Multiple sclerosis and bilingualism: some initial findings

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Abstract

It has been suggested that bilingualism is beneficial for executive control and could have positive long-term effects by delaying the onset of symptoms of degenerative diseases. This research project investigated, for the first time, the impact of bilingualism on executive control, specifically the monitoring and inhibitory control, in individuals with Multiple Sclerosis (MS), a neurodegenerative disease which commonly causes deficiencies in the cognitive system. Bilingual and monolingual adults, with and without an MS diagnosis, performed a flanker task in two degrees of monitoring demands (high monitoring vs. low monitoring). Results showed that bilingual MS patients had inhibitory control and monitoring abilities that were similar to healthy bilingual controls. In contrast, monolingual MS patients showed similar inhibitory control, but significantly worse monitoring abilities compared to monolingual healthy controls. We propose that the similar behaviour between bilingual groups suggests that bilingualism might counteract cognitive deficits related to MS, especially with respect to monitoring. The high monitoring cost observed in monolingual patients seems related to underlying deficits in the monitoring and possibly switching, executive control abilities commonly impaired in MS patients from an early stage. Our findings provide some preliminary evidence for the cognitive reserve hypothesis in bilingual MS patients.

Keywords: atypical bilingualism, Multiple Sclerosis, flanker task, bilingual, monolingual,

1. Introduction

A significant body of literature has suggested that being bilingual might be beneficial to domain-general cognition (e.g., Bialystok, Craik, Klein & Viswanathan, 2004; Bialystok, Craik & Luk, 2012; Colzato et al., 2008). Some studies have even proposed that this cognitive enhancement could positively affect the ageing brain and delay the onset of symptoms of degenerative illnesses, such as Alzheimer's Disease (Bialystok, Craik & Freedman, 2007; Craik, Bialystok & Freedman, 2010; Stern, 2002). This has led researchers to claim that bilingualism provides a "cognitive reserve"; that is, the assumption that some variables can positively affect the brain by delaying cognitive decline or improving its potential to deal with damage in older age (Craik et al., 2010). For example, research has found that being bilingual delays the onset of dementia by four to five years (Alladi, Bak, Duggirala, Surampudi, Shailaja & Shukla, 2013; Bialystok, Craik & Ryan, 2006; Craik et al., 2010). Most of the currently available studies depended on retrospective epidemiological analysis in dementia. However, these studies have opened the door to new research suggesting that bilingualism could be an environmental factor that protects the brain from cognitive decline. It is reasonable to expect that bilingualism might have the same protective function in other neurodegenerative diseases different from dementia. Nevertheless, experimental studies exploring the protective effects of bilingualism, especially in neurodegenerative conditions other than dementia, remain limited. Additionally, the bilingual advantage is not always supported, as several studies have suggested that the evidence for it is not consistent (e.g., Hilchey & Klein, 2011; Paap & Greenberg, 2013; Paap, Johnson & Sawi, 2015).

Regarding the cognitive reserve hypothesis, some opposing findings have also been reported in the literature (Zahodne, Schofield, Farrell, Stern & Manly, 2014; see Gold, 2015 for a review). The present research fills an important gap in the experimental literature of neurodegenerative diseases by investigating the effects of bilingualism on cognition in Multiple Sclerosis (MS).

MS is an autoimmune disease that affects over 2.5 million people worldwide and can impact patients' cognitive and neuropsychological abilities (see Amato, Zipoli & Portaccio, 2006 for a review). MS may affect both cerebral hemispheres, the cerebellum and brain-stem structures by inducing demyelination of the neuron axons, inflammation, neurodegeneration, and cerebral atrophy (Benedict, Bakshi, Simon, Priore, Miller & Munschauer, 2002). The disease is usually diagnosed in young adults between 20 and 40 years of age (Amato et al., 2006; Rao, 1986). The natural course of the disease causes a diverse range of symptoms that could be associated with a certain progression of physical disabilities, neuropsychiatric disorders (depression, fatigue), as well as cognitive impairments, with a proven impact on the quality of life (Benedict et al., 2005; Kobelt, Langdon & Jönsson, 2019). However, MS is heterogeneous, presenting different symptoms according to different phenotypes of the disease. This adds variability among individuals which renders investigating MS a challenging task (Chiaravalloti & DeLuca, 2008).

It has been demonstrated that 43% to 70% of individuals suffering from MS manifest difficulties in one or more cognitive domains, such as memory, attention, executive control, processing speed or verbal fluency (see Sokolov, Grivaz & Bove, 2018 for a review). The effect of MS on executive control is of particular interest when bilingual patients are considered because of the reported bilingualism-induced benefits on executive control, especially on attentional networks (Costa, Hernández, Costa-Faidella & Sebastián-Gallés, 2009). It has been agreed that both languages are constantly active in the bilingual mind; consequently, bilinguals

need to exert additional control compared to monolinguals in order to communicate in the intended language. This demanding task is performed by executive control components which, in turn, are enhanced by this experience (Green, 1998).

Executive control components are related to executive functions; that is, "the ability to respond in an adaptive manner to novel situations" (Lezak, Howieson, Bigler & Tranel, 2012, p. 666). The components of the executive control system include attention, shifting, inhibition (e.g., Beatty, Goodkin, Beatty & Monson, 1989; Drew, Tippett, Starkey & Isler, 2008) and they are needed to trigger the best response in competitive and/or new circumstances (Norman & Shallice, 1986).

Costa and colleagues provide an elegant explanation of how bilingualism enhances different components of executive control (Costa, Hernández & Sebastián-Gallés, 2008; Costa et al., 2009). They propose that there are two mechanisms at play: the monitoring mechanism (i.e., the ability to observe and evaluate a behaviour), and the inhibitory control (i.e., the ability to supress irrelevant information). Bilinguals not only use these executive control mechanisms by constantly inhibiting the conflict created by the non-intended active language (conflict resolution), but also by monitoring the contexts in which languages have to be used and adapting to these contexts for the use of the appropriate language (monitoring mechanism). Based on this rationale, bilinguals train their executive control mechanisms more vigorously in the process of speaking more than one language. This constant training of inhibition and monitoring enhances these mechanisms and possibly explains why bilinguals outperform monolinguals in tasks tapping executive control, such as the flanker, Stroop, and Simon tasks (Bialystok, 2006; Costa et al., 2008). Specifically, bilinguals seem to be overall faster and more accurate (i.e., indicative of the monitoring mechanism), and they show a shorter conflict effect (i.e., the time taken to solve conflicting information during tasks, such as the flanker, which requires inhibiting control resources) compared to monolinguals.

However, these advantages are not always observed in the literature. After reviewing 25 studies, Costa et al., (2009) conclude that the evidence on a bilingual advantage on the inhibitory control is scarce. However, it is more likely to be observed on the monitoring mechanism, particularly in task designs that are highly demanding of monitoring activity. Costa and colleagues provide a detailed explanation of how these tasks' designs work. For example, in a standard flanker task, a line with an odd number of arrows is presented on a screen to participants who have to decide whether the direction of the central arrow is to the right or to the left. The surrounding (flanking) arrows might follow the same direction of the central arrow (congruent trial) or have the opposite direction to the central arrow (incongruent trial). The task can be varied in design by presenting different proportions of congruent and incongruent trials, and by grouping them in a varied fashion. For instance, some flanker task conditions present congruent and incongruent trials independently in separate blocks; other conditions mix the types of trials, but their proportions vary (e.g., 25% incongruent vs. 75% congruent). When trials are highly mixed in blocks (e.g., 50% incongruent vs. 50% congruent), the demands on the monitoring mechanism increase as participants require constant adaptation to trials that either do or do not involve conflict resolution. This is observed in a generally slower performance compared to non-mixed designs, the so-called mixing cost, which reflects the mental flexibility and rapid adaptation to changes in task requirements (Costa et al., 2009). In contrast, in non-mixed or low-mixed designs (e.g., 8% congruent vs 92% incongruent), participants are generally confronted with one type of trial. Thus, high attentional behaviour and adaptation is not necessary. The behaviour observed when participants perform high monitoring tasks mirrors the bilingual speaker's experience, who in order to communicate in the intended language, needs to flexibly adapt their behaviour as both intended and non-intended languages are active. The hypothesis that the bilingual advantage is more evident

under high monitoring tasks has been supported by Costa et al., (2009) and Hofweber, Marinis and Treffers-Daller (2016).

In addition to enhanced executive control mechanisms, it has been suggested that the bilingual experience might restructure parts of the brain related to cognitive and language control (see Pliatsikas, 2019, for a review and a theoretical proposal for these effects). Specifically, it has been demonstrated that healthy young bilinguals have increased structural integrity compared to monolinguals in several language-related white matter tracts (Pliatsikas, Moschopoulou & Saddy, 2015). This is of particular interest to the study of MS in bilingual patients, as MS primarily targets white matter integrity. Therefore, bilingualism might interact with the expression and progression of the disease, as well as its cognitive outcomes, given that individuals with MS present deficits in the cognitive system and these deficits can be associated to attention and the executive control system (Chiaravalloti & DeLuca, 2008; Denney, Sworowski & Lynch, 2005). Research investigating the impact of bilingualism in MS stands to inform our theoretical and clinical understanding of the impact of bilingualism on cognitive control across healthy and clinically populations.

2. The present study

We investigated whether being bilingual impacts the monitoring mechanism and the inhibitory control in adults with MS. We compared two groups of MS patients (bilinguals and monolinguals) to age-matched healthy control groups (monolinguals and bilinguals) in two conditions of a flanker task. The selection of a flanker task is supported by previous studies that find this task suitable to measure relatively pure inhibitory control (Costa et al., 2009). Based on Costa et al.'s (2009) argument described above, we measured the monitoring mechanism and the inhibitory control in two monitoring conditions of the flanker task: High-Monitoring, HM, condition (50% incongruent trials; 50% congruent trials) and Low-

Monitoring, LM, condition (8% incongruent trials; 92% congruent trials). The monitoring mechanism was measured in two ways: i) by calculating the overall accuracy and RTs on congruent and incongruent trials in HM and LM conditions separately; that is, the Monitoring Load; and ii) by calculating the overall difference between HM and LM conditions collapsed across congruent and incongruent trials for both accuracy and RT; this is the so-called mixing cost by Costa and colleagues, which will be called the Monitoring Cost. The smaller the Monitoring Cost, the better the monitoring skills (Hofweber et al., 2016).

The inhibitory control was measured using the Conflict Effect. This was calculated by the difference between incongruent and congruent trials, and was measured in HM and LM conditions separately for both accuracy and RT. The conflict effect is affected by the monitoring conditions. It is expected to be larger in the LM condition, because more conflict resolution mechanisms are required to solve the conflicting information from non-expected incongruent trials. At the same time, having a high percentage of congruent trials favoured the performance which is generally non-conflicting. Finally, as conflict effect and monitoring skills can be independent behaviours, one or both can be impacted by bilingualism (see Costa et al., 2009, p. 137 for detailed explanation).

Our research questions addressed: 1) whether MS patients differ from healthy controls in their monitoring abilities (indexed by Monitoring Load in the HM and LM; Monitoring Cost) and in inhibitory control (indexed by the Conflict Effect in the HM and LM conditions); and 2) whether bilingualism differentially impacts monitoring abilities and inhibitory control in MS patients.

We tested the following exploratory hypotheses: firstly, if MS has an effect on executive control mechanisms, healthy controls will show better monitoring and inhibitory control abilities than MS patients; and secondly, if bilingualism has a protective function on executive control, (a) bilingual MS patients will outperform monolingual MS patients in both monitoring

and inhibitory control abilities (Bialystok et al., 2007; Craik et al., 2010), and also, (b) bilingual MS patients will not significantly differ from bilingual controls.

3. Methodology

3.1 Participants

Four adult groups of participants were recruited with ten participants in each group: bilinguals with MS; bilingual healthy controls; monolinguals with MS; and monolingual healthy controls. Table 1 provides their demographic information. Monolingual participants (MS vs. Control) were matched for age (F = 0.02; p = .89) and year of education (F = 2.68; p = .12); similarly, bilingual participants (MS vs. Control) were matched for age (F = 1.72; p = .21) and education (F = 1.96; p = .18). Bilinguals were systematically more educated than monolinguals in both groups (healthy controls, F = 4.78; p = .04 and MS patients F = 1.72; p < .001).

Table 1. Demographic information of the participants

Participants			*Age*			*YoE*			*Sex*	
		n	Range	*M*	*SD*	Range	*M*	*SD*	M	F
Bilingual	*Control*	10	23-44	32.1	5.65	16-22	18.3	2.11	5	5
	MS	10	24-58	37.1	9.93	12-20	16.9	2.56	5	5
Monolingual	*Control*	10	24-57	40.8	12.25	8-18	15.2	4.93	5	5
	MS	10	27-59	40.6	10.37	9-15	12.9	1.73	5	5

YoE = years of education; MS = Multiple Sclerosis

To characterise bilingual proficiency and usage, we administered the Language and Social Background Questionnaire (Anderson, Mak, Chahi & Bialystok, 2018). This is a self-administered questionnaire collecting information about the participants' language background (spoken languages, proficiency, time engaged speaking languages) and their social and

education background (profession, country of birth, where participants lived, etc). Monolingual speakers were all born in a Spanish-speaking country and used only Spanish for communication. All bilinguals were native speakers of Spanish with the exception of one participant (aged 59) who had been living in Madrid for more than 20 years and using Spanish on a daily basis (Spanish proficiency score 9.25/10). All participants lived and worked in Madrid, which is mainly a monolingual city. Table 2 shows the results from the questionnaire.

Table 2. Linguistic background of the bilingual speakers

	L1 Proficiency	L2 Proficiency	No. Participants with L3	L3 Proficiency		% time engage in L2	AoA < 7 years	AoA > 7 years
	M (SD)	*M (SD)*	N	Range	*M (SD)*	*M (SD)*	No	No
Control	10 (0)	8.45 (1.38)	7	4-9.25	7.1 (1.73)	42.27 (17.74)	5	5
MS	9.8 (0.63)	8.8 (0.92)	7	4-10	7.4 (2.1)	51.87 (21.05)	3	7

AoA = Age of Acquisition. Proficiency scale: 1-10 (1= no proficiency; 10=near native)

As observed in Table 2, Control and MS bilinguals had similar overall L2 proficiency. The main L2 was English. The groups were balanced in terms of the number of speakers with a L3 (mainly French, English, German, and Italian) and whether the languages were acquired before or after participants had reached seven years of age. The contexts of use of L2/L3 are mainly for work, communication, reading activities, and TV.

MS patients were recruited from the Demyelinating Diseases Unit at Gregorio Marañón Hospital in Madrid (Spain). They were diagnosed based on the McDonald (2010) criteria (Polman et al., 2011). All patients were diagnosed with relapsing-remitting MS, apart from one monolingual patient with the progressive type of MS. The mean age of onset of MS for monolingual and bilingual patients was 31.8 years (SD = 7.84) and 30.5 years (SD = 8.3); whilst the mean number of years with MS for monolingual and bilingual patients was 9.95 years (SD = 8.34) and 6.55 years (SD = 9.71). The degree of physical disability was measured

using the Expanded Disability Status Scale and results showed no difference between monolingual MS participants (Mean = 2.1; SD = 1.7) and bilingual MS participants (Mean = 1.6; SD = 1.37). There was no significant difference between the bilingual and monolingual MS participants on mean age of onset ($F = 0.13$; $p = .72$), mean years with MS ($F = 0.71$; $p = .41$), and degree of physical disability ($F = 0.53$; $p = .48$).

Cognitive diagnosis was obtained after neuropsychological evaluation. The assessment battery included measurements of information processing speed (Symbol Digit Modality Test, SDMT), verbal memory (via the Test of Verbal Learning España-Complutense, TAVEC, Spanish version of the CVLT-II), visual memory (via the Brief Visual Memory Test Revised, BVMT-R), attentional control and executive functioning (Paced Auditory Serial Addition Test, PASAT, 3 seconds and Five Digit Modality Test, 5-DIGIT), and executive function (verbal fluency task). See Appendix A and B for the scores of the tests and the diagnostic criteria, respectively. No cognitive impairment was present in the control groups. There was a similar distribution of MS participants, in terms of the presence of cognitive impairment across the monolingual and bilingual groups: six bilingual and four monolingual patients presented normal cognition (50% of MS participants); two bilingual and three monolingual patients showed mild cognitive deficits; and two bilingual and three monolingual patients showed moderate cognitive deficiency.

3.2. The flanker task

The flanker task included two conditions: HM with 50% of congruent and 50% incongruent trials; LM with 92% of congruent trials and 8% of incongruent trials. The HM and LM conditions were presented in two separate blocks. The pictures that were being monitored in the task were fish instead of arrows based on Rueda et al. (2004). All participants were presented with both conditions and the presentation order was counterbalanced across them.

We presented the flanker task on a laptop (13-inch MacBook) using *PsychoPy 1.81* software (Peirce, 2007). Each condition contained 100 trials. Each trial consisted of presenting participants with a row of five small fish and instructing them to focus their attention on only the central (target) fish. We presented an array of fish instead of typical arrows to overcome possible visuo-perceptual difficulties experienced by MS patients (Ortiz-Pérez et al., 2016). The test was administered after we had carried out 12 practice trials. Participants had to press a key that corresponded to the direction that the target fish faced, either L for right-facing fish or A for left-facing fish, as fast and as accurately as they could. Inter-trial intervals were jittered between 200ms to 2000ms. Each task had two experimental conditions: the congruent condition with all fish facing the same direction; and the incongruent condition, where surrounding fish faced in the opposite direction to the central one (Figure 1). The incongruent condition required participants to suppress the distractors, that is, to inhibit the conflicting information (i.e., the conflict resolution). This is expressed in higher RTs. In the congruent condition, there is no conflicting information and RTs should be shorter.

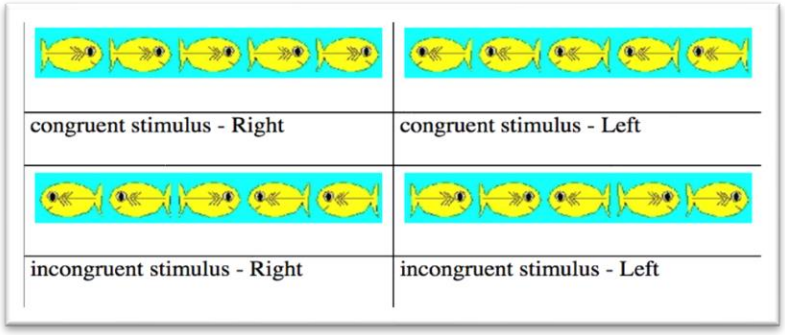

Figure 1. Conditions in the Flanker task

When performing a flanker task, participants are required to monitor conflicting information and adapt their forthcoming behaviour accordingly, exercising their monitoring mechanism. We measured two variables: Monitoring Load and Monitoring Cost.

Monitoring Load: this was measured by averaging the performance over congruent and incongruent trials in the HM and LM conditions separately. This was calculated for both the accuracy and RTs. Based on Costa et al. (2009), the smaller the overall RTs and the more accurate the overall responses (Monitoring Load), the better the monitoring mechanism.

Monitoring Cost: this was the difference in performance between HM and LM conditions, collapsed across congruent and incongruent trials (Hofweber et al., 2016). The smaller the Monitoring Cost, the better the monitoring skills, as the performances between HM and LM conditions would be closer (Hofweber et al., 2016). This was calculated for both the accuracy and RTs.

$$\text{Accuracy} = \%\ \text{Accuracy}_{\text{HM (incongruent trial+ congruent trial)}} - \%\ \text{Accuracy}_{\text{LM (incongruent trial+ congruent trial)}}$$

$$\text{RT} = \text{RT}_{\text{HM (incongruent trial+ congruent trial)}} - \text{RT}_{\text{LM (incongruent trial+ congruent trial)}}$$

In addition to the monitoring mechanism, the inhibitory control abilities were measured by calculating the Conflict Effect.

Conflict Effect: this was measured by the calculating the difference between congruent and incongruent trials for HM and LM conditions, separately. We calculated the conflict effect for both accuracy and RTs, thus, generating four variables (two for HM and two for LM).

$$\text{Accuracy} = \%\ \text{Accuracy}_{\text{incongruent trial}} - \%\ \text{Accuracy}_{\text{congruent trial}}$$

$$\text{RT} = \text{RT}_{\text{incongruent trial}} - \text{RT}_{\text{congruent trial}}$$

Given that the incongruent trials are expected to be more challenging, as distracting information would need to be suppressed, a smaller conflict effect will mean that participants exert their inhibitory control to a greater extent. As explained in Section 2, the conflict effect should be larger in the LM compared to the HM condition due to the small number of incongruent items.

3.3 Analysis

Prior to RT analysis, we eliminated incorrect responses. We also removed trials with RT values with +/- 3SD from the mean per type of trial (incongruent, congruent), group of participants (Control bilinguals, Control monolingual, MS bilingual, MS monolingual), and conditions (HM and LM). In total this resulted in discarding 27 trials (1.4%) in the bilingual Control group, 34 (0.98%) in the monolingual Control group, 29 (1.5%) in the bilingual patient group, and 20 (1.1%) in the monolingual patient group. Subsequently, we calculated the overall accuracy and RT for congruent and incongruent trials (Monitoring Load), the Monitoring Cost, and the Conflict Effect for both accuracy and RTs.

Raw accuracy and RTs (Monitoring Load) were analysed with separate multiple regression analyses; with Patient Group (Controls, MS), Language Group (monolingual, bilingual), Monitoring Condition (High, Low), Trial Type (Congruent, Incongruent), Age; a Monitoring Condition x Trial Type interaction; and a Language Group x Patient Group interaction as predictors. Because our language groups were not matched on education, Years of Education (YoE) was also added to the model as a continuous predictor, along with a YoE x Bilingualism interaction.

Following that, Monitoring Cost (accuracy and RT) was analysed separately in a model accounting for the effects of Patient Group, Language Group, YoE and Age, and the Patient Group x Language Group x YoE interaction. Finally, the Conflict Effect (accuracy and RT) was analysed separately for the HM and LM conditions in a model accounting for the same factors and their interactions: Patient Group, Language Group, YoE and Age, and the Patient Group x Language Group x YoE interaction. Data were analysed in R with the *lm* function.

4. Results

This section is organised as follows: Sections 4.1 and 4.2 report results for Monitoring Load and Monitoring Cost, respectively. These are indicative of the monitoring abilities of the

speakers' groups. Section 4.3 presents results of the Conflict Effect for RTs which reflects inhibitory control abilities. Means and standard deviations for accuracy and RT for Patient Group (Controls, MS), Trial Type (Congruent, Incongruent) and Monitoring Condition (High, Low), as well as the magnitude of the Monitoring Cost and Conflict Effect are presented in Table 3, for bilingual and monolingual participants, separately.

Table 3. Mean percent accuracy and RTs (msec) per condition, Monitoring Cost, and Conflict Effect for each group (standard deviation)

		Bilinguals				Monolinguals			
		Accuracy		RTs		Accuracy		RTs	
		Controls	MS patients	Controls	MS patients	Controls	MS patients	Controls	MS patients
HM	Congruent	99 (1.94)	99.2 (1.03)	467.30 (47.26)	489.29 (64.46)	99.2 (1.40)	99 (1.70)	478.13 (60.80)	513.38 (112.38)
	Incongruent	100 (0)	98.4(1.84)	476.61 (55.53)	503.72 (50.57)	99 (1.05)	97.4 (3.27)	491.21 (62.77)	521.44 (105.15)
	Overall Mean	99.5 (0.97)	98.8 (1.44)	471.96 (51.40)	496.50 (57.52)	99.1 (1.23)	98.2 (2.49)	484.67 (61.79)	517.41 (108.77)
LM	Congruent	99.2 (.79)	99.1(1.10)	437.24 (36.71)	485.80 (61.31)	99.6 (.52)	98.7 (1.34)	492.71 (58.74)	507.65 (124.73)
	Incongruent	97.5 (7.91)	100 (0)	488.89 (60.22)	524.59 (101.70)	100 (0)	98.8 (3.79)	540.0 (95.78)	519.81 (122.54)
	Overall Mean	98.35 (4.35)	99.55 (.55)	463.07 (48.47)	505.20 (81.51)	99.8 (.26)	98.75 (2.57)	516.36 (77.26)	513.73 (123.64)
Monitoring Cost		-0.2	-0.55	8.89	-8.69	0.65	-0.75	-31.70	3.69
Conflict	HM	1 (1.94)	-0.8 (1.94)	9.31 (21.03)	14.43 (25.44)	-0.2 (1.76)	-1.6 (2.07)	13.08 (6.12)	8.06 (15.31)
Effect	LM	-1.7 (8.22)	0.9 (1.09)	51.64 (34.72)	38.79 (60.47)	0.4 (.52)	0.1 (4.43)	47.33 (55.60)	12.16 (27.10)

HM = High Monitoring, LM = Low Monitoring

4.1. Monitoring Load

We first examined the overall means for accuracy and RT across the language groups for monitoring condition and type of trial. With respect to accuracy, Table 3 shows that all groups performed at near ceiling for both types of trials in both conditions, suggesting that this task was appropriate for the MS patients. This variable was not further analysed.

Table 4 summarises the results for the analysis of accuracy. The model did not reveal any significant main effects or interactions. Given that accuracy reached almost a ceiling level, this variable was not analysed any further.

Table 4. Multiple regression on raw accuracy scores in the Monitoring Load

	β	SE	t	*p*
(intercept)	100.38	2.70	37.2	<0.001
Patient Group	0.35	0.61	0.58	0.56
Language Group	1.09	2.79	0.39	0.69
Age	-0.03	0.03	-1.30	0.19
YoE	-0.02	0.13	-0.164	0.87
Monitoring Load	0.05	0.58	0.09	0.93
Trial Type	-0.40	0.58	-0.69	0.49
Monitoring Load x Trial Type	0.33	0.81	0.40	0.69
Language group x Patient group	-1.42	0.87	-1.64	0.10
Language Group x YoE	-0.02	0.16	-0.16	0.87

Overall model fit: R^2: 0.037

Table 5 summarises the results for the analysis of RTs. The model only revealed a significant main effect of Age, suggesting that the older the participants, the longer the RTs. No other significant main effects or interactions were found.

Table 5. Multiple regression on raw RTs in the Monitoring Load

	β	SE	t	*p*
(intercept)	211.39	73.69	2.87	<0.001
Patient Group	23.41	16.73	1.40	0.16
Language Group	120.79	76	1.59	0.11
Age	4.08	0.62	6.54	<0.001
YoE	6.18	3.53	1.75	0.08
Monitoring Load	-6.18	15.78	-0.39	0.7
Trial Type	11.21	15.78	0.71	0.48
Monitoring Load x Trial Type	26.26	22.30	1.18	0.24

Language group x Patient Group	-12.59	23.80	-0.53	0.60
Language Group x YoE	-6.73	4.26	-1.58	0.12

Overall model fit: R^2: 0.286

4.2. Monitoring Cost

Table 6 summarises the analysis for the Monitoring Cost only in RTs. The model revealed a significant main effect of Patient Group, suggesting that MS patients had higher cost than controls overall; a main effect of education, suggesting that the higher the education the smaller the cost; and a significant interaction between Language Group, Patient Group and YoE.

Table 6. Multiple regression on the Monitoring Cost (in RTs)

	β	SE	t	*p*
(intercept)	-191.98	97.43	-1.97	.05
Patient Group	257.79	84.07	3.06	.00
Language group	154.63	90.52	1.71	.09
Age	-1.14	0.73	-1.55	.13
YoE	-13.31	6.04	-2.20	.04
Language group x Patient Group x YoE	26.10	9.30	2.81	.01

Overall model fit: R^2: 0.361

To interpret the significant interaction by Language Group, we analysed bilingual speakers and monolingual speakers separately. Table 7 summarises the analysis for the bilinguals only. The model revealed YoE to have a significant effect on results. No other effects or interactions were significant. Critically, there was no main effect of Patient Group, suggesting that MS patients did not significantly differ from controls.

Table 7. Multiple regression on Monitoring Cost in the bilingual group (in RTs)

	β	SE	t	*p*
(intercept)	-178.96	123.53	-1.45	0.17
Patient Group	297.35	151.08	19.68	0.07
Age	-1.83	1.93	-1.41	0.18
YoE	13.27	6.10	2.17	0.046

Patient Group: YoE	-16.45	8.3	-2.02	0.06

Overall model fit: R^2: 0.346

Table 8 summarises the analysis for monolinguals only. The model revealed a significant main effect of Patient Group, but no other significant main effects or interactions. The significant differences between MS patients and Controls resulted from Controls showing lower monitoring cost (-31.7) than MS patients (3.69).

Table 8. Multiple regression on Monitoring Cost in the monolingual group (in RTs)

	β	SE	t	*p*
Intercept	-49.59	71.57	-0.69	0.49
Patient Group	252.31	109.60	2.30	0.043
Age	-0.85	0.96	-0.88	0.39
YoE	3.47	3.42	1.01	0.32
Patient Group x YoE	-16.35	8.19	-2.00	0.06

Overall model fit: R^2: 0.361

In conclusion, the analysis of the Monitoring Cost seems to indicate that there were not significant differences between bilingual MS and bilingual Controls. In contrast, there were significant differences between monolingual MS patients and monolingual Controls. Monolingual Controls showed a better monitoring cost performance compared to monolingual MS patients.

4.2. Conflict Effect (the inhibitory control)

The conflict effect in the HM and LM conditions in bilingual and monolingual MS and Control patients is presented in Table 3. The conflict effect was analysed statistically in the same fashion as the Monitoring Cost.

Table 9 summarises the analyses of the conflict effect for RTs, separately, for the HM condition and the LM condition. For the HM condition, the model did not reveal any

significant main effects or interactions. For the LM condition, there was a main effect of Age, suggesting that the older the participants, the higher the conflict effect.

Table 9. Multiple regression on the conflict effect in the HM and LM conditions (in RTs)

	High Monitoring (HM)				Low Monitoring (LM)			
	β	SE	t	*p*	β	SE	t	*p*
(intercept)	49.53	45.01	1.10	0.28	93.62	99.75	0.94	0.34
Patient Group	5.56	38.84	0.14	0.89	-174.81	86.08	-2.03	0.051
Language Group	-18.58	41.82	-0.44	0.66	-34.29	92.68	-0.37	0.71
Age	-0.32	0.34	-0.94	0.35	1.81	0.75	2.40	0.02
YoE	-1.15	2.79	-0.41	0.68	4.07	6.19	0.66	0.52
Language group x Patient Group x YoE	-0.43	4.29	-0.10	0.92	-9.50	9.52	-0.99	0.89

Overall model fit: HM: R^2: 0.06; LM: R^2:0.339

5. Discussion

This is the first study to investigate executive control using a flanker task in monolingual and bilingual MS patients in comparison to monolingual and bilingual healthy controls. Following Costa et al., (2009), we focused on two different executive control components: the monitoring mechanism and inhibitory control. These components, according to previous studies, are enhanced in bilinguals (Bialystok, Craik & Luk, 2008; Bialystok et al., 2004; Colzato et al., 2008; Costa et al., 2008; Costa et al., 2009).

Our research questions aimed to answer whether bilingualism has a protective function over these executive control components in MS patients. We explored three hypotheses: 1) healthy controls will show better monitoring mechanism and inhibitory control abilities than MS patients, as we assumed cognitive abilities in MS patients would be impaired even if only to a small degree; 2) if bilingualism has a protective function over executive control mechanisms: a) bilingual MS patients should outperform monolingual MS patients in both monitoring and inhibitory control, and also (b) bilingual MS patients should not significantly differ from bilingual controls. What follows is a discussion of our results in relation to the

different executive control components that were measured through the flanker task. Specifically, we discuss the results on the monitoring mechanism, followed by the findings on the inhibitory control.

Monitoring mechanism

The monitoring mechanism was analysed via Monitoring Load (mean performance in HM and LM conditions) and Monitoring Cost. Results from the analysis of Monitoring Load showed the expected pattern in the tasks according to Costa et al., (2009): firstly, incongruent items took longer to respond to than congruent ones; and secondly, congruent trials were responded to more slowly in the HM condition than in the LM condition, demonstrating that the performance in the LM condition was facilitated by the high proportion of congruent trials. RT responses correlated positively with age, in that the older the participants, the slower the responses. However, bilinguals and monolinguals (Controls and MS patients) both performed similarly in terms of overall accuracy and RTs.

In contrast, the results from the Monitoring Cost analysis showed some significant effects which provide some evidence to the hypothesis that bilingualism acts as a cognitive reserve factor. MS patients produced higher Monitoring Cost than Controls, that is, a less efficient monitoring mechanism. Further analyses revealed that the difference in performance was in the monolingual group. That is, monolingual MS patients had higher Monitoring Cost than monolingual controls. Bilingual MS patients and bilingual controls, on the other hand, did not differ in their performance. The fact that we found no differences in the monitoring abilities (Monitoring Load and Monitoring Cost) between two bilingual groups, and that both responded as predicted to the monitoring demands of the conditions (HM and LM), suggests that the monitoring mechanism might be spared in the bilingual MS patients.

Previous studies in cognition and MS suggest that cognitive impairment is present early in the disease (Foong et al., 1997; Schulz, Kopp, Kunkel & Faiss, 2006) in different degrees. This

is evidenced mainly in attention, shifting, and speed of processing (Drew et al., 2008; Fischer, Foley, Aikens, Ericson, Rao & Shindell, 1994; Rao, Leo, Bernardin & Unverzagt, 1991). These cognitive abilities are involved in the performance of the flanker task, in which participants need to monitor and evaluate stimuli to perform correctly. If bilingualism has a positive effect on MS cognition, we should expect bilingual MS patients to perform better than monolingual MS patients. We hypothesised that the equal performance in the two bilingual groups is attributed to the use of two languages, a complex sustained mental activity that may protect these patients against cognitive decline, as previously suggested (Bialystok et al., 2007; Craik et al., 2010; Stern, 2002). Specifically, the joint activation of two languages enhances frontal-posterior attentional control mechanisms and, consequently, other cognitive mechanisms (Bialystok et al., 2007). Bilingualism might thus be acting as an environmental factor that benefits some MS patients' cognitive abilities, as has been posited in previous studies about the effect of bilingualism on Alzheimer's disease and other dementias (Craik et al., 2010; Gollan, Salmon, Montoya & Galasko, 2011).

In contrast, the results indicate that monolingual MS patients performed poorly, by presenting higher Monitoring Cost compared to monolingual control. This seems to suggest that these patients have at least a minor impairment in their monitoring abilities. Indeed, deficits in the monitoring mechanism are not unusual in MS. The monitoring mechanism is part of the attentional network (Bialystok et al., 2012; Costa et al., 2009; Hofweber et al., 2016) and attentional deficits are among the most common impairments in MS, observed even in early stages of the disease. For example, Feinstein and colleagues reported attentional deficits in early stages of the MS disease when participants only have clinically isolated lesions (optic neuritis) detectable on MRI (Feinstein, Kartsounis, Miller, Youl & Ron, 1992). Also, it has been found that in early stages of MS, when attentional requirements are high, attentional deficits might arise (Dujardin, Donzew & Hautecouer, 1998). Kujala

and colleagues found attentional deficits in MS patients with cognitive damage in the task PASAT (Kujala, Portin, Revonsuo & Ruutiainen, 1995). Moreover, Clough found deficits in switching and sustained attention in MS patients with lower EDSS than in our study (1.17, SD=1.53) through an ocular motor task-switching paradigm (Clough et al., 2018). Other studies on MS that used equivalent tasks to the flanker commonly report errors and slower responses compared to healthy controls, even at early stages of the disease: Stroop task (Foong et al., 1997), Paced Auditory Serial Addition Task, PASAT (Kujala et al., 1995), and task-switching paradigms (Clough et al., 2018; Migliore et al., 2017). It is difficult to compare our study to previous ones due to the methodological differences; that is, most of the previous studies on the protective function of bilingualism are based on retrospective epidemiological analysis of dementias (Alladi et al., 2013; Bialystok, Craik & Ryan 2006; Craik et al., 2010). However, given the available evidence and our results, we hypothesise that the observed pattern in the monolingual MS group might reveal small deficits in attentional abilities and switching.

Inhibitory control

The results of the Conflict effect analysis in the HM and LM conditions suggest that bilinguals and monolinguals (controls and MS patients) show similar inhibitory control abilities. Only in the LM condition did the Conflict Effect seem to be affected by age, suggesting that the inhibitory control mechanism declines with age. Bilingual groups did not outperform monolingual groups on this executive control component, suggesting firstly that bilingualism did not affect inhibition, and secondly, that MS patients showed an unaltered inhibitory control. This finding was unexpected given the evidence that has shown that MS patients also present inhibitory control disabilities in MS (Sokolov et al., 2018). However, the result could be explained by the fact that most MS participants present the relapsing-remitting phenotype of MS, which shows less cognitive decline compared to other

phenotypes with a more progressive evolution (Chiaravalloti & DeLuca, 2008). An interesting hypothesis for future studies is that MS patients experience cognitive compensation and flexibility with the onset of cognitive decline. It is not uncommon to find MS patients with a small degree of cognitive deterioration, even when they do not match a proper diagnosis of cognitive impairment (Chiaravalloti & DeLuca, 2008; Dineen et al., 2009). More recently, studies with fMRI showed an increase on the cerebral connectivity in early stages of MS, which has been explained as an attempt to adapt to the incipient cognitive damage (Staffen et al., 2002; Rocca et al., 2018a; Rocca et al., 2018b).

Finally, a general lack of a bilingual advantage in inhibitory control, even in healthy controls, is consistent to Costa et al.'s (2009) observation that it is more likely to find bilingual benefits in the monitoring mechanism than in inhibitory control. In their review of previous studies, the authors found that in only 6 out of 25 studies was inhibition positively affected by bilingualism (i.e. Bialystok et al., 2004, Bialystok et al., 2006; Bialystok et al., 2005; Costa et al., 2008). Furthermore, in their own study, Costa et al. (2009) did not find any effect of bilingualism on the inhibitory control, only on the monitoring mechanism. In conclusion, the bilingual advantage over the inhibitory control is less likely to be observed. However, our study aimed to uncover why bilingual controls did not show a cognitive advantage over monolingual controls in the monitoring mechanism, when previous studies found significant effects, at least in high monitoring conditions (see Costa et al., 2009 for review). We hypothesised that two factors might hide the bilingual advantage in our healthy bilingual participants: 1) participants' age; 2) second language use. First, as recent literature suggests, bilingual benefits seem to be better observed in specific ontogenetical moments (i.e., infancy and older adults) when executive functions are either in development or in decline, respectively, compared to younger adults (e.g., aged 20-30) who show no bilingual advantages. At that point of young adulthood, they are described as in their better cognitive

capability; therefore, any possible benefit of bilingualism over monolingualism in this context might only be expressed in their older age, when biological cognitive decline can be expected (Bialystok, 2016). The fact that our sample is made up of young participants could be hiding the effects of bilingualism.

Secondly, the evidence also suggests that the amount of second language use could be a determinant factor in exerting the necessary training to enhance executive control mechanisms. Studies that focused on the effect of bilingualism on structural brain connectivity found that the most determinant factors for changes in brain structures are time spent using a L2 (Del Maschio, Sulpizio, Toti, Caprioglio, Del Mauro, Fedeli, & Abutalebi, 2019; DeLuca, Rothman, Bialystok & Pliatsikas, 2019) and immersion in a highly bilingual environment (Pliatsikas, DeLuca, Moschopoulou & Saddy, 2017). Connected to this hypothesis is the evidence that the bilingual advantage over executive functions is only exhibited in bilingual speakers involved in dense code-switching contexts (Hofweber et al., 2016). Our participants, despite being advanced L2 speakers, were not immersed in a bilingual community. Therefore, it is possible that the lack of sufficient use of both languages, combined with the young age of our control participants, may have hindered the effect of bilingualism on executive control.

Our study had several limitations that should be addressed in future research. Firstly, the number of participants was small due to difficulties in recruiting comparable samples. Secondly, although our bilingual and monolingual MS patients were comparable in terms of cognitive impairment, it would have been desirable to have tested matched populations, that is, participants with the same level of impairment. However, as observed in the literature, studies with MS patients with different degrees of cognitive impairment are not uncommon (e.g., Kujala et al., 1995; Migliore et al., 2017; Sumowski et al.,2018). These studies found that MS patients who do not show cognitive impairment after neuropsychological testing are not

necessarily free of cognitive deficits (Migliore et al., 2017). We also believe that, together with cognitive status, it would have been desirable to have access to brain lesion burden indexes, as there is a direct relationship between lesion burden and cognitive damage (Benedict et al., 2004; see Mollison et al., 2017 for a metanalysis) and loss of plasticity (Di Filippo, Portaccio, Mancini & Calabresi, 2018).

In conclusion, our results provide preliminary evidence for the cognitive reserve hypothesis in bilingual MS patients. The implications of our findings are important as they suggest that using more than one language might act as an environmental factor protecting the central nervous system from the decline expected from this neurodegenerative disease.

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Appendix A. Neuropsychological assessment battery scores

		CONTROL				*MS*			
		MONOL		*BILING*		*MONOL*		*BILING*	
		MEAN	SD	MEAN	SD	MEAN	SD	MEAN	SD
1.	SDMT	55.89	8.68	59.60	5.56	49.90	10.25	60.20	10.75
2. TAVEC	L1	8.22	2.11	9.20	2.57	8.50	2.42	8.10	2.47
	L5	13.67	2.06	15.40	0.70	13.40	2.12	14.50	2.12
	LT	57.89	12.73	67.90	5.80	58.60	10.29	62.80	10.94
	B	6.67	2.24	9.10	1.73	6.20	2.66	7.40	2.55
	ST_FR	11.33	2.40	14.40	1.58	12.10	2.77	14.00	2.71
	ST_CR	12.89	2.37	14.80	1.14	12.40	2.76	14.10	2.08
	LT_FR	13.00	2.69	14.60	1.51	12.30	2.91	14.20	2.78
	LT_CR	13.22	2.86	15.20	1.23	12.60	2.63	14.50	1.84
	R	6.44	3.78	3.70	4.37	6.10	3.90	3.50	2.55
	I_FR	2.67	1.80	1.00	1.56	3.80	2.66	2.00	2.40
	I_CR	1.78	2.22	0.40	0.84	1.50	1.78	0.80	1.40
	Rexecutive control	15.00	1.00	15.90	0.32	15.10	1.10	15.50	0.97
	FP	1.11	1.05	0.00	0.00	0.70	0.82	0.30	0.95
3. BVMT-R	BVMT_1	5.11	2.37	8.00	3.20	6.30	2.36	8.30	3.74
	BVMT_2	8.44	2.60	10.70	1.34	9.70	1.77	10.20	2.44
	BVMT_3	10.00	2.24	11.70	0.67	10.90	1.85	11.20	1.87
	BVMT_T	23.56	6.37	30.40	4.40	26.90	5.24	29.70	7.20
	BVMT_LEARN	4.89	2.15	2.90	2.33	5.10	2.08	2.90	3.31
	BVMT_LT	10.00	2.00	11.40	0.97	11.60	0.52	11.00	2.49
	BVMT_Rexecutive control	11.89	0.33	11.60	1.26	11.90	0.32	11.90	0.32
4. DIGIT	READ_HITS	17.56	2.30	17.40	3.37	19.50	4.97	19.30	4.32
	READ_ERR	0.00	0.00	0.00	0.00	0.10	0.32	0.00	0.00
	COUNT_HITS	20.33	3.35	20.50	2.88	22.20	5.03	21.20	5.47
	COUNT_ERR	0.00	0.00	0.00	0.00	0.20	0.63	0.00	0.00
	CHOICE_HIT	32.00	3.61	30.90	5.45	33.60	7.72	31.30	7.09
	CHOICE_ERR	0.67	1.00	0.50	0.53	1.00	0.82	0.50	0.97
	ALT_HIT	41.33	5.77	41.40	5.72	44.00	13.03	40.00	9.40
	ALT_ERR	0.33	0.50	2.40	2.22	2.80	2.78	1.40	1.51
	INHIB	16.00	4.87	14.80	5.09	14.10	4.18	12.10	3.81
	FLEX	19.00	5.66	19.60	8.66	22.10	9.77	18.90	6.05
5. PASAT	PASAT_Hit	45.00	11.96	52.10	6.95	48.00	10.72	48.00	10.68
	PASAT _Om	8.22	6.40	4.20	4.87	10.40	12.70	6.50	7.41
	PASAT _Int	1.00	1.12	0.80	1.87	1.20	1.62	1.90	1.73
	PASAT _Rep	1.89	1.83	1.30	1.34	1.30	1.83	1.50	1.35
	PASAT _Calc	4.56	6.25	1.50	1.84	1.90	1.66	1.00	1.49
	PASAT _Chk	2.11	3.14	1.10	2.23	0.90	1.29	1.90	2.51
	PASAT _DD	42.22	14.32	50.20	9.35	45.80	12.99	44.60	14.96
6. FLUENCY	ANIMALS	27.33	5.61	29.40	4.99	29.20	6.37	22.50	5.87
	SUPERM	29.44	8.37	34.00	8.40	28.40	5.66	28.40	7.28
	P	19.44	5.15	19.40	4.72	18.10	5.51	15.70	4.79
	M	15.00	4.61	14.20	5.90	17.70	5.70	11.20	2.04
	R	16.33	5.02	15.00	5.19	16.60	4.53	13.40	4.17
	No_e	16.00	4.33	17.30	4.92	14.40	3.31	15.10	4.31

Note. MS= Multiple Sclerosis; Monol= Monolingual; Biling= Bilingual; SD= Standard Deviation; SDMT= Hits at the Symbol Digit Modality Test.

2. TAVEC= Spanish version of the California Learning Verbal Test with the following measures:

L1= learning at first trial; L5= learning at last trial; LT = total learning; B= learning at list B; ST_FR = short-term free recall; ST_CR= short-term cued recall; LT_FR = long-term free recall; LT_CR= long term cued recall; R= repetitions; I_FR= intrusions at free recall; I_CR = intrusions at cued recall; Rexecutive control= recognition trial; FP= false positive responses.

3. BVMT-R= Brief Visual Memory Test Revised, with the following scores:

BVMT_1= learning at first trial; BVMT_2= learning at second trial; BVMT_3 = learning at third trial; BVMT_T= total learning; BVMT_LEARN= learning from third trial minus learning from first; BVMT_LT= long term recall; BVMT_Rexecutive control = recognition trial.

4. 5 DIGITS= Five-digit Test, with the following scores:

READ_HITS = hits for reading task; READ_ERR= errors at reading task; COUNT_HIT= hits for counting trial; COUNT_ERR = errors for counting trial; CHOICE_HIT= hits for choice trial; CHOICE_ERR= errors for choice trial; ALT_HIT= hits for alternant trial; ALT_ERR= errors for alternant trial; INHIB= inhibition score; FLEX= flexibility score.

5. PASAT= Paced Auditory Serial Addition Task with the following scores:

PASAT_Hit= hits; PASAT_OM= missing responses; PASAT_INT= intrusions; PASAT_REP= repetitions; PASAT_CALC= calculus error; PASAT_CHK= chunking response; PASAT_DD= dyads.
6. FLUENCY= fluency task, including with the following scores:
ANIM (animals); SUPERM (items found in a supermarket); P= words beginning with the letter P; M= beginning with letter M; R= beginning with letter R; No_e = words without the letter e.

Appendix B. Criteria for cognitive impairment diagnosis in MS patients

	No. of *Monolingual*	No. of *Bilingual*	*Cognitive areas impaired**	*Z scores*
Controls	10	10	None	None
No cognitive impairment	4	6	None	None
Mild cognitive deficit	3	2	1 or more	-1 to -1.5
Moderate cognitive deficit	3	2	2 or more	-2 or below

*Cognitive areas impaired: SDMT; TAVEC; BVMT-R; 5-DIGIT; PASAT; FLUENCY (see Appendix A)