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A systematic review of the gait characteristics associated with Cerebellar Ataxia

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ABSTRACT

Background: Cerebellar Ataxias are a group of gait disorders resulting from dysfunction of the cerebellum, commonly characterised by slowly progressing incoordination that manifests as problems with balance and walking leading to considerable disability. There is increasing acceptance of gait analysis techniques to quantify subtle gait characteristics that are unmeasurable by current clinical methods This systematic review aims to identify the gait characteristics able to differentiate between Cerebellar Ataxia and healthy controls.

Methods: Following systematic search and critical appraisal of the literature, gait data relating to preferred paced walking in Cerebellar Ataxia was extracted from 21 studies. A random-effect model meta-analysis was performed for 14 spatiotemporal parameters. Quality assessment was completed to detect risk of bias.

Results: There is strong evidence that compared with healthy controls, Cerebellar Ataxia patients walk with a reduced walking speed and cadence, reduced step length, stride length, and swing phase, increased walking base width, stride time, step time, stance phase and double limb support phase with increased variability of step length, stride length, and stride time.

Conclusion: The consensus description provided here, clarifies the gait pattern associated with ataxic gait disturbance in a large cohort of participants. High quality research and reporting is needed to explore specific genetic diagnoses and identify biomarkers for disease progression in order to develop well-evidenced clinical guidelines and interventions for Cerebellar Ataxia.

1. Introduction

Cerebellar Ataxias are a group of gait disorders resulting from dysfunction of the cerebellum and associated systems due to inherited and acquired causes. Cerebellar Ataxia (CA) is commonly characterised by slowly progressing incoordination which manifests as problems with balance and walking leading to considerable disability. Cerebellar Ataxias affect more than 10,000 adults in the UK [1], with variable age of onset and disease course.

Gait refers to the cyclic nature in which an individual walks, and is punctuated by consecutive heel strikes. An individual's body type, dictated by their sex, age and any natural physical asymmetries, affects their unique movement pattern [2]. Gait ataxia is clinically recognisable as a wide-based stance with truncal instability and irregular lurching steps, which can result in an increased risk of falls [3]. This can be accompanied or predominated by other symptoms depending on the ataxia subtype [4].

Presently, the principle methods of gait assessment in a clinical setting are through use of subjective rating scales such as the Scale for the Rating and Assessment of Ataxia (SARA) [5]. Although many of these are validated to detect progression of ataxia [6,7], there is evidence to suggest that clinical assessment scales might underestimate the severity of gait changes in CA [8].

Instrumented gait analysis techniques quantify subtle gait characteristics that would not be detected by clinical examination. There is increasing acceptance of the use of gait analysis methods such as 3D motion capture, pressure-sensitive walkways and inertial sensors for the assessment of neurological diseases that manifest with gait changes.

Improved classification of ataxic gait disturbance and definition of biomarkers for disease progression will enable quantification of the effect of novel and existing interventions to improve disease management in Cerebellar Ataxia while also clarifying the disease mechanisms in specific Cerebellar Ataxia subtypes [9].

Early studies using instrumented gait analysis in individuals with

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cerebellar syndromes described the spatiotemporal gait characteristics of Cerebellar Ataxia as: reduced cadence, step and length, gait velocity, and increased step and stride time and stance and swing phases [4,10]. However, other studies provide conflicting results and many report inconsistencies within cohorts. There are currently no guidelines to state the clinically relevant change in gait characteristics.

With technological advances making it quicker and easier to implement gait analysis, studies exploring neurological gait disorders are becoming more prevalent. It is now possible to seek a consensus description of the gait characteristics of Cerebellar Ataxia to explore the inconsistencies between published studies and to guide further research.

By evaluating and summarising the spatiotemporal gait characteristic measured using instrumented gait analysis techniques, this systematic review aims to answer the question: Which gait characteristics are able to differentiate between Cerebellar Ataxia and controls?

2. Methods

Available literature was systematically searched, following a predetermined protocol (PROSPERO 2016: CRD42016042149, Available from http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016042149).

Using the PICOS framework [11] the research question was explored in order to guide design of search strategy and selection criteria. Of interest were studies where straight lined self-paced walking was measured in adults (age 18yrs or older) with Cerebellar Ataxia. Quantification of gait should involve instrumented techniques. Participants were not required to undergo any type of intervention as baseline gait characteristics were of most interest. Where healthy controls were recruited they should be matched for age and gender as a minimum. Studies of all designs were considered, except review articles, if published since 1996 and available in English.

2.1. Search strategy

The search strategy and selection criteria were developed in line with the review questions and agreed on by two researchers (AM, EB). Titles and abstracts of articles within a number of electronic databases (MEDLINE via OVID, psyc-INFO via OVID, PubMed, IEEE-xplore, Cochrane trials library, web of science core collections, and Scopus) were searched systematically implementing MESH search terms and key words where appropriate to combine three search phrases (walking terms (Walk* or gait or Locomotion); measurement terms (Measur* OR assess* OR evaluat* OR examin* OR analysis OR analy*e OR Biomechanic OR kinematic OR instrumented) and ataxia terms (Cerebellar Ataxia OR gait ataxia)) (Supplementary material 1). Searches were completed in July 2016; repeated in November 2016; and the output restricted to those published since 1996 until the search date. Reference lists from eligible articles as well as relevant reviews and systematic reviews were hand searched and studies identified subjected to the same selection criteria. This aimed to reduce any restrictions of the search strategy in uncovering unpublished and published evidence. Records identified were imported into EndNote (Clarivate Analytics); and processed to remove duplicate records and any older articles that remained.

2.2. Study screening process

Article screening was guided by an Inclusion/Exclusion criteria, predefined in line with the research question (Supplementary material 2). Titles and abstracts of articles identified by searches were subjected to the selection criteria by two researchers independently. References were divided between assessors in the interest of time, while 10% of articles were dual-screened to confirm appropriate decision-making and adherence to the selection criteria.

Those articles that satisfied the screening criteria moved on to full text appraisal. This was completed in parallel by assessors and final selections made through discussion. Where articles were suspected or confirmed to report results from identical or overlapping cohorts of patients the earliest or most relevant article was selected for inclusion.

2.3. Data extraction

Study information and gait parameters were extracted from the selected articles and, where necessary, authors contacted to request additional results. All available study information and reported gait characteristics was collated in Microsoft Excel.

Results were converted to common units of measurement, so that all spatial parameters were expressed in terms of metres (m) and temporal parameters expressed in terms of seconds (s). Speed was expressed as metres per second (m/s), cadence as number of steps in a minute (steps/ min) while phases of the gait cycle were expressed as a percentage of the total stride duration (%). Gait variability was reported as either Coefficient of Variation ((CV) defined as Standard Deviation (SD)/mean (%)) or combined Standard Deviation ((cSD) defined as the square root of the mean variance of the left and right steps (cm)) [12].

Where necessary, authors of selected articles were contacted to clarify study details and obtain unreported results. This included requesting mean average and standard deviation of cohort gait characteristics where median and interquartile range was reported and coefficient of variation where other variability measures (such as combined standard deviation) were reported. Articles where information was not made available for assessment following repeated requests were excluded from further analysis despite being potentially relevant studies. Where multiple subgroups were examined in a single study, data were combined to a single result following Cochrane Review guidance [11].

2.4. Data synthesis & meta-analysis

For cohort demographics, descriptive statistics (mean average, standard deviation (SD) and range) will be computed using IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, N.Y., USA)

Meta-analysis was completed in Rstudio (version 3.3.2) [13], using the “meta” package [14]. For parameters where results were available for more than 3 studies, the weighted mean difference (MD), 95% Confidence intervals (CI) and the standardised Z-score for overall effect were computed. Heterogeneity was tested using I^2 statistic, although a single group random effect model (REM) used throughout to give a conservative approach to meta-analysis.

Forest plots were generated to display the comparison of walking gait characteristics in Cerebellar Ataxia and healthy controls from preferred/comfortable self-paced walking.

Studies without control cohorts were included in the meta-analysis but not given any weighting in the calculation of the pooled estimate. To ensure the uniformity of data processing, gait parameters that had been standardised for individual biomechanical features (e.g. leg length or height), were excluded from meta-analyses. For gait variability, only coefficient of variation was reported commonly enough for results to be meta-analysed.

2.5. Quality assessment

Studies that were eligible for inclusion underwent quality assessment to detect risk of bias using an adaptation of the criteria described by Littell et al. [15] (Supplementary material 3). Researcher’s independent findings were compared, and ratings were agreed on through discussion.

3. Results

3.1. Study selection

In total, 1363 records were identified through searches of 6 databases and numerous reference lists (Supplementary material 4). Of the 65 records that were screened as full texts, 21 articles [10,16–35] were selected for data extraction. Due to issues of data availability, 3 articles [20,21,25] were excluded from the meta-analysis.

3.2. Critical appraisal

A summary of the 21 included articles [10,16–35] is displayed in Supplementary material 5. Combined, these reflect gait assessments for 408 patients with established Cerebellar Ataxia and 403 healthy controls, with 44.12% and 48.14% females respectively (Supplementary material 6). Although only 16 articles had control cohorts, controls were always matched to the patient cohort's age and gender. Height and weight were also matched when reported. These clinical studies were completed across 10 countries (9 developed and 1 developing).

Patient cohorts were very often of mixed aetiology, but most (17) stated the specific diagnoses reflected in the group. Gait characteristics of more specific ataxia types were explored in 8 studies [17,18,20,24,26,27,30–32] encompassing Chromosome 16q-linked Autosomal Dominant Cerebellar Ataxia (16q-ADCA), Spinocerebellar Ataxias (SCA1/2/6/14), cerebellar subtype Multiple System Atrophy (MSAc), and Friedreich Ataxia (FRDA). Findings from these studies included: a correlation between plantar pressures and Double Limb Support phase (DLS) in SCA6 compared with MSAc and 16q-ADCA groups [18], a greater improvement with rehabilitative training in CA than afferent forms of ataxia [20] and a longer step length measured in individuals with SCA1/2 than with FRDA [30].

Twenty of the records included, related to published articles, accompanied by one conference abstract. This group of articles contains 2 intervention studies that explored the impact of rehabilitation and training on ataxic gait and 17 prospective observational studies investigating specific gait features of ataxic gait or validating new clinical tools and methods of analysis.

Follow-up assessments were completed in 4 studies, of which two were training studies [19,21] and the third incorporated data as independent samples [17]. The remaining study [23], performed a follow up assessment at 6 months on a subset of the initial cohort (n = 11/51) and identified no significant difference in velocity (the only spatiotemporal parameter reported).

Disease symptoms and balance/gait deficits were rated using clinical rating scales in 17 studies. Most commonly, International Cooperative Ataxia Rating Scale (ICARS) [36] or Scale for the Assessment and Rating of Ataxia (SARA) [5] were implemented, with 8 other rating scales used in the included studies. The ICARS and SARA scores reported confirm that patients included here showed gait difficulties but were still capable of independent walking [5,37]. Use of walking aids was expressly excluded in 14 studies while 11 studies excluded individuals with cognitive dysfunction.

Falls occurrence was reported in just 3 studies [26,28,34] where a higher rate of falls was apparent, with 43.18% (38/88) of those patients reported falling with the last 3–12months. Between these studies, only Schniepp et al. performed analysis exploring gait metrics associated with fall status [28]. They reported that a history of falls is associated with an increased stride length variability and stride time variability which correlates with preferred walking speed.

To track spatiotemporal characteristics of walking, the most commonly implemented gait analysis techniques within these studies were 3D Motion Capture, employed in 9 studies, and Pressure Sensitive Walkways, used in 8 studies. Other techniques used were: triaxial inertial sensors, pressure sensitive insoles, force plates and pressure sensitive treadmill. Within the included studies, all participants completed comparable short gait tasks to assess free unassisted, straight-line, self-determined speed walking in a laboratory setting. Walkway length for different studies was between 2.2 m and 20 m (mean ± SD = 9.1 m ± 3.4 m) and was principally controlled by the equipment type used. Participants walked barefoot in each of the 9 studies where 3D motion capture was used.

Eight studies explored the influence of pace on gait, through trials performed at different walking speeds. Different velocity walking trials were executed in 7 studies [5,16,21,22,24,28,31,32]. Participants within these studies completed walking tasks at a range of speeds between very slow and very fast. Upon full text appraisal, fast-paced walking by patients with ataxia was consistently associated with increased cadence, step and stride length, and swing phase as well as decreased in the stance and DLS phases, compared with preferred- and slow-paced walking. Meanwhile, variability of stride time and stride length, shows a U-shaped curve with the minimal CV magnitude observed in preferred paced walking and highest CV magnitude detected in slow paced walking [28,32].

Although 42 gait parameters were identified, only 14 were reported frequently enough to be explored further through meta-analysis. A summary of cohort mean values for gait metrics can be seen in Table 1.

3.3. Quality assessment

Upon quality assessment, 10 articles were rated "good" with low risk of bias, 10 rated "fair" with some risk of bias (Supplementary material 7). None were deemed to be of "poor" quality and at too high risk of bias for inclusion, but insufficient data was available from one study [25] to reach a full rating. All the published articles clearly stated appropriate research questions and hypotheses, participant inclusion criteria, gait analysis protocols and study findings.

Most (15) of the articles adjusted for confounding variables such as gait speed, or morphological features. Meanwhile, none of the articles provided a power calculation to justify the small cohort sizes.

3.4. Meta-analysis results

The included articles reported several distinct spatiotemporal gait characteristics measured during walking at a self-selected pace. A summary of each study's mean average and standard deviation of gait characteristics outcome with units displayed in Supplementary material 8.

Meta-analysis was completed for 14 spatiotemporal gait parameters extracted from 18 primary studies. Other parameters lacked sufficient evidence to assess between cohort differences. Exclusion of results standardised to leg length or height led to some data being excluded from meta-analysis.

3.4.1. Pace

Walking speed was studied by 14 studies [10,16,17,19,23,24,26–33] and in ataxia (n = 281) preferred walking speed was significantly reduced compared with healthy controls (n = 345) (REM, MD = −0.36 m/s, 95% CI (−0.43, −0.29), $p < 0.01$, $I^2 = 0\%$) (Fig. 1a). Similarly, in the 10 studies that reported cadence (number of steps per min) [10,16–18,23,24,26–28,31] the ataxia cohort (n = 208) demonstrated significantly reduced cadence than healthy controls (n = 267) (REM, MD = −13.28 steps/min, 95% CI (−19.99, −6.58), $p < 0.01$, $I^2 = 99\%$) (Fig. 1b).

3.4.2. Spatial

Step length, was studied by 7 studies [17,19,23,26,30,31,33] and was significantly reduced in ataxia cohort (n = 139) compared to healthy controls (n = 251) (−0.14 m (−0.20, −0.08), $p < 0.01$, $I^2 = 0\%$) (Fig. 2a). Stride length was also significantly reduced in ataxia (n = 94) compared to healthy controls (n = 142) (REM, MD = −0.20 m, 95% CI (−0.36, −0.04), $p = 0.01$, $I^2 = 0\%$) as

Table 1
Summary of Gait Characteristics.
See Supplementary material 4 for gait analysis results from each study. N = number of participants, k = number of articles featured in, results reported as mean average ± standard deviation (SD) (range).

	Cases			Controls			
	N	Mean Average ± SD	K	N	Mean Average ± SD	K	P value
Pace							
Speed (m/s)	281	0.91 ± 0.16	14	345	1.27 ± 0.15	12	< 0.01
Cadence (steps/min)	208	98.68 ± 10.85	10	267	111.97 ± 6.71	8	< 0.01
Spatial							
Step Length (m)	139	0.54 ± 0.09	7	251	0.68 ± 0.06	7	< 0.01
Stride Length (m)	94	1.17 ± 0.01	5	142	1.37 ± 0.04	3	0.01
Base Width (m)	192	0.17 ± 0.04	10	241	0.11 ± 0.03	8	< 0.01
Temporal							
Step Time (s)	42	0.63 ± 0.01	3	158	0.51 ± 0.02	3	0.01
Stride Time (s)	120	1.21 ± 0.06	7	177	1.03 ± 0.04	6	< 0.01
Gait Cycle							
Swing Phase (% cycle)	54	33.92 ± 3.44	4	146	39.25 ± 0.14	3	< 0.01
Stance Phase (% cycle)	57	65.99 ± 2.78	4	161	60.55 ± 0.22	4	< 0.01
Double Limb Support Phase (% cycle)	126	22.50 ± 6.77	7	170	16.76 ± 7.26	5	< 0.01
Variability							
Step Length Variability (%CV)	78	8.96 ± 1.94	5	184	3.07 ± 0.71	5	< 0.01
Stride Length Variability (%CV)	80	6.82 ± 1.70	4	142	1.95 ± 0.24	3	< 0.01
Stride Time Variability (%CV)	116	5.54 ± 1.05	6	187	2.24 ± 0.36	5	< 0.01
Speed Variability (%CV)	40	7.68 ± 4.31	3	148	3.46 ± 0.49	3	0.20

reported by 5 studies [17,24,28,31,32] (Fig. 2b). Meanwhile, walking base width was studied by 10 studies [17–19,24,26–30,32,33] and people with ataxia (n = 192) demonstrated significantly increased walking base width compared with healthy controls (n = 241) (REM, MD = −0.06 m, 95% CI (0.02, 0.10), p < 0.01, I^2 = 0%) (Fig. 2c).

3.4.3. Temporal

As reported by 3 studies [10,17,26], step time is significantly

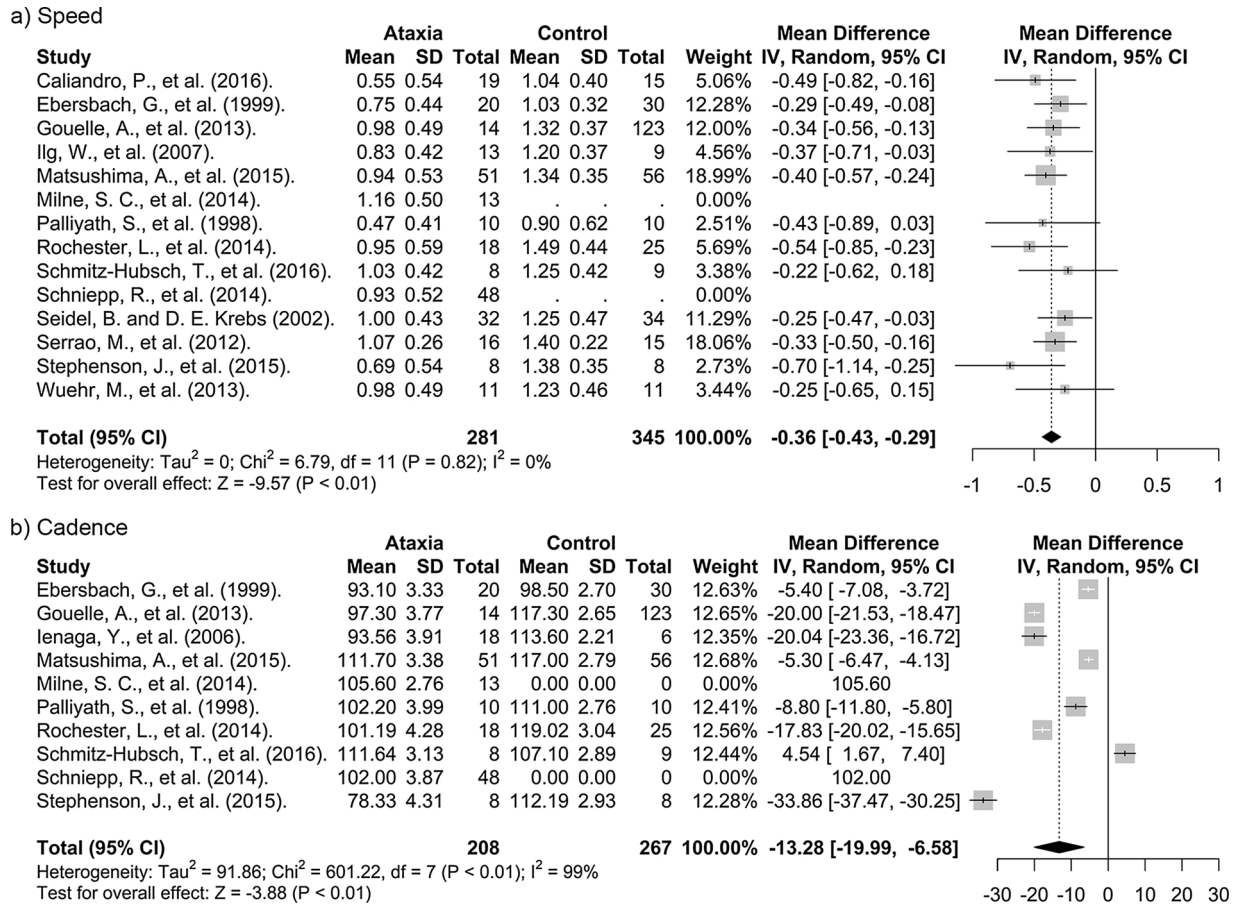

Fig. 1. Pace Domain. Mean difference in a) speed (m/s) and b) cadence (steps per min) during self-selected pace walking.

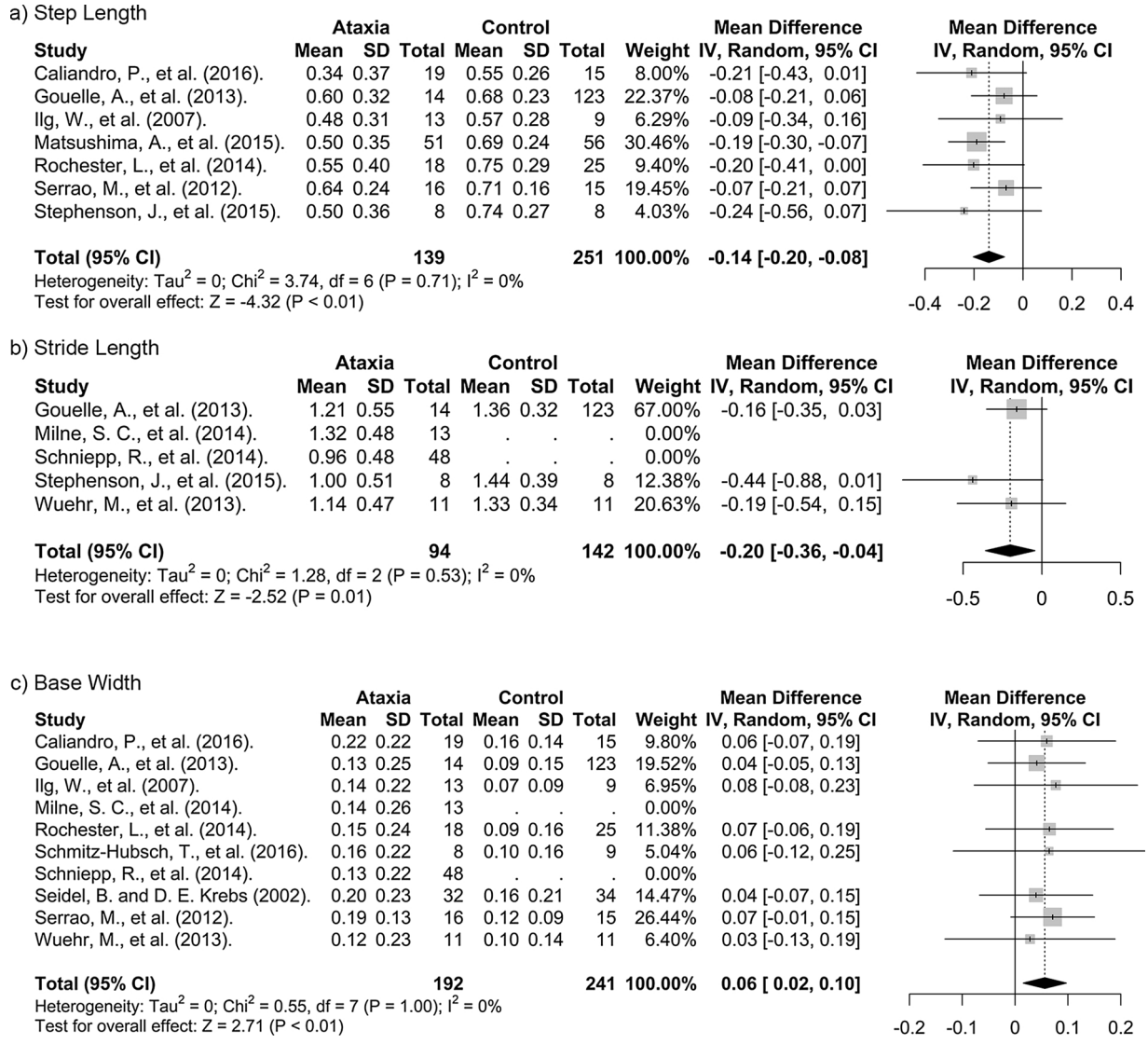

Fig. 2. Spatial Domain. Mean difference in a) step length (cm), b) stride length (cm) and c) base width (cm) during self-selected pace walking.

increased in ataxia (n = 42), compared with healthy controls (n = 158) (REM, MD = 0.11s, 95% CI (0.03, 0.20), p = 0.01, I^2 = 0%) (Fig. 3a). Stride time was studied by 7 studies [10,17,19,27,28,30,32] and overall, the ataxia cohort (n = 120) demonstrated significantly increased stride time than healthy controls (n = 177) (REM, MD = 0.18s, 95% CI (0.08, 0.27), p < 0.01, I^2 = 0%) (Fig. 3b).

3.4.4. Gait cycle

The swing phase of the gait cycle was explored by 4 studies [17,24,31,33]. People with ataxia (n = 54) exhibited a significantly reduced swing phase duration than healthy controls (n = 146) (REM, MD = −5.33%, 95% CI (−9.18, −1.43), p < 0.01, I^2 = 97%) (Fig. 4a). Meanwhile stance phase duration was significantly increased in the ataxia cohort (n = 57) than in healthy controls (n = 161) (REM, MD = 5.44%, 95% CI (2.12, 8.76), p < 0.01, I^2 = 97%) as reported by 4 studies [17,30,31,33] (Fig. 4b). Double limb support phase was studied by 7 studies [17,24,27,28,30,31,33] and the ataxia cohort (n = 126) demonstrated significantly increased double limb support phase duration than controls (n = 170) (REM, MD = 5.74%, 95% CI (3.81, 7.68), p < 0.01, I^2 = 93%) (Fig. 4c).

3.4.5. Variability

As shown in Fig. 5a, variability of step length was investigated by 5 studies [10,16–18,30]. The ataxia cohort (n = 78) demonstrated significantly increased step length variability compared to controls (n = 184) (REM, MD = 5.88%CV, 95% CI (3.42, 8.34), p < 0.01, I^2 = 97%). Meanwhile, variability of stride length was also significantly increased in people with ataxia (n = 80) compared to healthy controls (n = 142) (REM, MD = 4.87%CV, 95% CI (2.29, 7.45), p < 0.01, I^2 = 95%) [10,17,27,28] (Fig. 5b). Variability of stride time was considered by 6 studies [10,16,17,27,28,30], confirming a significant increase in ataxia (n = 116) compared with healthy controls (n = 187) (REM, MD = 3.17%CV, 95% CI (1.97. 4.37), p < 0.01, I^2 = 91%) (Fig. 5c).

4. Discussion

This systematic review objectively evaluated the existing evidence base for the gait characteristics of adult Cerebellar Ataxia. The 21 included studies reflect quantitative gait assessments for 408 Cerebellar Ataxia patients and 403 healthy controls. This forms a larger cohort than typically available in an individual descriptive study. Each individual study confirmed that cohort demographics (age, gender, height, leg length and Body Mass Index (BMI)) were equivalent and no significant differences between cases and control characteristics are present in the meta-analysis.

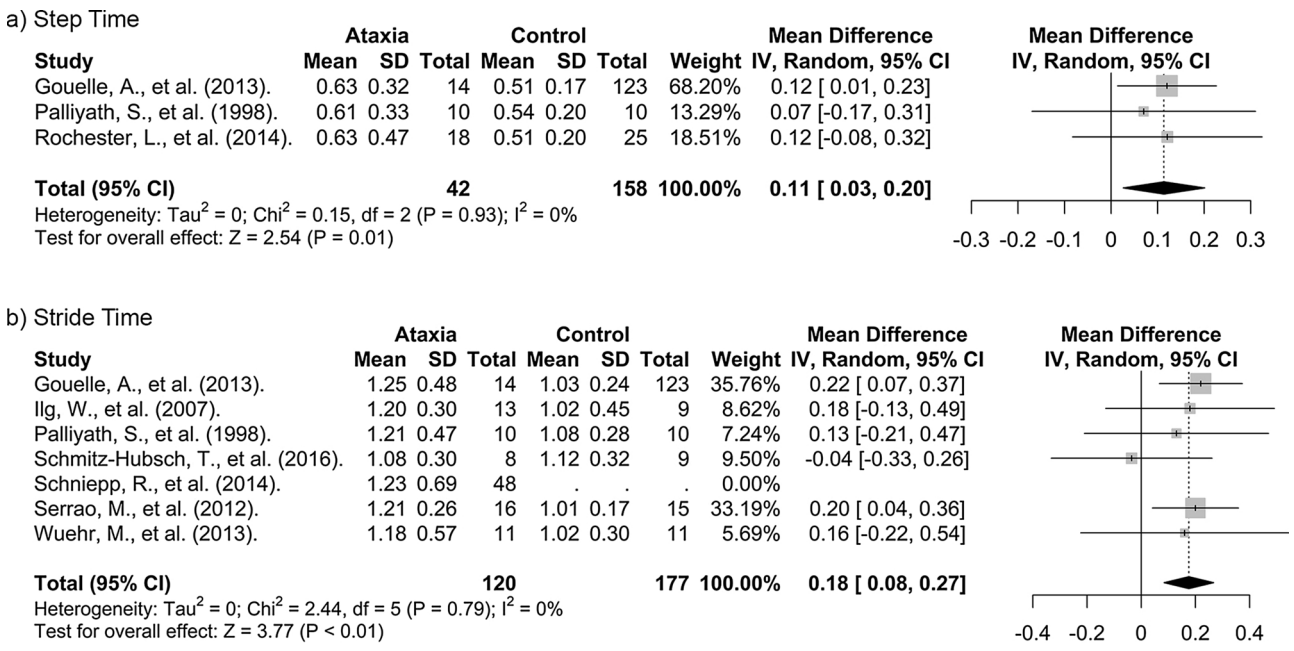

Fig. 3. Temporal Domain. Mean difference in a) step time (s) and b) stride time (s) during self-selected pace walking.

4.1. Headline results

During preferred paced walking, there is strong evidence that Cerebellar Ataxia patients display the following gait differences against healthy controls:

- reduced walking speed and cadence
- reduced step length, stride length, and swing phase
- increased base width, stride time, step time, stance phase and double limb support phase
- increased variability of step length, stride length, and stride time.

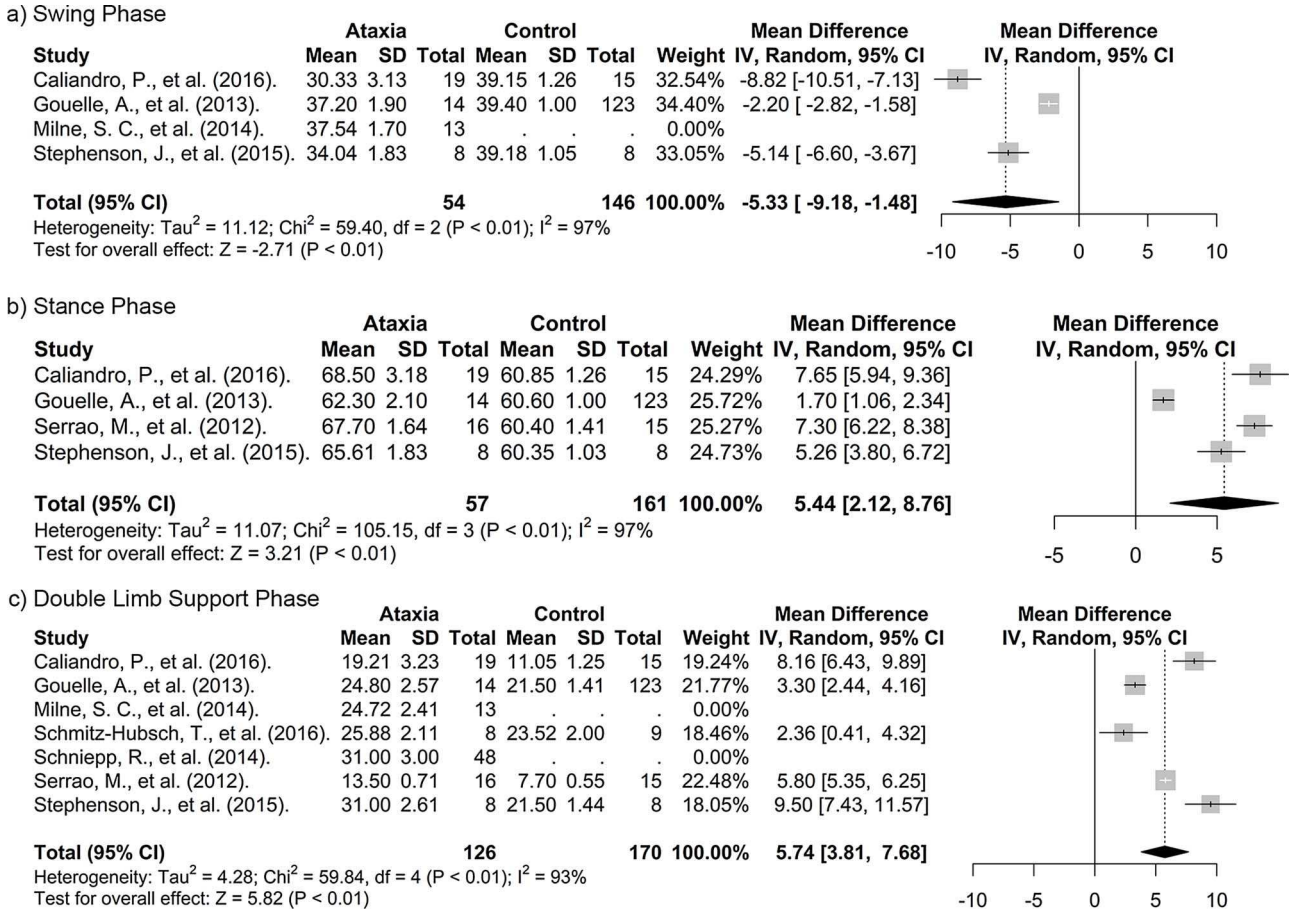

Fig. 4. Gait Cycle Domain. Mean difference in a) swing phase (%), b) stance phase (%) and c) Double Limb Support (DLS) phase (%) during self-selected paced walking.

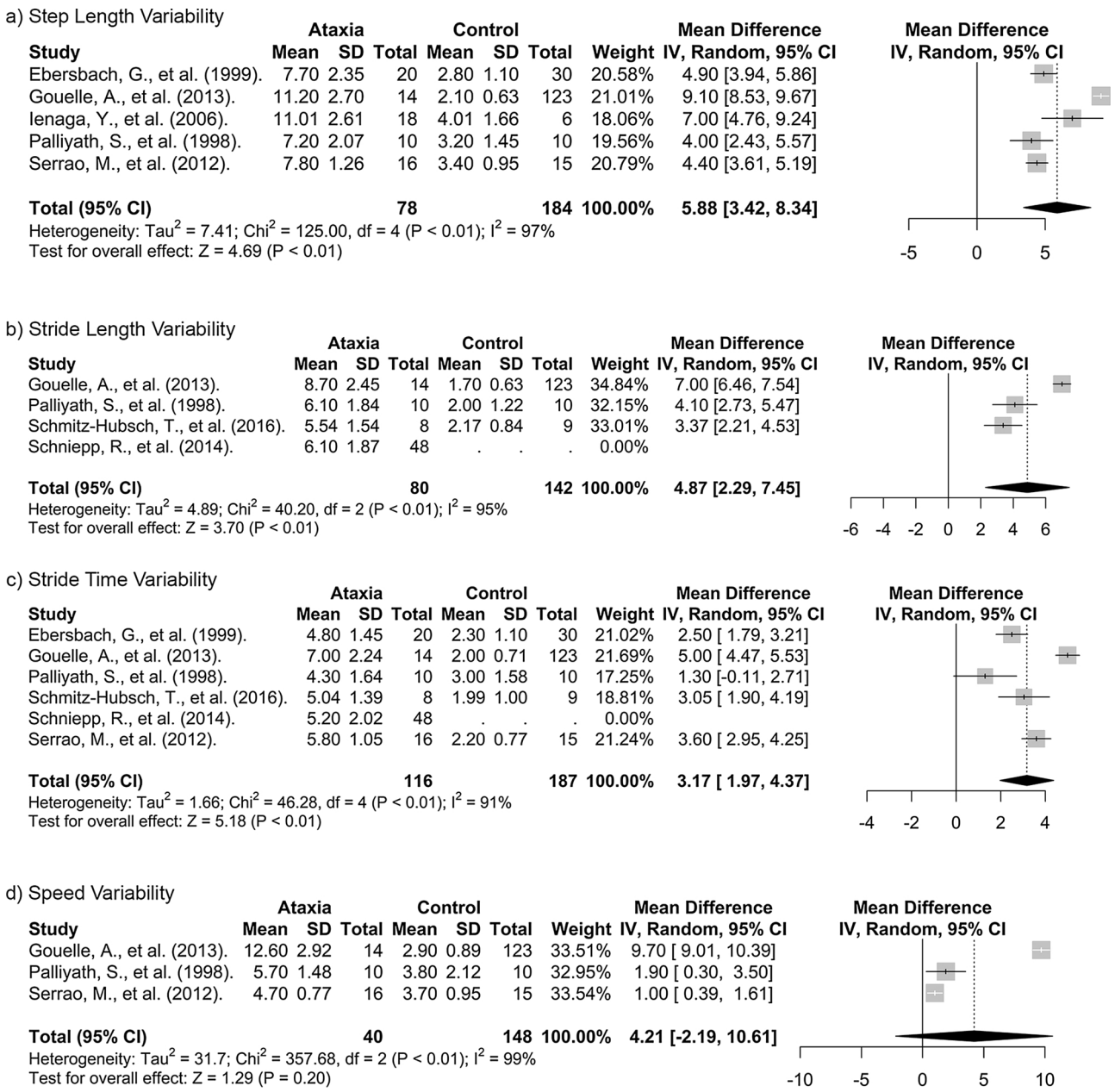

Fig. 5. Variability Domain. Mean difference in a) step length variability (% CV), b) stride length variability (% CV), c) stride time variability (% CV) and d) speed variability (% CV) during self-selected paced walking.

These adjustments were significantly different ($p < 0.01$) and consistently associated with a z-score greater than the 95% critical z-score (1.96). The gait parameters that were greatest affected in Cerebellar Ataxia (in terms of z-score) were Speed, Double Limb Support phase duration (%cycle) and stride time variability followed by Step Length Variability and Step Length. Although this suggests that these may be most useful in clinical practice, further research is necessary to consider a number of contributing factors.

4.2. Implications for practice/Future studies

Our findings corroborate reports that in ataxia gait modifications are employed to compensate for incoordination and trunk instability [38], possibly to reduce the falls risk common to these patients. Reduced velocity of self-selected walking and increased sagittal gait variability [28], as well as widened gait [34] correlate with risk of falls.

It is thought that while increased gait variability directly reflects the dynamic imbalance in Cerebellar Ataxia and is related to the presence of cerebellar damage [30,39], the increased step width, and decreased step length are compensations for trunk instability [30,40].

Although upper body metrics were reported in a minority of studies, there is evidence to indicate that exaggerations in trunk flexion-extension and an increased trunk rotation are present in cerebellar ataxia to increase stability [35]. In this way gait velocity and spatiotemporal parameters are preserved and maintain an energy efficient gait. In cerebellar ataxia, patients display increased trunk instability in all 3 directions but the anterior-posterior direction particularly [3,23,34]. While the overall instability correlates negatively with ICARS score, and positively with disease stage, this anterior-posterior instability may contribute to fall direction [41].

A number of articles report that in ataxia, walking at preferred speed minimises the gait abnormalities and recommend analysis of gait at a wide range of speeds [32]. However, since subjective rating scales incorporating self-selected paced walking remain the main method of

clinical gait assessment, our findings clarify ataxic gait characteristics as they would appear in a typical assessment.

In ataxia patients, with increasing speed walking, gait is characterised by increased cadence, step and stride length, and swing% phase as well as decreases in the stance% and DLS% phases [24]. Meanwhile, a nonlinear correlation is reported in stride time variability and stride length variability, with the highest CV in slow paced walking, and preferred paced walking associated with the minimal CV magnitude [28,32].

Many of these speed-dependent gait changes are also observed in healthy adults [42,43], and are more pronounced with age [44]. However, in controls gait variability is less closely associated with speed changes to allow flexibility and adaptability of walking strategy [45]. Although in Multiple Sclerosis [46], fast paced walking is reported to be more sensitive to gait changes, this complexity makes it less clear whether fast or slow walking is more clinically sensitive in Cerebellar Ataxia. It appears that different compensation strategies are at play in fast and slow paced walking. For instance, while more strongly significant differences have been reported in swing, stance and DLS phase between patients and controls in fast walking, than in preferred paced walking [31], the increased variability of slow paced walking is correlated with to falls risk [28]. However, spatiotemporal parameters of gait measured in slow paced conditions correlate with a fewer number of clinical markers than in fast and preferred paced walking [24].

There is also evidence to suggest that gait has potential to distinguish between neurological gait disorders, differentiate forms of Cerebellar Ataxia and be sensitive to disease progression. For instance, Parkinson's Disease and Huntington's disease, two diseases of the basal ganglia, are also characterised by decreased stride/step length with a reduced walking velocity [47] but have a number of differences from Cerebellar Ataxia and each other. In Parkinson's Disease, cadence remains normal, and a linear relationship between stride length and velocity is maintained, comparable to healthy controls [4,16,19]. Meanwhile gait variability is increased compared with healthy controls but remains lower than in Cerebellar Ataxia [48] although changes to step width are unclear, (either decreased or unaffected). However in manifest Huntington's disease, an increased step width and even more increased gait variability are apparent while stride time is not significantly different from Parkinson's Disease [4,48–50]. However, although a significant increase in width of walking base was found in the meta-analysis reported here, it has previously been suggested that stride width may not a disease specific gait characteristic but a compensation for the instability that occurs in many gait disorders [29]. While it is likely that through objective gait analysis, movement disorders of the basal ganglia can be distinguished from those of cerebellar origin, it is not possible to appraise specific changes across different pathologies from the present dataset [47].

Clarification of the objective differences between forms of ataxia has the potential to improve understanding of the underlying disease. While a number of studies explored the differences between specific forms of cerebellar ataxia there is insufficient evidence to categorically define the interaction between disease type and gait changes. However, there appears to be different gait features present between ataxia subtypes which may relate to the underlying disease differences, such as patterns of cerebellar degeneration, the presence of pyramidal signs and disease duration. This may contribute by affecting components of gait, or the patient's ability to apply compensations. Further work is required to clarify these interactions and their influence on falls status and link to clinical markers [24,41].

The studies included here that explored longitudinal gait changes were not sufficiently able to provide a conclusive description of gait disturbances with disease progression. However, follow-up studies to two others included here have recently been published [51,52]. In Friedreich Ataxia (FRDA) and mixed CAs, at 2 year and 4 year follow-up assessments respectively, these also reported reduced gait speed, an increase in gait variability, cadence and stride length, and step length as well as reduced swing and increased DLS phases. In comparison with baseline characteristics, these gait compensations and changes reflect an increase in postural instability with disease progression. Interestingly, these studies also observed that gait variability was able to predict loss of independent gait, and disease severity (measured by Friedreich's Ataxia Rating Scale (FARS) or SARA) was significantly different at follow-up from baseline, FARS scores changes did correlate well with objective gait characteristics, while SARA scores did not. Due to the complex nature of these findings, further assessment of the objective gait characteristics within a longitudinal study is required to clarify impact of disease progression on different cerebellar ataxia subtypes.

4.3. Strengths & weaknesses

In assessment of the methodological quality, all included studies were considered suitable, although some limitations were apparent. Findings should be interpreted in the context of its strengths and weaknesses.

Many studies considered confounding variables and all completed concurrent cohort assessments in an appropriate trial protocol for instance walkway lengths were relatively consistent between studies and mostly considered long enough to analyse a sufficient number of steps collected from steady state gait. Gait metrics were mostly well-defined and findings, research questions and inclusion/exclusion criteria were clearly reported. Study populations were usually well-defined and cohorts were representative and evenly matched for age, BMI and gender to restrict their influence on gait parameters. Patients with non-clinically "pure" ataxia were commonly excluded to avoid involvement of other neurological systems.

There are several limitations of the included studies that should be taken into account. Primarily, heterogeneity analysis revealed disparity between studies in meta-analyses for cadence, Swing (%cycle), Stance (%cycle), Double Limb Support phase (%cycle), Step length variability, Stride length variability, Stride time variability and Speed variability, but large within-study variability in the remaining variables (Speed, Base width, Stride length, Step length, Step time, Stride time).

The comparative rarity of Cerebellar Ataxia in the general population can lead to recruitment difficulties in observational clinical studies, and in fact many of these studies recruited in less than fifteen participants per cohort (on average, 19.43 (± 11.33) patients and 25.19 (± 29.03) healthy controls in each study). It is essential that studies report a sample size justification and attempt to reach statistical power where possible in order to reliably determine precise differences between cohorts.

Meanwhile, some intervention studies did not assess healthy individuals as control participants, as might be expected. In addition, a number of the studies reported results for specific parameters of interest and did not consider all possible parameters of gait despite possible associations.

Many of the patient cohorts were either not fully characterised in terms of diagnosis or several ataxia subtypes were grouped despite potential differences in the ataxia syndrome [53]. Disease severity was inconsistently characterised with a variety of rating scales employed. Most of the patients studied completed the walking task unaided, reflecting the relatively low disease severity in the cohort. This is a common problem in gait analysis studies as more severely affected patients are unable to take part without additional support.

One important consideration is the influence of technical restrictions of equipment on study design, walking protocol and parameter definitions. This impacts the length of walkway, whether participants complete the walking task barefoot and the ability of participants to reach steady state walking pace and can affect walking characteristics [54,55]. Also it should be noted that, despite studies validating equipment and techniques, differences in analytical approach may affect the results attained.

Unfortunately, due to limitations of the dataset it is not possible to

formally explore the influence of distinct confounding influences such as ataxia diagnosis type separately from equipment used, the correlations between upper body and spatiotemporal gait parameters, or the effect of changing velocity or disease progression on gait characteristics.

In addition, some articles did not report the full results of gait parameters analysed, opting to present a combined measure, or secondary analysis for example, the results of correlation analyses or the variability of gait parameters. However, several authors made additional data available for this systematic review.

Due to the heterogeneous nature of clinical studies, these were not deemed to be fatal flaws but informed restrictions on data included in meta-analysis. To overcome protocol differences and the influence of changing gait strategies with speed, only spatiotemporal gait characteristics measured using instrumented gait analysis techniques during preferred-paced straight-line walking in a laboratory setting at baseline assessment, were considered and standardised data excluded from meta-analysis.

Meanwhile, it should be considered that in walking gait, many characteristics are inherently interdependent. Therefore while they were each considered separately here, step/stride periods, and swing/stance/DLS phases inevitably contribute to each other [43,56]. Also, although results were excluded from meta-analysis where for contributing factors such as gait velocity and biomechanical features were controlled through standardisation, it is important to bear in mind that these do influence gait characteristics in the individual.

4.4. Closing statement

This systematic review provides a consensus description of the gait characteristics of Cerebellar Ataxia in a larger cohort than possible in a typical descriptive study.

It seems that due to trunk instability, in Cerebellar Ataxia an increased gait variability occurs. To compensate for this, walkers increase the width of the base of support, take smaller steps and increase the duration of foot contact to floor, sacrificing swing phase. They progress forward slower, with a lower cadence and preferred walking pace. The significant differences in spatiotemporal parameters uncovered by our meta-analysis reflect the considerable gait disability seen in these patients compared with healthy controls. These changes lead to an increased risk of falls and have potential as markers of disease progression due to the sensitivity to progression.

Advances in technology, have enabled gait analysis techniques to be more widely employed and genetic testing is also more readily available [57,58]. To accompany this, an increase in the quality of research and reporting in the future is needed to aid clinical decision making. Key criticisms such as studies lacking control cohorts, small participant numbers and specific genetic diagnoses should be addressed in future research.

Author contributions

EB – All aspects of study design and progression including data acquisition, analysis and interpretation and manuscript drafting and revision.

AM – Study conception and design, acquisition and interpretation of data, manuscript development and revision.

CM – Study design and interpretation of data, manuscript revision.

Conflict of interest statement

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.gaitpost.2017.11.024.

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