Anticipatory postural adjustment during gait initiation in multiple sclerosis patients: A systematic review

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Anticipatory postural adjustment during gait initiation in multiple sclerosis patients: A systematic review

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Background: Multiple sclerosis (MS) causes balance and walking disorders. Gait initiation is the complex tran-sition between standing and walking and is characterized by two distinct phases: the anticipatory postural adjustment (APA) phase followed by the execution of the first step phase.
Research aim: To determine alterations in the APA during gait initiation in patients with MS.
Methods: A systematic search was conducted in May 2018. The search was carried out by the use of the following databases: PubMed, Web of Science and the Cochrane Library. The following keywords were used: MS, gait initiation, step initiation, and postural adjustment(s). Outcomes of interest were the variables generally used to assess APA, including electromyography, force-plate data, or video-based data, duration of APA, and length of first step. The Ottawa scale was used to assess the quality of the studies.
Results: Eight case-control studies were included; one was a transverse study. A total of 215 MS patients and 116 healthy subjects were included with ages ranging from 22 to 76 years old. In MS patients, Expanded Disability Status Scale (EDSS) scores ranged from 0 to 7. APA CoP displacements were smaller in the anteroposterior axis. Four studies evaluated muscle activation during APA. The latencies of all muscles were delayed, and smaller magnitudes of muscle activity during APA were found, even in the early stage of disease. The first step was shorter in MS patients than in healthy patients. No previous study has reported joint movement or trunk in-clination during gait initiation.
Significance: This review illustrates the gap in knowledge of APA alterations in MS patients. APA assessment in the early stage of MS could be an interesting measure to characterize balance, dynamic control and risk of fall for such patients.

1. Introduction

Multiple sclerosis (MS) is an autoimmune inflammatory chronic disease of the central nervous system that affects young and middle-aged adults. The pathological and clinical presentations of MS are heterogeneous and include muscle weakness, somatosensory loss, ataxia, visual disturbance that impairs coordination, postural control and gait. Balance disturbance is often described as one of the initial consequence of these symptoms of the disease [1]. This balance disorder increases the risk of falling, contributes to a fear of falling, and reduces activity and social participation in MS patients [2,3]. A recent meta-analysis reported that the fall risk peak may be at the expanded disability status scale (EDSS) score of 4.0 [3]. At this EDSS, patients had also a reduction in walking distance. However, MS patients present postural instability and gait impairments before this stage of the disease [4,5]. Clinical measures of postural instability to determine the predictive value or validity in identifying risk of fall are poor [4,6]. In addition, quantification of orthostatic balance through posturography does not allow to highlight balance disorders at a such early stage of the disease [7]. However, the exploration of the mechanisms of postural instability in MS at early stage of the disease with objective measures is necessary to contribute to prevent fall and to improve rehabilitation of such patients.

Standing on unstable surfaces [8] or under induced somatosensory deficits [9] are means to assess the risk of falling. However, gait initiation is more challenging because of the dynamic postural control necessary to achieve the first step from quiet standing [10]. Gait initiation is characterized by two distinct phases: the anticipation phase

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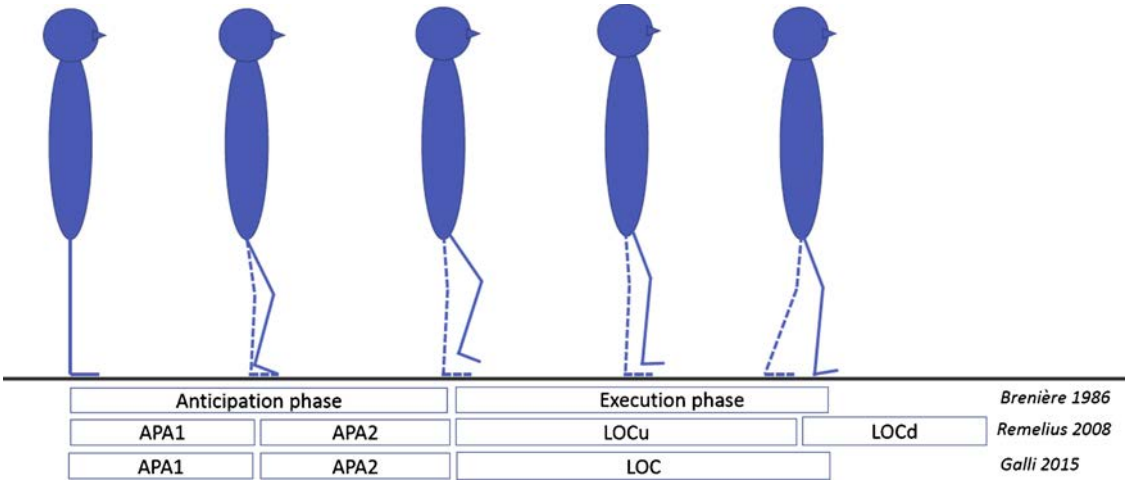

Fig. 1. Gait initiation phases according to Brenière at al.; Remelius et al. and Galli et al.
Abbreviations: APA Anticipatory Postural Adjustment; APA1 the first translation of the Center of Pressure in lateral and posterior directions together toward the swing foot heel; APA2 followed by a predominantly lateral Center of Pressure shift toward the stance foot. LOC locomotor phase; LOCu unidpodal phase; LOCd double support phase.

followed by the execution phase to achieve the first step from a quiet standing posture, presented in Fig. 1 [11,12]. The anticipation phase corresponds to Anticipatory Postural Adjustments (APA) that establish the dynamic conditions to move the body forward by specific motor activations. This necessary and daily repetitive destabilizing task requires the integration of multiple sensory systems (visual, vestibular and somatosensory systems) to develop a specific motor command [13]. Because falling is more common during transition movements [14], gait initiation is often used as an objective measure to evaluate postural instability and risk of fall. Gait initiation, especially APA is commonly used to assess postural instability in other populations such as older people or people with neurologic disorders, as Parkinson's disease (PD). Hence, evaluation of APA can be an objective measure to assess the postural instability of MS patients [15,16]. Currently, APA are still poorly investigated in the MS population, although MS is also a degenerative central nervous system disease characterized by balance and gait troubles. In the present study, the results described in Parkinson's patients will be compared with those found in MS patients.

APA are characterized by muscular patterns and spatiotemporal characteristics that are well identified. During quiet standing, the centre of mass (CoM) vertical projection and the CoP trajectories move together and are phased [17]. Gait initiation programmes induce dissociation of these trajectories through specific motor patterns, creating a disequilibrium torque in the sagittal plane. APA are characterized by a basic motor pattern that induces dissociation between the CoM and CoP trajectories. The motor pattern begins with a bilateral inhibition of the soleus followed by the activation of the tibialis anterior, which generates the posterior CoP displacement towards the initial swing heel [11,12], whereas the CoM moves towards the stance leg. This shift is associated with activation of the swing lower limb hip abductors. During the APA, the flexion of the stance knee is favoured by bilateral inhibition of the soleus and greater ipsilateral tibialis anterior activity, whereas hip flexion is associated with activation of the stance rectus femoris. Finally, from its posterior position, the CoP shifts laterally towards the stance leg. Functional roles are allocated to the displacements of the CoP during APA: displacement along the anteroposterior axis is predictive of motor performance, whereas displacements along the mediolateral axis are linked to postural stability of gait initiation [11,13,18,19].

The literature review of specific impairments in displacements of the CoP during APA in MS patients could allow us to understand and assess balance control in the early stage of the disease. Several studies have assessed APA in MS patients, but to date, no review about APA in this population has been published. The aim of this systematic review is to assess APA during gait initiation of MS patients.

2. Methods

2.1. Search strategy

This review was performed in accordance with PRISMA Guidelines PRISMA (http://www.prisma-statement.org/) Table 1. A systematic search was conducted in May 2018. The search was carried out using the following databases: PubMed, Web of Science, and the Cochrane Library. The following keywords and medical subject headings were used: multiple sclerosis AND gait initiation OR step initiation OR postural adjustment(s). Only articles published in the English language were considered. There was no limit to the year of publication. Articles were excluded if the article was a case report or if the article was not peer reviewed.

2.2. Study identification

The population of interest was MS patients with a definitive diagnosis of MS or clinically isolated syndrome (CIS). Outcomes of interest were the variables of APA including electromyography, CoP and CoM spatiotemporal parameters, kinematics, duration of APA, and ground reaction force. Additionally, the step length of gait initiation was reported to supplement previous data and illustrate the overall gait initiation process.

2.3. Data extraction

An eligibility assessment was performed by screening the title and reading the abstract (Fig. 2). Due to methodological study heterogeneity (differences in procedures to induce gait initiation), there was a lack of comparative data and the meta-analysis could not be performed; therefore, data are presented descriptively. The following data were extracted from selected studies: study design (case-control study, cohort study), population characteristics (gender, age, EDSS, MS form), instrumentation used, devices and procedures for gait initiation assessment (electromyography (EMG), force platform, instruction for gait initiation), reported outcome parameters, study results (CoP and CoM spatiotemporal parameters including displacements, velocity, and acceleration), kinematics, duration of APA, EMG results, and ground reaction force and step length.

Table 1
PRISMA checklist.

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	1
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	2
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	2
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	2
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	2
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	2
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	2
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	2
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	2
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	3
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	NA
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	NA
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	3
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	3
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	3
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	4
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	3-4
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	4-5
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	4-5
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	6
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	6

2.4. Quality assessment

The Newcastle-Ottawa Scale for case-control studies was used to assess the quality of included studies. Each study could obtain a maximum of nine stars: 4 stars for the selection of the study groups, 2 stars for the comparability of the groups, and 3 stars for the exposure or outcome of interest. Two reviewers used the Newcastle-Ottawa Scale checklist to rate the methodological quality. Any disagreements in ratings were resolved through discussion.

3. Results

After a systematic search of the databases, we retrieved 180 articles (Fig. 2). Nine articles were included in this review: 8 case-control studies and one transversal study [16,20–26]. A total of 215 MS patients (132 women, 49 men, sex was not specified for 34 patients) and 116 healthy subjects (76 women, 25 men, sex was not specified for 15 subjects) were included. The sex ratio for controls was similar to that for MS patients. For the 2 studies by Krishnan, the sample of MS patients and healthy subjects was the same; therefore, patients and healthy subjects were counted only once [21,22]. For all the studies, ages ranged from 22 to 76 years old. In MS patients, EDSS scores ranged from 1 to 7. Thirty-seven patients had relapsing-remitting multiple sclerosis (RRMS), 2 patients had secondary progressive multiple sclerosis (SPMS) and 1 patient had primary progressive multiple sclerosis (PPMS), 20 patients presented a Clinical Isolated Syndrome (CIS). The form of MS was not described for 155 patients (72%). In one study, MS patients were divided into 2 groups: fallers (patients with a history of at least one fall during the previous 6 months), and non-fallers [15].

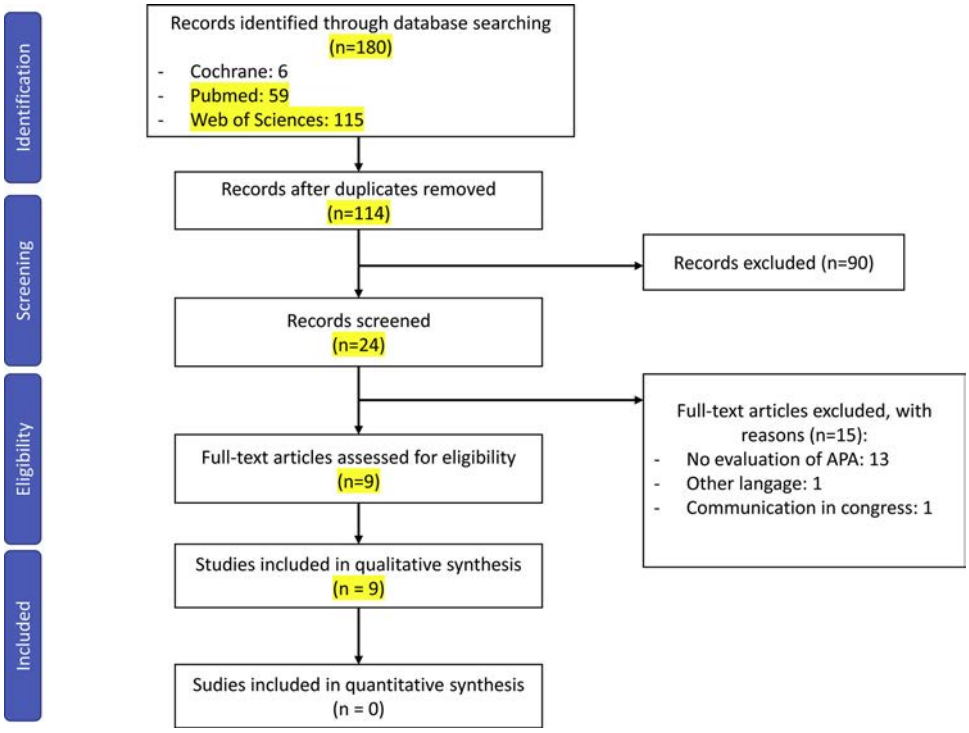

Fig. 2. Flow chart.

Population, procedures, outcomes and results are presented in Table 2.

3.1. CoP displacement, velocity and acceleration during APA

All included studies reported CoP displacements in the anteroposterior direction, and only 3 studies assessed mediolateral direction [20,23,24]. For MS patients, CoP displacements during APA were smaller, especially in the anteroposterior axis. No modification of the CoP displacement in the mediolateral direction was reported. Peak CoP displacements were larger [21,22] and velocity was decreased during APA.

3.2. CoM displacements and velocity during APA

CoM displacements were shorter and velocity was reduced in MS patients [20]. The maximal lateral displacement of the CoM was not significantly larger in MS patients compared to that in healthy controls [20].

Kinematics during APA: no one of the evaluated studies reported data about kinematics during the APA.

3.3. APA duration and APA phase

The duration of gait initiation was assessed in 4 studies [20,23–25]. APA were longer in MS patients. In the dual-task condition, the duration of gait initiation was longer than in the single-task condition [23]. The foot lift-off phase was delayed in the dual-task condition. APA were divided into different phases only in 2 studies, as presented in Fig. 1 [16,20]. The duration of APA2 (*i.e.* lateral translation of the CoP towards the stance limb), especially APA2b (*i.e* second part of CoP translation during APA2), was increased [20] in the Galli et al. study [16]. The velocities of APA1 (*i.e* posterior displacement of the CoP), APA2b and LOC (*i.e* anterior CoP displacement during swing phase) were decreased [16], and the double phase support was longer [20].

3.4. EMG during APA

EMG was reported in 4 studies [15,21,22,26]. The latencies of all studied muscles were delayed, and the magnitudes of muscle activity during APA were smaller. In the Krishnan study [21], subjects were required to perform rapid bilateral shoulder flexion and extension movements while standing on a force platform. MS patients did not present specific patterns of activation of muscles during flexion extension movement for the rectus femoris, soleus and tibialis anterior muscles when compared to healthy subjects (Table 2). In the Tajali study [15], MS fallers presented delayed activities in several muscles (rectus abdominis, erector spinae, biceps femoris and medial gastrocnemius) compared to MS non-fallers and healthy subjects.

3.5. Step length

The first step length was shorter for MS patients [20,23,24]. The effect of the dual-task condition on step length was different between 2 studies [23,24]: Jacobs et al. reported a smaller step length in the dual-task condition, whereas Brecl Jakob et al. did not find an effect of dual-task on step length. Remelius et al. noticed that the first step was wider for MS patients than for healthy subjects [20].

3.6. Testing procedures

Testing procedures were different for all the studies that evaluated APA in MS patients. Procedures included visual and auditory cues, external perturbation or dual tasks (cognitive task or motor task). Three studies analysed APA with a concurrent cognitive tasks [23–25], such as the auditory Stroop task, Brook's spatial memory task, the 2-back verbal working memory task or reciting alternating letters of the alphabet.

3.7. Quality assessment of studies

According to the Ottawa scale checklist, all the studies were of moderate quality. A detailed overview of the quality of the studies is

Table 2
Characteristics of the included studies.

Reference	Population	Intervention/Protocols	Outcome measures	Results	Discussion
Remelius et al. 2008	12 women EDSS mean 4.0 ± 1.4 SD, mean age 54.9 ± 8.5 12 healthy women mean age 52.9 ± 9.3	Subjects stood on the force platform and were instructed to initiate walking when they received a crosswalk signal. Ten markers provided references to joint centres: shoulder, elbow, knee, ankle.	Postural phase (APA1 : start of weight shift towards the swing foot, APA2 : begin at swing foot release and end at swing foot toe lift) Locomotor phase (LOCu : unipodal phase, LOCd : double support phase) CoP, CoM position, velocity and acceleration of CoP, anteroposterior and mediolateral displacements of CoP	In MS patients: Lower velocity in GI, smaller posterior CoP shift made during APA1, shorter first step length, longer GI duration. APA2 and LOCd were longer, and APA1 and LOCu were relatively shorter. Displacements and velocity of the CoM were reduced in MS patients.	MS patients had slower velocity and a smaller posterior CoP displacement during APA. MS patients limited LOCu and lengthening the dual support phase to create a safer stepping strategy. MS patients had different relative timing of APA and locomotor phase which suggested a safer stepping strategy. Smaller and slower CoP displacement decrease the risk of balance disturbance because CoP approach stability boundaries less directly.
Krishnan et al. 2012	11 patients (9 women, 2 men) with RRMS mean age 52 ± 13 EDSS mean 2.3 ± 0.9 11 healthy subjects (9 women, 2 men) age mean 51 ± 14	Subjects stood on the force platform and were instructed to hold a 2,27 kg load between their hands. They were instructed to release the load following an auditory cue « Go ».	EMG on the right side: TA, SOL, RF, ST, RA, ES APA : muscle activity, CoP displacements in anteroposterior direction	The latencies of all the muscles were delayed in MS patients. APA were of smaller magnitudes. APA CoP displacements were smaller and peak displacements were larger.	MS patients presented reduced magnitude of APA, APA were delayed, and CoP posterior displacement was decreased. These alterations could be due to a delayed conduction of information in the central transcortical loop. Alteration of cerebellar function could be induce a increased of magnitude of APA.
Krishnan et al. 2012	11 patients (9 women, 2 men) with RRMS mean age 52 ± 13 EDSS mean 2.3 ± 0.9 11 healthy subjects (9 women, 2 men) mean age 51 ± 14	The subjects were required to perform rapid bilateral shoulder flexion and extension movements while standing on a force platform; 5 trials were performed for each flexion and extension task.	EMG on the following: TA, SOL, RF, BF, RA, ES APA: muscle activity, CoP displacements in anteroposterior direction, CoP peak	The subjects in both groups showed directionally specific changes in the anticipatory activation of muscles. During arm flexion, bursts of activity appeared in ES and no activation in RA. In arm extension, anticipatory activation was shown in RA while there was no activation of ES prior to the onset of the movement. Similar but less pronounced patterns were observed in RF-BF and TA-SOL muscles. No directional specific patterns were observed in RF, SOL, and TA in MS patients when compared to healthy subjects. MS patients showed smaller magnitudes of APA. MS patients showed larger COP peak displacement in both the tasks vs healthy controls.	MS patients with moderate disability were able to produce APA but magnitude of muscles activations were smaller, and directional-specific activations of muscles were reduced. MS patients decreased their CoP displacements suggesting a weak balance control.
Jacobs et al. 2012	13 MS patients (8 women, 5 men), mean age 50 [43-56], EDSS range 2.5 [0-4.5] 13 healthy subjects (8 women, 5 men), mean age 50 [43-57]	Subjects stood on a force platform and were instructed to initiate walking in 3 conditions: cued step initiation, cued forward leaning to the limits of stability and feet in place postural responses to toes-up rotations. Patients performed the postural tasks alone or while also verbally responding to an auditory Stroop task.	Markers were placed to define the head, trunk, upper arms, forearms, thighs, shanks, and feet. CoP displacements (anteroposterior, mediolateral), CoP peak, velocity, step length, APA duration	The onset latencies of the posterior component of the APA were significantly more delayed in the dual-task condition vs the single-task condition for MS patients. The onset of the lateral component of APA was significantly later. APA durations were significantly longer, and foot lift onset latencies were significantly later in the dual-task condition than in the single-task condition in MS patients. Step lengths increased from the single-task to the dual-task condition for the subjects with MS, but step lengths decreased for the healthy subjects.	Regarding differences between groups, MS patients exhibited significantly longer APA durations and significantly later foot lift onset times than the healthy subjects. Sensitivity of APA depended on the method of recording them. APA measure may be more sensitive than the clinical assessment in MS patients with low disability.

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Table 2 (*continued*)

Reference	Population	Intervention/Protocols	Outcome measures	Results	Discussion
Wajda et al. 2014	20 patients (15 women, 5 men) age mean 58.6 ± 10.9 16 RRMS, 2 SPMS MS, 1 PPMS, and 1 individual did not report MS type. EDSS range 4.75 [2.6-6.0]	Subjects stood on a force platform and instructed to initiate walking in response to an auditory cue. During the cognitive challenge condition, the subjects simultaneously recited alternating letters of the alphabet aloud while performing the gait initiation task	Fall history in the previous 3 months. Kinematic parameters of gait initiation were quantified with a walkway which calculate CoP displacements, gait initiation duration, physiological profile assessment	GI was significantly delayed during the cognitive challenge compared with baseline values. Physiological profile assessment scores had a positive correlation with cognitive challenge gait initiation time. Cognitive challenge gait initiation time was primarily related to deficiencies in the leg strength and postural sway components of the physiological profile assessment. Positive correlation was observed between cognitive challenge gait initiation time and fall history in the previous 3 months.	MS patients with mild to moderate disability presented slower gait initiation, and cognitive distraction was correlated to falls and risk of fall. These results suggested that cognitive challenge represent a future target for falls prevention protocols.
Aruin et al. 2015	10 patients (8 women, 2 men), RRMS mean age 52 ± 13, EDSS mean 2.3 ± 0.9 10 healthy subjects (8 women, 2 men) mean age 51 ± 14	Subjects were instructed to maintain upright stance barefoot on the force platform. Pendulum paradigm: A load was attached to the pendulum and impact hand of the subjects. They received a series of perturbations with eyes opened (APA) and eyes closed (CPA).	APA EMG on right muscles: TA, GASL, VL, BF, RA, ES CoP anteroposterior displacements	For APA in MS patients, anticipatory muscles activity occurred closer to the moment of perturbation. The displacement of CoP was less.	MS patients were able to generate APA in response of a predictable perturbation, but the onset of activity muscle was delayed, as in elderly people.
Galli et al. 2015	95 patients (67 women, 28 men), mean age 38.8 ± 9.5, EDSS mean 2.44 ± 1.64 35 healthy subjects (26 women, 9 men), mean age 35.9 ± 13.1	Tests were performed on a force platform. patients were instructed to start walking following a verbal input.	Mediolateral and anteroposterior coordinates of points A (initial CoP position), B (maximal posterior CoP shift), C (maximal anterior CoP shift under swing foot), D (maximal posterior CoP shift under stance foot, and E (final CoP position). Track length of the segments APA1 (between A to B); APA2a (between B to C); APA2b (between C to D); LOC (between D to E); and track velocity and average value considering both mediolateral and anteroposterior displacements in the segments APA 1, APA2a, APA2b, LOC; track duration during APA1, APA2a, APA2b, LOC.	Significant difference were found: CoP displacements were reduced in the anteroposterior axis, velocity of APA1, APA 2a and LOC were reduced, and durations of APA2b and LOC were increased in MS patients. Significant positive correlations were observed between EDSS score and the anteroposterior coordinate of point B, the anteroposterior component of APA1 velocity, APA2b duration and LOC duration. Significant negative correlations were found with Y component of APA2a velocity and anteroposterior component of LOC velocity.	MS patients presented slowing and reduced of CoP displacements, as Parkinson's disease. The reduction of speed of CoP displacement during APA1 and 2a suggested a compensation to avoid the approach of stability boundaries. The reduction of CoP posterior displacement and reduction of speed during APA1 could be due to an incomplete desactivation of the tibialis anterior muscle. These alterations of the initial phase of APA involved a decrease of forward propulsion of CoM and LOC speed. These changes could represent a compensatory strategy to avoid the approach of stability boundaries and limited risk of fall.
Brecl Jakob et al. 2017	20 patients (13 women, 7 men), mean age 33.8 ± 8.5, patients with CIS (optic neuritis), EDSS 1 20 healthy subjects (13 women, 7 men), mean age 33.3 ± 8.5 SD	Neuropsychological tests were performed for all the patients. Tests were conducted on a treadmill with force-plates. Gait initiation was instructed when the bright light turned ON. APA were recorded alone and while dual tasking (Brook's spatial and 2-back verbal working memory)	Neuropsychological tests: TAP battery, SDMT, RFFT, the Stroop colour word interference test APA alone and with dual tasks maximal amplitudes of mediolateral (ML) and anteroposterior (AP) displacement of CoP, the length of the APA, duration, step length MFIS, ABC	47,3% of MS patients performed within normal range on all cognitive measures. Regarding mental tasks, 2b task and Br task significant difference between single vs dual tasking performance in MS patients were observed. Correlations between APA CoP and ML and AP CoP displacement were found in MS patients. Step length in MS patients was shorter. There were no effects of dual tasks on step length.	MS patients with low disability presented a reduced of step length. This change could be a compensation strategy to avoid the approach of stability boundaries during gait initiation. During cognitive tasks, MS patients prioritized motor task to maintain balance, that suggested reduced divided attention capacity.

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Table 2 (*continued*)

Reference	Population	Intervention/Protocols	Outcome measures	Results	Discussion
Tajali et al. 2018	17 MS fallers (one fall during the previous 6 months), mean age 37.1 ± 9.2 EDSS mean 3.8 ± 1.3 17 MS non-fallers mean age 36.4 ± 7.7, EDSS mean 3.8 ± 1.4 15 healthy subjects mean age 31.9 ± 11.5	Clinical balance scales were used: BBS, TUG test, and ABC scale. Patients and controls were instructed to stand barefoot on the force platform. An expected (APA) or unexpected (CPA) external perturbation was applied by an axillary belt connected to a system producing backward pull perturbation.	EMG on the following muscles: TA, MG, RF, BF, RA, ES. APA: muscle activity, CoP displacement	No significant difference was found for clinical balance scales between MS fallers and MS nonfallers. In MS patients, ES muscle activity was significantly delayed than healthy subjects. MS fallers presented a significantly delay in the initiation of muscle activities (RA, ES, RF, BF, MG). The RF and BF activities were smaller in MS fallers than healthy subjects. The MS non fallers had significantly smaller activities in BF and RF. No result of CoP displacement for APA.	Muscle activities were delayed in MS patients. MS fallers initiated significantly later muscles activities than MS nonfallers and controls. The inability to produce efficient APA could explain risk of fall and fall in MS patients. MS fallers presented more deficits in postural adjustment than MS nonfallers.

ABC : Activity-specific balance confidence scale; APA : Anticipatory postural adjustment; BBS: Berg Balance Scale; BF : Biceps femoris; CIS : Clinically isolated syndrome; CoM: Center of Mass; CoP: Center of Pressure; CPA : Compensatory postural adjustment; EMG : Electromyogram; ES : Erector spinae; GASL : Gastrocnemius lateral; GI : Gait initiation; MFIS : Modified fatigue impact scale; PPMS : Primary progressive MS; RA : Rectus abdominis; RFFT : The Ruff figural fluency test; RRMS : Relapsing-remitting MS; SDMT : Symbol digit modalities test; SOL : Soleus; SPMS : Secondary progressive MS; ST : Semitendinosus; TA : Tibialis anterior; TAP battery : Psychologische Test-systeme; TUG: Time up and go; VL : Vastus lateralis. Values in brackets represent the range.

provided in Table 3. Total scores ranged from 5 to 6 stars out of a possible nine stars. No study satisfied all the selection criteria. No study reported information about the selection of a healthy population (selection criteria 3), and no study described the manner in which MS patient data were collected (exposure criteria 1), highlighting potential selection bias.

4. Discussion

This systematic review aimed to report alterations in APA for MS patients. Meta-analysis was not possible because of the heterogeneity between studies in terms of populations, protocols, and outcome measures. This review highlights the fact that all MS patients were able to produce APA. Moreover, alterations of APA were reported, even at an early stage of the disease, and were more important in MS fallers than MS non-fallers [15].

Anteroposterior displacements of the CoP, due to a bilateral inhibition of soleus followed by a bilateral activation of tibialis anterior muscles [12,27], are predictive of motor performance in gait initiation [28]. In MS patients, the posterior displacement of the CoP was reduced at the initial phase of APA, suggesting a reduced motor performance in gait initiation. Nevertheless, anteroposterior displacements of the CoP are linked with the gait initiation speed [29] so the hypothesis of a decrease in gait initiation speed in MS patients cannot be excluded as a mechanical explanation of the altered CoP displacements during the APA. Indeed, the contraction of the tibialis anterior during APA generates sufficient ankle moment to move the CoP behind the ankles and create the disequilibrium required for gait initiation [11]. One can assume that in MS patients, the reduced and delayed muscle activities lead to a lesser ankle moment to move the CoP in the posterior direction. These alterations could explain the reduced initial forward propulsive force and step length in MS patients [20,25]. In 4 studies, the authors attributed these observations to a compensatory strategy to maintain the CoP trajectory away from the posterior stability boundary [16,20,21,24]. Moreover, no study has discussed spasticity, muscle weakness and somatosensory disorders, which are current phenomena in MS [30]. This perturbation could also be due to alterations in joint movements in the lower limb. Lesser and delayed activity of the tibialis anterior muscle or a delayed inhibition of the soleus in MS patients could decrease ankle moment and reduce posterior displacement of the CoP. Moreover, reduced ankle movement could be compensated for by an increase in the duration of APA to generate a sufficient movement to propel the swing leg [31].

Furthermore, trunk inclination is not reported in these studies. Trunk inclination changes the muscle activities in the soleus and tibialis anterior muscles [32]. At an early stage of MS disease, the activity of the rectus abdominis, internal obliques, and lateral flexor of muscles trunk was reduced [33]. Moreover, trunk flexion in MS patients is correlated with gait speed and gait activity [34,35]. Atypical inclination of the trunk induced by motor deficit of trunk muscles could also change APA and anteroposterior displacement of the CoP.

Mediolateral displacement was reported in only 3 studies, and no alteration was found in MS patients. However, these studies included patients at an early stage of disease. Mediolateral displacement predicts the stability of gait initiation and the risk of lateral fall [18,19]. This objective parameter could predict fall risk in MS patients. These reduced and delayed muscle activities in MS patients observed during APA could change the mediolateral displacement of the CoP and the movement of the hip, knee and ankle joints. Indeed, muscle synergy is observed during APA. This synergy generates the disequilibrium torque in the frontal plane. CoP displacement towards the swing foot is due to tibialis anterior activity, which is greater in the stance leg, knee flexion and hip abduction. Alteration of the mediolateral CoP could cause an increased velocity during a medial fall from a single stance due to a larger distance between the CoP and CoM during step execution. The risk of fall could be increased in MS patients if mediolateral CoP

Table 3
Methodological appraisal of studies with Newcastle Ottawa Scale.

	Selection				Comparability		Exposure			Total
	Criteria 1	Criteria 2	Criteria 3	Criteria 4	Criteria 1	Criteria 2	Criteria 1	Criteria 2	Criteria 3	
Remelius et al. 2008	X				X	X		X	X	5
Khrisnan et al. 2012	X				X	X		X	X	5
Khrisnan et al. 2012	X				X	X		X	X	5
Jacobs et al. 2012	X				X	X		X	X	5
Galli et al. 2015	X	X			X	X		X	X	6
Aruin et al. 2015	X				X	X		X	X	5
Brecl Jakob et al. 2017	X			X	X	X		X	X	6
Tajali et al. 2018	X				X	X		X	X	5

displacements are altered.

Similar changes in kinematic, kinetic and electromyographic parameters during APA have been found in the PD population. Reduced CoP displacements (in both anteroposterior and mediolateral axes), delayed muscle activities (especially for the tibialis anterior), longer duration of APA and shorter step length have also been reported [36,37]. These alterations can occur early in the evolution of PD [38] and are considered to be a major pathophysiological mechanism underlying impaired gait initiation. Given these similarities between PD and MS populations, one can reasonably assume that APA alterations significantly contribute to step impairments in MS. This literature review suggests a postural reeducation program, aimed at improving a forward body posture while moving the CoP backward.

In the PD population [36], it has been shown that gait initiation can be influenced by several factors. For example, Rogers et al. (2011) and Nieuwboer et al. (2008) showed that external sensory cues (visual or auditory) improve and facilitate gait initiation in PD patients [39,40]. Moreover, positive or negative emotions modulate gait initiation [41]. The reaction time of gait initiation was longer and step size was shorter in PD patients when they took a step forward in response to an unpleasant image. To the best of our knowledge, external cues or emotions were not evaluated in the gait initiation of MS patients. However, APA tend to be impaired in MS patients when dual-task paradigms are performed during gait initiation, such as in elderly fallers [42], whereas this was not observed in PD [43]. This difference between MS and PD for dual-task paradigms is explained by the cognitive decline of the MS patients, especially in terms of cognitive processing speed, even in the early stage [44], which suggests cognitive-motor interference in MS patients. Cognitive processing speed evaluation during gait initiation would be interesting to include in the assessment of APA at an early stage, but there is no cognitive test recommended for this analysis currently. Regarding these observations, rehabilitation programmes should nevertheless include cognitive-motor tasks, especially at the early stage of MS.

The present review revealed that all the included studies used different protocols to assess APA. This methodological heterogeneity made the results incomparable. Indeed, MS patients had an EDSS score range from 1 to 7, and no information on the form MS was recorded for half of the patients. The Newcastle-Ottawa Scale was used to assess the quality of the included studies. In addition, information about the recruitment of the healthy subjects was not described in all the studies. Consequently, a meta-analysis was not possible due to the different protocols used to assess the APA and the small number of studies with similar outcomes.

5. Conclusion

Alterations of APA are present in MS patients even at an early stage of the disease, principally characterized by a decrease in the posterior displacement of APA and reduced muscle activity of the lower limbs. APA evaluation at an early stage of MS seems to be an interesting measure to assess balance control and risk of fall in these patients. Nevertheless, this literature review highlights some potential improvements to better understand the underlying mechanisms of gait initiation in MS patients at the early stage of the disease. It would also be relevant to better correlate the gait initiation impairments with the risk of falling in MS patients to prevent falls and to adapt rehabilitation programmes at the early stage of the disease.

Declaration of Competing Interest

All authors declare that they have no conflicts of interest.

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