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Cerebral hemispherectomy: Sensory scores before and after Intensive Mobility Training

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Abstract

Purpose—It is unclear whether sensory modalities can be modified by rehabilitation and if sensory functions vary on the affected side many years after cerebral hemispherectomy. This pilot, proof-of-concept study assessed light touch and proprioception before and after 10 days of intensive mobility training in individuals after hemispherectomy.

Methods—Light touch and proprioception of the upper and lower extremity was measured using the Fugl-Meyer sensory subtest on the paretic side in 18 individuals with hemispherectomy before and after mobility training. Sensory scores and differences related to mobility training were compared with clinical variables.

Results—Patients were 7.1 ± 5.7 years from time of surgery to sensory assessment and mobility training. Light touch scores were $81 \pm 22\%$ and proprioception values were $64 \pm 23\%$ of normal ($p=0.0022$). Light Touch did not correlate with proprioception scores, and differences comparing after with before mobility training did not correlate. In multivariate analysis, younger age at seizure onset correlated with better light touch scores, and older age at onset correlated with improvements in light touch scores with mobility training. By comparison, proprioception scores were better in individuals with perinatal infarcts compared with Rasmussen encephalitis and Sturge-Weber. Post-training, proprioception scores were better in Sturge-Weber cases.

Conclusions—Light touch was less affected than proprioception on the paretic side after cerebral hemispherectomy. Improvements with mobility training correlated with older age at seizure onset and etiology. These findings suggest that many years after epilepsy surgery sensory functions are not static supporting the notion of existing developmental neuroplasticity of the remaining cerebral cortex along with brain stem and spinal cord pathways.

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Keywords

Neuroplasticity; rehabilitation therapy; surgery; epilepsy; cortical plasticity

Introduction

Cerebral hemispherectomy has been used for over 60 years as a treatment for medically refractory epilepsy involving extensive disease processes of half of the brain.[1–5]. Surgery results in motor-sensory impairments that vary depending on when during cortical development the operation occurred and adaptive reorganization of brain pathways [6–8]. Numerous studies have evaluated sensory functions on the paretic and non-paretic side after cerebral hemispherectomy with variable findings depending on the complexity of the test, upper versus lower extremity, and proximal or distal location on the limb tested [7, 9–11].

Our interest in sensory functions after cerebral hemispherectomy developed as part of our ongoing program to determine if intensive rehabilitation could be used to harness developmental neuroplasticity and improve function. Intensive therapy included 30 hours of mobility therapy with body weight supported treadmill training and over-ground practice for two weeks many years after surgery [8, 12]. We took the opportunity to investigate as a pilot project if sensory functions were static or changed with intensive rehabilitation therapy. The goals of this proof-of-concept study were to document measures of light touch and proprioception scores before and after two weeks of intensive rehabilitation and compare these measures against clinical variables to determine if sensory functions could be altered supporting a role for sensory neuroplasticity and adaptive change [13].

Methods/Subjects

Recruitment

This study was reviewed and approved by the Institutional Review Board of the University of South Carolina. Participants were recruited from a population of children that had undergone cerebral hemispherectomy and were participating in intensive gait and mobility therapy (for description of the cohort, surgical procedures, and inclusion/exclusion criteria see Fritz, et al 2011). Of 19 participants approached, 18 agreed to enroll in this study. All patients had hemiplegia post-cerebral hemispherectomy and their sensory scores were collected as part of pre- and post-therapy evaluation. Mental ages were determined using the Peabody Picture Vocabulary Test [14].

Additional clinical data was collected from the medical records. This included age at seizure onset, age at surgery, gender, side removed, and etiology (perinatal infarct, Rasmussen encephalitis, and Sturge-Weber syndrome) [15]. Epilepsy duration was calculated as the interval in years from age at seizure onset to age at surgery. Also calculated was the interval from age at surgery to age at sensory testing (in years).

Sensory Testing

The Fugl Meyer Assessment Sensory scale was used for measuring light touch and proprioception [16]. Light touch measures were performed with wisped end of a cotton swap in a quick short stroke on the skin over the biceps muscle belly on the upper arm, central palmar surface of the hand, anterior quadriceps muscle portion of the thigh and central part of the sole of the foot. The scoring criteria were defined as two points for normal sensation for each body part, one point for hyperesthesia or dysesthesia, and zero when no sensation was reported. Eight points was the maximal score for the light touch scale on the paretic side (normal score).

Proprioception was assessed over several joints of the paretic side. Each joint was moved in very small range of movements, upward and downward twice (four movements) while the subjects had their eyes closed. They reported verbally their joints position for the upper (shoulder, elbow, wrist and thumb) and lower extremity (hip, knee, ankle and toe). Two points were scored per joint if all answers were correct. If 75% of all answers were correct (three of four movements per joint), one point was given. More significant impairments were classified as zero points. A maximum of 16 points (normal score) was possible in testing proprioception (8 joints times 2 points).

Light touch and proprioception scores were collected twice over a two-week period. The first test was at the beginning of intensive gait and mobility therapy, and the second when therapy was completed. Therapy consisted of 10 days of 3 hours of Body Weight Supported Therapy and over ground training [7, 8] including a substantial amount of sensory stimulation and direction in over ground walking.

Data Analysis

Clinical data and sensory measures were entered into a database and analyzed using a statistical program (StatView 5; SAS Institute, Cary, NC). The light touch and proprioception scores were combined into a single repeated measure dependent variable for statistical testing of static performance. Univariate analysis involved linear regression and analysis of variance (ANOVA) when comparing clinical variables with sensory scores. Comparisons using nominal variables were performed using Chi-square tests. Multivariate analysis against continuous dependent variables used multi-step ANOVA progressively removing non-significant variables. Results were considered different at a minimal level of significance of $p < 0.05$.

Results

Patient Characteristics

The cerebral hemispherectomy cohort consisted of 18 individuals (7 females; 7 right-sided resections; Table 1) with clinical characteristics similar to other studies reported by our group [6–8, 12]. Mean ($\pm$ SD) age at seizure onset (Sz Onset) was 4.4 ± 3.7 years, age at surgery (Age Surgery) was 7.3 ± 4.6 years, epilepsy duration (Epilepsy Dur) was 2.9 ± 3.9 years, and the interval from surgery to intensive mobility therapy (Surg to Therapy) was 7.1 ± 5.7 years. Mean developmental quotients calculated from the mental ages of the Peabody Picture Vocabulary Test divided by age at testing was 77.8 ± 31 . There were three etiology groups in this cohort: Those with Perinatal Infarct (PI; $n=8$), Rasmussen Encephalitis (RE; $n=8$) and Sturge-Weber Syndrome (SW; $n=2$). Four participants did not have seizure control with infrequent simple partial seizures as reported by parents. We excluded patients with malformations of cortical development to limit our investigation of sensory reorganization to patients with confirmed unilateral cortical involvement.

Light Touch

Contralateral to the side of resection, light touch scores varied from 2 to 8 with a mean ($\pm$ SD) before mobility therapy of 6.2 ± 1.9 . After mobility therapy mean scores were 6.7 ± 1.6 ($p=NS$; Table 1). Before mobility therapy, seven (39%) patients had maximum light touch scores of eight (normal), and five (28%) had scores of five or less. After mobility therapy, light touch scores did not change in eight cases (44%) and were at the ceiling score of eight, and five (28%) cases had scores of five or less. Comparing light touch scores after with before two weeks of mobility therapy (Δ LT) showed no changes in eight (44%) patients, two (11%) cases with loss of one point (both less than age 4 years at seizure onset), and

seven (39%) gained one to two points (Table 1). Six of the seven patients that gained light touch scores after mobility therapy were age 5 years and older at the time of seizure onset.

Proprioception

Proprioception scores varied from 3 to 15 with none of the patients having the ceiling normal score of 16 (Table 1). Mean proprioception scores before mobility therapy was 10.1 ± 3.4 , and after therapy was 10.4 ± 3.9 ($p = \text{NS}$). Proprioception scores after mobility therapy compared with before (Δ Pro) showed that seven (39%) patients had gained from one to five points, three (17%) showed no changes, and eight (44%) had reduced scores from one to three points.

Comparison of Light Touch with Proprioception Scores

Repeated measure light touch scores were $81 \pm 22\%$ of normal and proprioception values were $64 \pm 23\%$ of normal (t -test; $p = 0.0022$). Light touch scores did not correlate with proprioception scores (LT vs. Pro; $p = 0.07$), and post- versus pre-mobility therapy differences in scores did not correlate (Δ LT vs. Δ Pro, $p = 0.59$). These findings indicate that proprioception was more impaired than light touch on the paretic side after cerebral hemispherectomy. Furthermore, light touch and proprioception scores did not correlate with each other, and gains or losses in these measures with mobility therapy did not occur in the same patient.

Comparison of Sensory Scores with Clinical Variables

Clinical variables were compared with light touch and proprioception scores and showed several findings (Table 2; Figs. 1 and 2). Univariate analysis found that light touch scores (repeated measures) negatively correlated with age at seizure onset (Table 2, Fig. 1A), and age at surgery (Fig. 1B). By comparison, differences in light touch scores post- versus pre-mobility therapy positively correlated with age at seizure onset (Fig. 1C). Proprioception scores (repeated measures) negatively correlated with age at seizure onset (Fig. 2A), and positively correlated with epilepsy duration (Fig. 2B). In addition, proprioception scores were different by etiology group (Fig. 2C) with those with Perinatal Infarcts (PI) showing higher scores at baseline than patients with Rasmussen encephalitis (RE; post-hoc; $p = 0.0033$). Differences in proprioception scores post- versus pre-mobility therapy also showed differences by etiology with those with Sturge-Weber showing greater improvement compared with Perinatal Infarct and Rasmussen encephalitis (Fig. 2D; post-hoc; $p < 0.012$).

Multivariate analysis using light touch scores as the dependent variable (repeated-ANOVA) found that age at seizure onset was more important ($p = 0.012$) than age at surgery ($p = 0.92$) without a significant interaction of these variables ($p = 0.08$). For proprioception etiology group was more critical ($p = 0.048$) than age at seizure onset ($p = 0.77$) and epilepsy duration ($p = 0.56$) without significant interactions ($p > 0.11$). Finally, we compared sensory scores in 14 patients who had seizure control with 4 individuals who were not seizure free post-hemispherectomy. These two groups did not differ from each other ($p > 0.09$).

Discussion

After cerebral hemispherectomy, this study assessed upper and lower extremity light touch and proprioception using the sensory scale of the Fugl-Meyer assessment before and after intensive mobility therapy and found correlations with clinical variables. On the paretic side, light touch scores were normal (score of 8) in about 40% of patients after cerebral hemispherectomy with a group average of 81% of normal. By comparison, proprioception scores were decreased in all patients with a mean of 64% of normal ($p = 0.0022$). Light touch and proprioception scores and differences comparing after with before mobility therapy did

not correlate with each other ($p>0.07$). However, there were correlations between sensory scores and clinical variables. Younger ages at seizure onset correlated with better Light Touch scores at baseline with many near the upper score of 8 (Fig. 1A), and an older age at seizure onset correlated with improved scores with mobility therapy (Fig. 1C). By comparison, proprioception scores were better in patients with perinatal infarcts compared with those with Rasmussen encephalitis (Fig. 2C), and greater improvements in scores post-mobility therapy were in cases of Sturge-Weber (Fig. 2D). Taken together, the results of our pilot study indicate that after cerebral hemispherectomy proprioception is more adversely affected compared with light touch on the paretic side, at baseline light touch scores correlate with age at seizure onset and proprioception with etiology, and that mobility therapy which includes a significant component of intensive sensory stimulation was linked with improvements in patients with certain etiologies and an older age at seizure onset.

Our results of the measures of light touch and proprioception before and after mobility therapy are consistent with previous observations in patients after cerebral hemispherectomy showing variable impairments. Studies have evaluated copious sensory tests including measures of light touch, pressure sensation, rolling ball direction, noxious stimulation, joint position, identifying objects in the palm, written numbers on the hand, two point discrimination of the index finger, vibratory thresholds, double stimulation of homologous points over both limbs, and temperature discrimination [10, 17–23]. These assessments show variable results ranging from near normal sensation to 80–90% loss of function depending on the test and site studied. Worse tests scores were generally reported for more complex tasks involving sensory integration and in tests of the distal compared with the proximal parts of the limbs. Such findings support the concept that recovery of sensory function after cerebral hemispherectomy is often adequate for tactile detection and intensity coding but are poorer for complex functions that involve sensory informational processing [17]. Furthermore, sensory tests have been previously linked with clinical variables supporting the notion that early damage or surgery is associated with better scores and with certain etiologies [6, 19, 22]. In addition, another study identified abnormalities involving the non-paretic ipsilateral limbs compared with normal for complex sensory tasks. These results raise the question of whether there are limitations of cortical plasticity when one hemisphere must do the work for ipsi- and contra-lateral limbs [20].

Our results are consistent with these prior studies by showing greater problems with proprioception mainly conducted by medial lemniscus systems compared with light touch of the paretic side's upper and lower extremity conducted by spinothalamic systems, and correlations with age at seizure onset and etiology. Such findings are consistent with a recent study using diffusion tensor imaging that suggested differences in the organization of brainstem corticospinal tracts and medial lemniscus systems after cerebral hemispherectomy [19]. In other words, sensory functions after cerebral hemispherectomy may depend not only on developmental neuroplasticity of the remaining sensory cortex but also on the underlying neuroanatomy of thalamic and brainstem systems where sensory information from spinal tracts are initially integrated. Future studies including brain imaging might want to focus on how those areas reorganize after cortical injury over variable developmental ages and etiologies.

The changes we observed in sensory tests before and after intensive mobility therapy may provide some useful insights into the potential for augmenting neuroplasticity after cerebral hemispherectomy as well as guide future studies of using rehabilitation therapy after cortical injury. We found no improvements in light touch and proprioception scores comparing the patients as a group before and after mobility therapy. This result is consistent with prior studies in individuals with cerebral palsy showing little sensory adaptation after cortical damage [24]. However, we did show correlations with greater improvement with an older

age at seizure onset for light touch and for Sturge-Weber patients for proprioception after intensive therapy in cerebral hemispherectomy patients. These correlations remained statistically significant in multi-variant analysis supporting the view that these correlations are real and not the consequence of inherent variability for the sensory scale of the Fugl-Meyer Assessment [25]. What these data mean clinically is that for light touch older patients at seizure onset and surgery who had scores less than normal improved the most while younger patients were already at the normal ceiling score or loss a point on the sensory score. This would suggest that younger patients had already maximized neuroplasticity of sensory systems for light touch after cerebral hemispherectomy while older patients had the most to gain from intensive mobility training. These concepts will need to be explored in further studies involving post-surgery therapy, but indicate at a minimum that sensory systems seem to be capable of changes linked with intensive sensory stimulation after cerebral hemispherectomy.

As this was a pilot study, the reader should be aware of the limitation in experimental design and methods when interpreting the results. For example, the sample size while large enough to demonstrate correlations with clinical variables did not contain an adequate sample size for some etiologies. The findings showing improved proprioception scores post-therapy in the Sturge-Weber group were based on two patients who had seizure onsets at 4 months and 3 years and surgery at age 1 and 7 years respectively. Further studies enlarging the cohort and including more cases of different etiologies are warranted to confirm our initial findings. Likewise, this study was designed to show proof-of-concept that sensory stimulation therapy could impact sensory functions. We do not know if other sensory measures involving more complex informational processing might or might not be linked with improvements pre- and post-intensive sensory therapy, if other types of sensory therapy involving one or both upper and lower limbs might show greater gains, and whether the therapy needs to be performed earlier, repeated, or for a longer period (greater dose) for best outcomes after cerebral hemispherectomy. Finally, correlation statistics used in our analyses indicate clinical associations but do not necessarily imply causality of the examined variables.

Despite these limitations, our study provides initial evidence that intensive mobility therapy that includes a substantial component of sensory stimulation can be linked with partial improvements in light touch and proprioception scores in the paretic limb in some patients and etiologies after cerebral hemispherectomy. These results offer hope that evidence based therapies can be developed for children after significant uni-hemispheric cortical injury that can have a lasting positive impact on quality of life and the ability to live more independently.

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Figure 1.

Scatterplots comparing Light Touch Scores against age at seizure onset (A) and age at surgery (B), and differences in Light Touch Scores post-pre mobility therapy ($LT2 - LT1 = \Delta LT$) compared with age at seizure onset (C). R-values and P-values are shown for each graph (from Table 2). Light Touch scores negatively correlated with age at seizure onset (A) and surgery (B). Improved Light Touch Scores post-mobility therapy positively correlated with age at seizure onset (C).

Figure 2.

Scatterplots comparing Proprioception Scores against age at seizure onset (A) and epilepsy duration (B), and bar graphs comparing etiology groups with Proprioception Scores, Pro2-Pro1= Δ Pro (C) and differences in post-pre mobility therapy. Proprioception Scores negatively correlated with age at seizure onset (A) and positively correlated with epilepsy duration (B). In addition, Proprioception Scores were greater in patients with Perinatal Infarcts compared with Rasmussen Encephalitis (RE; see *; Post-hoc; $p=0.0033$; C). Patients with Sturge-Weber ($n=2$) had greater improvements in Proprioception scores after mobility therapy compared with those with Perinatal Infarcts and RE (see **; Post-hoc; $p<0.012$; D).

Table 1

Patients in descending order based on age at seizure onset (1st Column), corresponding clinical variables and sensory scores

Seizure Onset, years	Age at Surgery, years	Epilepsy Duration, years	Surgery To Therapy years	Etiology	Side	Light Touch (0-8)			Δ LT	Propriocept (0-16)		Δ Pro
						LT1	LT2			Pro1	Pro2	
0.1	1.2	1.1	4.7	PI	Left	8	8		0	14	14	0
0.3	1.0	0.7	9.3	SW	Left	5	5		0	8	13	5
0.6	10.6	10.0	10.1	PI	Left	6	8		2	13	15	2
1.0	1.1	0.1	6.8	RE	Left	8	8		0	5	2	-3
2.0*	4.3	2.3	9.8	RE	Left	8	8		0	11	11	0
2.5	15.3	12.8	2.6	PI	Right	5	4		-1	15	13	-2
2.6	3.8	1.1	21.3	RE	Right	4	5		1	13	11	-2
2.6*	4.1	1.5	18.8	PI	Right	7	7		0	8	7	-1
3.0	7.3	4.3	2.1	SW	Right	8	8		0	7	11	4
3.0*	4.2	1.2	5.4	PI	Left	8	8		0	10	13	3
4.0	4.5	0.5	1.3	RE	Right	8	8		0	12	12	0
4.2	6.2	2.0	7.8	PI	Left	8	7		-1	10	13	3
5.0	9.1	4.1	0.1	PI	Left	6	7		1	11	13	2
7.0	11.4	4.4	8.6	PI	Left	6	7		1	14	12	-2
8.0	8.5	0.5	3.1	RE	Left	6	8		2	11	10	-1
10.0	11.1	1.1	9.8	RE	Right	6	7		1	12	11	-1
11.0	12.0	1.0	5.3	RE	Left	3	5		2	5	6	1
12.0*	15.3	3.3	1.2	RE	Right	2	3		1	3	1	-2

* participants with no seizure control (infrequent seizures)

Surgery To Therapy (Age at Therapy minus Age at Surgery). Etiology defined as Perinatal Infarct (PI), Sturge-Weber (SW), and Rasmussen Encephalitis (RE).

LT1/LT2 = Light Touch Score before and after Mobility Therapy.

Pro1/Pro2 = Proprioception score before and after Mobility Therapy

Δ LT is difference in Light Touch Score post- minus pre-mobility therapy.

Δ Pro is difference in Proprioception score post- minus pre-mobility therapy.

Table 2

Statistical Comparison of Light Touch and Proprioception Scores with Clinical Variables: Univariate Analysis.

Clinical Variable	Light Touch	Δ LT	Proprioception	Δ Pro
Seizure Onset	−0.492/0.0023	+0.509/0.031	−0.404/0.014	0.275/0.269
Age Surgery	−0.538/0.0007	0.365/0.136	0.036/0.833	0.391/0.215
EpilepsyDuration	0.206/0.229	0.07/0.784	+0.351/0.036	0.032/0.898
Surgery to Therapy	0.040/0.800	0.04/0.875	0.082/0.636	0.182/0.469
DQ Score	0.104/0.540	0.213/0.396	0.286/0.091	0.307/0.216
Etiology	0.875/0.426	1.29/0.305	5.08/0.011	8.39/0.0036
Side	3.060/0.089	0.602/0.449	0.54/0.468	1.78/0.202

Results presented as correlation coefficient and p-value, R/P, for continuous data (first five clinical variables) or the ratio of two independent estimates and p-value, F/P, for categorical values (Etiology & Resection Side). Analysis for Light Touch and Proprioception used a repeated measures incorporating first and second measurement before and after mobility therapy. Developmental Quotient, DQ Score, was calculated as the mental age divided by the chronological age at the time of therapy. Significant Results (p<0.05) indicated in **BOLD** type and in Figures 1 and 2.