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A Review of Gait Disorders in the Elderly and Neurological Patients for Robot Assisted Training

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A Review of Gait Disorders in the Elderly and Neurological Patients for Robot Assisted Training

Abstract:

Purpose: Ambulation is an important objective for people with pathological gaits. Exoskeleton robots can assist these people to complete their activities of daily living. There are exoskeletons that have been presented in literature to assist the elderly and other pathological gait users. This article presents a review of the degree of support required in the elderly and neurological gait disorders found in the human population. This will help to advance the design of robot assisted devices based on the needs of the end users.

Methods: The articles included in this review are collected from different databases including Science Direct, Springer Link, Web of Science, Medline and PubMed and with the purpose to investigate the gait parameters of elderly and neurological patients. Studies were included after considering the full texts and only those which focus on spatio-temporal, kinematic and kinetic gait parameters were selected as they are most relevant to the scope of this review. A systematic review and meta-analysis were conducted.

Results: The meta-analysis report on the spatio-temporal, kinematic and kinetic gait parameters of elderly and neurological patients revealed a significant difference based on the type and level of impairment. Healthy elderly population showed deviations in the gait parameters due to age, however significant difference is observed in the gait parameters of the neurological patients.

Conclusion: A level of agreement was observed in most of the studies however the review also noticed some controversies among different studies in the same group. The review on the spatio-temporal, kinematics and kinetic gait parameters will provide a summary of the fundamental needs of the users for the future design and development of robotic assistive devices.

Keywords: Pathological gait, Biomechanics of gait alterations, Elderly gait, Exoskeleton robots, Gait disorders

1. Introduction

Neurological conditions are the most common causes of gait disorders that affect people to perform activities of daily living independently [1]. These common conditions and the diseases associated with them include Parkinson disease (PD) which progresses over time and mostly found in older people [2], group of Ataxia (AT) patients are included that are mostly linked to difficulty in balance and walking [3, 4], people with a condition known as cerebral palsy (CP) is also a part of this study which is found in young children. This is due to the loss of proper muscle coordination in CP patients [5]. Limited sagittal plane motion and crouch gait is associated with CP [6]. Group of neuropathy patients are included that are linked to nerve problems causing weakness. A group known as Charcot Marie tooth (CMT) disease also falls under neuropathy group that linked to damage to the peripheral nerves is also a part of this study [7, 8, 9]. There are some conditions apart from the above described cases that lead people to hemiplegic (one side affected) or diplegic gait (both sides affected) [10]. Major incidences reported by elderly population are the frequent falls and as a result of its consequence, some aspects of the movement are affected [11]. They are described as the principal causes of the accidental deaths in the elderly [1]. There is also a slight divergence of gait associated with ageing and this irregularity can also lead to an impaired gait as a result of falls [12].

The assessment of gait impairment requires a clear distinction of pathological findings from the normal. To the authors' knowledge, no previous study has been done that takes into account a wide variety of neurological gaits together with the elderly gait to assess the biomechanical gait deviations associated with them. The aim of this review is to highlight the biomechanical gait deviations associated with elderly and neurological patients. The knowledge of these deviations is important so that robot assisted devices could be designed based on the needs of the individual users. An assistive exoskeleton is a wearable device that is provided with actuators at the joints and is worn by the human [13]. An exoskeleton is able to assist the user based on its requirements. It has been observed that a simple use of cane can significantly improve gait parameters when compared with those walking without a cane [14]. Therefore, with the use of exoskeletons, the level of performance is greatly increased [15]. There is a need to develop a systematic approach and to thoroughly investigate the biomechanical gait parameters of elderly and neurological patients to highlight the assistance required in each category. The study forms a basis in evaluating the assistance requirement among different clinical population. There has been a lack of study highlighting the lower limb support requirement by the end users of the robot assistive devices which emphasises the need of this study. The requirements of the users identified through this review will set up a design criteria for robot assisted devices, which is critical in order to make sure the devices to be developed are fit for purpose.

2. Methods

2.1 Literature search process

The articles in this review were obtained from various electronic database sources including Science Direct, Springer Link, Web of Science, Medline and PubMed. The search was systematically performed by the first author during the month of July-August 2017 reporting studies on biomechanical gait parameters of elderly and neurological patients. The search was restricted to articles published during the year 1985-2017. The keywords used for the search were Elderly, Parkinson, Ataxia, Cerebral Palsy, Charcot Marie Tooth, Neuropathy, Hemiplegia, Diplegia, Gait parameters, Kinematic and Kinetic characteristics, Robot assisted training, and Exoskeleton robots. The Boolean operator used –AND/OR. Full text articles were selected from the aforementioned duration.

2.2 Data collection process and criteria

A total of 2245 records were identified from all of the mentioned database sources, out of which 1843 were obtained after removing duplicates. The total records initially screened for abstract/title were based on the question 'Did the study reported at least one of the biomechanical areas of interest?' The articles that remained relevant after initial screening were reviewed for full text (n=102) and excluded those that were not containing the required sufficient data. Studies were selected based on the inclusion/exclusion criteria shown in Table 1. The selection of the studies was completed after reading full texts. Studies with a focus on spatio-temporal, kinematic and kinetic parameters were selected.

2.3 Search Results

The flowchart of the extensive literature search is outlined step wise in Figure 1. Studies were included in the review if they reported at least one parameter of interest in the three biomechanical areas of interests.

2.4 Assessment of Quality of Studies

The quality of the studies were assessed using a quality assessment tool developed by Downs and Black [16]. The overall scoring was done on 27 aspects however 11 questions in the Downs and Black assessment tool were found not relevant to the current reviewed articles. Therefore, a modified version of this tool was obtained which included 16 domains and the quality of the study was classified as poor (1-6/16), fair (7-12/16) and good (>12/16). The overall score of a study for each domain obtained during the assessment is shown in Table 2.

2.5 Data extraction

The process of data extraction was performed by the first author. All the extracted data from studies were entered into tables for easy comparison and grouping. Demographic characteristics of participants (number of participants, age, height, weight), and

inclusion/exclusion criteria used by this study were recorded. If the data from any study was identified as missing, an attempt was made to contact the authors for the missing data but if the authors did not respond, the articles were excluded from the review. Studies that reported the outcome measure of interest were included for statistical analysis.

2.6 Statistical Analysis

The data was transformed into standardized units for comparison and analysis. The demographic variables were calculated as means with standard deviations. The meta-analysis using forest plot was performed on each individual outcome measure which is reported in the results section. Since the review articles contained participants from different neurological conditions and the sample size was also not equally distributed, therefore random effect model was used in the forest plot that computes the combined effect of the distribution. The results were reported as mean differences with 95 % confidence intervals and p values. The heterogeneity was calculated using the I^2 statistic.

3. Results

3.1 Search results

There were 2245 articles that were initially obtained when performing the search, however only 39 articles were finally selected for review. There were reasonable backgrounds for excluding the articles such as inappropriate title, use of inappropriate comparison groups, unsuitable study design, missing data and other irrelevant data. Several studies investigated on more than one study area. Spatio-temporal characteristics were reported by most of the studies, however there were only few studies that recorded kinetic variables.

3.2 Quality of studies

The majority of studies selected in the review were of good quality as assessed by the assessment tool of Downs and Black [16] given in Table 2. No study obtained an overall score of less than 6. Few studies fell under a score of fair while majority of studies were having a score of more than 13. The difference between the fair and good quality studies was due to the fact that some of them reported the exact value of p rather than reporting the approximate values. Additionally, they described the demographic and exact sites of the selected participants.

3.3 Characteristics of Subjects

The participants included in this review were categorized as elderly group, neurological group and the comparison healthy control group. The elderly participants included were fit without any previous known disorder. The characteristics of the participants are reported in Table 3. The participants that form part of the comparison group were the age matched control group without any previous known disorder. The gait data from physically fit individuals were used as a reference benchmark to obtain the level of impairment among different groups.

3.4 Subject recruitment strategy

The subjects were recruited from a variety of sources as documented by the studies. These included hospitals, community outpatients and volunteers. The healthy subjects recruited in some cases were on voluntary basis.

3.5 Outcome results

The variables of interest found in the majority of studies were spatio-temporal, kinematic and kinetic parameters. These variables are discussed in detail in the next section.

3.6 Spatio-temporal characteristics

Gait speed

Gait speed was reported by four studies for elderly [17, 18, 19, 20] and many of them described for different neurological patients. These include ten studies for Parkinson [21, 22, 23, 24, 25, 26, 27, 28, 29, 30], five for Ataxia [4, 25, 31, 32, 33], four for Cerebral palsy [6, 34, 35, 36, 37], three for Charcot Marie Tooth [38, 39, 40], four for Neuropathy [41, 42, 43, 44], four for Hemiplegia [14, 45, 46, 47] and four for Diplegia group [48, 49, 50, 51]. The meta-analysis report on gait velocity for elderly showed a significant difference when compared with the young group. The gait velocity in elderly was reported as significantly lower than the young control group. The heterogeneity among the studies were $I^2 = 4\%$ (Figure 2a). When gait velocity was observed among different neurological patients, it was reported significantly lower in all of the patient group types. The overall heterogeneity among the neurological group studies was reported as $I^2 = 92\%$ (Figure 2b).

Stride length and Cadence

By observing the studies in the elderly group [17, 18, 19, 20], the meta-analysis report on stride length recorded significantly lower value in the elderly group (Figure 3a) whereas cadence was observed to be higher in elderly patients (Figure 4a). The heterogeneity among the studies for stride length and cadence were less $I^2 = 5\%$ and $I^2 = 21\%$ respectively. These parameters when observed in the neurological group, it was reported as significantly lower when compared to the healthy control group. Only CMT and hemiplegia group showed insignificant difference in the stride length as observed in Figure 3b whereas the cadence in the cerebral palsy patients was reported to be higher than the healthy group (Figure 4b). The overall heterogeneity among the neurological patients were 90 % for stride length and $I^2 = 79\%$ for cadence.

3.7 Kinematic characteristics

Hip range of movement (ROM)

The meta-analysis report on hip range of movement (ROM) included three studies for elderly group [17, 18, 20] and the individual studies for neurological group included Parkinson [21, 22, 25, 26, 28, 29, 30], Ataxia [4, 25, 31, 32, 33], Cerebral palsy [6, 34, 35, 36], Neuropathy [42, 52], Hemiplegia [46, 47, 53] and Diplegia [49, 50, 51, 54]. The studies on the elderly group reported lower ROM (mean difference as -1.79, 95 % CI -5.63 to 2.05, p=0.36) as compared to the young group with $I^2 = 78\%$ heterogeneity but it was not reported to be significant (Figure 5a). The seven studies that reported for Parkinson disease [21, 22, 25, 26, 28, 29, 30] also observed a significant lower hip ROM in the elderly group, though the heterogeneity was $I^2 = 64\%$. The five studies for Ataxia group [4, 25, 31, 32, 33], four for Cerebral palsy [6, 34, 35, 36], three for hemiplegia [46, 47, 53] and four for diplegia group [49, 50, 51, 54] reported a difference that was not significant. Only two studies were found for neuropathy group [42, 52] that recorded a significant lower ROM in the elderly group. The meta-analysis report showed an overall significant difference in the neurological patients as compared to the age matched healthy group (Figure 5b).

Knee range of movement (ROM)

The knee joint was reported by three authors [17, 18, 20] for the range of movement and observed a significant difference between elderly and young group. It was recorded to be significantly lower in the first group with a heterogeneity of $I^2 = 0\%$ (Figure 6a). The meta-analysis report on the neurological group also suggested a significantly lower range of motion in the patients group. Only studies by [4, 25, 32, 33] for Ataxia and [48, 49, 50, 51, 54] for Diplegia group showed no significant difference whereas the studies for Parkinson [21, 22, 25, 26, 29, 30], Cerebral palsy [6, 34, 35, 36], Neuropathy [42, 52] and Hemiplegia [46, 47,

53] observed a significant lower range of motion at the knee joint. The overall heterogeneity among the neurological studies were $I^2 = 90\%$ (Figure 6b).

Ankle range of movement (ROM)

The studies on the ankle range of movement (ROM) for elderly [17, 18, 20] and neurological patients [4, 6, 21, 22, 25, 26, 29, 31, 32, 33, 34, 35, 36, 42, 46, 51, 52, 53, 54] reported a significant lower value in the elderly and neurological group as compared to the healthy control group. In the neurological group, the meta-analysis report on all subgroup types suggested a lower ROM except Ataxia group in which no significant conclusion can be drawn. The heterogeneity among the studies in the elderly group was less $I^2 = 0\%$ (Figure 7a) but a high variability has been observed in the neurological group has $I^2 = 79\%$ (Figure 7b).

3.8 Kinetic characteristics

The kinetic variable of interest was joint moment. The studies reported for the elderly group for the peak flexion moment at hip, knee and ankle joint were not sufficient to perform a meta-analysis. Regarding the neurological group, three studies reported for Parkinson [21, 22, 29] at the hip and ankle joint and observed a significant lower peak joint moment. The heterogeneity was $I^2 = 0\%$ in both cases. No conclusion can be drawn for CP [34, 35, 37] at the hip and ankle joint, however it showed a significant higher peak flexion moment at the knee joint [35, 37]. Studies for diplegia [48, 51] showed a significant lower peak moment at hip and ankle whereas no significant conclusion can be drawn at the knee joint. There were only two studies [41, 42] found for neuropathy patients at the ankle joint and showed a significant lower peak ankle dorsiflexion moment. Overall the meta-analysis report on the kinetic variables suggested no significant difference at the hip (Figure 8) and knee flexion moment (Figure 9) but a significant lower peak ankle dorsiflexion moment (Figure 10). There was also a lot of variability observed among the studies for peak flexion moment ($I^2 = 98\%$, $I^2 = 99\%$ and $I^2 = 89\%$ for hip, knee and ankle joint respectively).

4. Discussion

This study is a comprehensive analysis of the biomechanical alterations in elderly and neurological patients. The gait pattern was analysed in comparison with the healthy groups in terms of spatio-temporal, kinematic and kinetic characteristics and highlighted the support requirement in each category of the deviated gait. From the above findings and results, it appeared that there was a degree of agreement in reporting most of the spatio-temporal, kinematic and kinetic variables of various gait impairment types, though some inconsistency and variability has also been observed in describing certain parameters among the authors. The inconsistency among the studies could be as a result of different measurement approaches employed, varied number, age, mass and gender of subjects, the reference frame used, etc. It has been observed that there are difficulties in categorising patients as some of them do not match a single set of gait pattern. An improper coordination in any one of the input source can lead to gait impairment [10]. For better understanding, it would be appropriate to explore the parameters according to the review findings and results discussed above. From meta-analysis of the spatio-temporal parameters, it could be suggested that participants of Parkinson's disease walked slower than CMT and Neuropathy patients but faster than participants of Diplegic gait. The main reason for slow gait speed in Parkinson disease (PD) is the disorder in the regulation of stride size [2, 55]. A large variation of gait speed, stride length and cadence exists in studies of Hemiplegic gait. The walking speed of Hemiplegic patients were directly related to the stage of motor recovery [56]. In elderly gait, the three spatio-temporal parameters of interests showed a decreasing trend that indicates a decline in the gait performance at older age. In cerebral palsy patients, the deterioration of the gait pattern was suggested to be responsible for decrease in spatio-temporal variables [57]. The overall results of the meta-analysis for the spatio-temporal characteristics showed a decreasing trend in elderly and neurological patients that indicates the need of the patients to use the robot assisted devices so that the deviations among them could be minimized. The study of these deviations in spatio-temporal parameters will also be helpful in the design of robot assisted devices.

The results obtained for the kinematics of hip, knee and ankle joints also showed some degree of inconsistency among them but the overall results of the meta-analysis favoured elderly and neurological patients i.e. a decrease in hip, knee and ankle range of movement (ROM) is recorded and hence the need of robot assisted devices is highlighted. The meta-analysis report on the hip ROM of elderly showed a decrease in the ROM as it is reported that even a small reduction in hip ROM alters gait in elderly [19]. In order to produce the same output, there is a large contribution required from hip extensors [19] and small contribution from knee extensors and ankle flexors [58]. Knee ROM in elderly also showed a significant reduction and the studies also reported an increase in the knee extension angle during mid stance and a decrease during the swing phase [17, 18, 20]. The decrease in the ankle is associated with the ankle dorsi-flexion (DF) and plantar-flexion (PF) muscles weakness [18, 20]. The ROM of the Parkinson disease was observed to be significantly affected at the later stages of the disease. Knee flexion was usually observed to be increased in advanced stages of Parkinson [59]. Change in knee extension caused an overall reduction in the ROM of knee. Studies of the kinetic parameters showed a lot of variability among them in reporting most of the parameters. In Parkinson's disease, more abnormalities were observed in kinetic profiles than the kinematics with the moments reaching peaks that were significantly different from the healthy group [60]. The peaks of the moment profile in Parkinson disease were observed to be different than normal, hip showed a prolonged and increase in the flexion moment, peaks

of the knee extension moment were observed to be lowered [22]. The ankle ROM was reduced during push off and recorded a reduction of PF at toe off [24, 26, 29]. In PD patients, it was reported that there was an increase of PF moment at heel strike and a reduction before push off [22]. Studies of the Ataxic gait showed a lot of variability among them. A lack of inter joint coordination was suggested to be the main reason for gait impairment in Ataxic gait [31]. Studies documented on the kinematic and kinetic changes in ataxic gait observed the changes in stepping and lack of coordination of limb motion [3, 4]. This may lead to lurching in unusual directions. Ataxic patients showed less hip flexion at toe off [32]. The ROM in ataxic patients was reduced [4, 25, 33] and the effects were correlated with clinical severity. [32] pointed out a decrease in knee flexion at heel contact and mid stance and an increase in the flexion during swing. Changes in the kinematics of ankle joint were appeared to be significant in Ataxic gait even at moderate speed [25]. Limited sagittal plane motion and crouch gait is associated with CP [6]. Hip demonstrated a delay in shifting from extension to flexion moment. Hip extension was appeared to be reduced during mid stance [34]. There existed at least eight different clusters of gait; [61] and [49] used Principal Component Analysis (PCA) to classify gait patterns in CP. [62] established a correlation between higher gait speed and ankle ROM. Peak ankle PF and knee flexion at initial contact were observed to be decreased [34]. The increase in the moment of knee flexors was explained by [63] due to the large moment required for hip extension during walking. Although findings of the kinematic and kinetic variables for CMT were not significant to perform a meta-analysis report but it showed excessive hip extension in [38]. The CMT patients showed a delay in the peak DF in the terminal stance associated with the weakness in the ankle plantar flexors [40]. Two distinct gait patterns were reported in CMT, a steppage pattern and a clumsy pattern [64]. A delay in the peak value of ankle DF is a common finding in CMT patients [40]. The results of the findings of the hemiplegia and diplegia group

showed a significant difference at the ankle joint and therefore favours the need of the use of an assistive device.

The findings of this review will be helpful in proposing the design criteria for lower limb robot assisted training. By observing the torque deviations involved in different impaired gaits, maximum deviated value of the joint torque could be determined. This would indicate a threshold requirement of elderly and neurological gaits, hence a general support requirement from the robotic assistive devices is established. It was also noticed that the torque and angle profile of the lower limb joints varies to a large extent among different categories of gait impairments so it was not possible to group patients with similar gait characteristics based on the joint angular displacement and torque profile. Even subjects belonging to the same category of neurological gait significantly differ among each other. The study reported a significant difference in the spatio-temporal, kinematic and kinetic variables in elderly and neurological patients, hence the need for robot assisted devices is highlighted. However, deviations in few parameters were observed to be insignificant.

5. Conclusion

The work presented in this paper is of great importance in analysing the design requirements of robotic assistive devices. It outlines the requirements among different types of gait impairments that will be beneficial in the design of assistive devices to help users complete the activities of daily living independently. The review and meta-analysis identified the gait deviations in spatio-temporal, kinematic and kinetic parameters among elderly and neurological groups. A systematic approach was developed to organise the gait data according to the alterations in the biomechanical parameters related with the various gait pathologies. The review was able to gather evidences of gait malfunctions in different categories of patients and established a general trend in the support requirements among them. The work covered in this review is helpful to define the end users of the robot assistive devices by investigating the support required for them in the spatio-temporal, kinematic and

kinetic parameters involved in locomotion. Based on this review, future devices can be

proposed based on the individual needs of the specific users to overcome the altered gait

biomechanics.

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No potential conflict of interest was reported by the authors.

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Inclusion criteria	Exclusion criteria
Studies reporting elderly and neurological gaits in comparison to a healthy control group	Studies that did not compare elderly or neurological gait with the normal individuals
Studies that include a barefoot biomechanical analysis	Studies that did not include a barefoot analysis or including an analysis using an assistive device
Studies have full text available Outcome measure of interest- (a) Spatio-temporal parameters (gait speed, stride length and cadence) (b) Kinematic variables of hip, knee and ankle (peak flexion/extension and range	 Studies that did not report at least one outcome measure of interest Studies that include elderly people with a previous known disorder Studies that include pathological gaits
ankle (peak flexion/extension and range of movement (ROM))	other than neurological origin
(c) Kinetic variables of hip, knee and ankle (peak flexion/extension moment)	

Table 1. Inclusion and Exclusion Criteria for Studies

Downs and black questions	Anderson et al. [19]	Judge et al. [20]	Kerrigan et al. [17]	Kerrigan et al. [18]	Peppe et al. [27]	Ferrain et al. [21]	Roiz et al. [28]	Ferrarin et al. [22]
1	Y	Y	Y	Y	Ν	Ν	Y	Ν
2	Y	Y	Y	Y	Y	Y	Y	Y
3	Y	Y	Y	Y	Y	Y	Y	Y
4	NR	NR	NR	NR	NR	NR	NR	NR
5	N	Y	Y	Y	Y	Y	Y	Y
6	Y	Ŷ	Ŷ	Ŷ	Ŷ	Ŷ	Ŷ	Y
7	N	Y	Y	N	Y	Y	Y	Y
8	NR	NR	NR	NR	NR	NR	NR	NR
9	NR	NR	NR	NR	NR	NR	NR	NR
10	N	N	Y	N	N	N	Y	N
11	UTD	Y	Y	N	Y	Y	Y	UTD
12	UTD	Y	Y	UTD	Y	Y	UTD	UTD
12	UTD	I UTD	NR	Y	Y	Y	UTD	UTD
13	NR	NR	NR	NR	NR	NR	NR	NR
15	NR	NR	NR	NR	NR	NR	NR	NR
15	V	V	V	V	V	N	V	V
10	I ND	I ND	I ND	I ND	I ND	ND	I ND	ND
17	V	V	V	N	NK	N	V	N
10	1 ND	I ND	1 ND	IN ND	I ND	IN ND	1 ND	IN ND
19		NK V	NK V	NK	NK	NK	NK V	NK V
20		I UTD	Y N	Y V	I UTD	Y V	Y V	Y V
21				I V				
22				I ND	VID			
23	NR	NK	NR	NR	Y	NR	NK	NK
24	NK	NK	NK	NK		NK	NK	NK
25	UID				Y	Y	Y	Y
26	NR	NR	NR	NR	NR	NR	NR	NR
27	NR	NR	NR	NR	NR	NR	NR	NR
Total score	6	11	12	10	13	11	13	9
Downs and black questions	Sofuwa et al. [29]	Zijlman s et al. [30]	Lewis et al. [24]	Morris et al. [26]	Mitoma et al. [25]	Vasco et al. [32]	Serraro et al. [31]	Stolze et al. [33]
1	Y	Y	Y	Y	Y	Y	Y	Y
2	Ŷ	Ŷ	Ŷ	Ŷ	Ŷ	Ŷ	Y	Y
3	Ŷ	Ŷ	Y	Y	Y	Y	Y	Y
4	NR	NR	NR	NR	NR	NR	NR	NR
5	Y	Y	NR	Y	Y	Y	Y	Y
6	Y	Y	Y	Y	Y	Y	Y	Y
7	Y	Y	Y	Y	Y	Y	Y	Y
8	NR	NR	NR	NR	NR	NR	NR	NR
9	NR	NR	NR	NR	NR	NR	NR	NR
10	V	NR	V	V	N	N	V	N
10	I V	V	I V	v	N			
12	v V	v		ı V	V		V	
12	т ПТD		V	т ПТП	т ПДД		ı V	
13			1 ND				1 ND	
14		ND	ND	ND	ND	ND		ND
15	INK V	INK V	INK V	INK V	INK V	INK V	INK V	INK V
10	I ND	I ND	I ND	I ND	I ND	I ND	I ND	I ND
1/	INK V	INK	INK V	INK V	INK V	INK V	INK V	INK
18	I	IN NID	I ND	I ND	I ND	I ND	I ND	IN NID
19	INK	INK	INK	INK	INK	INK	INK	INK

 Table 2. Study Quality Assessment (Downs and Black [16])

20	Y	Y	Y	Y	Y	Y	Y	Y
21	Y	Y	Y	Y	Y	Y	Ν	Y
22	UTD	UTD	UTD	UTD	Y	Y	Y	Y
23	NR	NR	NR	NR	NR	NR	NR	NR
23	NR	NR	NR	NR	NR	NR	NR	NR
24	N	V	V	N	V	V	N	V
25		I ND	I ND		I ND	I ND		1 ND
20		INK		NK ND				NK
27	NK	NK 12	NK 12	NK 12	NK 12	NK 12	NK	NK
Total score	13	12	13	13	13	12	13	11
Downs and black questions	Palliyath et al. [4]	Chen et al. [45]	Galli et al. [46]	Kuan et al. [14]	Mazure et al. [54]	Romkes et al. [53]	Adolfsen et al. [34]	Gomes et al. [52]
1	Y	у	Y	Y	N	Y	Y	Y
2	Y	Y	Y	Y	Y	Y	Y	Y
3	Y	Y	Y	Y	Y	Y	Y	Y
4	NR	NR	NR	NR	NR	NR	NR	NR
5	Y	Y	Y	Y	Y	Y	Y	Y
6	Ŷ	Ŷ	Ŷ	Ŷ	Y	Ŷ	Ŷ	Ŷ
7	Ŷ	Ŷ	Y	Y	Ŷ	Y	Ŷ	Y
, 8	NR	NR	NR	NR	NR	NR	NR	NR
0 0	NR	NP	NR	NR	NR	NR	NR	NR
10	V	N	N	V	V	N	V	V
10		IN V			I V	N N	I V	1 N
11	UID	ľ V		UID	I	Y N	Y N	IN N
12	UID	Y	Y	UID	UID	Y	Y	Y
13	Y	Y	Y	UTD	UTD	Y	Y	Y
14	NR	NR	NR	NR	NR	NR	NR	NR
15	NR	NR	NR	NR	NR	NR	NR	NR
16	Y	Y	Y	Y	Y	Y	Y	Y
17	NR	NR	NR	NR	NR	NR	NR	NR
18	Y	Y	Ν	Y	Y	Ν	Y	Y
19	NR	NR	NR	NR	NR	NR	NR	NR
20	Y	Y	Y	Y	Y	Y	Y	Y
21	Y	UTD	Ν	Y	Y	Y	Ν	Y
22	Y	UTD	Y	Y	Y	Y	UTD	UTD
23	NR	NR	NR	NR	NR	NR	NR	NR
24	NR	NR	NR	NR	NR	NR	NR	NR
25	UTD	Y	Y	Y	Ν	Y	Y	Y
26	NR	NR	NR	NR	NR	NR	NR	NR
27	NR	NR	NR	NR	NR	NR	NR	NR
Z / Total score	13	13	12	13	12	14	14	14
	15	15	12	15	12	14	14	14
Downs and black questions	Davids et al. [35]	Steinwe nder et al. [36]	Eek et al. [37]	Sawacha et al. [44]	Carreiro et al. [49]	Langrak et al. [50]	Saraph et al. [51]	Bianco et al. [38]
1	Y	Y	Y	Y	Y	Y	Y	Y
2	Y	Y	Y	Y	Y	Y	Y	Y
3	Ν	Y	Y	Y	Y	Y	Y	Y
4	NR	NR	NR	NR	NR	NR	NR	NR
5	Ν	Y	Y	Y	Y	Y	Y	Y
6	Y	Y	Y	Y	Y	Y	Y	Y
7	Y	Y	Y	Y	Y	Ν	Y	Y
8	-	-	-	-	-		-	-
0	NR	NR	NR	NR	NR	NR	NR	NR
9	NR NR	NR NR	NR NR	NR NR	NR NR	NR NR	NR NR	NR NR
9 10	NR NR N	NR NR N	NR NR V	NR NR V	NR NR V	NR NR V	NR NR V	NR NR N
9 10 11	NR NR N	NR NR N	NR NR Y V	NR NR Y V	NR NR Y V	NR NR Y	NR NR Y V	NR NR N
9 10 11	NR NR N Y	NR NR N N	NR NR Y Y	NR NR Y Y	NR NR Y Y	NR NR Y N	NR NR Y Y	NR NR N N

13	Y	UTD	Y	Y	Y	Y	UTD	Y
14	NR	NR	NR	NR	NR	NR	NR	NR
15	NR	NR	NR	NR	NR	NR	NR	NR
16	Y	Y	Y	Y	Y	Y	Y	Y
17	NR	NR	NR	NR	NR	NR	NR	NR
18	Ν	Y	Y	Y	Y	Y	Y	Ν
19	NR	NR	NR	NR	NR	NR	NR	NR
20	Y	Y	Y	Y	Y	Y	Y	Y
21	Ν	Y	Y	Y	Y	Y	Y	Y
22	Y	Y	Ν	Ν	UTD	Ν	Y	Y
23	NR	NR	NR	NR	NR	NR	NR	NR
24	NR	NR	NR	NR	NR	NR	NR	NR
25	Ν	Y	UTD	Ν	UTD	Ν	Y	Y
26	NR	NR	NR	NR	NR	NR	NR	NR
27	NR	NR	NR	NR	NR	NR	NR	NR
Total score	10	12	14	14	14	12	14	13

Downs and black questions	Ferrain et al. [39]	Onupu u et al. [40]	Rao et al. [41]	Raspovic et al. [42]
1	Y	Y	Y	Y
2	Y	Y	Y	Y
3	Y	Y	Y	Y
4	NR	NR	NR	NR
5	Y	Y	Y	Y
6	Y	Y	Y	Y
7	Y	Y	Ν	Y
8	NR	NR	NR	NR
9	NR	NR	NR	NR
10	Y	Y	Y	Y
11	Ν	Ν	Y	Y
12	Y	Y	Y	Y
13	Y	Y	Y	Y
14	NR	NR	NR	NR
15	NR	NR	NR	NR
16	Y	Y	Y	Y
17	NR	NR	NR	NR
18	Y	Y	Y	Y
19	NR	NR	NR	NR
20	Y	Y	UTD	Y
21	Y	Y	UTD	UTD
22	Y	Ν	Y	Y
23	NR	NR	NR	NR
24	NR	NR	NR	NR
25	Ν	Ν	Y	Ν
26	NR	NR	NR	NR
27	NR	NR	NR	NR
Total score	14	13	13	14

*Y=1, N=0, NR=not relevant, UTD=unable to determine

Demographics	Elderly	Pathological	Normal
	$Mean \pm SD$	$Mean \pm SD$	$Mean \pm SD$
Number of Subjects (n)	90	647	676
Age (years)	76.3 ±5.28	42.61 ±7.6	41.78±5.1
Height (m)	1.61 ±8.7	1.63 ± 10.9	163.41±8
Weight (kg)	66.4 ±11.7	72.91 ±13.56	65.69±11.53

 Table 3. Demographic data of participants from included studies



Figure 1.



Figure 2a.

Study or Subaroup	Mean	SD SD	Total	Mean	SD	Total	Weight	Mean Difference	Mean Difference IV. Random, 95% Cl
1.1.1 Parkinson	moun	30	Total	aroun	30	Total	Teight	, runuoni, 5570 Cl	iv, randin, 35% G
Corrorin 2002	0.61	0.2	4	1 1 2	0.10	4	2.106	0.6110.70 0.241	
-errann 2002	0.01	0.2	4	1.12	0.19	4	2.170	-0.31 [-0.76, -0.24]	
Perranni 2005	0.00	0.24	10	1.13	0.19	10	2.0%	-0.57 [-0.76, -0.36]	
Hong 2005	0.82	0.25	10	1.01	0.9	10	0.9%	-0.19 [-0.77, 0.39]	
.ewis 2000	1.06	0.21	14	1.39	0.22	14	2.8%	-0.33 [-0.49, -0.17]	
litoma 2000	0.46	0.2	9	0.63	0.16	12	2.8%	-0.17 [-0.33, -0.01]	
lorris 2005	0.94	0.2	12	1.51	0.15	12	2.9%	-0.57 [-0.71, -0.43]	
eppe 2006	0.76	0.12	16	1.16	0.12	13	3.2%	-0.40 [-0.49, -0.31]	
loiz 2010	0.77	0.14	12	0.59	0.2	15	2.9%	0.18 [0.05, 0.31]	
ofuwa 2005	0.94	0.21	15	1.19	0.11	9	2.9%	-0.25 (-0.38, -0.12)	<u> </u>
iiilmans 1996	0.66	0.25	12	1 1 7	0.24	10	2.5%	-0.51 [-0.72 -0.30]	
Subtotal (95% CI)	0.00	0.20	114		0.2.1	109	25.4%	-0.33 [-0.49, -0.17]	◆
leterogeneity: Tau² = 'est for overall effect: :	0.06; Chi ^a Z = 4.09 (I	² = 89.85, P < 0.000	df = 9 (1)	P < 0.0	0001);	l² = 90°	%		
.1.2 Ataxia									
ditoma 2000	0.44	0.10	14	ເລດ	016	10	2.0%	-0106030 0.00	
allivath 4000	0.44	0.13	14	0.03	0.10	12	3.0%	-0.15["0.30, -0.08]	
ramyatri 1998 Samaa 2040	0.47	0.17	10	0.9	0.39	10	2.1%	-0.43[-0.69, -0.17]	
errao 2012	1.07	0.07	16	1.4	0.05	15	3.3%	-0.33 [-0.37, -0.29]	
tolze 2002	0.96	0.31	12	1.11	0.18	12	2.5%	-0.15 [-0.35, 0.05]	
asco 2016	0.9	0.07	11	1.2	0.04	13	3.3%	-0.30 [-0.35, -0.25]	±
ubtotal (95% CI)			63			62	14.2%	-0.29 [-0.35, -0.23]	◆
leterogeneity: Tau² = 'est for overall effect: J	0.00; Chi ^a Z = 10.06	² = 8.43, 0 (P < 0.00	3f = 4 (P 1001)	= 0.08)); I² = 5	3%			
.1.3 Cerebral Palsy									
dolfsen 2007	1.05	016	31	1 1 9	0.14	31	3 2%	-0.14 I-0 21 -0 071	
Sell 2002	0.90 0.90	0.27	28	1 1 7	0.15	28	3.0%	-0.28[-0.30 -0.17]	
avids 1998	1.05	0.21	10	1.22	0.16	15	3,0%	-0.17[-0.20]-0.77]	
anus 1990 Joli 2011	1.00	0.2	19	1.22	0.10	20	2.0%	-0.17[-0.28]-0.00]	
toinuonder 2000	1.1	0.21	20	1.3	0.24	20	2.9%	-0.20[-0.34,-0.06]	
terriwender 2000	1.24	0.12	20	1.33	U.1	20	3.2%	-0.09 [-0.16, -0.02]	
Heterogeneity: Tou? -	0.001068	= 8 67 <i>4</i>	118 1f= 4 /⊡	= 0.07): 2 = 6	114	13.4%	-0.10[-0.23, -0.10]	▼
est for overall effect:)	Z = 5.01 (I	F ~ 0.000	.017						
Test for overall effect: J J .1.4 Charcot Marie T Jianco 2008 Terrain 2011 Jnupuu 2013	Z = 5.01 (I ooth (CM 0.78 0.76 1.11	T) 0.05 0.11 0.16	1 21 33	1.06 0.77 1.27	0.1 0.07 0.1	6 18 21	3.0% 3.3% 3.2%	-0.28 [-0.41, -0.15] -0.01 [-0.07, 0.05] -0.16 [-0.23, -0.09]	
Fest for overall effect: . I .1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Dnupuu 2013 Subtotal (95% CI)	Z = 5.01 (I ooth (CM 0.78 0.76 1.11	T) 0.05 0.11 0.16	1 21 33 55	1.06 0.77 1.27	0.1 0.07 0.1	6 18 21 45	3.0% 3.3% 3.2% 9.5 %	-0.28 [-0.41, -0.15] -0.01 [-0.07, 0.05] -0.16 [-0.23, -0.09] - 0.14 [-0.29, 0.00]	
Fest for overall effect: . I. 1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Onupuu 2013 Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect: .	Z = 5.01 (1 ooth (CM 0.78 0.76 1.11 0.01; Chi ^a Z = 1.93 (1	T) 0.05 0.11 0.16 F = 20.10, P = 0.05)	1 21 33 55 df= 2 (1.06 0.77 1.27 P < 0.01	0.1 0.07 0.1 001); P	6 18 21 45 *= 90%	3.0% 3.3% 3.2% 9.5 %	-0.28 [-0.41, -0.15] -0.01 [-0.07, 0.05] -0.16 [-0.23, -0.09] - 0.14 [-0.29, 0.00]	
est for overall effect: . .1.4 Charcot Marie T Dianco 2008 errain 2011 Dupuu 2013 Jubtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect . .1.5 Neuropathy	Z = 5.01 (I 0.78 0.76 1.11 0.01; Chi ² Z = 1.93 (I	T) 0.05 0.11 0.16 = 20.10, P = 0.05)	1 21 33 55 df=2(1.06 0.77 1.27 P < 0.01	0.1 0.07 0.1 001); P	6 18 21 45 2 90%	3.0% 3.3% 3.2% 9.5 %	-0.28 [-0.41, -0.15] -0.01 [-0.07, 0.05] -0.16 [-0.23, -0.09] - 0.14 [-0.29, 0.00]	
est for overall effect: . .1.4 Charcot Marie T Jianco 2008 errain 2011 Dupuu 2013 Subtotal (95% Cl) leterogeneity: Tau ² = est for overall effect: . .1.5 Neuropathy Rao 2005	Z = 5.01 (i 0.78 0.76 1.11 0.01; Chi ² Z = 1.93 (i 0.91	 C.000 T) 0.05 0.11 0.16 ² = 20.10, P = 0.05) 0.07 	1 21 33 55 df=2(1.06 0.77 1.27 P < 0.01	0.1 0.07 0.1 001); P 0.05	6 18 21 45 *= 90%	3.0% 3.3% 3.2% 9.5%	-0.28 [-0.41, -0.15] -0.01 [-0.07, 0.05] -0.16 [-0.23, -0.09] - 0.14 [-0.29, 0.00] -0.14 [-0.29, 0.00]	 —
est for overall effect: . .1.4 Charcot Marie T Blanco 2008 errain 2011 prupuu 2013 subtotal (95% CI) Heterogeneity: Tau ² = est for overall effect: . .1.5 Neuropathy Rao 2005 Pasenvic 2012	Z = 5.01 () ooth (CM 0.78 0.76 1.11 0.01; Chi ^a Z = 1.93 () 0.91	C.000 T) 0.05 0.11 0.16 ² = 20.10, P = 0.05) 0.07 0.2	1 21 33 55 df=2(10	1.06 0.77 1.27 P < 0.01 0.92 1.2	0.1 0.07 0.1 001); ^p 0.05	6 18 21 45 *= 90% 10	3.0% 3.3% 3.2% 9.5%	-0.28 [-0.41, -0.15] -0.01 [-0.07, 0.05] -0.16 [-0.23, -0.09] -0.14 [-0.29, 0.00]	
est for overall effect: . .1.4 Charcot Marie T Banco 2008 Terrain 2011 Soupout 2013 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: . .1.5 Neuropathy Rao 2005 Raspovic 2013 Sovelberr 2010	Z = 5.01 (i ooth (CM 0.78 0.76 1.11 0.01; Chi ² Z = 1.93 (i 0.91 1.1	 T) 0.05 0.11 0.16 ² = 20.10, P = 0.05) 0.07 0.2 0.42 	1 21 33 55 df = 2 (10	1.06 0.77 1.27 P < 0.01 0.92 1.3 1.19	0.1 0.07 0.1 001); ¹³ 0.05 0.1	6 18 21 45 *= 90% 10 10	3.0% 3.3% 3.2% 9.5% 3.3% 2.9%	-0.28 [-0.41, -0.15] -0.01 [-0.07, 0.05] -0.16 [-0.23, -0.09] -0.14 [-0.29, 0.00] -0.01 [-0.06, 0.04] -0.20 [-0.34, -0.06] -0.16 [-0.20, 0.03]	
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Fest for overall effect: . 1.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Drupuu 2013 Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect: . 1.1.5 Neuropathy Rao 2005 Raspovic 2013 Savelberg 2010 Savecha 2008 Chetral (05% CI)	2 = 5.01 (i ooth (CM 0.78 0.76 1.11 0.01; Chi Z = 1.93 (i 0.91 1.1 1.02 1.1	T) 0.05 0.11 0.16 ² = 20.10, P = 0.05) 0.07 0.2 0.13 0.2	1 21 33 55 df= 2 (10 10 8 26	1.06 0.77 1.27 P < 0.04 0.92 1.3 1.18 1.27	0.1 0.07 0.1 001); ¹² 0.05 0.1 0.22 0.1	6 18 21 45 *= 90% 10 10 20	3.0% 3.3% 3.2% 9.5% 3.3% 2.9% 2.7% 3.2%	-0.28 [-0.41, -0.15] -0.01 [-0.23, -0.09] -0.16 [-0.23, -0.09] -0.14 [-0.29, 0.00] -0.14 [-0.29, 0.00] -0.16 [-0.20, 0.04] -0.20 [-0.34, -0.06] -0.16 [-0.32, 0.00] -0.17 [-0.26, -0.08] -0.12 [-0.29, -0.08]	
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est for overall effect : .1.4 Charcot Marie T bianco 2008 errain 2011 onupuu 2013 subtotal (95% CI) leterogeneity: Tau ² = est for overall effect : .1.5 Neuropathy Rao 2005 Raspovic 2013 savelberg 2010 savacha 2008 subtotal (95% CI) leterogeneity: Tau ² = est for overall effect : .1.6 Hemiplegia	Z = 5.01 (i ooth (CM 0.78 0.76 1.11 0.01; Chi ^a Z = 1.93 (i 1.02 1.1 0.01; Chi ^a Z = 2.23 (i	T) 0.05 0.11 0.16 = 20.10, P = 0.05) 0.07 0.2 0.13 0.2 = 14.29, P = 0.03)	1 21 33 55 df = 2 (10 10 8 26 54 df = 3 (1.06 0.77 1.27 P < 0.00 0.92 1.3 1.18 1.27 P = 0.00	0.1 0.07 0.1 001); I ² 0.05 0.1 0.22 0.1 0.3); I ² =	6 18 21 *= 90% 10 10 10 20 50 = 79%	3.0% 3.2% 9.5% 3.3% 2.9% 2.7% 3.2% 12.1%	-0.28 [-0.41, -0.15] -0.01 [-0.23, -0.09] -0.16 [-0.23, -0.09] -0.14 [-0.29, 0.00] -0.14 [-0.29, 0.00] -0.16 [-0.34, -0.06] -0.16 [-0.32, 0.00] -0.17 [-0.26, -0.08] -0.12 [-0.23, -0.01]	
est for overall effect: . .1.4 Charcot Marie T ianco 2008 errain 2011 youpuu 2013 ubtotal (95% CI) leterogeneity: Tau ² = est for overall effect: . .1.5 Neuropathy tao 2005 caspovic 2013 iavelberg 2010 iavacha 2008 ubtotal (95% CI) leterogeneity: Tau ² = est for overall effect: . .1.6 Hemiplegia then 2005	Z = 5.01 (i ooth (CM 0.78 0.76 1.11 0.01; Chi ^p 2 = 1.93 (i 0.91 1.1 1.02 1.1 0.01; Chi ^p Z = 2.23 (i 0.34	T) 0.05 0.11 0.16 * = 20.10, P = 0.05) 0.07 0.2 0.13 0.2 * = 14.29, P = 0.03) 0.11	1 21 33 55 df = 2 (10 10 8 26 54 df = 3 (1.06 0.77 1.27 P < 0.01 0.92 1.3 1.18 1.27 P = 0.01 0.34	0.1 0.07 0.1 0001); P 0.05 0.1 0.22 0.1 03); P :	6 18 21 45 *= 90% 10 10 10 20 50 = 79%	3.0% 3.3% 9.5% 3.3% 2.9% 2.7% 3.2% 12.1%	-0.28 [-0.41, -0.15] -0.01 [-0.07, 0.05] -0.16 [-0.23, -0.09] -0.14 [-0.29, 0.00] -0.14 [-0.29, 0.00] -0.20 [-0.34, -0.06] -0.16 [-0.32, 0.00] -0.17 [-0.26, -0.08] -0.12 [-0.23, -0.01]	
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Fest for overall effect : I.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Drupuu 2013 Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect : I.1.5 Neuropathy Rao 2005 Raspovic 2013 Savelberg 2010 Savelberg 2010 Savelberg 2010 Savelberg 2010 Savelberg 2010 Savelberg 2010 Savelberg 2010 Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect : I.1.6 Hemiplegia Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect : I.1.7 Diplegia Suckon 2004 Saraph 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect : Subtotal (95% CI) Subtotal (95% CI) Subtotal (95% CI) Subtotal (95% CI) Subtotal (95% CI) Subtotal (95%	Z = 5.01 (i) ooth (CM 0.78 0.76 1.11 0.01; Chi ² Z = 1.93 (i) 0.91 1.1 1.02 1.1 0.01; Chi ² Z = 2.23 (i) 0.34 0.6 0.29 0.87 0.87 0.08; Chi ² Z = 2.81 (i) 1.08 0.86 0.71 1.06 0.03; Chi ² Z = 4.24 (i) 0.03; Chi ² Z = 4.24 (i)	 C 0.000 T) 0.05 0.11 0.16 * = 20.10, P = 0.05) 0.07 0.2 0.13 0.2 * = 14.29, P = 0.03) 0.11 0.18 0.2 * = 88.62, P = 0.005 0.22 0.32 0.27 0.23 * = 19.56, P < 0.000 * = 451.61 	1 21 3 55 df = 2 (10 10 8 26 54 df = 3 (6 118 df = 3 (9 46 118 df = 3 (9 46 118 df = 3 (10 15 46 118 df = 3 (10 15 46 118 df = 3 (10 15 46 118 df = 3 (10 15 46 118 15 46 118 15 46 118 15 15 15 15 15 15 15 15 15 15 15 15 15	1.06 0.77 1.27 P < 0.01 0.92 1.3 1.18 1.27 P = 0.01 0.34 1.17 P < 0.01 1.26 1.36 1.26 1.38 P = 0.01 4 (P < 0	0.1 0.07 0.1 001); F 0.05 0.1 0.22 0.1 0.3); F 0.1 0.3; F 0.1 0.18 0.14 0.16 0.17 0.18 0.17 0.18 0.02); F	6 18 21 45 5 90% 10 10 20 50 6 15 46 82 71 5 71 5 85% 533 1): F = (3.0% 3.3% 3.2% 9.5% 3.2% 2.9% 3.2% 12.1% 3.0% 3.0% 3.0% 3.2% 12.2% % 2.9% 3.2% 12.2% 5.0% 3.0% 3.0% 3.0% 3.0% 3.0% 3.0% 5.0% 11.3%	-0.28 [-0.41, -0.15] -0.01 [-0.07, 0.05] -0.16 [-0.23, -0.09] -0.14 [-0.29, 0.00] -0.14 [-0.29, 0.00] -0.16 [-0.32, 0.00] -0.16 [-0.32, 0.00] -0.17 [-0.26, -0.8] -0.12 [-0.23, -0.01] 0.00 [-0.12, 0.12] -0.70 [-0.81, -0.59] -0.56 [-0.78, -0.52] -0.30 [-0.37, -0.23] -0.41 [-0.70, -0.13] -0.55 [-0.66, -0.44] -0.32 [-0.43, -0.21] -0.38 [-0.56, -0.21]	
Fest for overall effect : I.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Drupuu 2013 Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect : I.1.5 Neuropathy Rao 2005 Raspovic 2013 Bavelberg 2010 Bavelberg 2	Z = 5.01 (i) ooth (CM 0.78 0.76 1.11 0.01; Chi ^p Z = 1.93 (i) 0.91 1.1 1.02 1.1 0.01; Chi ^p Z = 2.23 (i) 0.34 0.6 0.29 0.87 0.08; Chi ^p Z = 2.81 (i) 1.08 0.86 0.71 1.06 0.03; Chi ^p Z = 4.24 (i) 0.03; Chi ^p Z = 8.66 /i)	 C 0.000 T) 0.05 0.11 0.16 ² = 20.10, P = 0.05) 0.07 0.2 0.13 0.2 ² = 14.29, P = 0.03) 0.11 0.18 0.18 0.18 0.18 0.2 ² = 88.62, P = 0.005 0.22 0.32 0.27 0.23 ² = 19.56, P < 0.000 ² = 451.66 P < 0.000 	1 21 35 55 df = 2 (10 10 8 26 54 df = 3 (118 df = 3 (118 df = 3 (119 10 16 9 40 25 90 df = 3 (11) 10 10 10 10 11)	1.06 0.77 1.27 P < 0.01 0.92 1.3 1.18 1.27 P = 0.01 0.34 1.3 0.94 1.17 P < 0.01 1.26 1.36 1.26 1.38 P = 0.01 4 (P < C	0.1 0.07 0.1 0001); F 0.22 0.1 0.22 0.1 0.3); F 0.12 0.3; F 0.14 0.14 0001); 0.16 0.17 0.18 0.14 0001); F	6 18 21 45 2*= 90% 10 10 10 10 50 50 50 51 5 48 82 15 15 48 82 17 97' 16 10 20 25 71 *= 97' 16 10 20 50 50 50 50 50 50 50 50 50 5	3.0% 3.3% 3.2% 9.5% 3.2% 2.9% 3.2% 12.1% 3.0% 3.0% 3.0% 3.2% 12.2% 2.9% 3.2% 12.2%	-0.28 [-0.41, -0.15] -0.01 [-0.07, 0.05] -0.16 [-0.23, -0.09] -0.14 [-0.29, 0.00] -0.14 [-0.29, 0.00] -0.16 [-0.32, 0.00] -0.17 [-0.26, -0.08] -0.17 [-0.26, -0.08] -0.12 [-0.23, -0.01] 0.065 [-0.78, -0.52] -0.30 [-0.37, -0.23] -0.41 [-0.70, -0.13] -0.55 [-0.66, -0.44] -0.32 [-0.43, -0.21] -0.38 [-0.56, -0.21] -0.27 [-0.33, -0.21]	





	E	derly		Y	oung			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
Anderson 2014	1.3	0.1	10	1.4	0.08	10	17.5%	-0.10 [-0.18, -0.02]	
Judge 1996	1.3	0.14	26	1.48	0.08	32	29.3%	-0.18 [-0.24, -0.12]	_
Kerrigan 1998	1.2	0.12	31	1.38	0.11	31	32.5%	-0.18 [-0.24, -0.12]	_
Kerrigan 2001	1.22	0.12	23	1.37	0.15	30	20.7%	-0.15 [-0.22, -0.08]	
Total (95% CI)			90			103	100.0%	-0.16 [-0.19, -0.13]	•
Heterogeneity: Tau ² =	= 0.00; C	hi = 3.	.15, df=	= 3 (P =	0.37);	l² = 5%			
Test for overall effect:	Z = 9.27	'(P < 0	0.00001)					-0.2 -0.1 0 0.1 0.2 Favours [Elderly] Favours [Young]
			Fo	orest	Plot	Stric	de Len	gth – Elderly vs	Young

Figure 3a.

study of Subgroup	Mean	SD SD	oup Total	C Mean	ontrol SD	Total	Weight	Mean Difference IV, Random, 95% Cl	Mean Difference IV, Random, 95% Cl
2.1.1 Parkinson									
Ferrarin 2002	0.72	0.23	4	1.28	0.1	4	2.4%	-0.56 [-0.81, -0.31]	
Ferrarin 2005	0.68	0.2	10	1.27	0.13	10	3.3%	-0.59 [-0.74, -0.44]	
Hong 2005	0.89	0.26	30	1.09	0.13	30	3.7%	-0.20 [-0.30, -0.10]	
Lewis 2000	1.1	0.25	14	1.42	0.18	14	3.2%	-0.32 [-0.48, -0.16]	
Mitoma 2000	0.52	0.24	9	0.79	0.19	12	2.9%	-0.27 [-0.46, -0.08]	
Morris 2005	0.96	0.19	12	1.46	0.08	12	3.6%	-0.50 [-0.62, -0.38]	
Peppe 2006	0.87	0.24	16	1.27	0.12	13	3.4%	-0.40 [-0.53, -0.27]	_ —
Roiz 2010	1.03	0.13	12	0.79	0.22	15	3.4%	0.24 [0.11, 0.37]	
Sofuwa 2005	1.03	0.16	15	1.24	0.1	9	3.7%	-0.21 [-0.31, -0.11]	<u> </u>
Zijilmans 1996	0.86	0.28	12	1.29	0.19	10	2.8%	-0.43 [-0.63, -0.23]	
Subtotal (95% CI)			134			129	32.2%	-0.32 [-0.47, -0.17]	◆
Heterogeneity: Tau² = Test for overall effect:	0.05; Chř Z = 4.12 (² = 103.3 P < 0.000	2, df = 9 01)	I(P < 0.	.00001); I ² = 9	1%		
2.1.2 Ataxia									
Mitoma 2000	0.54	0.22	14	0.79	0.19	12	3.2%	-0.25 [-0.41, -0.09]	<u> </u>
Palliyath 1998	1.04	0.25	10	1.65	0.69	10	1.2%	-0.61 [-1.060.16]	
Serrao 2012	1.27	0.11	16	1.4	0.52	15	2.2%	-0.13 [-0.40. 0.14]	
Stolze 2002	1.07	0.32	12	1.13	0.14	12	2.8%	-0.06 [-0.26. 0.14]	
Vasco 2016	0.71	0.3	11	0.82	0.03	13	3.0%	-0.11 [-0.29, 0.07]	
Subtotal (95% CI)			63			62	12.4%	-0.17 [-0.30, -0.05]	◆
Heterogeneity: Tau² = Test for overall effect:	0.01; Chi Z = 2.79 (² = 6.30, (P = 0.005	df = 4 (F 5)	P = 0.18); ² = 3	86%			
2.1.3 Cerebral Palsv									
Adolfsen 2007	0.92	0.11	31	1 1 1	015	31	3.9%	-0.19/-0.26 -0.121	
Rell 2002	0.32	0.13	28	1.1.9	0.10	28	3.8%	-0.34 [-0.43 -0.26]	
Dell 2002 Dovide 1009	0.04	0.15	10	1.10	0.13	15	2.0%	-0.34 [-0.43, -0.23]	
Eak 2011	1 1	0.13	20	1.1	0.12	20	1.0%	-0.21 [-0.30, -0.12]	
Steinwender 2000	1.1	0.1 0.00	20	1.3	0.09	20	4.070 1/100	-0.20["0.20, "0.14] -0.14[-0.19] 0.10]	+
Subtotal (95% CI)	1.07	0.00	118	1.21	0.07	114	4.1 % 19.6%	-0.21 [-0.270.15]	▲
Test for overall effect:	Z = 6.73 (P < 0.000		•					
Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008	Z = 6.73 (ooth (CM 1.02	P < 0.000 T) 0.05)01) 1	1.22	0.03	6	3.7%	-0.20 [-0.30, -0.10]	
Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008 Ferrain 2011	Z = 6.73 (i iooth (CM 1.02 0.78	P < 0.000 T) 0.05 0.07	001) 1 21	1.22 0.79	0.03 0.04	6 18	3.7% 4.1%	-0.20 [-0.30, -0.10] -0.01 [-0.05, 0.03]	
Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect:	Z = 6.73 () ooth (CM 1.02 0.78 0.02; Chi ² Z = 1.04 ()	P < 0.000 T) 0.05 0.07 ² = 12.15, P = 0.30)	001) 1 21 22 , df = 1	1.22 0.79 (P = 0.0	0.03 0.04 005); P	6 18 24 ² = 92%	3.7% 4.1% 7.8 %	-0.20 [-0.30, -0.10] -0.01 [-0.05, 0.03] - 0.10 [-0.28, 0.09]	
Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.5 Neuropathy	Z = 6.73 () ooth (CM 1.02 0.78 0.02; Chi ² Z = 1.04 ()	P < 0.000 T) 0.05 0.07 ² = 12.15 P = 0.30)	001) 1 21 22 , df = 1	1.22 0.79 (P = 0.0	0.03 0.04 005); F	6 18 24 *= 92%	3.7% 4.1% 7.8 %	-0.20 [-0.30, -0.10] -0.01 [-0.05, 0.03] - 0.10 [-0.28, 0.09]	
Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.5 Neuropathy Bao 2005	Z = 6.73 () ooth (CM 1.02 0.78 0.02; Chi ² Z = 1.04 () 1.06	P < 0.000 T) 0.05 0.07 *= 12.15 P = 0.30)	001) 1 21 22 , df = 1	1.22 0.79 (P = 0.0	0.03 0.04 005); F	6 18 24 ² = 92%	3.7% 4.1% 7.8%	-0.20 [-0.30, -0.10] -0.01 [-0.05, 0.03] - 0.10 [-0.28, 0.09]	
Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.5 Neuropathy Rao 2005 Rao 2005	Z = 6.73 () ooth (CM 1.02 0.78 0.02; Chi ² Z = 1.04 () 1.06 1.2	P < 0.000 T) 0.05 0.07 F = 12.15 P = 0.30) 0.1 0.2	1 21 22 , df = 1	1.22 0.79 (P = 0.0 1.21	0.03 0.04 005); F 0.07 0.1	6 18 24 ² = 92% 10	3.7% 4.1% 7.8% 3.9%	-0.20 [-0.30, -0.10] -0.01 [-0.05, 0.03] - 0.10 [-0.28, 0.09] -0.15 [-0.23, -0.07]	
Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: 2.1.5 Neuropathy Rao 2005 Raspovic 2013 Savelbace 2010	Z = 6.73 () ooth (CM 1.02 0.78 0.02; Chi ² Z = 1.04 () 1.06 1.2 1.15	P < 0.000 T) 0.05 0.07 * = 12.15, P = 0.30) 0.1 0.2 0.2	1 21 22 , df = 1 10 10	1.22 0.79 (P = 0.0 1.21 1.3	0.03 0.04 005); F 0.07 0.1	6 18 24 *= 92% 10 10	3.7% 4.1% 7.8% 3.9% 3.4%	-0.20 [-0.30, -0.10] -0.01 [-0.05, 0.03] - 0.10 [-0.28, 0.09] -0.15 [-0.23, -0.07] -0.10 [-0.24, 0.04]	
Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: 2.1.5 Neuropathy Rao 2005 Raspovic 2013 Savelberg 2010 Savescho 2009	Z= 6.73 (ooth (CM 1.02 0.78 0.02; Chi ² Z= 1.04 (1.06 1.2 1.15 1.2	P < 0.000 T) 0.05 0.07 * = 12.15, P = 0.30) 0.1 0.2 0.15 1.2	1 21 22 , df = 1 10 10 8 26	1.22 0.79 (P = 0.0 1.21 1.3 1.28	0.03 0.04 005); F 0.07 0.1 0.15 0.1	6 18 24 *= 92% 10 10 10 20	3.7% 4.1% 7.8% 3.9% 3.4% 3.4%	-0.20 [-0.30, -0.10] -0.01 [-0.05, 0.03] - 0.10 [-0.28, 0.09] -0.15 [-0.23, -0.07] -0.10 [-0.24, 0.04] -0.13 [-0.27, 0.01] -0.20 [-0.26, 0.26]	
Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.5 Neuropathy Rao 2005 Raspovic 2013 Savelberg 2010 Sawacha 2008 Subtotal (95% Cl)	 a. 73 (i a. 78 (i) a. 78 (i)	P < 0.000 T) 0.05 0.07 = 12.15, P = 0.30) 0.1 0.2 0.15 1.2	1 21 22 , df = 1 10 10 8 26 54	1.22 0.79 (P = 0.0 1.21 1.3 1.28 1.4	0.03 0.04 005); F 0.07 0.1 0.15 0.1	6 18 24 * = 92% 10 10 10 20 50	3.7% 4.1% 7.8% 3.9% 3.4% 3.4% 1.1%	-0.20 [-0.30, -0.10] -0.01 [-0.05, 0.03] - 0.10 [-0.28, 0.09] -0.15 [-0.23, -0.07] -0.10 [-0.24, 0.04] -0.13 [-0.27, 0.01] -0.20 [-0.66, 0.26] -0.14 [-0.26, 0.08]	
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Test for overall effect: Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.5 Neuropathy Rao 2005 Raspovic 2013 Savelberg 2010 Sawacha 2008 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.6 Hemiplegia Chen 2005 Kuan 1999 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.7 Diplegia Buckon 2004 Carriero 2009 Saraph 2002 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.7 Diplegia Buckon 2004 Carriero 2009 Saraph 2002 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.4 LOS% Cl)	Z = 6.73 () ioth (CM 1.02 0.78 0.02; Chi ² Z = 1.04 () 1.06 1.2 1.15 1.2 0.00; Chi ² Z = 4.55 () 0.52 0.49 0.13; Chi ² Z = 1.07 () 0.91 0.8 0.95 0.01; Chi ² Z = 3.85 ()	P < 0.000 T) 0.05 0.07 * = 12.15, P = 0.30) 0.1 0.2 0.15 1.2 * = 0.47, (P < 0.000 0.22 0.19 * = 13.82, P = 0.29) 0.15 0.23 0.14 * = 11.83, P = 0.000	1 1 21 22 2 2 4 df = 1 10 10 10 8 5 4 4 df = 3 (f 5 4 4 df = 3 (f 15 2 1) 001) 6 15 21 10 10 10 8 6 5 4 4 11 10 10 10 10 10 10 10 10 10 10 10 10	1.22 0.79 (P = 0.0 1.21 1.3 1.28 1.4 0.53 1.03 (P = 0.0 1.08 1.16 1.33 (P = 0.0	0.03 0.04 005); F 0.07 0.1 0.15 0.1 0.19 0.24 002); F 0.12 0.12 0.12 0.14 0.14 03); F	6 18 24 = 92% 10 10 10 20 8 % 6 15 21 = 93% 16 10 25 51 16 10 25 51 16	3.7% 4.1% 7.8% 3.9% 3.4% 3.4% 1.1% 1.1% 1.1% 1.7% 2.5% 3.2% 5.7% 3.0% 3.9% 10.6%	-0.20 [-0.30, -0.10] -0.01 [-0.05, 0.03] -0.10 [-0.28, 0.09] -0.10 [-0.28, 0.09] -0.10 [-0.24, 0.04] -0.13 [-0.27, 0.01] -0.20 [-0.66, 0.26] -0.14 [-0.20, -0.08] -0.14 [-0.20, -0.08] -0.54 [-0.69, -0.39] -0.28 [-0.80, 0.24] -0.36 [-0.54, -0.18] -0.36 [-0.54, -0.18] -0.38 [-0.46, -0.30] -0.30 [-0.45, -0.15]	
Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.5 Neuropathy Rao 2005 Raspovic 2013 Savelberg 2010 Sawacha 2008 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.6 Hemiplegia Chen 2005 Kuan 1999 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.7 Diplegia Buckon 2004 Carriero 2009 Saraph 2002 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: 2.1.7 Diplegia Buckon 2004 Carriero 2009 Saraph 2002 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: Total (95% Cl)	$\begin{aligned} z &= 6.73 (i) \\ \hline \textbf{rooth} (CM) \\ 1.02 \\ 0.78 \\ 0.02; Chi^2 \\ z &= 1.04 (i) \\ 1.06 \\ 1.2 \\ 1.15 \\ 1.2 \\ 0.00; Chi^2 \\ z &= 4.55 (i) \\ 0.52 \\ 0.49 \\ 0.13; Chi^2 \\ z &= 1.07 (i) \\ 0.91 \\ 0.8 \\ 0.95 \\ 0.01; Chi^2 \\ z &= 3.85 (i) \\ \end{aligned}$	P < 0.000 T) 0.05 0.07 * = 12.15, P = 0.30) 0.1 0.2 0.15 1.2 * = 0.47, (P < 0.000 0.22 0.19 * = 13.82, P = 0.29) 0.15 0.23 0.14 * = 11.83, P = 0.000	1 1 21 22 2 4f=1 10 10 8 26 54 6 54 6 54 6 54 10 001) 6 54 6 54 7 10 10 8 26 50 10 10 10 8 26 51 10 10 10 10 10 10 10 10 10 10 10 10 10	1.22 0.79 (P = 0.0 1.21 1.3 1.28 1.4 2 = 0.93 (P = 0.0 1.08 1.16 1.33 (P = 0.0	0.03 0.04 0005); F 0.07 0.1 0.15 0.1 0.15 0.1 0.19 0.24 002); F 0.12 0.12 0.12 0.14 003); F;	6 18 24 *= 92% 10 10 20 50 % 6 55 21 *= 93% 16 10 25 51 = 83% 451	3.7% 4.1% 7.8% 3.9% 3.4% 3.4% 1.1% 1.1% 1.7% 2.5% 3.2% 5.7% 5.7% 3.0% 3.9% 10.6%	-0.20 [-0.30, -0.10] -0.01 [-0.05, 0.03] -0.10 [-0.28, 0.09] -0.10 [-0.28, 0.09] -0.10 [-0.24, 0.04] -0.13 [-0.27, 0.01] -0.20 [-0.66, 0.26] -0.14 [-0.20, -0.08] -0.54 [-0.69, -0.39] -0.28 [-0.80, 0.24] -0.36 [-0.54, -0.18] -0.38 [-0.46, -0.30] -0.30 [-0.45, -0.15] -0.24 [-0.30, -0.18]	
Test for overall effect: Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: 2.1.5 Neuropathy Rao 2005 Raspovic 2013 Savelberg 2010 Sawacha 2008 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: 2.1.6 Hemiplegia Chen 2005 Kuan 1999 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: 2.1.7 Diplegia Buckon 2004 Carriero 2009 Saraph 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: 2.1.7 Diplegia Buckon 2004 Carriero 2009 Saraph 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: Total (95% CI) Heterogeneity: Tau ² =	<pre>Content Content C</pre>	P < 0.000 T) 0.05 0.07 * = 12.15, P = 0.30) 0.1 0.2 0.15 1.2 * = 0.47, I P < 0.000 0.22 0.19 * = 13.82; P = 0.29) 0.15 0.23 0.14 * = 11.83; P = 0.000 * = 294.1;	1 1 22 22 , df = 1 10 10 10 8 26 54 4 54 21 001) 6 5 5 21 16 9 25 50 0, df = 2 21) 462 25	1.22 0.79 (P = 0.0 1.21 1.3 1.28 1.4 2 = 0.93 (P = 0.0 1.08 1.16 1.33 (P = 0.0	0.03 0.04 0005); i 0.07 0.1 0.15 0.1 0.15 0.1 0.19 0.24 002); i 0.12 0.12 0.12 0.12 0.14 0.012 0.14 0.03); i ² :	6 18 24 *= 92% 10 10 10 20 50 % 6 51 21 10 25 51 = 83% 451 1); I*=	3.7% 4.1% 7.8% 3.9% 3.4% 3.4% 1.1% 1.7% 2.5% 3.2% 3.2% 3.2% 3.2% 3.2% 3.2% 3.0% 3.9% 10.6% 90%	-0.20 [-0.30, -0.10] -0.01 [-0.05, 0.03] -0.10 [-0.28, 0.09] -0.10 [-0.28, 0.09] -0.10 [-0.24, 0.04] -0.13 [-0.27, 0.01] -0.20 [-0.66, 0.26] -0.14 [-0.20, -0.08] -0.54 [-0.69, -0.39] -0.28 [-0.80, 0.24] -0.17 [-0.26, -0.08] -0.38 [-0.46, -0.30] -0.38 [-0.45, -0.15] -0.30 [-0.45, -0.18]	
Test for overall effect: 2.1.4 Charcot Marie T Bianco 2008 Ferrain 2011 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: 2.1.5 Neuropathy Rao 2005 Raspovic 2013 Savelberg 2010 Sawacha 2008 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: 2.1.6 Hemiplegia Chen 2005 Kuan 1999 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: 2.1.7 Diplegia Buckon 2004 Carriero 2009 Saraph 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: Fotal (95% CI)	Z = 6.73 () footh (CM 1.02 0.78 0.02; Chi ⁷ Z = 1.04 () 1.06 1.2 1.15 1.2 0.00; Chi ⁷ Z = 4.55 () 0.52 0.49 0.13; Chi ⁷ Z = 1.07 () 0.91 0.8 0.95 0.01; Chi ⁷ Z = 3.85 () 0.02; Chi ⁷ Z = 8.03 ()	$P < 0.000$ T) 0.05 0.07 $^{2} = 12.15$ $P = 0.30$ 0.1 0.2 0.15 1.2 $^{2} = 0.47, \mu$ $P < 0.000$ 0.22 0.19 $^{2} = 13.82$ $P = 0.29$ 0.15 0.23 0.14 $^{2} = 11.83,$ $P = 0.000$ $^{2} = 294.1$ $P < 0.000$	1 21 22 , df = 1 10 10 10 8 6 54 4 df = 3 (F 15 21 16 9 25 50 0 (df = 2 21) 462 20 21 21 22 20 21 20 20 20 20 20 20 20 20 20 20	1.22 0.79 1.21 1.3 1.28 1.4 P = 0.93 0.53 1.03 (P = 0.0 1.08 1.16 1.33 (P = 0.0	0.03 0.04 005); i 0.07 0.1 0.15 0.1 0.15 0.1 0.19 0.24 0.12 0.16 0.14 0.12 0.16 0.14 0.03); i ^{F}	6 18 24 10 10 10 20 20 50 (% 6 15 21 21 21 21 21 21 21 21 21 21	3.7% 4.1% 7.8% 3.9% 3.4% 3.4% 1.1% 1.1% 2.5% 3.2% 5.7% 3.2% 5.7% 3.9% 3.9% 3.9% 3.9% 3.9% 3.9% 3.9% 3.9	-0.20 [-0.30, -0.10] -0.01 [-0.05, 0.03] -0.10 [-0.28, 0.09] -0.10 [-0.28, 0.09] -0.10 [-0.24, 0.04] -0.13 [-0.27, 0.01] -0.20 [-0.66, 0.26] -0.14 [-0.20, -0.08] -0.54 [-0.69, -0.39] -0.28 [-0.80, 0.24] -0.17 [-0.26, -0.08] -0.36 [-0.54, -0.18] -0.38 [-0.46, -0.30] -0.30 [-0.45, -0.15] -0.30 [-0.45, -0.18]	+ + + + + + + + + + + + + + + + + + +

Figure 3b.

	Ele	Elderly Young						Mean Difference	Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl		
Anderson 2014	110	10	10	108	6	10	13.4%	2.00 [-5.23, 9.23]			
Judge 1996	116	7	26	110	9	32	33.4%	6.00 [1.88, 10.12]	_		
Kerrigan 1998	119	9	31	119	10	31	27.1%	0.00 [-4.74, 4.74]			
Kerrigan 2001	120	7	23	118	11	30	26.0%	2.00 [-2.87, 6.87]			
Total (95% CI)			90			103	100.0%	2.79 [-0.02, 5.61]	-		
Heterogeneity: Tau ² =	: 1.77; C	hi ² =	3.81, d	f= 3 (P :	= 0.2	8); I ² =	21%				
Test for overall effect:	Z = 1.94	(P =	0.05)						Favours [Elderly] Favours [Young]		
				Fore	est F	lot: (Cadeno	ce – Elderly vs Y	oung		

Figure 4a.

	Neurolo	ogical Gr	oup	0	ontrol			Mean Difference	Mean Difference
Study or Subaroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% Cl	IV. Random, 95% Cl
3.1.1 Parkinson								,	
Ferrarin 2002	100	17.5	4	105	10	4	24%	-5 00 [-24 75 14 75]	
Ferrarin 2002	94.6	18.2	10	105 9	8.5	10	2.470	-11 30 [-23 75 1 15]	
Hong 2005	108.6	14.9	30	110.1	9.5	30	5.5%	-1 50 [23.13, 1.13]	
Lewis 2000	120	11	14	117	0.0	14	5 3 %	3 00 64 12 10 12	_ _
Lewis 2000 Morrie 2005	110 0	16.2	19	124.1	126	17	4.200	5.00 [4,12,10,12]	
Montis 2003 Ponno 2006	105.3	7.26	12	1411 5	7.6	12	4.270	-0.00[17.01, 0.41] 6.40[11.05_0.05]	
перре 2000 Собимо 2006	100.1	10	10	116.0	0.1	13	5.770	-0.40[-11.00,-0.90]	
Sultated (95% CI)	106.5	12	101	115.5	0.0	92	32 1%	-0.60 [-14.25, 0.65] 3 98 [7 30 0.66]	
Unteressensity Tou ² -	2.06.068	8-700	4f = 0 /1		. .	50	32.170	-5.50 [-7.50, -0.00]	•
Test for overall effect:	Z= 2.35 (P = 0.03	ui – 0 (r	0.32), i – i	570			
3.1.2 Ataxia									
Palliyath 1998	102.2	15.9	10	111	7.6	10	4.3%	-8.80 [-19.72, 2.12]	
Stolze 2002	106.4	14.2	12	119.1	14.4	12	4.1%	-12.70 [-24.14, -1.26]	- _
Subtotal (95% CI)			22			22	8.4%	-10.66 [-18.56, -2.76]	◆
Heterogeneity: Tau² = Test for overall effect:	0.00; Chi Z = 2.64 (² = 0.23, P = 0.008	df=1(F 3)	P = 0.63); ² = ()%			
3.1.3 Cerebral Palsy									
Adolfsen 2007	136	11	31	130	13	31	5.6%	6.00 [0.01, 11.99]	⊢ ⊷−
Bell 2002	123	19.5	28	130	12.5	28	4.9%	-7.00 [-15.58, 1.58]	_ - +
Davids 1998	144	17	19	133	15	15	4.3%	11.00 [0.23, 21.77]	├
Eek 2011	129	9.5	20	120	9.3	20	5.6%	9.00 [3.17, 14.83]	
Steinwender 2000	139.3	8.2	20	131.7	7.4	20	5.8%	7.60 [2.76, 12.44]	
Subtotal (95% CI)			118			114	26.2%	5.56 [0.54, 10.58]	◆
3.1.4 Charcot Marie T	ooth (CM	T)	4	104	0.5	c	4.000	40.001.04.74 4.061	
Bianco 2008 Formain 2014	91	2.8	1	104	8.5	10	4.8%	-13.00 [-21.74, -4.26]	
Ferrain 2011	110	9	21	110	11	18	5.5%	0.00[0.37,0.37]	
Onupuu 2013 Subtotal (95% CI)	122	10	33	125	12.5	21	5.5% 15.9%	-3.00 [-9.34, 3.34]	
Heterogeneity: Tau ² = Test for overall effect:	23.79; Cł Z = 1.35 (ni² = 5.68 P = 0.18)	, df = 2	(P = 0.0	6); I ² =	65%	101070		•
3.1.5 Hemiplegia									
Chen 2005	83.4	12.8	6	78.9	21.7	6	2.4%	4.50 [-15.66, 24.66]	
Kuan 1999	67.2	20.6	15	110.1	23	15	3.2%	-42.90 [-58.53, -27.27]	
Subtotal (95% Cl)			21			21	5.5%	- 19.65 [-66.09, 26.80]	
Heterogeneity: Tau² = Test for overall effect:	1038.71; Z = 0.83 (Chi ² = 13 P = 0.41)	3.27, df	= 1 (P =	0.000	3); I² =	92%		
3.1.6 Diplegia									
Buckon 2004	142	23	16	140	12	16	3.8%	2.00 [-10.71, 14.71]	
Carriero 2009	126.7	17	9	143.3	21	10	2.9%	-16.60 [-33.71, 0.51]	
Saraph 2002	133.8	14	25	124.2	12	25	5.2%	9.60 [2.37, 16.83]	
Subtotal (95% CI)			50			51	11.9%	0.11 [-13.61, 13.84]	
Heterogeneity: Tau² = Test for overall effect:	107.50; C Z = 0.02 (>hi² = 7.8 P = 0.99)	9, df = 2	2 (P = 0.	02); I²	= 75%			
Total (95% CI)			367			345	100.0%	-2.88 [-6.79, 1.03]	•
Heterogeneity: Tau ² =	62.21: Ch	ni² = 98.9	1. df = 3	21 (P < 0		1); I ² =	79%		
Test for overall effect: Test for subgroup diff	Z = 1.44 (erences: (P = 0.15) Chi ² = 15	.81, df=	= 5 (P =	0.007)	, I ² = 68	3.4%		-50 -25 Ó 25 50 Favours (neurological) Favours (control)
			For	est P	lot:	Cade	ence –	Neurological vs	Healthy

Figure 4b.



Figure 5a.

	Neurolo	ogical Gro	up	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
4.1.1 Parkinson									
Ferrarin 2002	30.6	5.8	4	49.3	3.6	4	4.0%	-18.70 [-25.39, -12.01]	
Ferrarin 2005	28.8	7.9	10	46.2	5.5	10	4.0%	-17.40 [-23.37, -11.43]	
Mitoma 2000	21.5	5.4	9	30.6	5.4	12	4.1%	-9.10 [-13.77, -4.43]	
Morris 2005	33.2	8.5	12	47.6	4.1	12	4.1%	-14.40 [-19.74, -9.06]	
Roiz 2010	32.3	13.5	12	40.4	8.2	15	3.7%	-8.10 [-16.79, 0.59]	_
Sofuwa 2005	39.8	10.3	15	45.6	8.1	9	3.9%	-5.80 [-13.23, 1.63]	
Zijilmans 1996	39	20.8	12	39	3	10	3.4%	0.00 [-11.91, 11.91]	
Subtotal (95% CI)			74			72	27.1%	-11.45 [-15.68, -7.21]	◆
Heterogeneity: Tau² = Test for overall effect:	19.82; Ch Z = 5.30 (i	ni² = 16.61 P < 0.000	, df = 6 01)	(P = 0.1	01); I²∶	= 64%			
4.1.2 Ataxia									
Mitoma 2000	25.3	6.6	14	30.6	5.4	12	41%	-5 30 (-9 91 -0 69)	
Pallivath 1998	31.3	47	10	34.3	5.9	10	41%	-3 00 [-7 68 1 68]	_ ___
Serran 2012	44 A	16.6	16	48.1	4.0	15	3 8%	-3 70 [-12 13 / 72]	
Stolze 2002	++.+ 26	10.0	10	90.1	7.4	10	3.0% 2.0%	5.00[12.13, 4.73] 5.00[1.1.00_11.00]	
SIGIZE 2002	20	12	12	46.0	2	40	3.970	0.00[11.00, 11.00] 0.40.00 40 5 703	
Zubtotal (95% CP	50	3.0	63	40.9	2.1	13	4.2% 20.2%	3.10 [0.42, 3.78] 0.66 [4.95 3.63]	
Heterogeneity: Tau ² =	15.40: Ch	ni ² = 14,41	. df = 4	(P = 01	006): P	<u>مح</u> ¥= 72%	20.270	-0.00 [-4.65, 5.55]	T
Test for overall effect:	Z = 0.31 (P = 0.76)			,,.				
1.1.3 Cerebral Palsy									
Adolfsen 2007	47	5	31	48	9	31	4.2%	-1.00 [-4.62, 2.62]	
Bell 2002	45	9	28	47	8.5	28	4.1%	-2.00 [-6.59, 2.59]	-+
Davids 1998	45	9	19	45	6	15	4.1%	0.00 [-5.06, 5.06]	_
Steinwender 2000	48.8	5.6	20	48.8	3	20	4.2%	0.00 [-2.78, 2.78]	+
Subtotal (95% CI)			98			94	16.7%	-0.59 [-2.44, 1.26]	
Heterogeneity: Tau² = Test for overall effect: .	0.00; Chi ^a Z = 0.62 (i	² = 0.64, d P = 0.53)	lf = 3 (F	' = 0.89)); I² = 0	%			
4.1.4 Neuropathy									
Gomes 2011	5.63	1.72	23	26	3.6	23	4.3%	-20.37 [-22.00, -18.74]	+
Raspovic 2013	11.8	2.7	10	44.7	4.1	10	4.2%	-32.90 [-35.94, -29.86]	
Subtotal (95% CI)			33			33	8.5%	-26.57 [-38.84, -14.29]	
Heterogeneity: Tau² = Test for overall effect: .	76.95; Ch Z = 4.24 (i	ni² = 50.61 P < 0.000	,df=1 1)	(P < 0.1	00001); I² = 9;	8%		
4.1.5 Hemiplegia									
Galli 2010	33.3	7.6	51	36.5	8.9	15	4.1%	-3.20 [-8.16, 1.76]	+
Romkes 2002	20.9	10.4	12	37.1	7.7	10	3.9%	-16.20 [-23.78, -8.62]	
Thomas 1987	41.3	6.8	46	42	3	46	4.3%	-0.70 [-2.85, 1.45]	
Subtotal (95% CI)			109			71	12.2%	-5.87 [-13.21, 1.47]	
Heterogeneity: Tau² = Test for overall effect:	35.34; Ch Z = 1.57 (i	ni² = 15.12 P = 0.12)	?, df = 2	(P = 0.1	0005);	l² = 87	%		
4.1.6 Diplegia									
Carriero 2009	47.1	18.1	9	49.9	7.2	10	3.3%	-2.80 [-15.44, 9.84]	
Langerak 2008	44.8	12.3	40	39.4	8.3	20	4.1%	5.40 [0.13. 10.67]	⊢
Mazure 2013	45	94	12	49.1	8.1	17	4 0 %	-4 10 [-10 67 2 47]	_ _+
Baranh 2002	47.9	10	25	40.7	14.2	26	30%	-6.40[-13.21 0.41]	
Subtotal (95% CI)	42.0	10	86	43.2	14.2	72	15.2%	-1.60 [-7.85, 4.65]	•
Heterogeneity: Tau ² = Test for overall effect	25.86; Ch 7 = 0.50.0	ni² = 8.98, P = 0.62)	df = 3 ((P = 0.0)	3); I² =	67%	1012 /0	100 [-100,-100]	
	L - 0.00 (- 0.02)	105				100.00		
i otal (95% Cl)			463			404	100.0%	-6.54 [-11.18, -1.90]	
· · · · · · · · · · · · · · · · · · ·	130.23; C	≈ni² = 728.	.97, df:	= 24 (P	< 0.00	UO1); l²	= 97%		-20 -10 0 10 20
Heterogeneity: au* =		D 0.000							20 10 0 10 20
Heterogeneity: au* = Test for overall effect: .	Z = 2.76 (P = 0.006))						Favours (neurological) Favours (control)

Figure 5b.



Figure 6a.

	Neurolo	ogical Gr	oup	C	ontrol			Mean Difference	Mean Difference
Study or Subaroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random. 95% CI	IV. Random, 95% Cl
5.1.1 Parkinson								,	,
Ferrarin 2002	40	63	4	57.9	18	4	41%	-17 90 [-24 32 -11 48]	
Ferrarin 2005	36	10.3	10	58.2	1.3	10	41%	-22 20 [-28 63 -15 77]	
Mitoma 2000	43.2	94	9	58.6	7.8	12	3.9%	-15 40 [-22 96 -7 84]	
Morris 2005	47.9	7.5	12	58.1	6.3	12	4.3%	-10 20 [-15 74 -4 66]	<u> </u>
Sofuwa 2005	52.5	8.6	15	59.4	6.4	, ç	4.2%	-6.90 [-12.94 -0.86]	
Zijilmans 1996	45	11.7	12	62	4	10	4.0%	-17 00 [-74 07 -9 93]	<u> </u>
Subtotal (95% CI)	40		62	02	7	57	24.6%	-14.78 [-19.4210.13]	•
Heterogeneity: Tau ² =	22.69 [.] Ch	u² = 15.5	1 df = 4	5 (P = 0	008) 1	₹= 689	6		•
Test for overall effect:	Z = 6.24 (I	P < 0.000	001)	, - o.	,,	- 00,			
5.1.2 Ataxia									
Mitoma 2000	38.8	9.9	14	58.6	7.8	12	4.0%	-19.80 [-26.61, -12.99]	
Palliyath 1998	53.9	7.7	10	58.5	2.1	10	4.4%	-4.60 [-9.55, 0.35]	
Stolze 2002	50	8	12	53	3	12	4.4%	-3.00 [-7.83, 1.83]	
Vasco 2016	66.3	4.4	11	58.4	3.6	13	4.7%	7.90 [4.65, 11.15]	
Subtotal (95% CI)			47			47	17.6%	-4.60 [-15.17, 5.98]	
Heterogeneity: Tau ² =	109.65; C	;hi² = 59.	92, df=	3 (P < 0	0.000	1); I² =	95%		
Test for overall effect:	Z = 0.85 (I	P = 0.39)							
5.1.3 Cerebral Palsy									
Adolfsen 2007	44	16	31	63	7	31	4.2%	-19.00 [-25.15, -12.85]	
Bell 2002	47	12	28	63	8.5	28	4.3%	-16.00 [-21.45, -10.55]	
Davids 1998	45	13	19	56	5	15	4.1%	-11.00 [-17.37, -4.63]	
Steinwender 2000	52.7	4.9	20	59	1.4	20	4.8%	-6.30 [-8.53, -4.07]	-
Subtotal (95% CI)			98			94	17.5%	-12.76 [-19.29, -6.23]	-
Test for overall effect:	37.37; Ch Z = 3.83 (I	P = 0.000	0, ar = 3 01)	3 (P < U.	0001);	, r= 87	70		
5.1.4 Neuropathy									
Gomes 2011	58.3	4.15	23	61.33	3.9	23	4.8%	-3.03 [-5.36, -0.70]	
Raspovic 2013	26.9	4.3	10	30.7	4.7	10	4.6%	-3.80 [-7.75, 0.15]	
Subtotal (95% CI)	0.00.01.0		33			33	9.4%	-3.23 [-3.23, -1.22]	•
Heterogeneity: 1 au ² = Test for overall effect:	Z = 3.16 (I	P = 0.002	at = 1 (F 2)	⁹ = 0.74);	1%			
5.1.5 Hemiplegia									
Galli 2010	52.3	9.7	51	58.3	6.9	15	4.5%	-6.00 [-10.39, -1.61]	
Romkes 2002	50.8	13.7	12	68.6	3.3	10	3.8%	-17.80 [-25.82, -9.78]	
Thomas 1987	45.3	9.5	46	56	4	46	4.7%	-10.70 [-13.68, -7.72]	
Subtotal (95% CI)			109			71	13.0%	-10.59 [-15.72, -5.46]	◆
Heterogeneity: Tau ² = Test for overall effect:	14.04; Ch Z = 4.05 (I	ni² = 7.04 P < 0.00(, df = 2 01)	(P = 0.0	3); I² =	72%			
5.1.6 Diplegia									
Buckon 2004	47.7	12.5	16	55.2	8.57	16	3.9%	-7.50 [-14.930.07]	
Carriero 2009	41.3	27.4	9	64.8	6.4	10	1.9%	-23.50 [-41.845.16]	
Langerak 2008	56.8	14.8	40	56.2	7.1	20	4.3%	0.60 [-4.94. 6.14]	_ _
Mazure 2013	57.9	5.1	12	45.8	15.8	17	3.8%	12.10 [4.05, 20.15]	—
Saraph 2002	40.3	14	25	57.5	9.4	25	4.1%	-17.20 [-23.81, -10.59]	<u> </u>
Subtotal (95% CI)			102			88	17.9%	-5.98 [-16.86, 4.91]	
Heterogeneity: Tau ² = Test for overall effect:	131.14; C Z = 1.08 (I	:hi² = 38. P = 0.28)	52, df =	4 (P < (0.0000	1); I²=	90%		
Total (95% CI)			451			390	100.0%	-9.38 [-12.566.20]	•
Heterogeneity: Tau ² =	53 29° Ch	ji ² = 238	29 df=	23 (P <	: n nnn	01) P:	= 90%	000 [- 12:00, -0:20]	
Test for overall effect:	Z = 5.78 (P < 0.000	, 201)	v ·	2.500	2.01.2	~		-20 -10 0 10 20
Test for subaroup diff	erences (Chi ² = 28	.32, df=	= 5 (P <	0.0001	1), ² = 8	32.3%		Favours (neurological) Favours (control)



Figure 6b.



Figure 7a.

Marchar and Dashaman	Neurolo	gical Gro	up	Co	ontrol	T	104-1-1-1	Mean Difference	Mean Difference
Study of Subgroup	wean	SD	rotal	mean	SD	rotal	vveight	iv, Random, 95% Cl	IV, Kandom, 95% CI
5.1.1 Parkinson									
errarin 2002	12.6	3.7	4	24.4	4.7	4	4.2%	-11.80 [-17.66, -5.94]	
errarin 2005	13.4	3.2	10	24.5	4.5	10	5.6%	-11.10 [-14.52, -7.68]	
Aitoma 2000	24.2	6.2	9	32.8	7	12	4.3%	-8.60 [-14.27, -2.93]	
Aorris 2005	19.1	4	12	23.8	4.8	12	5.5%	-4.70 [-8.24, -1.16]	
Sofuwa 2005 Subtotal (95% CI)	21.54	5.13	15 50	25.7	5.6	9 47	5.0% 24.5%	-4.16 [-8.65, 0.33] -7 89 [-11 17 -4 62]	
Heterogeneity: Tau ² = Fest for overall effect:	8.58; Chi² Z = 4.73 (F	° = 10.92, ° < 0.000	df = 4 (01)	(P = 0.0	3); ² :	= 63%	24.370	-1.05 [-11.17, -4.02]	
5.1.2 Ataxia									
Aitoma 2000	19.5	5.1	14	32.8	7	12	4.8%	-13.30 [-18.08, -8.52]	
Pallivath 1998	23.5	5.1	10	31.5	62	10	47%	-8 00 [-12 98 -3 02]	
Serran 2012	16.2	53	16	20	49	15	5.5%	-12 80 [-16 39 -9 21]	
Stolze 2002	25	5	12	 10	7.5	12	5.5%	12.00 [10.00, -0.21]	
/00/20 2002 /00/20 2016	20	U Na	12	19	4 5 5	12	J.U.70 1/00/	-210[2.30, 8.02]	
Subtotal (95% CI)	20.9	0.4	63	30	0.0	13 62	4.8% 25.2%	-3.10[-7.92, 1.72] -6.20[-14.01, 1.61]	
Heterogeneity: Tau ² = Test for overall effect:	74.34; Ch 7 = 1.56 (F	i ² = 66.74 P = 0.12)	, df = 4	(P < 0.	0000	1); I² =	94%		
1 3 Corobral Daley		,							
	~~	~	~ 1	~ 4	-	~ 4	E 000	0.0017.01.1.01	
aoifsen 2007	28	9	31	31		31	5.2%	-3.00 [-7.01, 1.01]	
ieli 2002	27	8.5	28	31	5.5	28	5.4%	-4.00 [-7.75, -0.25]	
avids 1998	26	9	19	29	4	15	4.9%	-3.00 [-7.52, 1.52]	
teinwender 2000 Jubtotal (95% Cl)	22.6	9.2	20 98	25.8	8.5	20 94	4.4% 19.9%	-3.20 [-8.69, 2.29] - 3.36 [-5.521.21]	•
Heterogeneity: Tau² = Test for overall effect:	0.00; Chi ² Z = 3.06 (F	²= 0.17, d P = 0.002)	f=3(P)	9 = 0.98); 2 =	0%			
6.1.5 Neuropathy									
Fomes 2011	11.1	3	23	16.6	4	23	6.3%	-5.50 [-7.54, -3.46]	_
Raspovic 2013	20.2	4	10	25.7	4	10	5.5% 11.8%	-5.50 [-9.01, -1.99]	
Subtotal (95% Ch									•
Subtotal (95% CI)	0.00.01.2		33	4 00	. 17	0.01	111070		
Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect:	0.00; Chi² Z = 6.11 (F	° = 0.00, d ° < 0.0001	33 f = 1 (P 01)	? = 1.00); ² =	0%	110,0		
Subtotal (95% CI) Heterogeneity: Tau² = Test for overall effect: 5.1.6 Hemiplegia	0.00; Chi Z = 6.11 (F	² = 0.00, d ° < 0.0001	33 f=1(P 01)	9 = 1.00); ² =	0%	1107		
Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect: 5. 1.6 Hemiplegia 3alli 2010	0.00; Chi² Z = 6.11 (F 18.4	²= 0.00, d º < 0.0001 9.5	33 f=1(P 01) 51	25.5 ² = 1.00); l²= 6.8	0%	5.1%	-7.10 -11.42 -2.781	
subtotal (95% CI) leterogeneity: Tau ² = 'est for overall effect: i. 1.6 Hemiplegia Salli 2010 Romkes 2002	0.00; Chi [≈] Z = 6.11 (F 18.4 21 8	² = 0.00, d P < 0.0001 9.5 15 4	33 f = 1 (P 01) 51 12	25.5 27.8); I ^z = 6.8 8 6	0% 15 10	5.1% 2.4%	-7.10 [-11.42, -2.78] -6.00 [-16 21 4 21]	
Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: 5.1.6 Hemiplegia Salli 2010 Romkes 2002 Subtotal (95% CI)	0.00; Chi ^a Z = 6.11 (F 18.4 21.8	[:] = 0.00, d ^o < 0.0001 9.5 15.4	33 f = 1 (P 01) 51 12 63	25.5 27.8); I² = 6.8 8.6	0% 15 10 25	5.1% 2.4% 7.4%	-7.10 [-11.42, -2.78] -6.00 [-16.21, 4.21] - 6.93 [-10.91, -2.96]	
Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect: Salli 2010 Romkes 2002 Subtotal (95% Cl) Heterogeneity: Tau ² = Test for overall effect:	0.00; Chi ^z Z = 6.11 (F 18.4 21.8 0.00; Chi ^z Z = 3.42 (F	² = 0.00, d P < 0.000 9.5 15.4 ² = 0.04, d P = 0.000	33 f=1(P 01) 51 12 63 f=1(P 6)	25.5 27.8 2 = 0.85); I ² = 6.8 8.6); I ² =	0% 15 10 25 0%	5.1% 2.4% 7.4%	-7.10 [-11.42, -2.78] -6.00 [-16.21, 4.21] - 6.93 [-10.91, -2.96]	
Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: S.1.6 Hemiplegia Salli 2010 Romkes 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: S.1.7 Diplegia	0.00; Chi ² Z = 6.11 (F 18.4 21.8 0.00; Chi ² Z = 3.42 (F	² = 0.00, d ⁹ < 0.000 9.5 15.4 ² = 0.04, d ⁹ = 0.000	33 f = 1 (P 01) 51 12 63 f = 1 (P 6)	25.5 27.8 2 0.85); I ² = 6.8 8.6); I ² =	0% 15 10 25 0%	5.1% 2.4% 7.4%	-7.10 [-11.42, -2.78] -6.00 [-16.21, 4.21] -6.93 [-10.91, -2.96]	
Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: 5.1.6 Hemiplegia Salli 2010 Romkes 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: 5.1.7 Diplegia dazure 2013	0.00; Chi ² Z = 6.11 (F 18.4 21.8 0.00; Chi ² Z = 3.42 (F 29.1	² = 0.00, d ⁹ < 0.000 9.5 15.4 ² = 0.04, d ² = 0.000 3.2	33 f = 1 (P 01) 51 12 63 f = 1 (P 6) 12	25.5 27.8 2 0.85); I ² = 6.8 8.6); I ² =	0% 15 10 25 0%	5.1% 2.4% 7.4%	-7.10 [-11.42, -2.78] -6.00 [-16.21, 4.21] - 6.93 [-10.91, -2.96]	
iubtotal (95% CI) leterogeneity: Tau ² = 'est for overall effect: .1.6 Hemiplegia Salli 2010 Comkes 2002 Soubtotal (95% CI) leterogeneity: Tau ² = 'est for overall effect: .1.7 Diplegia lazure 2013 Lazure 2013	0.00; Chi [≠] Z = 6.11 (F 18.4 21.8 0.00; Chi [≠] Z = 3.42 (F 29.1 24 5	2 = 0.00, d 9 < 0.0000 9.5 15.4 2 = 0.04, d 9 = 0.0000 3.2 7	33 f = 1 (P 01) 51 12 63 f = 1 (P 6) 12 25	25.5 27.8 2 = 0.85 33.7); I ² = 6.8 8.6); I ² = 6.6	0% 15 10 25 0% 17	5.1% 2.4% 7.4% 5.5%	-7.10 [-11.42, -2.78] -6.00 [-16.21, 4.21] - 6.93 [-10.91, -2.96] -4.60 [-8.22, -0.98]	
Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: Salli 2010 Romkes 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Test for overall effect: S.1.7 Diplegia Mazure 2013 Saraph 2002 Subtotal (95% CI)	0.00; Chi [≥] Z = 6.11 (F 18.4 21.8 0.00; Chi [≥] Z = 3.42 (F 29.1 21.6	2 = 0.00, d 9 < 0.0001 9.5 15.4 2 = 0.04, d 2 = 0.0001 3.2 7	33 f = 1 (P 01) 51 12 63 f = 1 (P 6) 12 25 37	25.5 27.8 2 = 0.85 33.7 25.9); I ² = 6.8 8.6); I ² = 6.6 4	0% 15 10 25 0% 17 25 42	5.1% 2.4% 7.4% 5.5% 5.7% 11.2%	-7.10 [-11.42, -2.78] -6.00 [-16.21, 4.21] -6.93 [-10.91, -2.96] -4.60 [-8.22, -0.98] -4.30 [-7.46, -1.14] -4.43 [-6.81, -2.05]	
Subtotal (95% CI) Heterogeneitly: Tau ² = Fest for overall effect: S.1.6 Hemiplegia Salli 2010 Romkes 2002 Subtotal (95% CI) Heterogeneitly: Tau ² = Test for overall effect: Subtotal (95% CI) Heterogeneitly: Tau ² = 'est for overall effect: 'est for overall effect:	0.00; Chi [≇] Z = 6.11 (F 18.4 21.8 0.00; Chi [≇] Z = 3.42 (F 29.1 21.6 0.00; Chi [≇] Z = 3.65 (F	= 0.00, d 9.5 15.4 = 0.04, d 3.2 7 = 0.01, d = 0.000	33 f = 1 (P 01) 51 12 63 f = 1 (P 6) 12 25 37 f = 1 (P 3)	25.5 27.8 2 = 0.85 33.7 25.9 2 = 0.90); I ² = 6.8 8.6); I ² = 6.6 4); I ² =	0% 15 10 25 0% 17 25 42 0%	5.1% 2.4% 7.4% 5.5% 5.7% 11.2%	-7.10 [-11.42, -2.78] -6.00 [-16.21, 4.21] -6.93 [-10.91, -2.96] -4.60 [-8.22, -0.98] -4.30 [-7.46, -1.14] -4.43 [-6.81, -2.05]	
Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect: S.1.6 Hemiplegia Salli 2010 Romkes 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect: S.1.7 Diplegia Mazure 2013 Saraph 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect: Fotal (95% CI)	0.00; Chi [≥] Z = 6.11 (F 18.4 21.8 0.00; Chi [≥] Z = 3.42 (F 29.1 21.6 0.00; Chi [≥] Z = 3.65 (F	= 0.00, d 9.5 15.4 = 0.004, d = 0.0001 3.2 7 = 0.01, d P = 0.0001	33 f=1 (P 01) 51 12 63 f=1 (P 6) 12 25 37 f=1 (P 3) 344	25.5 27.8 9 = 0.85 33.7 25.9 9 = 0.90); ² = 6.8 8.6); ² = 6.6 4); ² =	0% 15 10 25 0% 17 25 42 0% 303	5.1% 2.4% 7.4% 5.5% 5.7% 11.2%	-7.10 [-11.42, -2.78] -6.00 [-16.21, 4.21] -6.93 [-10.91, -2.96] -4.60 [-8.22, -0.98] -4.30 [-7.46, -1.14] -4.43 [-6.81, -2.05]	
Subtotal (95% CI) Heterogeneitly: Tau ² = Fest for overall effect: S.1.6 Hemiplegia Salli 2010 Romkes 2002 Subtotal (95% CI) Heterogeneitly: Tau ² = Fest for overall effect: S.1.7 Diplegia Mazure 2013 Saraph 2002 Subtotal (95% CI) Heterogeneitly: Tau ² = Fest for overall effect: Fotal (95% CI)	0.00; Chi [≇] Z = 6.11 (F 18.4 21.8 0.00; Chi [≇] Z = 3.42 (F 29.1 21.6 0.00; Chi [≇] Z = 3.65 (F	= 0.00, d 9.5 15.4 = 0.04, d = 0.000 3.2 7 = 0.01, d = 0.000	33 f=1 (P 01) 51 12 63 f=1 (P 6) 12 25 37 f=1 (P 3) 344	25.5 27.8 25.9 27.8 27.8 25.9 25.9 25.9); ² = 6.8 8.6); ² = 6.6 4); ² =	0% 15 10 25 0% 17 25 42 0% 303	5.1% 2.4% 7.4% 5.5% 5.7% 11.2%	-7.10 [-11.42, -2.78] -6.00 [-16.21, 4.21] -6.93 [-10.91, -2.96] -4.60 [-8.22, -0.98] -4.30 [-7.46, -1.14] -4.43 [-6.81, -2.05]	
Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect: S.1.6 Hemiplegia Balli 2010 Romkes 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect: S.1.7 Diplegia Mazure 2013 Baraph 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect: Fotal (95% CI) Heterogeneity: Tau ² =	0.00; Chi [≥] Z = 6.11 (F 18.4 21.8 0.00; Chi [≥] Z = 3.42 (F 29.1 21.6 0.00; Chi [≥] Z = 3.65 (F	² = 0.00, d 9.5 15.4 ² = 0.04, d ² = 0.04, d ^{3.2} 7 ² = 0.01, d ² = 0.000 ³	33 f=1 (P 01) 51 12 63 f=1 (P 6) 12 25 37 f=1 (P 3) 344 ,df=1	25.5 27.8 2 = 0.85 33.7 25.9 2 = 0.90 9 (P < (); ² = 6.8 8.6); ² = 6.6 4); ² =	0% 15 10 25 0% 17 25 42 0% 303 01); I [≠] =	5.1% 2.4% 7.4% 5.5% 5.7% 11.2%	-7.10 [-11.42, -2.78] -6.00 [-16.21, 4.21] -6.93 [-10.91, -2.96] -4.60 [-8.22, -0.98] -4.30 [-7.46, -1.14] -4.43 [-6.81, -2.05] -5.79 [-7.73, -3.84]	
Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect: S.1.6 Hemiplegia Salli 2010 Romkes 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect: Aazure 2013 Saraph 2002 Subtotal (95% CI) Heterogeneity: Tau ² = Fest for overall effect: Fotal (95% CI) Heterogeneity: Tau ² =	0.00; Chi [≇] Z = 6.11 (F 18.4 21.8 0.00; Chi [≇] Z = 3.42 (F 29.1 21.6 0.00; Chi [≇] Z = 3.65 (F 14.64; Ch Z = 5.83 (F	<pre>'= 0.00, d 9 < 0.0000 9.5 15.4 '= 0.04, d P = 0.0000 3.2 7 '= 0.01, d P = 0.0000 i² = 88.41 C < 0.0000</pre>	333 f=1 (F 01) 51 12 63 f=1 (P 65) 12 25 37 f=1 (P 3) 344 , df=1 01)	25.5 27.8 9 = 0.85 33.7 25.9 9 = 0.90 9 (P < (); ² = 6.8 8.6); ² = 6.6 4); ² = 0.000	0% 15 10 25 0% 17 25 42 0% 303 303 303	5.1% 2.4% 7.4% 5.5% 5.7% 11.2%	-7.10 [-11.42, -2.78] -6.00 [-16.21, 4.21] -6.93 [-10.91, -2.96] -4.60 [-8.22, -0.98] -4.30 [-7.46, -1.14] -4.43 [-6.81, -2.05]	-10 -5 0 5 10 Favours [neurologicall] Favours [control]



Figure 7b.

	Neurolo	ogical Gr	oup	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
7.1.1 Parkinson									
Ferrarin 2002	0.76	0.24	4	1.08	0.16	4	12.1%	-0.32 [-0.60, -0.04]	_
Ferrarin 2005	0.88	0.27	10	0.97	0.26	10	12.4%	-0.09 [-0.32, 0.14]	
Sofuwa 2005	0.71	0.21	15	0.83	0.12	9	12.7%	-0.12 [-0.25, 0.01]	
Subtotal (95% CI)			29			23	37.2%	-0.14 [-0.25, -0.04]	◆
Heterogeneity: Tau ² :	= 0.00; Chi ^a	^e = 1.82,	df = 2 (ł	P = 0.40	l); I ^z = (0%			
Test for overall effect	: Z = 2.62 (F	P = 0.00!	9)						
7.1.2 Cerebral Palsy	,								
Adolfsen 2007	0.74	0.3	31	1.1	0.52	31	12.5%	-0.36 [-0.57, -0.15]	_
Davids 1998	0.63	0.3	19	-0.57	0.12	15	12.7%	1.20 [1.05, 1.35]	
Eek 2011	1.65	0.45	20	0.99	0.15	20	12.5%	0.66 [0.45, 0.87]	_
Subtotal (95% CI)			70			66	37.6%	0.50 [-0.40, 1.41]	
Heterogeneity: Tau ² :	= 0.63; Chi ^a	² = 140.5	3, df = 0	2 (P < 0.	.00001); l² = 9	9%		
Test for overall effect	.: Z = 1.09 (F	P = 0.28))						
7.1.3 Diplegia									
Buckon 2004	0.7	0.23	16	0.82	0.16	16	12.7%	-0.12 [-0.26, 0.02]	
Saraph 2002	1.13	0.4	25	0.94	0.4	25	12.4%	0.19 [-0.03, 0.41]	
Subtotal (95% CI)			41			41	25.1%	0.02 [-0.28, 0.33]	
Heterogeneity: Tau ² :	= 0.04; Chi ^a	² = 5.43,	df = 1 (f	P = 0.02	(); 2 = 8	32%			
Test for overall effect	: Z = 0.14 (F	P = 0.89)							
Total (95% CI)			140			130	100.0%	0.13 [-0.28, 0.54]	
Heterogeneity: Tau ² :	= 0.34; Chi ^a	² = 283.5	4. df = 3	7 (P < 0	.00001); ² = 9	8%	-	
Test for overall effect	: Z = 0.64 (I	P = 0.53	1						-1 -0.5 0 0.5 1
Test for subaroup dit	fferences: (Chi² = 2.8	32 df=	2 (P = 0	124) P	'= 29 O	%		Favours (neurological) Favours (control)
Test for subgroup dif	ferences: (Chi² = 2.8	32. df=	2 (P = 0	1.24), l ^a	'= 29.0	%		
	Fore	est Plo	ot: Pe	eak F	lexic	on M	omen	t at Hip – Neuro	ological vs Healthy

Figure 8.



Figure 9.

	Neurolo	gical G	oup	C	ontrol			Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% Cl	IV, Fixed, 95% Cl
9.1.1 Parkinson									
Ferrarin 2002	1.15	0.25	4	1.33	0.04	4	1.2%	-0.18 [-0.43, 0.07]	
Ferrarin 2005	1.08	0.21	10	1.37	0.14	10	2.9%	-0.29 [-0.45, -0.13]	
Sofuwa 2005	1.32	0.05	15	1.5	0.05	9	42.1%	-0.18 [-0.22, -0.14]	+
Subtotal (95% CI)			29			23	46.2%	-0.19 [-0.23, -0.15]	•
Heterogeneity: Chi² = Test for overall effect:	1.78, df = Z = 9.29 (F	2 (P = 0. P < 0.00	.41); I² = 001)	0%					
9.1.2 Cerebral Palsy									
Adolfsen 2007	1.19	0.22	31	0.95	0.26	31	5.0%	0.24 [0.12, 0.36]	
Davids 1998	1.02	0.2	19	1.03	0.15	15	5.2%	-0.01 [-0.13, 0.11]	_
Eek 2011	1.59	0.15	20	1.71	0.22	20	5.3%	-0.12 [-0.24, -0.00]	
Subtotal (95% CI)			70			66	15.5%	0.03 [-0.03, 0.10]	◆
Heterogeneity: Chi² = Test for overall effect:	18.57, df= Z = 0.96 (F	= 2 (P ≺ I P = 0.34	D.0001))	; I ² = 899	6				
9.1.3 Charcot Marie T	ooth (CM	T)							
Bianco 2008	0.83	0.03	1	1.02	0.024	6	18.8%	-0.19 [-0.25, -0.13]	
Ferrain 2011	0	0	21	0.98	0	18		Not estimable	
Onupuu 2013	1.07	0.17	33	1.31	0.19	21	7.2%	-0.24 [-0.34, -0.14]	
Subtotal (95% Cl)			34			27	26.0 %	-0.20 [-0.26, -0.15]	•
Heterogeneity: Chi² = Test for overall effect:	0.70, df= Z = 7.60 (F	1 (P = 0. P < 0.00	40); I² = 001)	0%					
9.1.4 Neuropathy									
Rao 2005	1.21	0.18	10	1.4	0.25	10	2.0%	-0.19 [-0.38, 0.00]	
Raspovic 2013	1.27	0.17	10	1.38	0.18	10	3.1%	-0.11 [-0.26, 0.04]	
Subtotal (95% CI)			20			20	5.0%	-0.14 [-0.26, -0.02]	◆
Heterogeneity: Chi² = Test for overall effect:	0.41, df= Z= 2.32 (F	1 (P = 0. P = 0.02	.52); I² =)	0%					
9.1.5 Diplegia									
Buckon 2004	0.84	0.18	16	1.29	0.15	16	5.5%	-0.45 [-0.56, -0.34]	
Saraph 2002	0.72	0.4	25	1.29	0.3	25	1.9%	-0.57 [-0.77, -0.37]	
Subtotal (95% Cl)			41			41	7.3%	-0.48 [-0.58, -0.38]	◆
Heterogeneity: Chi² = Test for overall effect:	1.07, df= Z=9.51 (F	1 (P = 0. P < 0.00	30); I ² = 001)	7%					
Total (95% CI)			194			177	100.0%	-0.18 [-0.20, -0.15]	•
Heterogeneity: Chi ² =	96.76, df=	= 11 (P <	0.0000	1); l² = 8	39%			-	
Test for overall effect:	Z = 12.91	(P < 0.0	0001)						Favours [neurological] Favours [control]
		biz = 7	24 df-	A/D ~	0 00004	$1 \times 12 = 0$	203.10		ravous [reuningical] ravous [control]

Figure 10.

FIGURE CAPTIONS

Figure 1. Flowchart Outlining Literature Search Process

Figure 2a. Meta-analysis report for gait velocity comparing elderly with young group. A negative mean difference indicates a lower gait velocity in the elderly

Figure 2b. Meta-analysis report for gait velocity comparing neurological with healthy group. A negative mean difference indicates a lower gait velocity in the neurological group

Figure 3a. Meta-analysis report for stride length comparing elderly with young group. A negative mean difference indicates a lower stride length in the elderly

Figure 3b. Meta-analysis report for stride length comparing neurological with healthy group. A negative mean difference indicates a lower stride length in the neurological group

Figure 4a. Meta-analysis report for cadence comparing elderly with young group. A positive mean difference indicates a higher value of cadence in the elderly

Figure 4b. Meta-analysis report for cadence comparing neurological with healthy group. A negative mean difference indicates a lower value of cadence in the neurological group

Figure 5a. Meta-analysis report for hip range of movement (ROM) comparing elderly with young group. A negative mean difference indicates a lower hip ROM in the elderly

Figure 5b. Meta-analysis report for hip range of movement (ROM) comparing neurological with healthy group. A negative mean difference indicates a lower hip ROM in the neurological group

Figure 6a. Meta-analysis report for knee range of movement (ROM) comparing elderly with young group. A negative mean difference indicates a lower knee ROM in the elderly

Figure 6b. Meta-analysis report for knee range of movement (ROM) comparing neurological with healthy group. A negative mean difference indicates a lower knee ROM in the neurological group

Figure 7a. Meta-analysis report for ankle range of movement (ROM) comparing elderly with young group. A negative mean difference indicates a lower ankle ROM in the elderly

Figure 7b. Meta-analysis report for ankle range of movement (ROM) comparing neurological with young group. A negative mean difference indicates a lower ankle ROM in the neurological group

Figure 8. Meta-analysis report for peak flexion moment at hip comparing neurological with healthy group. A negative mean difference in Parkinson indicates a lower value of peak flexion moment at hip. Results do not favour any group in cerebral palsy and diplegia

Figure 9. Meta-analysis report for peak flexion moment at knee comparing neurological with healthy group. A positive mean difference in cerebral palsy indicates a higher value of peak flexion moment at knee. Results do not favour any group in diplegia

Figure 10. Meta-analysis report for peak dorsi-flexion at ankle comparing neurological with healthy group. A negative mean difference indicates a lower value of peak dorsi-flexion moment in the neurological group