Evaluation of Cognitive Control and Distraction Using Event-Related Potentials in Healthy Individuals and Patients with Multiple Sclerosis

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Abstract. Multiple Sclerosis (MS) is a disorder of the central nervous system that can result in cognitive dysfunction. Despite the prevalence of cognitive impairments in MS, few studies have directly examined dysfunction in the domain of cognitive control, which involves the monitoring of conflicting stimulus input and response options and the subsequent selection of an appropriate response (and inhibition of inappropriate responses). The present study examined event-related potential (ERP) indices of brain function in MS patients and healthy controls (HCs) for a Go/Nogo Flanker task of cognitive control. The task required participants to respond appropriately to a central target arrow stimulus that was flanked by non-target stimuli that were congruent, incongruent, or neutral with respect to the target. On some trials, a two-sided target arrow was presented, which required the inhibition of a response (Nogo). The Nogo stimulus also was surrounded by flankers (arrow primes or neutral). MS patients had slower reaction times during Go trials compared to HCs. Patients exhibited prolonged latencies for P1, frontal P2, N2, and P3 components compared to HCs. MS patients, compared to HCs, also had a more pronounced anteriorization for P3 amplitude during Nogo compared to Go trials, possibly indicating inhibitory dysfunction. Finally, decreased amplitude was also observed in MS patients compared to HCs for a positive-negative complex with very early latency onset, which may reflect dysfunction in early processing of the flanker stimuli. The findings indicate dysfunction at multiple stages of processing in MS patients during cognitive control.

Keywords: Cognitive control · Inhibition · Multiple sclerosis · ERPs

1 Introduction

Multiple Sclerosis (MS) is a neurodegenerative disorder that can result in demyelination, multi-focal lesions, and cortical atrophy [1–3]. Cognitive impairments are prevalent in MS in the domains of attention, working memory, learning, and executive functioning [4]. Brain structural abnormalities and atrophy in patients are predictive of deficits on tasks of cognitive performance [5–8]. Previous work examining cognitive

impairments in MS has covered a variety of cognitive domains; however, to date, few studies have specifically examined potential deficits in the domain of cognitive control in MS. Cognitive control involves the ability to monitor conflicting response options and the subsequent decision to respond (or inhibit a response) in a context-dependent manner. Selective attention to relevant information and the inhibition of distracting information are involved in this process. Given the profile of cognitive impairments commonly observed and the underlying neuropathology, it is plausible that MS patients may have deficits in cognitive control processes, particularly in inhibitory functioning.

Cognitive control has typically been studied using Go/Nogo type tasks (and also the Stop-Signal task, not discussed here). During a typical Go/Nogo task, participants are required to respond whenever they see a "Go" stimulus (e.g., a green circle) and withhold their response whenever they observe a "Nogo" stimulus (e.g., a red circle). Ongoing electroencephalographic (EEG) data can also be recorded while participants are completing the task, and event-related potential (ERP) measures of stimulus-specific brain processes can be derived. There has been extensive research on ERP measures obtained during Go/Nogo tasks. The P3 and N2 components, in particular, have been observed to be modulated by the demands of cognitive control tasks (for a review, see [9]). The P3 ERP component is a positivity that occurs at approximately 300–500 ms post-stimulus; the N2 component is a negativity observed at approximately 200–350 ms post-stimulus. A consistent finding has been that there is a more frontal-central scalp electrode maxima of P3 component amplitude for Nogo stimuli compared to Go stimuli, for which P3 has a more parietal maxima. This finding has been termed the "Nogo anteriorization" effect and is thought to be an index of response inhibition and/or evaluation of inhibitory processes. A typically frontal-central maximal N2 component has also been observed for Nogo stimuli, but the N2 has been posited to reflect conflict monitoring processes, and not necessarily response inhibition per se [9].

Flanker tasks have also been useful for studying processes that are related to cognitive control, such as selective attention and conflict monitoring. Flanker tasks typically involve the presentation of a central target arrow stimulus that is flanked by non-target arrow stimuli that are either directionally congruent (e.g., →→→), or directionally incongruent (e.g., →←→). Congruent flankers result in faster responding (facilitation of attention), whereas prolonged response speeds are observed when the flankers are incongruent (increased distraction) [10, 11]. Several studies have examined ERPs during a Go/Nogo task with flanker stimuli [10, 11]. In these studies, Go trials had left or right target arrows that had congruent or incongruent flankers; Nogo stimuli also had flankers ("directional primes"). This work suggests that ERPs, including the N2 and P3 components, can potentially be modulated by flanker-target congruency, in addition to inhibitory control requirements. This methodology provides a useful means for examining cognitive control processes such as conflict monitoring and response inhibition while also being able to manipulate the level of distraction created by non-target flanker stimuli.

There have been only a few studies that have examined brain function in MS during Go/Nogo or flanker tasks. MS patients in a functional magnetic resonance imaging (fMRI) study [12] had greater activation of bilateral inferior frontal cortical regions compared to HCs for incongruent trials (incongruent > congruent contrast). In another study [13], participants were presented with congruent or incongruent target/flanker

arrow stimuli. But on a small percentage of trials, the central target arrow turned red after a 150 ms delay, during which participants had to actively inhibit their response, if possible. The authors examined the error-related negativity (ERN), a negative component derived by averaging the EEG data for stop trials where there was an error of commission. The ERN was found to be significantly higher for MS patients compared to HCs. These studies suggest that MS patients may have disrupted brain function during flanker type tasks that require selective attention and inhibitory control.

In the present study, we used a Go/NoGo task that incorporated flanker stimuli to manipulate the level of conflict during the decision making process (Go/Nogo Flanker; adapted from [11]). This task allowed us to examine neural substrates of selective attention, inhibition, and distraction in HCs and MS patients. The task included congruent (facilitation), incongruent (increased distraction), and neutral stimulus types for Go trials; During Nogo trials, directional primes (increased distraction and response priming) or neutral flankers were also presented. Our primary goal was to assess differences in ERP components elicited during different task conditions between MS patients and HCs. We were particularly interested in whether there were differential effects for MS vs. HCs regarding P3 and N2 amplitude and latency during response inhibition (Nogo stimuli). Additional components reflecting different stages of processing were also examined.

2 Methods

2.1 Participants

Participant sample demographics can be found in Table 1. All individuals were tested as part of a larger study on cognitive training. Participants were administered the North American Adult Reading Test to estimate IQ (NAART; [14]). In the present manuscript, pre-training data for the Go/Nogo Flanker task are reported. One of two alternate versions of the task (both with equal difficulty) were semi-randomly administered to participants. Patients with clinically definite MS [15] were tested. The majority of MS patients had the relapsing remitting subtype (N = 10; relapsing progressive, N = 2, secondary progressive, N = 2, primary progressive, N = 1). Fifteen HC participants were semi-randomly selected, keeping demographic characteristics in mind, from a pool of 43 healthy individuals that had participated in the study, to achieve a sample size for the HC group that was similar to the MS group. The HC group participants were selected prior to and separate from any knowledge about behavioral performance and ERP measures and data viability (i.e. noise in the ERP). All participants were screened prior to testing, and excluded from the study if they had psychiatric, neurologic, or medical conditions (other than MS), history of head trauma, hearing problems, uncorrectable visual problems, or learning disorders. All participants provided informed consent and received compensation for participation. The study met the standards of the Internal Review Board of the State University of New York at Buffalo.

Table 1. Participant Demographics.

	Multiple sclerosis			Healthy controls		
	Mean	SD	N	Mean	SD	N
Age	34.73	8.34	15	27.40	4.58	15
Years of education	15.47	1.81	15	17.00	2.56	15
NAART est IQ	105.12	6.69	14	109.70	8.20	15
Years MS	11.53	8.06	15	–	–	–
Gender (% female)	73 %			73 %		

2.2   Go/Nogo Flanker Task

Participants were seated in front of a computer monitor that displayed the task stimuli and were given a four button response pad. Each trial was 2,050 ms long and began with a fixation cross. There was a 1,000 ms inter-stimulus interval. Participants were instructed to press the inner buttons on the response pad with their index fingers if a central target stimulus was a down arrow; press the outer buttons if the central target was an up arrow (equal number of up and down targets; these were Go trials, 70 % of all trials); or to withhold their response if the central target stimulus was a two-sided arrow (Nogo trials, 30 % of all trials). On each trial of the task, the central target arrow stimulus was surrounded by flanker stimuli, which preceded the onset of the target stimulus by 50 ms in order to induce a priming effect. Flanker stimuli then remained on the screen for the duration of target presentation (1,000 ms). See Fig. 1 for a depiction of the flanker/target combinations: For one third of the Go trials, the target and flanker pointed in the same direction (Go Congruent); for another third, the target and flanker pointed in opposite directions (Go Incongruent); and another third of the Go trials had flankers that were rectangles (Go Neutral). Up or down flankers were also presented for 2/3 of the NoGo trials (NoGo Prime trials). The other 1/3 of NoGos had rectangle flankers (NoGo Neutral). There were 250 total trials, and a short practice preceded the task block. Trial types were pseudo-randomly presented. Performance accuracy was recorded for all trials, and RT data were recorded for all Go trials. Measures examined in the present study include percent correct responses and correct response reaction time (RT) for Go Congruent, Go Incongruent, and Go Neutral trials; as well as accuracy and false alarms for Nogo Prime trials.
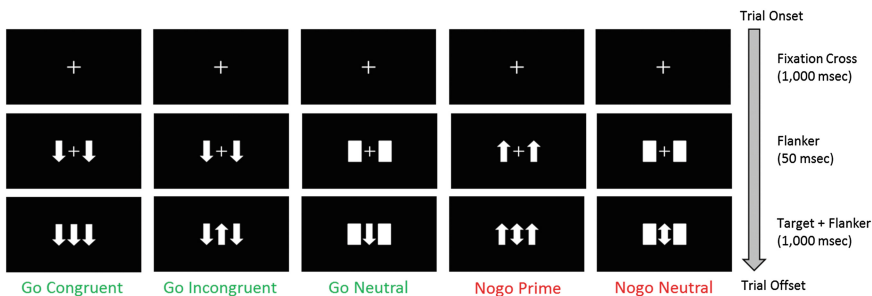

Fig. 1. Go/Nogo Flanker task

2.3   Event-Related Potential Analyses

Participants performed the task in a sound attenuated, dimly lit testing chamber while sitting in a comfortable chair. EEG recordings were obtained during the task using a 256 channel dense electrode array HydroCel Geodesic Sensor Net (Electrical Geodesics, Inc., Eugene OR) using a vertex reference. Impedances was generally kept below 60 kΩ. A bandpass filter of 0.1–100 Hz was applied during EEG recording and data were digitized at a sampling rate of 250 Hz. Data were then processed offline using Netstation version 4.4 (Electrical Geodesics, Inc., Eugene OR). A 25 Hz low pass filter was applied, then data were segmented into 1,100 ms epochs (200 ms prior to target onset, 900 ms post-target onset). Segment categories included Go Congruent, Go Incongruent, Go Neutral, Nogo Prime, and Nogo Neutral trial types. Following segmentation, automated artifact rejection algorithms were run and bad data were removed, as per previously described methods [16].

After automated artifact detection, each trial segment was then visually inspected. Segments that were not rejected using the automated algorithms but were observed to still contain artifact were then marked by the experimenter and rejected from subsequent averaging. Next, electrodes that were marked as bad either via the automated algorithms or by the experimenter were replaced by estimated data that were interpolated from other scalp locations. Data were then averaged for each trial category and re-referenced using the averaged reference derived from all scalp electrodes. Baseline correction was then applied to all averaged waveforms using the 150 ms time period prior to the onset of the flanker stimuli. Four participants were not included in ERP analyses due to excessive artifact resulting in a low trial count in the averaged waveforms. Thus, for all ERP analyses: HC, N = 14 and MS, N = 12. Nogo Neutral trials were not analyzed in the present study due to low trial counts. The average number of trials used to generate the averaged waveforms for the analysis in the present study, after all artifact rejection procedures is as follows: For MS, Go Congruent, M = 42.42, SD = 11.54; Go Incongruent, M = 41.17, SD = 10.55; Go Neutral, M = 42.00, SD = 12.34; Nogo Prime, M = 30.75, SD = 9.58; for HCs, Go Congruent, M = 43.86, SD = 10.54; Go Incongruent, M = 44.93, SD = 7.85; Go Neutral, M = 46.14, SD = 9.44; Nogo Prime M = 35.29, SD = 11.37.

ERPs at three midline clusters of electrodes (Fz, Cz, and Pz) were identified for statistical analyses, corresponding with the 10–20 electrode placement system. Analysis of the electrode clusters was conducted as described previously [16]. P1 and P3 components were observed at all clusters and analyzed accordingly (Fz, Cz, and Pz; see description in Results for additional detail regarding ERPs). P2 and N2 ERP components were observed primarily at Fz and analyses were restricted to this region. An early positive-negative complex at parietal leads (PN_p) was also observed prior to the onset of P1, so analysis for this complex was restricted to Pz. Based on the grand averages across all participants for each condition, windows for these components were applied to each individual participant's ERP data, and an automated algorithm was used to extract the peak amplitude and latency for each component for each subject. The ERP component windows were visually inspected prior to running the peak/latency extraction procedure to ensure that the correct ERP component was selected.

2.4 Statistical Analyses

Independent samples t-tests and chi-square tests were used to analyze demographic differences between groups. Behavioral and ERP data were analyzed using repeated measures ANOVAs. Greenhouse-Geisser corrected values were used in cases where sphericity was violated (noted as "gg corrected"). Partial eta squared (η_p^2) served as estimates of effect size for all ANOVAs. Independent samples t-tests were used to examine differences between groups when probing significant effects. Paired samples t-tests were used for all comparisons between conditions or leads. Alpha level was set at p ≤ .05.

3 Results

3.1 Participant Demographics

MS patients and HCs did not significantly differ on IQ (estimated from NAART performance) or years of education. MS patients did, however, have a significantly higher mean age compared to HCs (p = .006). Chi-square analyses indicated that there were no significant differences between groups on gender proportion, left/right handedness, or ethnicity/race.

3.2 Go/Nogo Flanker Behavioral Performance

Behavioral data were analyzed for all subjects, regardless of their inclusion in the ERP analyses (N = 15 for both groups). Condition (Go Congruent, Go Incongruent, Go Neutral) X Group (MS, HC) repeated measures ANOVAs were used for Go accuracy and RT. For Go accuracy (% correct) there was a borderline Condition effect ($F(2, 56) = 2.765$, p = .072, $\eta_p^2 = .090$), but in general, accuracy was high across all conditions (around a mean of 95 % or greater). For Go RT, there was a significant Condition effect ($F(2, 56) = 63.324$, p < .001, $\eta_p^2 = .693$) and Group effect ($F(1, 28) = 6.266$, p = .018, $\eta_p^2 = .183$; see Fig. 2A). Post-hoc tests indicated a pattern for Go RT in which Incongruent > Neutral > Congruent (p < .001 for all comparisons). The Group effect was observed because MS patients had significantly slower RT compared to HCs, across all Go conditions. MS patients and HCs also did not differ on the number of errors of commission during Nogo Prime trials (false alarms).
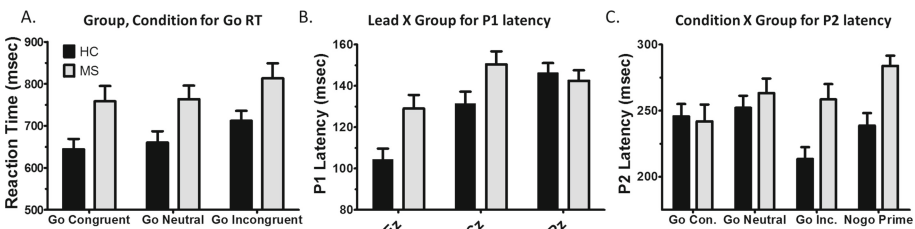

Fig. 2. Response speed and ERP latency effects.

3.3   Event-Related Potential Analyses

Figure 3 shows the grand averaged ERPs for midline electrodes. The P3 component was identified across all midline leads and conditions at approximately 300–600 ms post-target. The P1 component was also identified for all midline leads and conditions at approximately 80–180 ms post-target. The P1 and P3 components were analyzed across all midline clusters (Fz, Cz, Pz). Other components were more restricted to specific cluster leads. An N2 component was identified at frontal scalp sites at approximately 220–380 ms (analyses restricted to Fz). A positive frontal component was also identified at approximately 200–320 ms (P2 component, analyses restricted to Fz). There was also an early positivity and negativity observed at parietal leads, with the positivity peaking at approximately 30–40 ms post-target and a subsequent negatively peaking at approximately 60–80 ms (early parietal positive-negative complex, PN_p, analyses restricted to Pz). The PN_p component occurred prior to the onset of P1, and due to the early onset it may reflect early processing of the flanker stimulus and/or the flanker/target comparison. Condition (Go Congruent, Go Incongruent, Go Neutral, Nogo Prime) X Lead (Fz, Cz, Pz) X Group (MS, HC) ANOVAs were conducted for P1 and P3 amplitude and latency measures. Condition X Group ANOVAs were conducted for the frontal P2 and N2, and parietal PN_p measures.
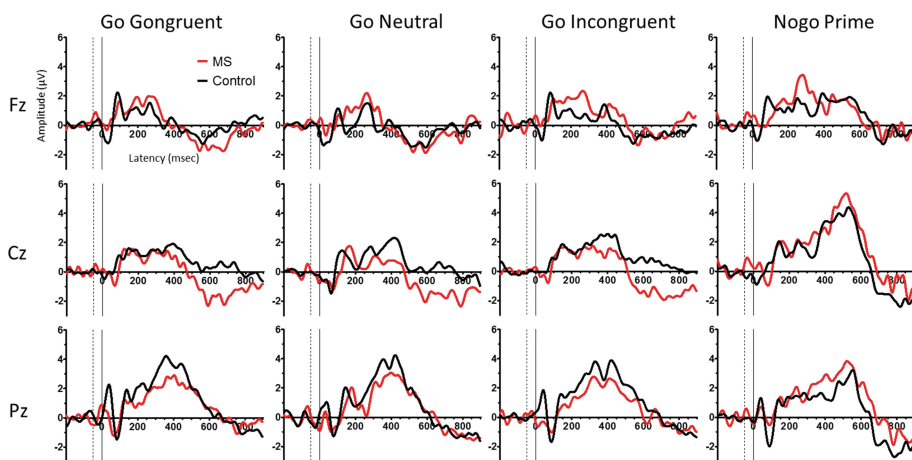

Fig. 3. Grand averaged ERPs for each trial type of the Go/Nogo Flanker task. The dashed line at −50 ms represents flanker onset. The solid line at 0 ms represents target onset. (Color figure online)

P3 Component. The P3 amplitude ANOVA yielded significant Condition X Group (F (3, 72) = 3.364, p = .034, gg corrected, η_p^2 = .123) and Condition X Lead (F(6, 144) = 7.419, p < .001, gg corrected, η_p^2 = .236) interactions. First we probed the Condition X Group interaction (see Fig. 4A and B). There were no statistically significant differences between the groups at any condition. However, it can be observed in the grand averages in Fig. 3, as well as the topographic maps in Fig. 4A that MS

patients tended to have lower P3 Amplitude for Go trials, but higher P3 Amplitude for the Nogo Prime trials (especially at Cz and Pz), compared to HCs. For HCs, P3 amplitude was greater during Nogo Prime compared to Go Neutral and Congruent trials ($p < .05$ for both comparisons). For MS patients, the general pattern was that Nogo Prime > Go Incongruent > other Go conditions ($p < .05$ all comparisons). The Condition X Group interaction therefore appears to be driven by a larger relative difference between Nogo Prime and Go trial P3 amplitude in MS patients compared to HCs.

Next we probed the Condition X Lead effect (See Fig. 4A and C). For the Go Congruent and Go Neutral trials, P3 amplitude exhibited a pattern of Pz > Cz > Fz (parietal maxima, $p \leq .002$ all comparisons). For Go Incongruent trials, P3 amplitude was lower at Fz compared to both Cz and Pz ($p < .05$ both comparisons). For Nogo Prime trials, P3 amplitude was greater at Cz compared to both Fz and Pz ($p \leq .019$ both comparisons). In sum, the Condition X Lead effect for P3 amplitude appears to illustrate the typical Nogo anteriorization effect, wherein Nogo Prime trials exhibited a more anterior P3 amplitude compared to the Go trials.
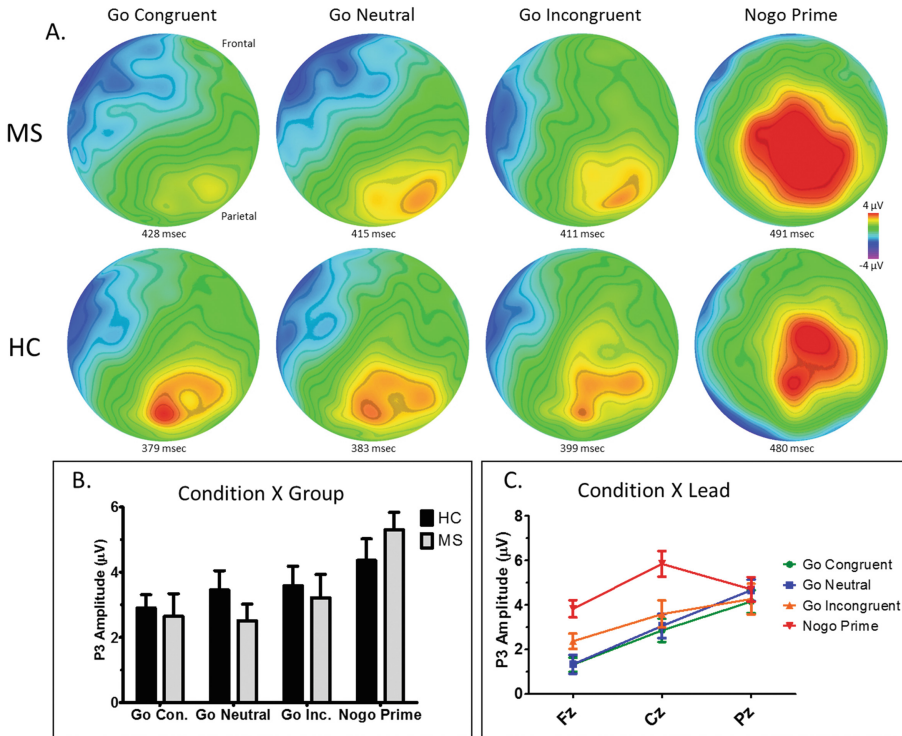

Fig. 4. (A) Topographic maps depict amplitude data above the canthomeatal line. The time point depicted is listed beneath each map (in msec) and corresponds to the group average for that condition. (B) and (C) depict mean and SEM for relevant P3 amplitude effects. (Color figure online)

The ANOVA for P3 latency revealed significant effects for Condition (F(3, 72) = 22.089, p < .001, η_p^2 = .479) and Group (F(1, 24) = 4.644, p = .041, $\eta p2$ = .162). Post-hoc tests revealed that the Condition effect was driven by longer P3 latency for Nogo Prime compared to Go trials (p < .001 all comparisons). Longer P3 latency across conditions in MS patients compared to HCs accounts for the Group effect.

Frontal N2 Component. There were no significant main effects or interactions for the ANOVA for N2 amplitude. The N2 latency ANOVA revealed a significant Group effect (F(1, 24) = 9.486, p = .005, η_p^2 = .283), and a borderline Condition effect (F(3, 72) = 2.426, p = .073, η_p^2 = .092). The Group effect can be accounted for by longer N2 latencies in MS patients compared to HCs, irrespective of Condition (see Fig. 3).

P1 Component. The ANOVA for P1 amplitude yielded a significant Condition X Lead interaction (F(6, 144) = 2.595, p = .015, gg corrected, η_p^2 = .130). Post-hoc tests revealed that P1 amplitude at Fz was lower for Go Neutral compared to Go Congruent and Incongruent trials (p ≤ .008 for both comparisons); whereas P1 amplitude was greater for Go Neutral compared to Go Incongruent trials at Pz (p = .049, see Fig. 3). Notably, P1 amplitude was not different between groups.

For P1 latency, the ANOVA revealed a significant Lead X Group interaction (see Fig. 2B; F(2, 48) = 3.993, p = .025, η_p^2 = .143). There was a borderline Condition X Group interaction (F(3, 72) = 2.448, p = .071, η_p^2 = .093), and a significant effect for Condition (F(3, 72) = 5.228, p = .003, η_p^2 = .179). Probing the Lead X Group effect revealed that MS patients had longer P1 latency compared to HCs at Fz and Cz (p < .05 both comparisons), but not at Pz. Post-hoc tests for the Condition effect revealed that P1 latency was earlier for the Go Congruent trials compared to Go Neutral and Nogo Prime trials (p < .05). There was also a trend for earlier P1 latency for Go Incongruent compared to Go Neutral trials (p = .053).

Frontal P2 Component. For the P2 amplitude ANOVA, there was a significant Condition effect (F(3, 72) = 2.884, p = .042, η_p^2 = .107), but no effect or interaction involving the Group factor. The Condition effect was driven by greater overall P2 amplitude for the Nogo Prime trials compared to the other conditions (p < .05 all comparisons, see Fig. 3). The ANOVA for P2 latency revealed a significant Condition X Group interaction (see Fig. 2C; F(3, 72) = 4.544, p = .006, η_p^2 = .159). MS patients had longer frontal P2 latency compared to HCs for Go Incongruent and Nogo Prime trials (p ≤ .005 both comparisons, see Fig. 3), only. Thus, the interaction for P2 latency appears to be driven by prolonged latencies in MS patients compared to HCs for trials with distracting flankers.

Parietal Early Positive-Negative Complex (PN$_p$). The pronounced early parietal positivity and immediate subsequent negativity of the PN$_p$ appeared to be closely coupled in time, and we were therefore interested in examining this complex as a unit. We derived an amplitude measure for PN$_p$ by subtracting the negative peak amplitude from the positive peak amplitude of the complex for each subject, at each condition. The ANOVA for PN$_p$ yielded a significant Group effect (F(1, 24) = 5.087, p = .033, η_p^2 = .175, see Fig. 3), which can be accounted for by lower overall amplitude in MS patients compared to HCs.

4 Discussion

In the present study we examined ERPs obtained for a Go/Nogo Flanker task in MS patients and HCs. This task allowed for the assessment of conflict monitoring and response inhibition while also manipulating the level of distraction induced by the flanker stimuli. For Go trials, RT was enhanced by congruent flankers and delayed by incongruent flankers, across both groups. However, MS patients had delayed RT in general compared to HCs, across all Go trial types. The ERP results indicated disruptions at multiple stages of cognitive control in MS patients compared to HCs. MS patients exhibited (1) delays in ERP components reflecting early selective attention (longer P1 and frontal P2 latencies), (2) delayed latencies in components reflecting conflict monitoring (N2) and inhibitory control (P3), and (3) alterations in neural resources underlying inhibitory functioning, as evidenced by P3 amplitude effects. Reduced amplitude was also observed in MS patients for an ERP component complex with a very early onset that may reflect initial processing of the flanker stimuli (PN_p).

The Nogo P3 anteriorization effect was observed in both groups (Condition X Lead effect, Fig. 3A and C), consistent with the extant literature [9] and previous work that has used a Go/Nogo Flanker type task [10]. The P3 did not appear to be very strongly modulated by congruency of the Go flanker stimuli (but there were perhaps subtle differences for incongruent trials, see Fig. 4C). While this finding was true for both groups, MS patients exhibited a general attenuation of Go P3 amplitude and an enhancement of Nogo P3 amplitude compared to HCs (Condition X Group effect, see Figs. 3 and 4). Enhanced Nogo P3 amplitude in MS patients may reflect the need for additional recruitment of inhibitory resources to inhibit a response during Nogo trials. Attenuation of P3 amplitude during Go trials for MS patients may mean something different; it could potentially be an index of inefficient processing, altered resource allocation, or decreased resource recruitment, during response selection and stimulus/response evaluation. Further, P3 latency was also delayed in MS patients compared to HCs, across all conditions, indicating delayed central processing speed with respect to stimulus evaluation and/or inhibitory control.

N2 amplitude was not modulated as a function of trial type, nor was it different between groups, contrasting with some previous findings [10, 13, 18]. One possibility for this is that the flankers in our study, which occurred 50 ms prior to stimulus onset, engaged conflict monitoring processes (which are thought to be reflected by the N2 [9]) similarly across conditions. N2 latency, however, was prolonged in MS patients compared to HCs, which may reflect poorer efficiency and/or greater processing time to resolve conflict in MS.

Longer latencies were also observed in MS patients for several other ERP components. MS patients had longer P1 latency at frontal-central leads compared to HCs across all conditions of the task. While it is not typically examined in Go/Nogo paradigms, the P1 component is generally thought to reflect early selective attention and suppression of distracting information [17]. The delay in P1 latency in MS compared to HCs could possibly reflect delays in selective attention to the target stimulus and away from the flankers. The frontal P2 component had a longer latency in MS compared to HCs, but only for the Go Incongruent and Nogo Prime trials, which had the most distracting

flanker stimuli. The delay in P2 latency in MS patient may therefore reflect delayed central processing speed under conditions for which there are incongruent or highly distracting non-target/flanker stimuli. This notion is also consistent with the belief that the P2 reflects selective attention and stimulus evaluation [17].

We identified an early positive-negative complex (PN_p) which emerged prior to the onset of the identified target related P1 component. The positive and negative components of this complex are clearly observed at parietal leads for the HCs, but they seem to be visibly attenuated in the MS group. This observation was confirmed with statistical analysis. This complex has not been examined previously in similar paradigms, but a positive-negative complex with similar timing can be observed in the grand averages reported in earlier studies that used a similar task [11, 18], although no analyses were conducted for these components. Given the timing of the PN_p, one could speculate that it may reflect very early processing of the flanker primes. It may be analogous to a P1-N1 complex, but in this case it may be associated with the flanker presentation, reflecting processing prior to the onset of the target-associated P1. Given the lack of prior research regarding this complex in this paradigm, this analysis should be regarded as exploratory. Further work is required to determine the nature of this complex and whether it may reflect legitimate dysfunction in MS. But it is nonetheless intriguing as a potential early marker of the dysfunction of priming processes in MS patients.

The present study was the first to examine a broad range of ERP components during a Go/Nogo Flanker task in MS patients. There were several limitations, including a relatively small sample size, age differences between groups, and the exploratory nature of some of the analyses (i.e., PN_p). The only previous study that examined ERPs in MS patients using a similar task focused the analysis on the error-related negativity (ERN) during "stop" trials [13]. The present study found that MS patients had longer RT compared to HCs during Go trials. Longer latencies were observed in MS patients for components that reflect early selective attention (P1, frontal P2), conflict monitoring processes (N2), and inhibitory processing/evaluation (P3). Frontal P2 latency delays in MS, in particular, may reflect delayed processing when the flankers are particularly distracting (Go Incongruent, Nogo Prime). Further, the Nogo P3 anteriorization effect was generally stronger in MS patients compared to HCs, likely reflecting a need to recruit additional neural resources to adequately perform the task and inhibit a response. The results demonstrate dysfunction in stimulus evaluation and in cognitive control processes in MS at multiple stages of processing.

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