The group of patients also underwent an extended neuropsychological baseline, including particularly, anterograde memory and executive functions. The results showed that the MS patients' scores on the baseline were mildly or not impaired. On the contrary, the Autobiographical Interview measure, i.e., the mean number of internal details, for each of the two phases of the test – free recall and specific probe – was significantly lower in simulated past and future events in comparison with the healthy controls. Within each group, autobiographical memory performance was superior to episodic future thought performance. A strong positive correlation was observed between past and future mental simulation scores in both groups.

In conclusion, our results showed, for the first time, the co-occurrence of deficit of remembering the past and imagining the future in MS patients. They also showed more difficulty in imagining future events than remembering past events for both patients and normal controls. MS being a neurological condition very frequent in the young adult population, the clinical considerations of our study might be of interest. Indeed, they give rise to new insights on MS patients' daily life difficulties related to impaired mental simulation of personal events despite general abilities, including anterograde memory, only mildly or not impaired.

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1. Introduction

The occurrence of cognitive impairment in multiple sclerosis (MS) has been established for the past 20 years [10,38], covering a wide range of cognitive functions such as anterograde memory, executive functions, attentional processes, and information processing speed, among others [44].

More recently, the investigation of autobiographical memory (AM) in MS patients has attracted some attention. Briefly stated, AM is the capacity of reliving detailed events, within their specific spatio-temporal context, as they are remembered [58]. An overview of AM studies in MS [20,21,25,35,37] shows some conflicting results, which seem to rely mainly on some methodological discrepancies, particularly, the sensitivity of the test used to assess AM in MS. The call for a stringent AM test is also motivated by the fact that notwithstanding the variability of AM test performance, MS patients' complaints are frequent. These clinical observations together with neuroanatomical and conceptual considerations (see below), led to the suggestion that AM impairment in MS patients is likely caused by a deficit of retrieval strategies rather than a loss of personal recollections [20,21]. The deficit would be then attributed to dysfunctional prefrontal regions ([7,8,30]).

From a neuroanatomical standpoint, MS patients' difficulties in remembering past events are coherent with both the multifocal nature of MS lesions and the widespread cerebral network recruited during AM tasks [53,57]. This cerebral network encompasses predominantly the left and medial cerebral regions, namely, the prefrontal cortex, medial and lateral temporal cortices, parieto-occipital regions, temporoparietal junctions and cerebellum. Consistent with these findings, the

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preliminary fMRI results obtained by Ernst et al. [21] showed enhanced bilateral prefrontal region activations during the initial retrieval phase of past events, which seemed to corroborate the retrieval-deficit hypothesis. Moreover, the enhanced prefrontal activation having been observed bilaterally, the suggestion was one of a compensation mechanism attempt, although insufficient to result in normal AM performance [21].

Recent neuroimaging and clinical studies have examined the ability to mentally simulate hypothetical scenarios from not only past recollections but also those that may potentially occur in the future, i.e., the relationships between remembering the past and imagining the future. Imagining future personal events or episodic future thought (EFT; [55]; see [45] for a review), is the ability to mentally pre-experience a personal event that may happen in the future. The relation between AM and EFT, sometimes referred to as "mental time travel" [50,51], has been extensively studied in the healthy subject (e.g. [1,8,54]), revealing a common cerebral network assumed to reflect the engagement of similar cognitive processes. Indeed, AM and EFT involve not only the self-referential processes, but also the retrieval and binding of details into a coherent event representation, which include conceptual and sensory information, with a strong reliance on visual imagery processes [1].

Subsequently, in clinical studies, it was surmised that EFT would also be deficient whenever AM impairment had been observed. Investigations carried out in several clinical conditions such as Alzheimer disease (e.g. [3]), amnesic mild cognitive impairment (e.g. [22]), schizophrenia (e.g. [15]), depression (e.g. [62]), or medial temporal lobe amnesia (e.g. [24,39]) confirmed the co-occurrence of deficit in the simulation of past and future personal events.

To our knowledge, EFT has never before been explored in MS patients despite the characteristic onset of the illness occurring during young adulthood and despite the clinical value of the central role of mental time travel in everyday life. Indeed, AM contributes to the construction and the continuity of the personal identity, plays at least two social roles, the development of new relationships and the nurturing of existing ones, and involves also a directive function, where the past serves as a basis for guiding present and future behaviours [9,40]. With regard to EFT, three main functional benefits have also been described [55] comprising a role in (i) coping skills for stressful events, with an implication in emotion regulation and problem solving; (ii) goal achievement, for which the act of imagining various scenarios helps to reach the desired goal; and finally, (iii) the implementation of intentions, for which a higher likelihood of completing an action is observed when there is an intention to implement this action. Furthermore, D'Argembeau, Lardi & Van der Linden [17] suggested that EFT, similarly to AM and, particularly, self-defining EFTs contribute to a person's sense of self and, together with self defining AMs, give rise to a strong sense of personal continuity over time.

Based on both the abovementioned works on the interdependence between AM and EFT in terms of common cognitive processes, and previous reports on AM in MS patients, the aims of the present study were (i) to explore autobiographical memory and episodic future thought in non-depressed relapsing–remitting MS patients, (ii) to investigate the influence of a high retrieval support condition on MS patients' past and future simulations, and (iii) to obtain the patients' reports about their difficulties during the test, and in everyday life. To that end, we probed the ability of MS patients to generate future episodic events, as well as to remember recent past events and remote past events from across lifespan. The rationale for exploring remote past events relied on the importance of having a comprehensive view of MS patients' AM performance. Effectively, taking into account the suggestion of an AM retrieval-deficit hypothesis in MS patients, exploring only recent past events, which are generally more accessible memories, could result in an underestimation of the AM impairment. A similar pattern of impairment was expected between future events and both time intervals, and recent and remote past events in MS patients. Complementarily, a correlation between AM and EFT scores in our patients was also expected.

As the AM test sensitivity is a main concern in the exploration of AM functioning, we carried out the research with the Autobiographical Interview (AI; kindly communicated by Brian Levine to one of us, LM), based on its sensitivity to detect AM and EFT deficits in different clinical populations (e.g. [3,19,22]). Moreover, as the AI includes both a free recall and a high retrieval support condition (i.e. the specific probe phase), a further aim was to investigate the influence of this last condition on AM and EFT performance in MS patients. Finally, we also aimed at obtaining the patients' self-reports on their difficulties during the mental simulation testing, and also more generally in their everyday life.

2. Methods

2.1. Participants

Thirty-nine patients with definite MS according to the McDonald criteria [31] were recruited at the Neurology Units of two French hospitals (Strasbourg and Colmar). Inclusion criteria were as follows: RR-MS disease course, Expanded Disability Status Scale (EDSS; [27]) score ≤5, absence of major signs of depression according to the Montgomery and Asberg Depression Rating Scale (MADRS; [33]: significant clinical threshold score ≥15), and no recent exacerbation of MS symptoms.

Thirty-four healthy controls matched for gender, age and education level were also recruited. Exclusion criteria for all the participants included documented psychiatric illness, neurological disorder (other than MS for the patient group) and poor knowledge of French. Demographic and clinical data are summarised in Table 1. The present study was approved by the 'Committee for Protection of Persons' (CPP/CNRS No. 07023) and we complied with the APA ethical standards.

2.2. Neuropsychological baseline examination

The patients completed a comprehensive baseline examination in order to verify their cognitive status allowing us to control any potential confounding variables on the AM and EFT performance. It comprised the following functions, general verbal abilities, tested with the Verbal IQ, short form [4] of the WAIS-III [61], and nonverbal reasoning assessed using the Advanced Progressive Matrices Set 1 [41]. Anterograde memory was examined with the Rey Auditory Verbal Learning Test (RAVLT; [42]), and the Rey–Osterrieth Complex Figure (ROCF; [36,43]). The executive functions were probed by means of the National Hospital, London's phonological and categorical fluency tests, the Brixton Spatial Anticipation Test [11], the Tower of London Test [46,48], and the Cognitive Estimation Task [47]. The attentional abilities and information processing were assessed using the Information Processing Speed Test from the Adult Memory Information Processing Battery (AMIPB; [13]), the Stroop Test [49], and the Months Backwards Test (National Hospital, London). Language was tested with the Déno 100 test [26], and the visuo-perceptual and visuo-spatial abilities with the Silhouettes and Cube Analysis Sub-Tests from the Visual Object and Space Perception Battery (VOSP; [60]). Additionally, the effects of fatigue in everyday life were assessed using the "Echelle de Mesure de l'Impact de la Fatigue", (EMIF-SEP; [18]).

Finally, in the interest of obtaining qualitative information about MS patients' perception of potential AM/EFT difficulties during the assessment, and also in everyday life, we proposed a semi-structured interview (described in [20]) at the end of the AI session.

2.3. Assessment of mental simulation of past and future events

The assessment of AM and EFT was based on the AI described in Levine et al. [28]. The AI general instructions for both AM and EFT conditions were as follows: to retrieve/imagine personal unique events, temporally and contextually specific, occurring over minutes to hours and to generate freely as many details as possible about the event. We used the adapted version of the AI [2,3], introducing cue-words for