Explaining the variability improvements in gait quality as a result of single event multi-level surgery in cerebral palsy

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Purpose: This is a study of all children with spastic diplegic cerebral palsy (Gross Motor Classification System levels II and III) who had single event multi-level surgery (SEMLS) at a single tertiary referral hospital between 1995 and 2008 to identify factors predicting improvement in gait quality as quantified by the gait profile score (GPS). 9 factors (5 dichotomous and 4 continuous, including preoperative GPS) that might be expected to predict outcomes were identified and univariate and multivariable analysis used to explore how these affected outcomes.

Scope: Data from 121 children were included. The mean improvement in GPS of 4.3° was 2.7 times the minimal clinically important difference. Univariate analysis suggested that preoperative GPS is a very strong predictor of improvement in GPS (p < 10^-5) and when this is considered as a covariate only GMFCS level (p = 10^-5) and having had previous surgery (p = 0.026) were found to be statistically significant predictors of GPS improvement (p < 0.05). Children of GMFCS level II improved on average by 2° more than those of level III once differences in preoperative GPS had been accounted for.

Conclusion: Children with the most abnormal gait patterns preoperatively, and hence those with the most potential to improve are those that improve the most and surgery has clearly been beneficial. Over a quarter of children show changes in GPS which were less than the MCID. The majority of these were those with the least abnormal gait patterns preoperatively and further research is required to establish whether and how such children benefit from SEMLS.

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1. Introduction

Single event multi-level surgery (SEMLS) is becoming a more and more widely accepted technique for correcting orthopaedic impairments of children with cerebral palsy [1–4]. A recent systematic review concluded that there is now robust evidence for substantial improvements in gait dysfunction following SEMLS with much weaker evidence for improvements in gross motor function, gait efficiency and health related quality of life [5]. A number of studies [6–12] have reported improvements in gait quality in terms of gait indices such as the Gillette Gait Index [13], Gait Deviation Index [14] or Gait Profile Score [15–17]. These all reported statistically significant improvements. All show considerable heterogeneity within the cohorts at baseline and follow-up.

Two studies [6,11] contain sufficient detail to demonstrate that there is also considerable heterogeneity in how gait quality is affected by SEMLS across the groups. The purpose of this study was to thus investigate the outcomes of SEMLS for children with cerebral palsy from a single centre using the Gait Profile Score (GPS) and to identify the factors which might be predictive of outcome.

2. Methods

This was single centre, retrospective cohort study, investigating the outcome of SEMLS, followed by postoperative physiotherapy, in which the child’s outcome was compared to their preoperative status using the Gait Profile Score (GPS) and Movement Analysis Profile (MAP) [16]. Ethical approval for this study was given by the Ethics in Human Research Committee of the institution No 23144C. The records of all children who had had surgery for gait correction at the Royal Children’s Hospital between 1995 and 2008 were searched to identify children satisfying the following criteria:
A diagnosis of bilateral spastic cerebral palsy [18]  
GMFCS levels II and III [19]  
Gait analysis before and more than 12 months after SEMLS.

Before any data was examined, the authors determined a list of parameters which they considered might be predictors of outcome. Dichotomous variables were GMFCS (II or III), private health insurance (yes/no, as a surrogate for socio-economic status as clinical pathways are similar), adverse events and prior gait correction surgery (both classified as yes or no). Continuous variables were age at surgery, number of surgical procedures and preoperative GPS. During the analysis two other variables were added; gender [following, 20] and date of surgery (months since the first child was operated upon) as it was expected that improving surgical and rehabilitation techniques might lead to improved outcomes.

2.1. Indications

The indication for SEMLS was principally to improve gait dysfunction. However, eight children had significant hip displacement (MP > 40%). The primary indication for surgery in these children was to stabilise the hips, with improvements in gait being a secondary goal. Eleven children had been assessed for possible selective dorsal rhizotomy (SDR) and were rejected by the rigorous screening process required for this procedure in our institution. As such these children were less than ideal candidates for SEMLS. The gait dysfunction in this group was in part related to spasticity and in part to fixed contractures or other musculoskeletal pathology.

Selection of surgical procedures had been based on the diagnostic matrix, in which information from the patient’s clinical history, physical examination, instrumented gait analysis, radiological examination and examination under anaesthesia are synthesised [21]. The technical details of the operative procedures have been described in previous publications and included a strong commitment to selecting the correct “surgical dose” [4,12,22,23].

Rehabilitation was provided by community physiotherapists. Children were discharged after a mean of five days in the hospital. Inpatient rehabilitation was not available.

Quantitative three-dimensional gait data had been collected using one of a number of Vicon systems but all with same marker placement protocol and post-processing through Plug-in Gait (Vicon, Oxford, United Kingdom). The GPS provides a single index of gait quality as the RMS difference between data from one gait cycle and averaged data from a control cohort of typically developing children taken across the 9 most clinically relevant kinematic variables [16]. The equivalent RMS differences for the individual kinematic variables are known as Gait Variable Scores (GVS) and can be displayed in a bar chart called the Movement Analysis Profile (MAP). GPS and MAP were calculated for both legs on four individual gait cycles. The median GPS and MAP were calculated for each leg and averaged to provide a single index for each child using GaiaBase, a web-interfaced repository for gait analysis data [24].

Linear regression analysis was used to determine whether each of the proposed predictors of change had an effect on the GPS improvement following surgery. The original analysis plan was to perform separate bivariate regression analyses for each predictor and select those found to be significant at p < 0.05 for a subsequent multivariable regression analysis. Preoperative GPS was found to be such a strong predictor (p < 10^{-5}), however, that the separate regression analyses were repeated for the other potential predictors with preoperative GPS as a covariate. Any predictors that showed a statistical significance of less than 0.05 for this regression were then used as inputs to the multivariable analysis.

One of the advantages of the GPS is that it can be decomposed into individual gait variables scores (GVS) that constitute the MAP [16]. To account for variation in preoperative GPS the participants were grouped by preoperative GPS into three equal groups. Within these groups the median improvement in the different gait variables were calculated.

3. Results

One hundred and twenty one children with spastic diplegia, 48 girls and 73 boys of mean age 10.7 (standard deviation 2.7 years) were identified as fulfilling the inclusion criteria. All had had a preoperative gait analysis mean of 7.3 months before surgery (s.d. 6.0 months) and a subsequent postoperative analysis mean of 1.3 after surgery (s.d. 1.0 year). GPS was 15.5 (s.d. 3.9) preoperatively and 11.2 (s.d. 2.5) postoperatively with a change of 4.3 (s.d. 3.7). The change in GPS (ΔGPS) was statistically significant (p < 0.001). An MCID of 1.6 has recently been defined for the GPS [15]. On the basis of this 86 children (71%) improved (ΔGPS > 1.6), 32 (26%) showed no evidence of clinically important change (1.6 > ΔGPS > −1.6), and 3 (2%) had deteriorated (ΔGPS < −1.6).

Results of the simple linear regression analysis and with pre-op GPS as a covariate are presented in Table 1. The two regression analyses give quite different results confirming the importance of considering Pre-op GPS as a covariate. Only GMFCS level and previous surgery showed statistically significant regressions when pre-op GPS is controlled for in this way. Table 2 represents the result of the multivariable regression involving these three predictors. The r^2 value for this is 0.69 and the RMS residual 2.1. It can be seen that the effect of previous surgery is no longer significant reflecting a correlation between previous surgery and

| Table 1 | Results of bivariate linear regression and linear regression with preoperative GPS as a covariate for the different potential predictor variables. Figures in bold are statistically significant (p < 0.05). |
|---|---|---|---|---|---|---|---|
| Dichotomous variables | Proportions | Bivariate analysis | With pre-op GPS as covariate | |
| | | Effect (standard error) | p-Value | Effect (standard error) | p-Value |
| GMFCS level | II:III | 66:34 | −0.34 (0.72)^* | 0.641 | 2.11 (0.44)^* | 4·10^{-6} |
| Gender | Female:Male | 74:26 | −0.75 (0.73)^* | 0.285 | −0.46 (0.43)^* | 0.297 |
| Health insurance | No:yes | 35:65 | 0.73 (0.71)^* | 0.306 | 0.32 (0.45)^* | 0.471 |
| Adverse events | No:yes | 10:90 | 3.17 (1.11)^* | 0.005 | 1.15 (0.72)^* | 0.112 |
| Previous surgery | No:yes | 19:81 | 1.01 (0.87)^* | 0.306 | 1.20 (0.53)^* | 0.026 |
| Continuous predictors | Mean | Standard deviation | Bivariate analysis | With pre-op GPS as covariate | |
| | | | Effect (standard error) | p-Value | Effect (standard error) | p-Value |
| GPS pre-op(^*) | 15.5 | 3.8 | −0.76 (0.06)^* | 1·10^{-26} | 0.00 (0.01)/month | 0.670 | −0.01 (0.01)/month | 0.092 |
| Date of surgery (months) | 72.0 | 39.0 | 0.00 (0.01)/month | 0.670 | 0.00 (0.01)/month | 0.670 | 0.01 (0.08)/year | 0.188 |
| Age at surgery (years) | 10.7 | 2.7 | 0.33 (0.12)/year | 0.009 | 0.11 (0.08)/year | 0.188 |
| Number of procedures | 7.6 | 2.1 | 0.00 (0.16)/proc | 0.996 | 0.00 (0.10)/proc | 0.608 |
GMFCS level. Fig. 1 plots GPS improvement against pre-op GPS for GMFCS II and III separately.

Given the strength of this relationship children were divided into three equal groups on the basis of preoperative GPS to study the GVS comprising the MAP. None of the children could be described as mildly affected so children with the lowest preoperative GPS (<14) were labelled “moderate”, the next third (14 < GPS < 18) as “severe” and the most affected third (GPS > 18) as “very severe”. The median changes for each GVS (taken across both legs for all children) and quartile range are plotted in Fig. 2.

4. Discussion

The mean improvement (decrease) in GPS is 4.3°. This compares with the 4.6° decrease in GPS at 12 months reported from the randomised controlled trial of SEMLS conducted by Thomason et al. [12]. That study was conducted under near ideal conditions whereas this study represents all children who underwent SEMLS over a 13 year time period. This suggests that the excellent results reported from that trial are very similar to outcomes of routine clinical practice at the same hospital.

The regression analysis indicates that once pre-op GPS has been accounted for the only other predictor of improvement is GMFCS level. On average children at level II have a GPS 2° higher after surgery than those at level III with the same pre-op GPS. GMFCS is an indication of the severity of underlying neurology. It thus makes sense that the children at level II who are less affected have more potential for improvement as a result of SEMLS. The $r^2$ value suggests that 69% of variability in improvement can be attributed to GMFCS level and preoperative GPS and the low RMS residual (2.1°) confirms that once these factors have been accounted for the results of SEMLS are actually quite consistent.

The relationship between improvement in GPS and pre-op GPS as illustrated in Fig. 1 is interesting. Improvement is clearly better in the children with more abnormal gait patterns preoperatively. This is unsurprising as these are the children who have the most potential for improvement. The data suggest that SEMLS will reduce GPS by about 86% of each degree above a threshold value (9.6° for GMFCS II and 12.2° for GMFCS III). These thresholds still fall well outside the range of GPS values for children with no neuromusculoskeletal pathology serving as a reminder that even after orthopaedic impairments have been removed that the children still have cerebral palsy and do not walk “normally”.

Horizontal lines representing the minimal clinically important difference (MCID) for the GPS of 1.6° [15] are displayed in Fig. 1. 71% of children exceeded this and the average improvement was 2.7 times this value reinforcing the excellence of overall outcomes for the group. Correspondingly, however, 28% of children showed deterioration or improvement of less than this value and these are, predominantly, those who have the least abnormal gait patterns (lowest preoperative GPS) to start with. It is tempting to suggest that these children might be too good to improve from surgery but it should be noted that both values are considerably in excess of the 97.5th percentile of GPS scores for typically developing children (8.5°) and that all children were considered to have sufficiently poor gait patterns to warrant SEMLS which, by definition, involves at least four orthopaedic procedures. It is premature to extrapolate from this data to the conclusion that children with less abnormal gait patterns will not benefit from surgery. GPS is only one outcome measure. It has been shown to be mathematically related.
to the other recent indicator of gait quality, GDI, and highly correlated with GDI suggesting that it is unlikely that other measures of gait quality will show substantially different results. There is strong evidence, however, that without SEMLS children with CP are susceptible to some deterioration in gait quality [25-27] and that surgery may act to prevent this. Factors other than gait quality may also be important, the most obvious of these being function which is not addressed by this study. For example some children with small changes in GPS, required less external support to ambulate after SEMLS, documented using the Functional Mobility Scale (FMS).

Fig. 2 shows that improvements in the GVS that constitute the MAP vary considerably with preoperative GPS. Again, children with the most abnormal gait patterns preoperatively are those who show most improvement. Improvement varies considerably across the different variables with foot progression, ankle dorsiflexion and knee flexion showing most evidence of improvement. For the third of children with the least abnormal preoperative gait patterns the variability in the GVS change is considerably greater than the mean improvement. This suggests that, in this group in particular, surgery leads to different but not necessarily more normal gait patterns. In line with the GPS analysis children in GMFCS II generally do better than those in GMFCS III. There is some evidence that within the moderate and severe groups SEMLS may be leading to deterioration in pelvic tilt, hip flexion and pelvic rotation for children in GMFCS III.

Understanding the relationship between preoperative GPS and change in GPS is important in understanding outcome studies. It is very clear from Fig. 1 that studies involving children with more abnormal gait patterns are likely to result in greater mean improvements than ones involving children with less involved gait patterns. Meaningful comparison of results from different studies is thus only possible if the range of preoperative GPS scores is clearly stated. In designing comparative studies stratification or minimisation approaches will be useful to ensure groups are matched for preoperative GPS and in analysing these it will be useful to include postoperative GPS as a covariate.

This is, of course, a factor affecting any clinical research in which a condition with considerable variation in severity is being studied and is not limited to use of the GPS.

Finally it is worth mentioning one statistical issue which is that the correlation between change scores and baseline data (as in Fig. 2) will be exaggerated if the measurement variability associated with the outcome measure is substantial. To investigate the likely effects of this a Monte Carlo analysis was performed which is fully reported in Appendix A. The findings of this where that measurement error is likely to lead to over-estimation the gradient of the regression line by around 4% and the intercept with the x-axis by less than a degree. Effects on $r^2$ and the p-value will actually be to reduce the strength of the correlation. Measurement error is thus very unlikely to influence either the presentation of the results or the clinical interpretation that has been placed upon it.

Assessing improvement after intervention amongst heterogeneous groups of patients is very common in many fields of medicine. Investigating change scores as a function of baseline score has been demonstrated in this study to be lead to intuitively to an understanding of the underlying patterns in the data. This approach tends to be criticised as introducing a risk of misinterpretation of data as a consequence of the effects of measurement error. The Monte Carlo analysis described in Appendix A suggests that such effects have a minimal likely effect in this particular case and thus that such methods may be more useful than has been assumed. Further work will be required, however, to establish methods to determine the circumstance under which these risks are, or are not acceptable.

5. Conclusion

In summary we conclude that SEMLS can lead to substantial improvements in gait quality with a mean change in GPS of 4.3° (in comparison to an MCID of 1.6°) for children with cerebral palsy at GMFCS level II or III. The children with the most abnormal gait patterns show the largest improvements and surgery has clearly been beneficial. Over a quarter of children shows changes in GPS which were less than the MCID. The majority of these were those with the least abnormal gait patterns despite all of them still lying well outside normal ranges and being considered subjectively as having problems severe enough to require complex orthopaedic surgery. Further research is required to establish whether and how such children benefit from SEMLS.

Conflicts of interest

There are no conflicts of interest to declare.

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Appendix A. Investigating potential effects of measurement error on the line of regression

A1. Introduction

The results of the analysis reported in the full paper are that the outcome of SEMLS (change in GPS from baseline) correlates strongly with the preoperative GPS score. Some care is needed however in such an analysis if the measurement variability is substantial as this will lead to a correlation between change scores and baseline measures even if there is no treatment effect. To understand this consider that a given measurement of GPS is a consequence of some “true” score that is characteristic of the person and some random variability associated with the measurement process (this may include variability of the measurement itself and the performance of the individual on different occasions). Those people measured with high pre-operative scores are likely to be those with high true scores and for whom the random element was high as well. If they are re-assessed and the true score is the same but actual score is likely to reduce because the random element is unlikely to be so high on the second occasion. A similar effect means that low scores are likely to increase. The overall result is that there is likely to be a correlation between the change score and the baseline measurement even if the true scores are unchanged.

This can be illustrated by modelling the data. Preoperative GPS scores were represented by 41 points (the number of participants in the smaller GMFCS III group) uniformly distributed across the range of preoperatively recorded scores. No change was assumed and the postoperative scores were thus assumed to be equal to the preoperative scores. Measurement variability was then applied to both pre- and postoperative scores with a Gaussian distribution specified by its standard deviation. Fig. A1 shows the results of one such model in which variability with a standard deviation of 3° gives rise to an apparent correlation with $R^2 = 0.39$. Repeating this process 100 times gave an average slope of 0.29 and $r^2$ of 0.29. This
suggests that the effects of this phenomenon are sufficiently large to merit further investigation.

A.2. Method

A Monte Carlo analysis was performed to estimate the potential effect of measurement error on the data presented in this study. Clearly true scores are unknown so for the purposes of this analysis the measured values were taken as estimates of the true pre- and postoperative GPS scores and Gaussian error specified by its standard deviation was applied to both of these. The regression coefficient, p-value, slope and intercept with the x-axis where calculated for the relationship between the change score and the pre-operative score. This analysis was repeated one thousand times and the mean and standard deviation of the listed statistical parameters were calculated. The whole process was repeated for a range of error standard deviations between 0° and 4°.

A.3. Results

The results of the analysis are plotted in Fig. A2. When the variance is zero the analysis gives the same results as the original data as expected. As the variability rises there are increases in the slope and x-intercept as expected but these are very small. The effect of increased variability is to decrease r² value and increase the p-value suggesting that the potential for regression to the mean effects to reinforce the correlation is outweighed by the direct effect of increasing the variability about the line of regression.

A.4. Discussion

There have been no formal studies to estimate the variability of repeat measures of the GPS. Thomason et al. [12] reported a cohort of nine children fulfilling the eligibility criteria for this study who did not have study and were reassessed after a 12 month period. The mean score for these children suggested a deterioration (average = 1.3°) over this period and the difference score thus may include some change in true score as well as measurement error. The RMS difference between pre- and postoperative scores for this cohort (2.3°) can therefore be taken as an upper bound for the measurement variability associated with the GPS over this time period. Reading from the graphs suggests that the likely effect of measurement error is likely to reduce the slope by less than 4% and increase the intercept by less than 1° from the values calculated directly from the measured results. These effects are very unlikely to influence the clinical interpretation that is based on the data. As commented above, the effect of measurement error is to reduce the strength of correlation as represented by r² and the p-value suggesting that the underlying correlation will be even stronger than reflected by r² and p-values calculated from the original data. The overall conclusion is thus that there is little potential for effects of measurement variability to significantly affect the findings of this study.

Fig. A2. Results of Monte Carlo analysis. Plotted value represent the mean from 1000 simulations and the error bars represent standard deviation.