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The long-term effects of aggressive spasticity reducing treatment, including selective dorsal rhizotomy, on joint kinematic outcomes of persons with cerebral palsy

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ABSTRACT

Background: Selective dorsal rhizotomy (SDR) creates a large and permanent reduction of spasticity for children with cerebral palsy (CP). Previous SDR outcomes studies have generally lacked appropriate control groups, had limited sample sizes, or reported short-term follow-up, limiting evidence for improvement in long-term gait function.

Research question: Does aggressive spasticity management for individuals with CP improve long-term gait kinematics (discrete joint kinematics) compared to a control group of individuals with CP with minimal spasticity management?

Methods: This study was a secondary analysis – focused on joint-level kinematics – of a previous study evaluating the long-term outcomes of SDR. Two groups of participants were recruited based on a retrospectively completed baseline clinical gait study. One group received aggressive spasticity treatment including a selective dorsal rhizotomy (Yes-SDR group), while the other group had minimal spasticity management (No-SDR group). Both groups had orthopedic surgery treatment. Groups were matched on baseline spasticity. All participants prospectively returned for a follow-up gait study in young adulthood (greater than 21 years of age and at least 10 years after baseline). Change scores in discrete kinematic variables from baseline to follow-up were assessed using a linear model that included treatment arm (Yes-SDR, No-SDR), baseline age, and baseline kinematic value. For treatment arm, 5° and 5 Gait Deviation Index points were selected as thresholds to be considered a meaningful difference between treatment groups.

Results: At follow-up, there were no meaningful differences in pelvis, hip, knee, or ankle kinematic variable changes between treatment arms. Max knee flexion – swing showed a moderate treatment effect for Yes-SDR, although it did not reach the defined threshold.

Significance: Aggressive spasticity treatment does not result in meaningful differences in gait kinematics for persons with cerebral palsy in young adulthood compared to minimal spasticity management with both groups having orthopedic surgery.

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1. Introduction

The purpose of the current study was to understand the long-term effects of spasticity reduction on gait kinematics. To isolate the effect of spasticity, long-term gait kinematics for individuals with cerebral palsy (CP) treated with aggressive spasticity management, including selective dorsal rhizotomy (SDR), were compared to a control group of individuals with CP who underwent minimal spasticity management. Discrete kinematic variables at the ankle, knee, hip, and pelvis were investigated at baseline (<10.5 years of age) and follow-up in young adulthood. Change scores (baseline to follow-up) were compared between treatment groups to assess the effects of spasticity. Previous gait outcomes between groups were only assessed using a summary metric, the Gait Deviation Index (GDI) [1].

Spasticity is defined as a velocity dependent stretch reflex and is a common concern in children with CP [2]. Spasticity is not part of typical development, and thus has been considered a significant pathology for children with CP and treated with varying methods including oral medications [3], botulinum toxin [4,5], intrathecal baclofen pumps [6], and SDR [7,8]. SDR creates a large and permanent reduction of spasticity; however, there is limited evidence for improvement in long-term gait kinematics following SDR. Previous studies of SDR outcomes have either lacked an appropriate control group, had a small sample size, or solely investigated short-term follow-up [9–21]. A recent systematic review of the long-term effects of SDR showed no functional improvements due to SDR compared to routine care without SDR, in part due to low evidence levels and bias [22].

Studies investigating the long-term effects of SDR on function were recently reported, with many of the authors of the current study involved in three of the publications [1,23–25]. The first study found minimal differences in gait, energy consumption, and function between groups treated with and without an SDR at one center [23]. However, the control group in this study had other anti-spasticity treatment including neurotoxin injections and baclofen pump implantation. To more comprehensively compare aggressive to minimal spasticity treatment, a second study compared a group with aggressive spasticity treatment (all participants in group undergoing SDR, some also undergoing neurotoxin injections) (Yes-SDR), to a control group with minimal spasticity treatment (No-SDR) [1,24]. Both groups had orthopedic surgery. This multi-center, pre-registered, long-term study found no meaningful long-term differences in contracture, function, energy expenditure, quality of life, or overall amount of orthopedic surgery, between groups. Although the overall amount of orthopedic surgery was not different between groups, the Yes-SDR group had more bony surgeries (femoral and tibial derotation osteotomies, foot stabilization procedures) while the No-SDR group had more soft tissue surgeries, likely reflecting philosophical differences in orthopedic management between centers. Effects on gait were only assessed using GDI [26] and non-dimensional speed. The authors reported both Yes-SDR and No-SDR groups improved with the Yes-SDR group improving by a modestly larger amount. Individual parameters (e.g., hip rotation, knee extension, ankle dorsiflexion, etc.) were not reported [1]. A third study investigated short (1 year) and medium term (5 year) kinematics outcomes for Yes-SDR vs. No-SDR groups [25]. At the 1 year follow-up, the Yes-SDR group had significant kinematics improvements compared to No-SDR, but at 5 years, both groups had kinematic improvements with no differences between Yes-SDR and No-SDR groups [25].

Prior to analysis, four baseline variables were identified that were likely confounders of long-term kinematic outcomes of young adults with CP. The following factors were considered for model inclusion: (1) baseline deformity (contractures, bony alignment, or spasticity) (2) treatment history (spasticity or orthopedic treatment), (3) baseline age, and (4) baseline kinematic values. Baseline deformity was not significantly different between groups based on multiple physical exam measures at baseline [1] and was excluded from our model to assess outcomes. Similarly, treatment history prior to baseline (matched on baseline spasticity, no history of prior SDR, and no significant differences in prior orthopedic surgery [1]) was similar between groups and excluded from analysis.

Children develop gross motor skills as they age, independent of spasticity treatment. While matching between the groups was effective for the pre-registered age range (3.5–10.5 years), it was not perfect. Median age for the Yes-SDR group (5.0 years) was two years younger than the No-SDR group (7.1 years) [1]. Potential developmental effects for the Yes-SDR group starting at a younger age might have led to a portion of the overall GDI improvement at follow-up. Therefore, an adjustment for baseline age is necessary to account for its impact on kinematic outcomes.

Baseline kinematic value differences between treatment groups might affect outcomes. Some baseline kinematics were different between Yes-SDR and No-SDR groups [1]. For example, baseline median minimum knee flexion in stance for Yes-SDR was 15° flexion while No-SDR group was 6°. Prior studies have demonstrated that individuals with greater baseline kinematic deviations generally had greater post-treatment improvements [27–29]. The concept of regression to the mean can account for part of these improvements. Further, larger baseline deviations may have led to a greater propensity of orthopedic treatment and again led to greater kinematic change scores. Therefore, baseline kinematic values for each treatment group need to be accounted for in the outcome analysis.

For the current study, we hypothesized that children treated with aggressive spasticity management (Yes-SDR) will have significantly larger improvements in discrete gait kinematic variables in early adulthood compared to children treated with minimal spasticity management (No-SDR). Since some kinematic outcomes could be due to baseline differences along with regression to the mean impacting change scores, we chose to assess differences in kinematics due to spasticity management while adjusting for any significant baseline differences with linear models.

2. Materials and methods

The methods and design of the previously published long term SDR study were pre-registered in a protocol paper [24]. Further methods and results were reported in the overall outcomes study [1]. Institutional Review Board (IRB) approval was granted by the University of Minnesota and the Western IRB. Informed consent was obtained from all participants prior to joining in the study.

2.1. Participants

Two groups of participants were recruited from three centers. One group of participants received aggressive spasticity reducing treatment at one of the centers (Gillette Children's, St. Paul, MN, USA) including, a selective dorsal rhizotomy (Yes-SDR group). The other group had minimal spasticity management (No-SDR group) consisting of less than three episodes of neurotoxin injections and oral or intrathecal baclofen for <1 year. This No-SDR control group was recruited from two centers (Shriners Children's – Salt Lake City, UT, USA and Shriners Children's – Spokane, WA, USA).

Yes-SDR and No-SDR groups included participants with a diagnosis of bilateral CP and were matched on baseline spasticity distributions and age range (3.5 – 10.5 years) [24]. All centers established an eligible pool of participants that had a baseline study (prior to SDR for Yes-SDR group) and met the criteria for baseline age. Potential participants were 21 years or older at the time of recruitment and at least 10 years from baseline. Individuals meeting these criteria were randomly contacted to return to the same baseline center for a follow-up evaluation between October 2018-February 2020.

2.2. Protocol

This manuscript focuses on three-dimensional instrumented gait analysis testing. Each center collected kinematics using their typical data collection, modeling, and processing methods. All centers had a 12 + camera Vicon Motion Capture system (Oxford Metrics, Oxford, UK). The Shriners Children's centers used similar models to assess lower extremity movement based on Plug-in-Gait (Vicon, Oxford Metrics). Gillette Children's used the Plug-in-Gait model with functional methods for hip joint center and knee axis [30,31]. All three centers were accredited by the Commission for Motion Laboratory Accreditation [32]. Kinematic data were collected barefoot, at self-selected walking speed, using samples of three to five trials.

2.3. Statistical analysis

To determine sample size, a power analysis (0.75 effect size, 0.05 significance level, 0.9 power) was conducted based on mean change in GDI as an overall outcome measure [24]. A total sample size of 80 individuals with 40 in each group, Yes-SDR and No-SDR, was determined to be appropriate.

Analyses were completed using R software, version 4.0.3 (R Foundation for Statistical Computing, Vienna, Austria). Change scores from baseline to follow-up were calculated for each participant and kinematic variable of interest. A limited set of discrete kinematic variables were selected to 1) represent the majority of concerns describing the multiplanar and multi-level kinematic changes anticipated in CP gait and 2) prevent over-analysis of too many discrete variables. The following kinematic change scores were considered as dependent variables for analysis:

1. mean pelvic tilt over the entire gait cycle
2. pelvic tilt range of motion over the entire gait cycle
3. minimum hip flexion during stance phase
4. mean hip rotation during stance phase
5. mean hip adduction during stance phase
6. minimum knee flexion during stance phase
7. maximum knee flexion during swing phase
8. timing of maximum knee flexion during swing phase
9. mean ankle dorsiflexion during stance phase
10. mean ankle dorsiflexion during swing phase
11. mean foot progression during stance phase
12. GDI

2.4. Linear model analysis

Each kinematic dependent variable was analyzed with a linear regression model that included the following variables: 1) treatment arm (dichotomous variable: Yes-SDR vs No-SDR), along with the potential confounding variables of 2) baseline age, and 3) baseline value of relevant kinematic variable. This regression model assumed a linear relationship between the variables; no interactions were included in the model. With the adjustments for the confounding variables, treatment arm coefficients reflected differences in outcomes due to treatment (Yes-SDR vs No-SDR), the primary focus of the current study. Treatment arm coefficients >5 degrees (kinematic differences) or points (GDI differences) were selected as a meaningful difference. Therefore, the entire 95 % CI would need to be larger than 5° for conclusive evidence that there is a meaningful difference in treatment arm kinematic outcomes.

3. Results

3.1. Participant characteristics and matching

Participants were well matched on many characteristics at baseline for spasticity, sex, passive joint range of motion, and GDI [1]. The sample size for the Yes-SDR was slightly lower than 40 due to COVID-19 restrictions starting in March 2020 and subsequent recruitment being closed. The age of the Yes-SDR group at baseline was significantly younger than the No-SDR group, attributed to practice patterns for consideration of SDR for spasticity management at a younger age. Some baseline kinematic values were significantly different between groups: pelvic tilt range of motion-gait cycle, minimum hip flexion-gait cycle, mean hip rotation-stance, minimum knee flexion-stance, and maximum knee flexion-swing (Table 1). The Yes-SDR group had a larger number of bony orthopedic surgeries between baseline and follow-up, with the No-SDR group having a greater number of soft tissue orthopedic surgeries (Table 2).

Table 1
Patient characteristics at baseline.

Characteristic	Yes-SDR, n = 35[a]	No-SDR, n = 40[a]	p-value[b]
Age (years)	5.0 (4.6, 5.7)	7.1 (5.8, 8.6)	<0.001
Mean Pelvic Tilt GC (°)	19.6 (15.2, 23.6)	19.7 (14.3, 25.3)	0.7
Pelvic Tilt ROM GC (°)	7.0 (5.8, 9.4)	9.1 (7.5, 10.2)	0.02
Min. Hip Flexion GC (°)	6.5 (−0.1, 8.9)	0.1 (−6.8, 4.8)	0.003
Mean Hip Rotation Stance (°)	17.5 (11.7, 23.5)	2.0 (−1.9, 9.0)	<0.001
Mean Hip Adduction Stance (°)	3.0 (0.5, 4.8)	2.1 (0.0, 4.3)	0.5
Min. Knee Flexion Stance (°)	14.8 (7.8, 20.8)	5.8 (−0.1, 16.3)	0.009
Max. Knee Flexion Swing (°)	64.0 (56.8, 66.7)	53.7 (47.2, 57.8)	<0.001
Time Max. Knee Flexion (% GC)	80.9 (79.4, 84.1)	80.0 (76.8, 83.2)	0.3
Mean Ankle DF Stance (°)	-2.9 (−12.6, 2.8)	2.0 (−6.7, 7.2)	0.06
Mean Ankle DF Swing (°)	-15.5 (−22.7, −9.3)	-11.4 (−22.5, −0.6)	0.3
Mean Foot Progression Stance (°)	5.5 (−0.3, 10.9)	6.9 (−2.3, 16.4)	0.5
Gait Deviation Index (GDI)	63.6 (58.7, 71.1)	66.2 (59.0, 74.0)	0.6

SDR - selective dorsal rhizotomy. GC – Gait Cycle, ROM – Range of Motion, DF - dorsiflexion, Min. – minimum, Max. – Maximum, ankle dorsiflexion: positive = dorsiflexion; knee flexion: positive = flexion; hip flexion: positive = flexion
[a] Median (Interquartile range)
[b] Wilcoxon rank sum test

Table 2
Summary of Orthopedic Surgeries by Treatment Group. Note: the number of surgeries is the total between baseline and follow-up. Some limbs had repeat surgeries (for example hamstring) that are included in the count for that surgery type.

Surgery Category	Yes-SDR, 70 limbs	No-SDR, 80 limbs
Soft Tissue		
Psoas lengthening	16	27
Adductor release	13	17
Hamstring lengthening	11	70
Rectus femoris transfer/lengthening	11	46
Gastrocnemius/soleus lengthening	48	63
Foot and ankle soft tissue	38	13
Soft tissue other	11	1
Bony		
Pelvic osteotomy	3	0
Femoral derotation osteotomy	54	37
Distal femoral extension osteotomy	16	5
Patellar advancement	21	8
Tibial derotation osteotomy	28	14
Foot and ankle bone	54	15
Bone other	13	6
Leg length	9	3

SDR - selective dorsal rhizotomy

3.2. Unadjusted gait kinematics

Mean kinematic graphs (Fig. 1) and tables (Table 1) illustrate unadjusted overall trends comparing baseline and long-term Yes-SDR and No-SDR data (i.e., not adjusted for baseline age or kinematic

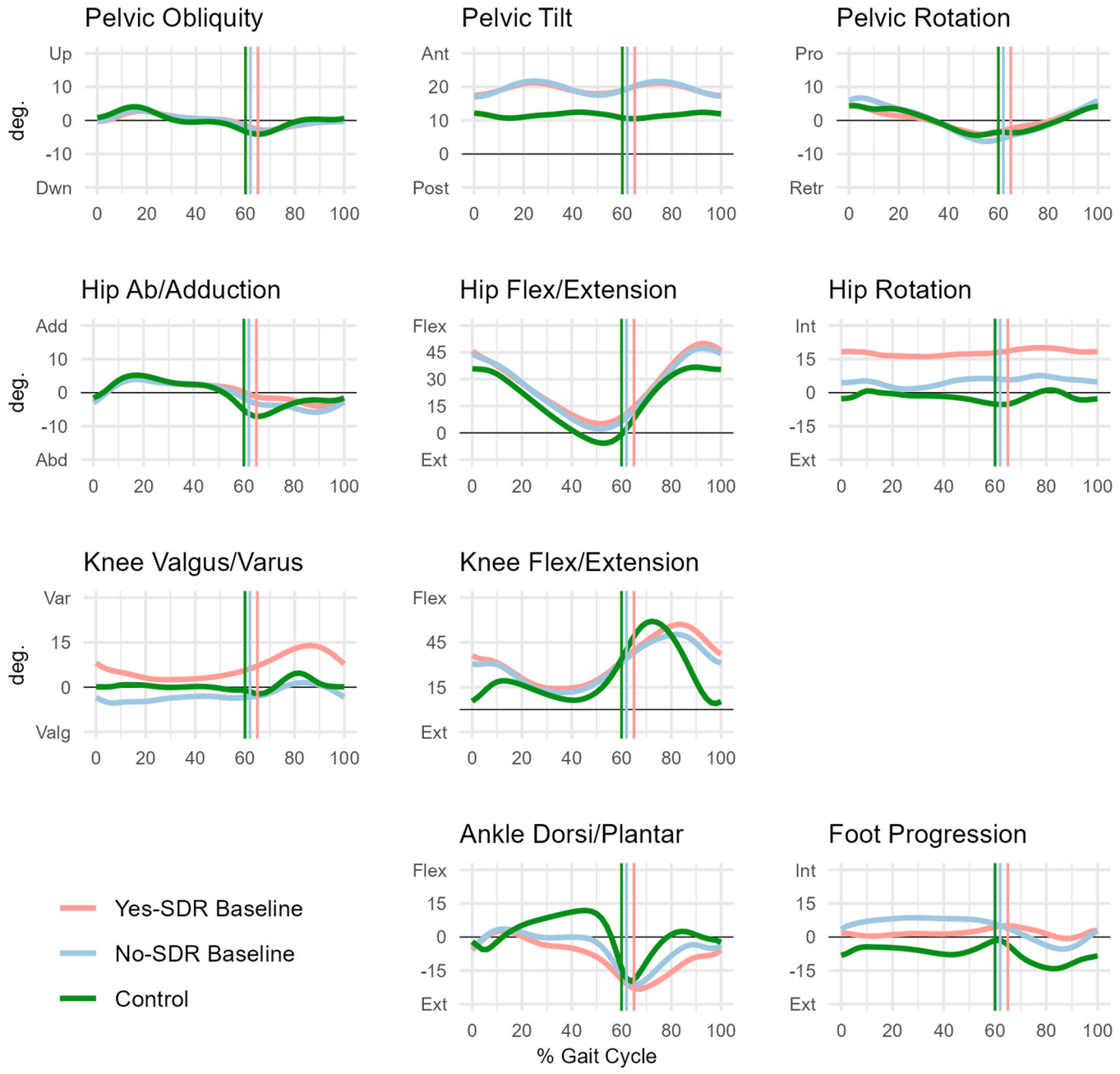


Fig. 1. Mean kinematic graphs of Yes and No Selective Dorsal Rhizotomy (SDR) groups, provided for a visual impression of baseline and follow up in young adulthood for Yes and No-SDR groups.

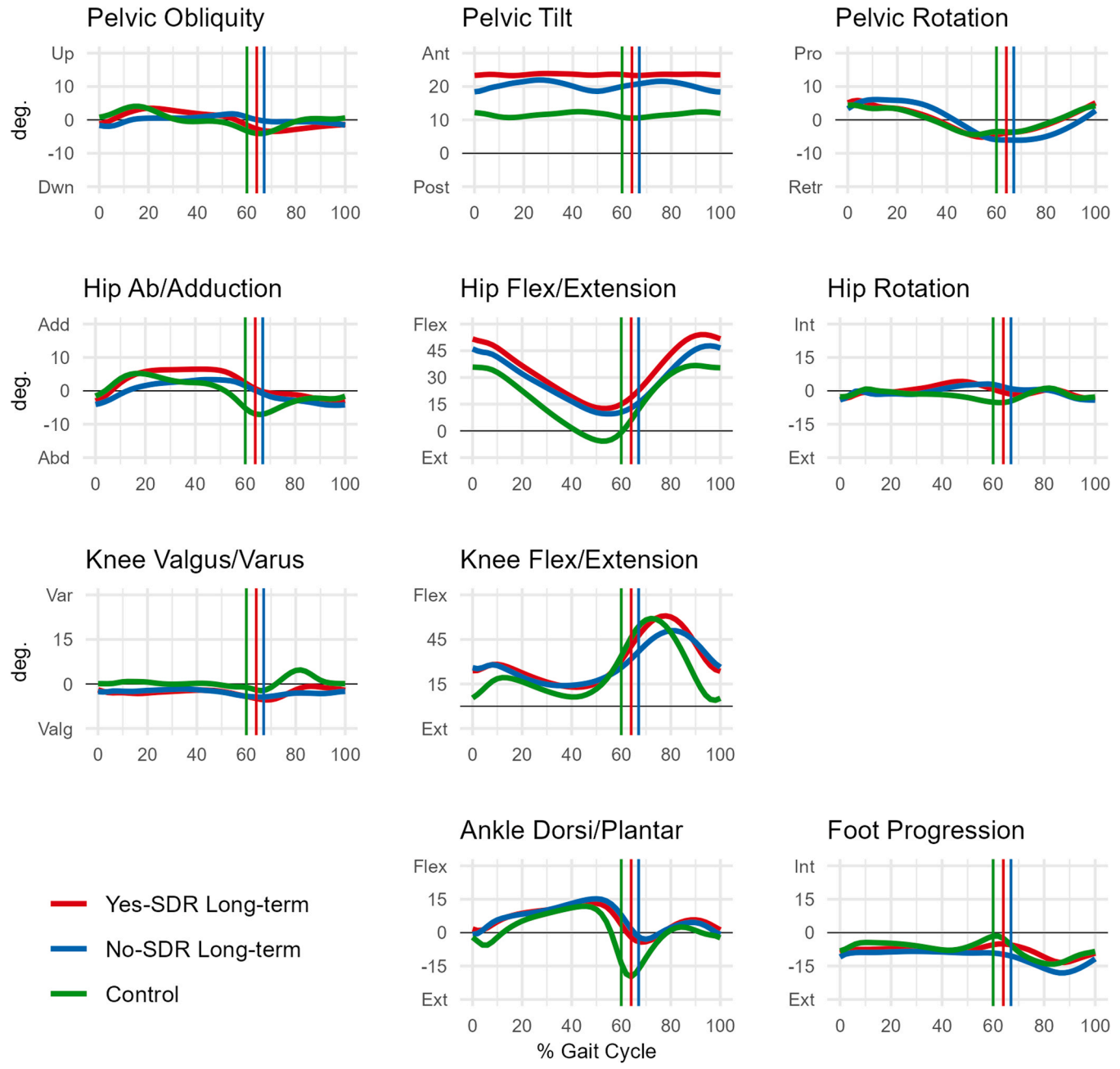
differences). Baseline Yes-SDR group had increased knee flexion in swing, greater internal hip rotation, and less internal foot progression compared to the No-SDR group (Fig. 1a). Long-term Yes-SDR group had increased knee flexion in swing, increased hip adduction, and increased pelvic tilt compared to the No-SDR group (Fig. 1b). Comparing baseline to follow-up for the Yes-SDR group (Fig. 1c) and the No-SDR group (Fig. 1d) showed similar improvements. As previously reported, both groups had significantly overall improvement in the GDI [1].

3.3. Adjusted gait kinematics

After adjusting for baseline age and kinematics, there were no meaningful differences in kinematic outcomes between treatment groups (Fig. 2). Either point estimates were <5 or CIs included 5. All but one discrete parameter mean was within ± 5°. Maximum knee flexion – swing had a mean coefficient value of 7.3° with only a slight overlap of the 5° boundary. This suggests moderate evidence of Yes-SDR maintaining knee flexion in swing.

4. Discussion

Aggressive spasticity management during childhood did not result in beneficial discrete kinematic outcomes in young adulthood when compared to a minimal spasticity management strategy. This outcome



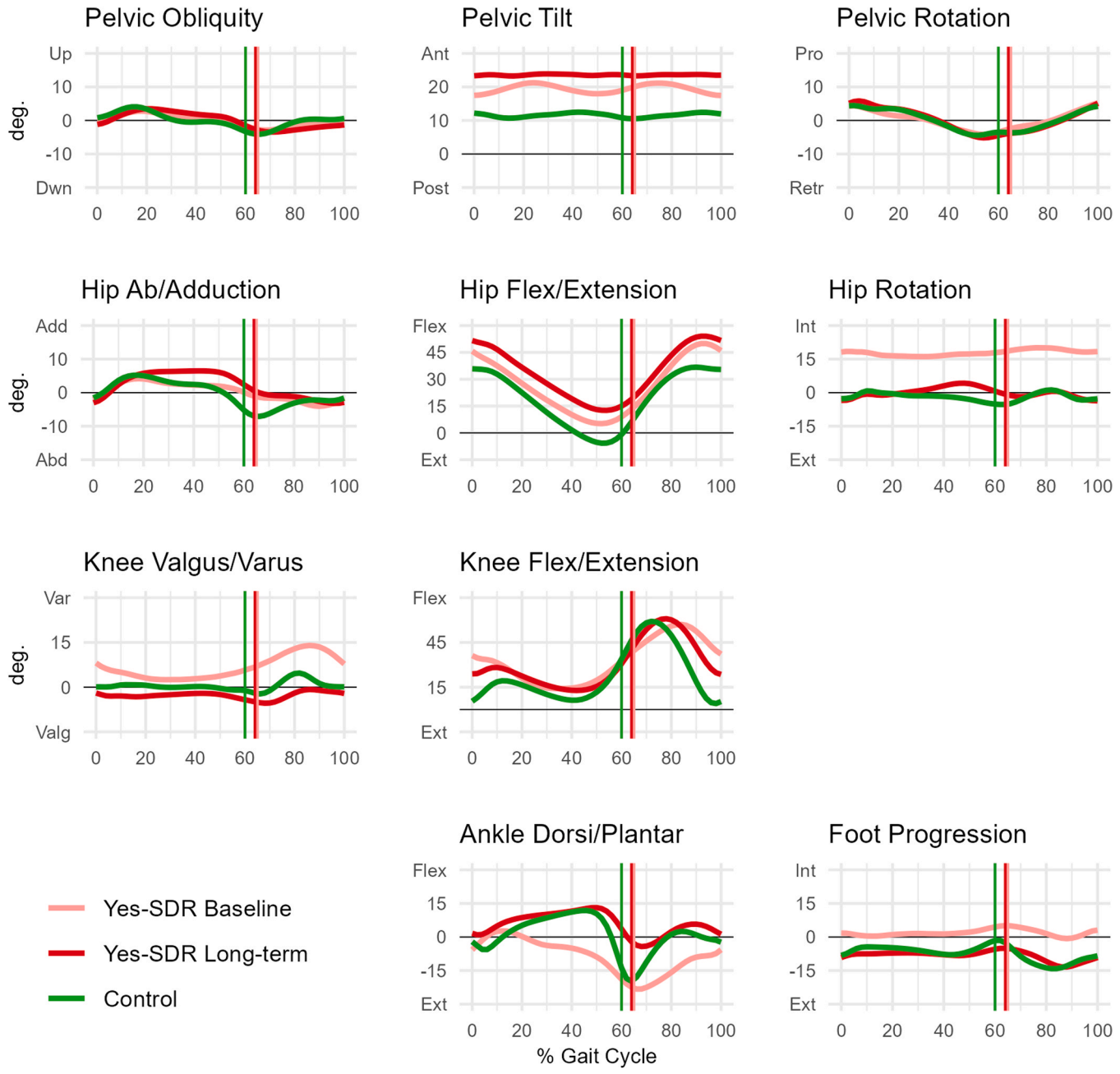
(b) Long-term Yes-SDR and No-SDR

Fig. 1. (*continued*).

was contrary to the proposed hypothesis. The 95 % CI of the treatment arm coefficients were not greater than a 5° established cut-off, and were therefore not considered to be meaningfully different between aggressive and minimal spasticity management groups.

The advantage of the adjusted linear regression models employed in this study was to assess treatment arm (Yes-SDR vs No-SDR) effects while accounting for baseline age and kinematic differences (Table 1). As an example, an unadjusted difference (not accounting for baseline age and kinematic value) initially showed 7° more improvement in minimum knee flexion in stance for the Yes-SDR group, while the adjusted difference was only 2°.

To specifically illustrate the importance of accounting for baseline kinematic values, consider that a larger gain for the Yes-SDR group came from mean hip rotation during stance phase that improved from a baseline median of 18° internal to 1° internal at follow-up (Fig. 1). However, this change did not seem attributable to aggressive spasticity management for two main reasons. First, the baseline Yes-SDR kinematics had a large internal hip rotation bias due to experimental errors, based on the marked difference seen in knee varus/valgus estimation (Fig. 3). The marked increase in knee varus/valgus motion in swing is an indicator of errant experimental methodology leading to an overestimation of internal rotation of the knee flexion/extension axis and increase in estimation of internal hip rotation [27]. The improvement observed at follow-up is almost certainly due, in part, to regression to the mean [28] as well as changes in modeling and improved quality assurance checks over the time between baseline and follow-up studies. Second, an increase in internal hip rotation could confirm a decision to perform derotation osteotomies. The rate of femoral derotation



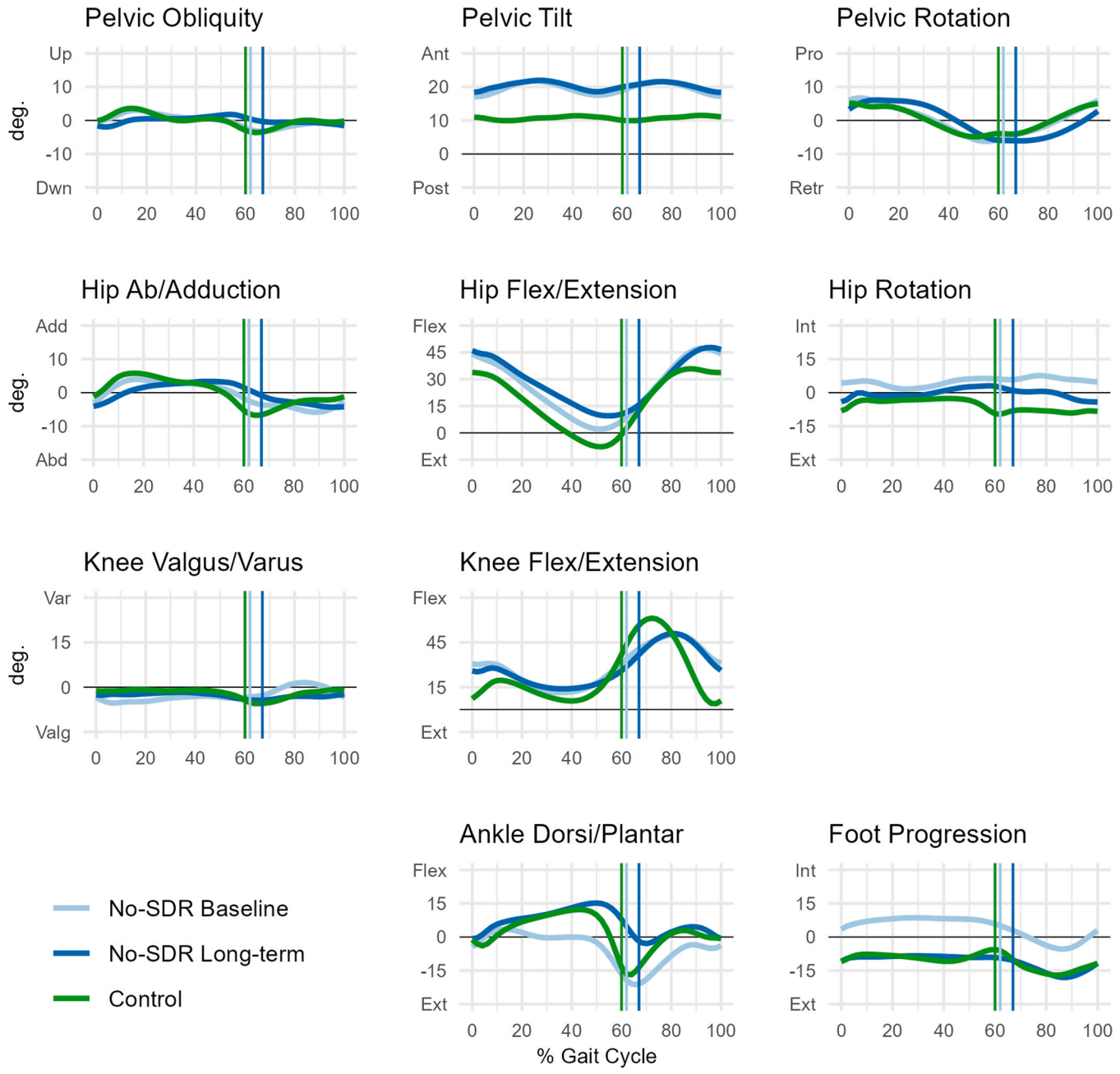
(c) Baseline and Long-term for Yes-SDR

Fig. 1. (*continued*).

osteotomies was about two times greater in the Yes-SDR group (with increased baseline internal hip rotation) compared to the No-SDR group (Table 2). This illustrated the concept of larger kinematic deviations leading to increased treatment. In summary, when baseline age and kinematic values were accounted for, treatment arm had no effect on the change in hip rotation in stance (Fig. 2).

Surgical management for children with CP is commonly recommended to address deficits in gait prerequisites. Limited swing phase knee range of motion is common in CP and causes difficulties with clearance in swing and prepositioning of the leg for initial contact. Max knee flexion – swing showed a moderate treatment effect for Yes-SDR. The Yes-SDR group had a baseline median of 64° max knee flexion – swing with a follow-up value of 65° (Fig. 1c). To clarify, there was not a 7° gain of max knee flexion – swing (treatment coefficient when adjusting for baseline age and kinematic value, Fig. 2). The 7° max knee flexion – swing treatment coefficient can be explained by the No-SDR group having a baseline median of 54° and follow up of 56° (Fig. 1d). The No-SDR group had the potential for improvement from a lower baseline value but did not improve. The No-SDR group had a greater rate of rectus femoris surgery compared to the Yes-SDR group (Table 2) yet still did not have increased max knee flexion – swing. When adjusting for baseline kinematic value, the Yes-SDR group had a moderate treatment effect in maintaining median max knee flexion – swing, that might mechanistically be attributed to spasticity reduction with potential benefit for foot clearance in swing.

In a previous publication comparing aggressive spasticity treatment to minimal spasticity treatment, GDI for both Yes-SDR and No-SDR groups improved with the Yes-SDR group improving by a modestly



(d) Baseline and Long-term for No-SDR

Fig. 1. (*continued*).

larger amount of 6 points [1]. The current report found the same GDI difference between Yes-SDR and No-SDR when adjusting for baseline age and baseline GDI. However, biased baseline internal hip rotation in the Yes-SDR group led to an erroneously lower baseline GDI. The Yes-SDR group likely should have started with a higher baseline GDI than the No-SDR group. Excessive internal hip rotation has been shown to account for approximately 5 points in the GDI [33], corresponding to the modestly larger improvement in the Yes-SDR group.

Previous studies have reported the kinematic gait outcomes of children with CP undergoing an SDR [12,14,15,34]. Feger et al. compared children with CP that underwent orthopedic surgery, an SDR, or no surgery and reported greater improvements for the SDR group in knee and hip flexion-extension [12]. However, this small study (SDR group, n = 8) did not match groups for spasticity at baseline, had a short-term follow-up, and did not adjust outcomes for baseline age and kinematics. A different short-term outcome study of SDR treatment indicated improvement of knee extension and dorsiflexion in stance similar to the current study; however, they had no control group of children with CP that did not undergo an SDR [34]. Two studies that reported longer term outcomes of adults with CP undergoing an SDR as children reported participants walking in mild crouch with adequate knee loading response, swing phase knee flexion, and swing phase ankle dorsiflexion, but they again lacked an appropriate control group of adults with CP not undergoing an SDR [14,15]. Similar outcomes for the Yes-SDR group were found in the current study; however, the same outcomes were also found for the No-SDR group.

With an appropriate control group and adequate follow-up (5 years), Marron et al. [25] reported no differences in gait kinematics between

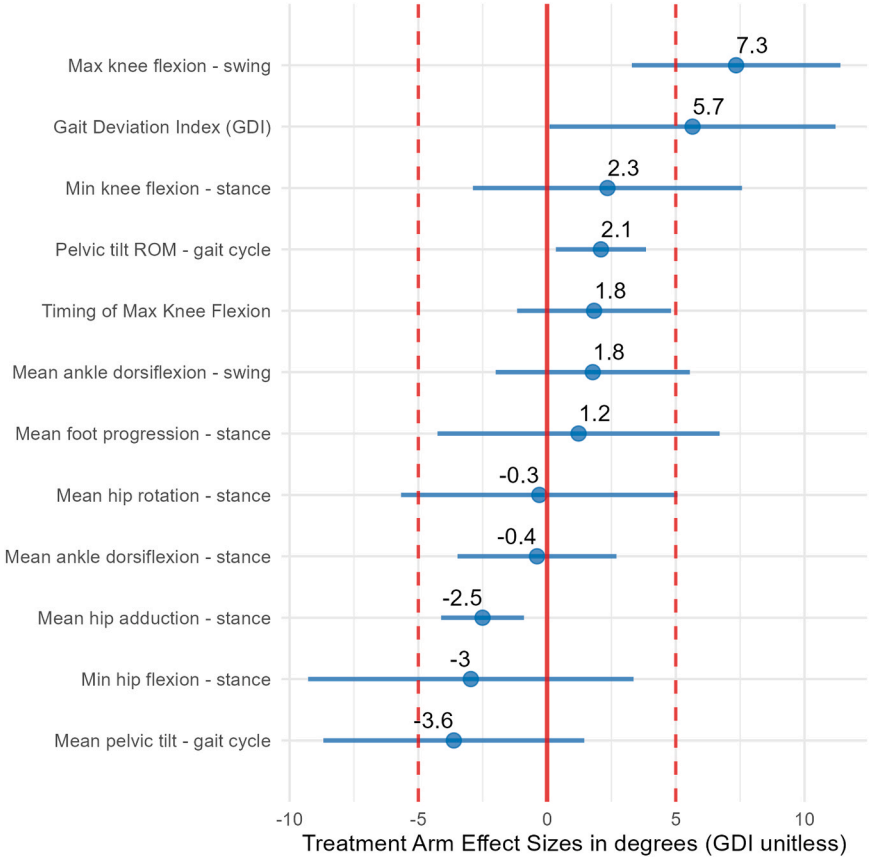


Fig. 2. Treatment arm coefficients with 95 % confidence interval for change baseline to follow-up. The coefficients represent differences in outcomes between the Yes-SDR and No-SDR groups (both groups having orthopedic surgery), adjusted for baseline age and kinematic value. None of the coefficients had an interval greater than ± 5° indicating no meaningful differences in any kinematic variable changes between spasticity treatment strategies. Max – Maximum; Min – Minimum; ROM – Range of Motion.

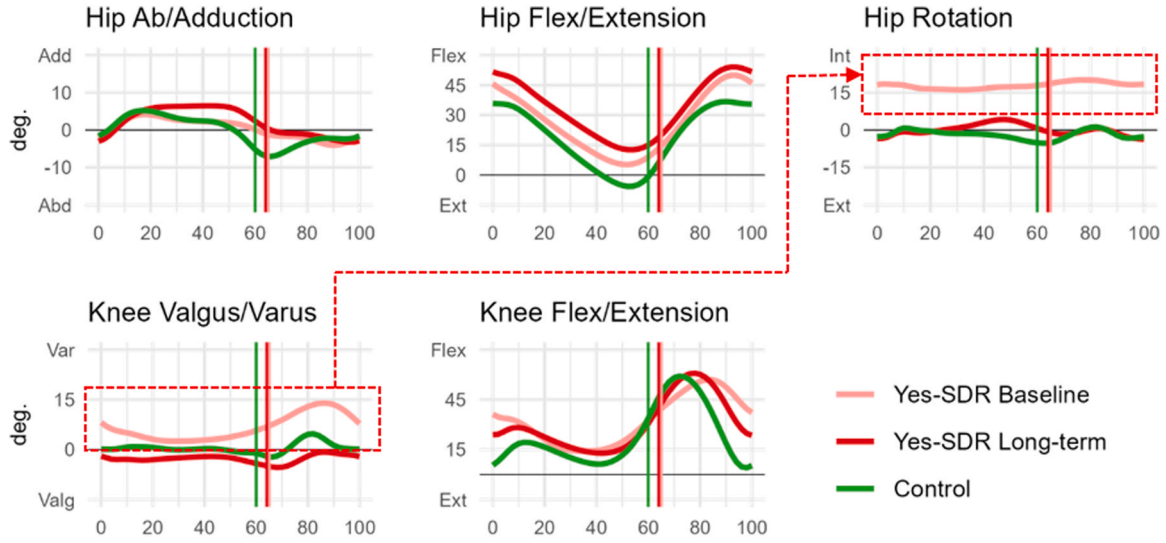


Fig. 3. Baseline kinematics for Yes-SDR group had a large internal hip rotation bias/overestimation due to errant experimental methodology, based on the marked increase in knee varus/valgus motion in swing phase of gait.

Yes-SDR vs. No-SDR groups. The current study with a 10 + year follow-up found the same kinematic outcomes for both Yes-SDR vs. No-SDR groups. Taken together these studies illustrate aggressive spasticity management when compared to a matched control group (both having orthopedic surgery) with an adequate follow-up is less promising than originally expected.

This study has several limitations. The orthopedic surgical intervention was not controlled between the two groups, and likely accounted for some of the differences reported here. We evaluated a limited set of discrete kinematic variables that conceivably did not fully capture all of the changes that were present between groups. Conversely, we found no evidence to suggest other clinically relevant kinematic parameters would lead to a different conclusion. The GDI provided an analysis of the kinematic curves as a whole. Participant recruitment was regionally based due to the location of the centers. Therefore, we assumed the presentation of individuals with cerebral palsy was similarly distributed. Small personnel and protocol differences between and within labs over time may have affected results, although

the three centers have a history of cooperation and sharing of methodology.

5. Conclusion

Aggressive spasticity treatment during childhood did not result in meaningful differences in gait kinematics for young adults with cerebral palsy compared to minimal spasticity treatment.

Source of Funding

This work was supported by the Gait and Motion Outcomes Fund of the Gillette Children's Foundation, USA.

Brief explanation

This study investigated the outcomes in young adulthood of a group of children with cerebral palsy undergoing aggressive spasticity management (including a selective dorsal rhizotomy) compared to control group (minimal spasticity management). The study was conducted at three sites requiring research, medical, recruitment, and 3D gait data collection expertise at each site. Multiple authors from each site (approximately 4 per site) should be included on this manuscript.

CRediT authorship contribution statement

Mark L. McMulkin: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Supervision, Validation, Visualization, Roles/Writing - original draft, Bruce A. MacWilliams: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Supervision, Validation, Visualization, Roles/Writing - original draft, Elizabeth A. Nelson: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Visualization, Writing - review & editing, Meghan E. Munger: Conceptualization, Formal analysis, Methodology, Project administration, Resources, Supervision, Writing - review & editing, Brian Po-Jung Chen: Conceptualization, Formal analysis, Investigation, Methodology, Visualization, Writing - review & editing, Tom F. Novacheck: Conceptualization, Formal analysis, Funding acquisition, Methodology, Supervision, Writing - review & editing, Kristen L. Carroll: Conceptualization, Formal analysis, Methodology, Writing - review & editing, Alan K. Stotts: Conceptualization, Formal analysis, Methodology, Writing - review & editing, Lisa H. Carter: Conceptualization, Formal analysis, Investigation, Methodology, Writing - review & editing, Shelley L. Mader: Conceptualization, Formal analysis, Investigation, Methodology, Writing - review & editing, Brianna Hayes: Conceptualization, Formal analysis, Investigation, Methodology, Writing - review & editing, Glen O. Baird: Conceptualization, Formal analysis, Methodology, Writing - review & editing, Michael H. Schwartz: Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Project administration, Software, Supervision, Validation, Visualization, Writing - review & editing.

Confirmation

Based on the contributions of each author listed, it is confirmed that Mark L. McMulkin, Bruce A. MacWilliams, Elizabeth A. Nelson, Meghan E. Munger, Brian Po-Jung Chen, Tom F. Novacheck, Kristen L. Carroll, Alan K. Stotts, Lisa H. Carter, Shelley L. Mader, Brianna Hayes, Glen O. Baird, and Michael H. Schwartz all meet the criteria for authorship.

Declaration of Competing Interest

No conflict of interest.

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