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ORIGINAL RESEARCH

Factors Associated With Long-Term Improvement of Gait After Selective Dorsal Rhizotomy

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Abstract

Objective: To identify factors associated with long-term improvement in gait in children after selective dorsal rhizotomy (SDR).

Design: Retrospective cohort study.

Setting: University medical center.

Participants: Children (N=36) (age 4-13y) with spastic diplegia of Gross Motor Function Classification System (GMFCS) level I (n=14), II (n=15), and III (n=7) were included retrospectively from the database of our hospital. Children underwent SDR between January 1999 and May 2011. Patients were included if they received clinical gait analysis before and 5 years post-SDR, age >4 years at time of SDR and if brain magnetic resonance imaging (MRI) scan was available.

Intervention: Selective dorsal rhizotomy.

Main Outcome Measures: Overall gait quality was assessed with Edinburgh visual gait score (EVGS), before and 5 years after SDR. In addition, knee and ankle angles at initial contact and midstance were evaluated. To identify predictors for gait improvement, several factors were evaluated including functional mobility level GMFCS, presence of white matter abnormalities on brain MRI, and selective motor control during gait (synergy analysis).

Results: Overall gait quality improved after SDR, with a large variation between patients. Multiple linear regression analysis revealed that worse score on EVGS and better GMFCS were independently related to gait improvement. Gait improved more in children with GMFCS I and II compared to III. No differences were observed between children with or without white matter abnormalities on brain MRI. Selective motor control during gait was predictive for improvement of knee angle at initial contact and midstance, but not for EVGS.

Conclusion: Functional mobility level and baseline gait quality are both important factors to predict gait outcomes after SDR. If candidates are well selected, SDR can be a successful intervention to improve gait both in children with brain MRI abnormalities as well as other causes of spastic diplegia.

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Cerebral palsy (CP) is the most common cause of childhood disability, caused by a permanent injury to the brain before the age of 1 year or by a congenital malformation. Preferably, CP is diagnosed based on the presence of abnormalities on brain magnetic resonance imaging (MRI) matching the diagnosis.[1] If no brain abnormalities are visible, the origin of the disability might be different and alternative diagnoses should be explored, such as hereditary spastic paraplegia (HSP). Although the pathogenesis of CP and HSP is different, symptoms are comparable and treatment of its consequences is often similar. Both disorders are typically associated with abnormal muscle tone, often manifesting in the form of spasticity.[2] Spasticity in children is associated with development of contractures and joint deformities, which tend to

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worsen during growth. Since these impairments can lead to limited walking capacity, treatments in ambulant children with spastic diplegia are aimed at preserving or improving walking capacity for the long term.[2]

Several treatment options are available to reduce spasticity in children with spastic diplegia. For temporary effects, botulinum toxin-A (BoNT-A) is frequently applied. Although BoNT-A has been shown to reduce the effects of spasticity and increase the range of motion of joints, effects diminish over time and treatment has to be repeated to retain results.[3] An alternative treatment is intrathecal baclofen (ITB), offering more long-term effects. However, ITB treatment is a less specific treatment. Furthermore, it is expensive, pumps have to be filled regularly and there is a risk of complications associated with the pump placement and the catheter function. In contrast, selective dorsal rhizotomy (SDR) is a single event surgical intervention, which decreases spasticity through reduction of the excitatory input of dorsal nerve rootlets.[4,5] A large number of studies support the effectiveness of SDR for reduction of spasticity and increase in range of motion.[4,6,7] However, concerning gross motor function and gait, SDR outcomes appear to be variable between individuals.[5,6,8-10]

Since SDR is an invasive, irreversible and permanent treatment, it is of great importance to select only candidates who are likely to benefit from the procedure.[5,8,11] Although selective motor control, MRI-derived parameters and age have been reported as selection criteria for SDR, this is mainly driven by clinical experience, and literature on the topic is scarce.[4,5,8,11] For diagnoses other than CP, even less is known.[12,13] The search for selection criteria is further complicated by the fact that, although the aim of SDR is to improve long-term functioning, most studies evaluate only short term outcomes (1-2y). Studies on long-term effects (ie, 5y or longer) are rare and complicated by interfering additional treatment and natural development during growth.[14]

A recent study proposed that quality of selective motor control during gait is a strong predictor for SDR outcomes.[15] In patients with neurologic disorders, selective motor control is altered and patients seem to use a more a simplified control strategy for the execution of movements.[16-18] During gait, this simplified control strategy can be quantified through investigation of muscle activation, looking at the number of synergies observed during walking or the variance accounted for (VAF) by 1 synergy.[17] With novel techniques such as non-negative matrix factorization (NNMF) muscle synergies can be assessed relatively easily using surface electromyography during gait analysis. Although synergy analysis could potentially provide more in depth insight into underlying mechanisms, it is unlikely that one parameter can predict individual outcomes for all patients. Given the heterogeneity of the group and complexity of the disorder, interactions between parameters are likely to occur. Therefore, it is important consider a large set of variables including brain MRI, age, birth weight and Gross Motor Function Classification System (GMFCS) level, when searching for predictive variables for improvement.[8,18]

The aim of the present study was to investigate long-term effects of SDR on gait quality and to identify parameters presurgery that can predict SDR outcomes. Amongst others, evaluated predictors included selective motor control during gait, GMFCS level, presence of abnormalities on brain MRI, and several gait kinematics-related baseline scores. Since the main treatment goal in this group of ambulant children was to improve or preserve walking capacity, outcome measures were focused on gait. We hypothesized a large variation in outcomes after SDR. Furthermore, we expected that children with a higher level of selective motor during gait control would improve more than children with a more synergetic control strategy.

List of abbreviations:

BoNT-A	**botulinum toxin-A**
CP	**cerebral palsy**
EVGS	**Edinburgh Visual Gait Score**
GDI	**gait deviation index**
GMFCS	**Gross Motor Function Classification System**
HSP	**hereditary spastic paraplegia**
ITB	**intrathecal baclofen**
MRI	**magnetic resonance imaging**
NNMF	**non-negative matrix factorization**
PVL	**periventricular leukomalacia**
SDR	**selective dorsal rhizotomy**
VAF	**variance accounted for**

Methods

Participants

Forty-eight ambulant children underwent SDR surgery at the VU Medical Center in Amsterdam between January 1999 and May 2011. Patients were included retrospectively in this study if they received clinical gait analysis before and 5 years following SDR, including biplanar video recordings and electromyography, and were 4 years or older at the time of SDR surgery. Children below the age of 4 years were excluded, because selective motor control could potentially be still highly developing under this age.[19] Children were classified as GMFCS I to III; for non-CP patients their GMFCS level was estimated as I to III on the basis of their mobility. Characteristics of included patients are presented in table 1. All patients were informed and gave consent. The study protocol was approved by the local medical ethics committee.

According to the clinical protocol of the hospital, patients were selected for SDR based on the following criteria: bilateral spasticity that interferes with walking performance; spasticity (defined as a velocity dependent resistance to passive stretch observed during clinical examination) in at least 6 muscles groups of the lower limbs; no severe contractures or structural bony deformities at hip, knee or ankle; ability to crawl alternately; sufficient strength of quadriceps (ability to squat >7 times) and hip extensors (maintain high knee pose); and moderate to good selective control. All selection criteria were evaluated through observation of functional assessments by a multidisciplinary team, under supervision of the rehabilitation physician. Furthermore, patients had to be motivated and receive support from parents and the rehabilitation setting.

Procedures

Prior to SDR surgery, patients underwent video-based clinical gait analysis on a 10-mile walkway at self-selected comfortable walking speed. Sagittal, frontal and dorsal videos were recorded for both legs. Surface electromyography was collected bilaterally for at least 5 leg muscles (rectus femoris, vastus lateralis, semitendinosus, tibialis anterior, gastrocnemius medialis). Electrodes were placed according to the guidelines of the Surface ElectroMyoGraphy for the Non-Invasive Assessment of Muscles project, with an electrode center distance of 2 centimeters. According to the hospital's protocols, gait analyses were repeated yearly until

Table 1 Patient characteristics as defined at baseline, before SDR surgery

Participants							Brain MRI			
							Abnormalities in Brain MRI		No Abnormalities	
Pre-SDR	n	Men/Women	Walking Aid	Age SDR	Birth Weight (g)	Gestational Age (wk)	PVL	Hydrocephalus	Other Diagnosis	No Definitive Cause Found for Spastic Diplegia
GMFCS I	14	7/7	0	7.4±2.2	3100±1151	36.8±5.01	6	0	2	6
GMFCS II	15	12/3	2	7.2±1.97	2305±1244	33.8±6.144	11*	1	0	4
GMFCS III	7	4/3	7	6.1±1.88	2156±949	33.6±5.48	6	1	0	0
Total	36	23/13	9	7.2±1.9	2558±1203	34.83±5.71	23	2	2	10

NOTE. Values are mean ± SD or number of participants. Walking aid was specified as the use of an assistive device during gait analysis. MRIs were analyzed for the presence of brain abnormalities to confirm the diagnosis of CP. For children where no abnormalities were present on brain MRI, diagnoses were incontinentia pigmenti (n = 1), HIV myelopathy (n = 1), and no cause found for spastic diplegia (n = 10).
* Note that 1 child was diagnosed with PVL as well as hydrocephalus (GMFCS level II) and another child demonstrated a porencephalic cyst in addition to PVL.

the child was fully grown (girls 16y, boys 18y). For the present study, data of assessments before SDR as well as 5 years after SDR were included. To confirm the diagnosis, MRI scans were collected for all subjects after the age 2 years.

SDR procedure was performed by the same neurosurgeon for all children. Trans-section of the rootlets was done after electro-stimulation, according to the palpable muscle contraction and electromyography response. After laminotomy from L2 to S2, approximately 50% of the rootlets at level L2 to S1 were selected by electrical stimulation and transected. Post-operative rehabilitation included prescription of ankle foot orthoses and intensive physical therapy for 12 months.

Medical records were searched for additional patient information including birth weight, gestational age and to determine whether patients received additional surgery after SDR that could influence the postresults. In case of absence of postmeasurements motives were explored.

Data analysis

MRI scans were analyzed by a specialized child neurologist to evaluate presence of brain abnormalities. Neurologic diagnoses were classified and patients were grouped into those with abnormalities on brain MRI (periventricular leukomalacia [PVL] or hydrocephalus) and those without abnormalities on brain MRI.

Kinematic data were analyzed using a custom-made open source software package (MoXie Viewer)[a] that includes a digital screen goniometer, based on the alignment of a stick figure, which allows for quantification of 2D sagittal kinematics.[20] All data were analyzed by the same assessor for one representative step of each leg in each condition. The assessor was blinded, meaning that she was naive whether data concerned a pre- or post-measurement, and trials were analyzed in random order. Overall gait quality was assessed using the Edinburgh Visual Gait Score (EVGS, scale 0-34 for assessment of individual limbs, where 0 indicates no gait abnormalities).[20,21] EVGS was considered as the sum of scores of both legs. In addition, several key kinematic parameters were analyzed, ie, knee and ankle angles at initial contact and mid-stance. Reproducibility and validity of EVGS in children with CP has been reported previously.[20,21]

Synergy analysis was performed for the most affected leg (based on their physical examination) to assess selective motor control during gait. Because we included retrospective data, not all raw electromyography data were available and we were restricted to the filter frequencies used at the time. All electromyography data were high-pass filtered (20Hz), rectified and subsequently low-pass filtered (2Hz) to obtain the envelope. Data of three strides per subject were time-normalized to 100% gait cycle, amplitude-normalized to their own peak value, and concatenated for further analysis. NNMF was applied to calculate selective motor control during gait. Selective motor control was quantified as the VAF by 1 synergy (following).[17] In addition to VAF, the number of synergies was calculated, with a cutoff of 90%, meaning that the number of synergies was reached if at least 90% of each individual electromyography signal was explained by the reconstructed electromyogram.

Statistical analysis

Pre-post effects 5 years after SDR were evaluated with a paired-samples t test ($P<.05$). Multiple backward linear regression analysis was performed to identify factors associated with

Table 2 Kinematics before and 5 years after SDR

Measurement	Pre-SDR	5y Post-SDR	*p*
EVGS	35.9±7.9	23.4±9.8	.001*
Knee MST (deg)	23.2±15.7	23.5±15.6	.132
Ankle MST (deg)	-10.6±13.0	3.4±9.0	.001*
Knee IC (deg)	36.8±5.7	25.8±7.6	.001*
Ankle IC (deg)	-20.5±9.3	-10.1±11.4	.001*

NOTE. Values are mean ± SD or as otherwise indicated. EVGS is presented as the summed score for both legs. Knee and ankle angles are presented at midstance and initial contact for the most affected leg in the sagittal plane. Positive angles represent knee flexion and ankle dorsiflexion, respectively.
Abbreviations: IC, initial contact; MST, midstance.
* Signifiant *p* value.

improvement after SDR. The following parameters at baseline were included in the analysis: sex, age at time of SDR, GMFCS level, presence of abnormalities on brain MRI, gestational age, birth weight, EVGS, VAF, number of synergies, knee and ankle angles at both midstance and initial contact. Categorical variables (MRI abnormalities, GMFCS, sex) were entered as dummy variables. GMFCS I was used as a reference variable and compared to GMFCS level II and III. For the linear regression, individual parameters were evaluated in a separate univariate linear regression first. In order not to miss any relevant parameters, $P<.2$ was used in the initial selection of parameters. Parameters with $P<.2$ were entered in a multivariate regression. This step was repeated several times and for each repetition, 1 parameter with the least significant contribution was excluded. The final model was accepted if (1) the overall regression model was significant ($P<.05$); (2) all included parameters had a P value $<.01$.

Results

Of the 48 operated children, 36 children met the inclusion criteria (mean age at SDR: 7.2±1.94y [range: 4-13], 23 boys, 13 girls). Patient characteristics are presented in table 1. Other patients were excluded because of incomplete/incorrect electromyography data (n=8) and absence of post-measurements at the medical site (n=2).

On brain MRI, 24 children showed abnormalities, of whom 23 children were diagnosed with PVL and 2 children were diagnosed with hydrocephalus (n=2) (see table 1). One child was diagnosed with PVL as well as hydrocephalus and another child demonstrated a porencephalic cyst in addition to PVL. Other children were diagnosed with incontinentia pigmenti (n=1) and HIV myelopathy (n=1). For the rest of the children (n=10), no abnormalities were found on MRI and no definitive diagnosis could be made. A genetic etiology like in HSP was presumed, but no definitive genetic diagnosis was made in any of the participants. Children were grouped as abnormalities on brain MRI (n=24) vs no abnormalities (n=12).

Five years following SDR, EVGS improved on average by 12.5 points ($P<.005$), with a large SD of 10.2; and a range from 34-point improvement to 5 points worsening (table 2). This was accompanied by more knee extension at initial contact (11.4±12.7°; $P<.005$), and less ankle plantarflexion at initial contact (10.4±9.9°; $P<.005$) and midstance (7.2±12.8°; $P<.005$). Knee angle at mid stance did not change significantly.

As for additional treatments, 9 out of 36 children underwent orthopedic surgery within 5 years following SDR (GMFCS I: 5, GMFCS II: 1, GMFCS III: 3). Applied surgeries were subtalar arthrodesis (Fulford, n=3), derotation osteotomy of the tibia (n=3), proximal and distal interphalangeal arthrodesis (n=1), peroneus brevis lengthening (n=1), triple arthrodesis (n=2), triceps myotenotomy (n=1), and tibialis posterior transfer (n=1). Some children received a combination of procedures. In addition, several children received BoNT-A injections and/or serial casting.

Multiple regression analysis revealed that baseline EVGS and functional ability level (GMFCS) were significantly related to improvement in EVGS score ($P<.001$, $R^2=0.61$; table 3, fig 1). A higher EVGS score at baseline (more deviations from a typical gait pattern) was related to greater improvements ($P<.01$). GMFCS III improved less than GMFCS I ($P<.001$), but no differences were observed between GMFCS II and GMFCS I or II and III. Contributions of the individual parameters can be found in table 3.

Significant models were also found for knee angle at midstance and at initial contact as well as for ankle angle at midstance (see table 3). Number of synergies was a predictive factor for knee angle at initial contact and at midstance, where a higher number of synergies (better selective motor control) was related to better outcomes. Baseline scores of knee and ankle angles at midstance were predictive for changes of these parameters themselves. No significant model was found for changes in ankle angle at initial contact. Sex, age at SDR, gestational age, birth weight, neurologic diagnosis, VAF, and knee/ankle flexion at initial contact, did not contribute to any of the models.

Discussion

SDR surgery is generally performed to improve long-term motor functions, especially walking capacity, in children who are expected to deteriorate due to severe spasticity. The aim of the current study was to investigate predictors for long-term improvement of gait. Multiple outcome parameters were evaluated and effects were compared between children of whom diagnosis of CP was confirmed by abnormalities on brain MRI (PVL/hydrocephalus) and children without abnormalities on brain MRI.

At group level, overall gait quality (EVGS), knee angle at IC and ankle angles at IC and MST improved 5 years after SDR. As hypothesized, large variation between patients was found, which allowed for investigation of associated factors. In line with Schwartz et al,[15] within the individual GMFCS levels, more gait deviations (higher EVGS scores) at baseline were related to greater improvement 5 years after SDR. This may be due to the fact that children with less gait deviations before SDR have less room for improvement compared to children who are more severely affected. In contrast, on a functional scale, children with GMFCS III gained less improvement than children with GMFCS I. Although children were already selected as SDR candidates and our sample did not represent the full range of GMFCS I and III levels, our results imply that adding a functional term such as GMFCS classification, strengthens the prognostic prediction compared to baseline gait quality (EVGS) alone.

Brain MRI abnormalities, birth weight, gestational age and sex were not predictive for any of the outcomes. Although little is known about long-term effects of SDR in children with diagnoses other than CP, changes were comparable for children whose

Table 3 Results of the regression analysis

Dependent Variable	Constant		GMFCS I		GMFCS II		GMFCS III		EVGS Pre		No. of Synergies		Knee MST		Ankle MST		Model Overall		
	B	*p*	B	*p*	B	*p*	B	*p*	β	*p*	B	*p*	β	*p*	B	*p*	R^2	*p*	SE
Δ EVGS	14.16	.01*	ref	ref	3.94	.18	19.2	.001*	-0.89	.001*	NA	NA	NA	NA	NA	NA	0.61	.001*	6.9
Δ knee IC (deg)	-14.3	.14	ref	ref	NA	NA	NA	NA	NA	NA	-9.90	0.01*	NA	NA	NA	NA	0.186	.01*	11.6
Δ knee MST (deg)	-35.0	11.8	ref	ref	NA	NA	NA	NA	NA	NA	-9.28	0.05*	0.47	0.01*	NA	NA	0.32	.001*	14.3
Δ ankle IC (deg)	ref	ref	ref	ref	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	ref	ref	ref
Δ ankle MST (deg)	4.4	.03*	ref	ref	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	-0.8	0.001*	0.53	.001*	8.9

NOTE. Dependent variables are difference scores between before and 5 years after SDR. Data are presented for significant regression models. Not applicable represents parameters which are not included in the final model. GMFCS was used as a reference variable. Sex, age at SDR, gestational age, birth weight, neurologic diagnosis, VAF, and knee/ankle flexion at initial contact did not contribute to any of the models.
Abbreviations: NA, not applicable; ref, reference variable.
* Significant *p* value.

diagnosis was confirmed by brain MRI, compared to children without presence of abnormalities on brain MRI. This indicates that SDR can be a good option for this latter group of patients, if well selected. Although no definitive genetic diagnosis was made in any of the patients, HSP was suspected in some children. Although HSP can be progressive and spasticity could still increase over time, results 5 years after SDR seem promising. Future studies should look at results after even longer periods of time and development into adulthood.

In contrast to Schwartz et al,[15] we did not find an association between better selective motor control during gait (lower VAF or higher number of synergies) and improvement in overall gait quality. This can partly be explained by the small number of patients in combination with the large heterogeneity of the population. Secondly, there is a general difference between the EVGS score and scores such as the gait deviation index (GDI), as used by Schwartz et al.[15] Where EVGS is restricted to specific events of the gait cycle, GDI includes complete gait cycle kinematics. In addition, for the synergy analysis only a limited number of strides and muscles were included and we were restricted to a relatively low low-pass electromyography filter frequency. Although the number of included muscles was comparable to Schwarz et al,[15] addition of more strides, inclusion of more muscles and a higher filter frequency could potentially allow for better discrimination between patients.[16,22,23]

When looking at specific gait events, we found an association between selective motor control during gait (number of synergies) and improvements in knee angle at initial contact and midstance. This may be explained by the fact that these kinematic features require a high level of selective motor control during gait. Especially knee angle at initial contact can be hindered by either a hip-knee flexion synergy or by excessive hamstring spasticity at the end of swing phase. After SDR, if hamstrings spasticity is absent, children with better motor control can perform this movement, whereas children with poorer selective control can be expected to still be hindered by the hip-knee flexion synergy. Thus, our results indicate that synergy outcomes can be related to changes in specific kinematic parameters, but due to different responses within the group, these results could not be translated to an overall EVGS score.

Study limitations

Some children received additional treatment between SDR and the 5-year follow-up measurement including orthopedic surgery. Although most interventions were single-level foot and lower leg surgery, these could have affected the outcome parameters. We do not know if more or less orthopedic surgery would have been necessary without SDR. Therefore, the present results cannot be attributed to SDR only, but should be interpreted as a combination of SDR, additional treatment where needed, and natural development. Especially the latter seems important, since natural development of gait is related to the severity of the disorder.[24] Nevertheless, we chose to use a 5-year follow up, because SDR is generally performed to improve long-term function and additional treatments are often part of the trajectory of patients. Another limitation of this study was the use of 2-dimensional clinical gait analysis. Although good reliability of the EVGS score has been reported previously,[20,21,25] several children walked with rotations and motion out of the sagittal plane was likely to occur. In addition, our results are restricted to effects on gait quality and do not include functional capacity

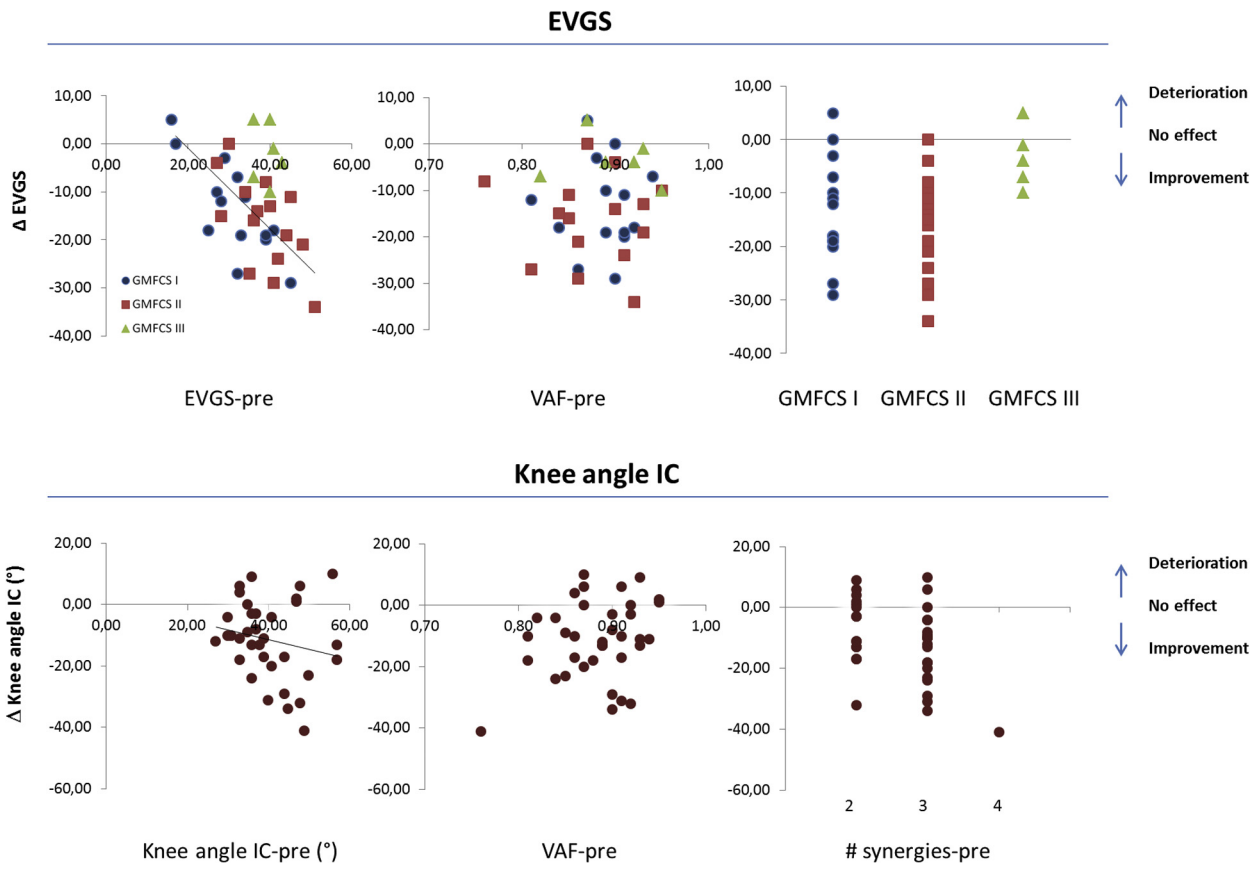

Fig 1 Changes (Δ) in EVGS (upper panel) and knee angle at initial contact (lower panel) before and 5 years after SDR. Negative values indicate improvement, whereas positive values indicate deterioration. EVGS score before SDR and GMFCS were significant for Δ EVGS, whereas knee angles before SDR and number of synergies were significant for Δ knee angle at initial contact.

or quality of daily life. Finally, it is important to realize that we did not investigate a random group, but a subgroup of children who were already selected for SDR. We can assume that children in our sample with GMFCS level I were relatively more affected than peers within the same functional level, while children with GMFCS level III in our sample functioned relatively well within their GMFCS level, and these factors should be considered when translating the current findings to a larger population.

Conclusion

In summary, children improved overall gait quality 5 years after SDR surgery, where children with GMFCS I and II in combination with worse overall gait quality at baseline, reached greatest improvement. Gait improvement was not related to the presence of brain MRI abnormalities. Although results should be interpreted in the light of natural growth and development, these findings may help to guide clinicians to set realistic goals for individual patients after SDR.

Supplier

a. MoXie Viewer; VU University Medical Center.

Keywords

Cerebral palsy; Kinematics; Selective motor control; Spastic diplegia; Rehabilitation

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