Outcome following multiple subpial transection in Landau-Kleffner syndrome and related regression

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SUMMARY

Objective: To determine whether multiple subpial transection in the posterior temporal lobe has an impact on long-term outcome in children who have drug-resistant Landau-Kleffner syndrome or other 'electrical status epilepticus during sleep' related regression. Given the wide variability in outcomes reported in the literature, a secondary aim was to explore predictors of outcome.

Methods: The current study includes a surgery group (n=14) who underwent multiple subpial transection of the posterior temporal lobe and a non-surgery comparison group (n=21) who underwent pre-surgical investigations for the procedure, but did not undergo surgery. Outcomes were assessed utilising clinical note review as well as direct assessment and questionnaires.

Results: The distribution of non-classical cases was comparable between groups. There were some differences between the surgery and non-surgery groups at pre-surgical investigation including laterality of discharges, level of language impairment and age, therefore follow-up analyses focused on change over time and predictors of outcome. There were no statistically significant differences between the groups in language, non-verbal ability, adaptive behaviour or quality of life at follow-up. There was no difference in the proportion of patients showing improvement or deterioration in language category over time for either group. Continuing seizures and an earlier age of onset were most predictive of poorer quality of life at long-term follow-up ($F_{2,23} = 26.2$, $p=<.001$, $R2= .714$).

Significance: Both surgery and non-surgery groups had similar proportions of classic LKS and ESES related regression. As no significant differences were found in the changes observed from baseline to follow-up between the two groups, it is argued that there is insufficient evidence to suggest that multiple subpial transection provides additional benefits over and above the mixed recovery often seen in Landau-Kleffner syndrome and related regressive epilepsies.

Key words: Landau-Kleffner syndrome; electrical status epilepticus during sleep; multiple subpial transection; neurosurgery; neurocognitive outcome

INTRODUCTION

Historically, patients with proven seizure onset within cortex serving eloquent function have been considered poor candidates for resective surgery in view of the high risk of devastating neurocognitive sequelae. Morrell and colleagues[1] proposed multiple subpial transection (MST) as a solution. This surgical procedure aims to preserve the functional capacity of eloquent cortex (presumed to be served by longitudinal fibres) while eliminating electrical discharge and spread (facilitated by horizontal fibres). It is difficult to establish the efficacy of MST in childhood epilepsy, as there are many methodological issues that may account for variability in results including the fact that MST is usually used as part of resective procedures[2] and children are often combined with adult populations in small case series.[3,4] The efficacy of MST in adults appears to be supported by a growing body of research. [5-7] However, its effectiveness in the treatment of the developing brain has not been as readily established.[8]

Landau-Kleffner syndrome (LKS) is commonly associated with electrical status epilepticus during sleep (ESES) of centro-temporo-parietal origin and marked by a language-led regression between the ages of two and seven years. [9,10] It is often accompanied by behavioural changes such as hyperactivity, impulsivity, aggression, and symptoms of autism.[11-14] The epileptiform activity integral to a diagnosis of LKS tends to remit in the second decade of life and there is often some neurocognitive recovery though many are left with permanent deficits. [15] These persistent neuropsychological deficits associated with LKS are considered to be the most debilitating aspect of this disorder[16] and appear related to an earlier age of onset and a longer period of ESES. [12,17]

On the premise that LKS was the result of an epileptogenic lesion arising in the speech cortex, Morrell and colleagues proposed MST guided by electrocorticography over the posterior temporal lobe and into the sylvian fissure on the determined driving side.[11] They reported use of the technique in 14 cases, seven of whom recovered age-appropriate speech and four of whom showed a marked improvement. The group subsequently report longer-term follow-up, [18] finding statistically significant improvements in expressive and receptive language measures of single word vocabulary post-surgery. However, only one other group has reported use of the technique[19] in children with ESES associated with language regression. Irwin et al. [19] did not replicate the findings and showed only subtle improvement in neurocognitive functioning, but more dramatic improvement in behaviour. Grote and colleagues[18] noted that the children assessed the longest time after surgery showed the greatest gains on standardised tests. Given that LKS often is a remitting disorder it has been suggested that post-operative improvements could be attributed to the natural recovery of the condition.[19] Utilisation of a non-surgery comparison group would be particularly important given that LKS presents with a fluctuating course, the long-term outcome of LKS is variable and a proportion of patients with a previously refractory presentation show good recovery over time without surgical intervention.[12]

We report on children who have undergone MST as part of their management of LKS and ESES related regression, and for the first time, compare their outcome to a comparative group who underwent pre-surgical investigations but did not proceed with MST. Here we compare language, cognitive, quality of life, and functional and behavioural outcomes. The primary aim of this study was to determine whether MST has an impact on long-term outcome in children who have drug-resistant LKS or other ESES related regression, and given the wide variability in outcomes reported in the literature, a secondary aim was to explore predictors of outcome.

METHODS

All children included in this study had been diagnosed with sleep-activated discharges within the ESES spectrum of 40-90% in the first sleep cycle and at least 30% in subsequent cycles.[20] There remains debate around the diagnosis and description of LKS and for the purpose of this study, the patients who did not fit within the criteria boundaries for 'classical' LKS[11,21] but instead presented with a more global pattern of regression have been recorded here as ESES related regression. [22] All children had a language led regression (LKS) or more global regression (ESES related regression) leading to a significant language impairment (generally single word level or less) that had shown no recovery with adequate dose and course of steroids (at least 2 mg/kg/day for six weeks; usually tried on two occasions) and at least two conventional anticonvulsants (including benzodiazepines) for more than six months and had available follow-up data. Ethical approval for long-term follow-up was obtained from Great Ormond Street Hospital Foundation Trust NHS Research Ethics Committee.

All children underwent pre-surgical investigations at Great Ormond Street Hospital NHS Foundation Trust between 1992 and 2010, to determine lateralisation of their epileptiform activity, and to exclude a lesional cause for their epilepsy that would be amenable to a resection. This included epilepsy-protocol MRI scans, EEG evaluation, neurodevelopmental assessment and neuropsychiatric review. Lateralisation was determined by methohexitone suppression test as described by Morrell[1] and/ or magnetoencephalography (MEG) [23] at Helsinki University Hospital. Surgery was only offered where there was good temporal definition and normal MRI scans and so children with widespread or remote generators and/or evidence of structural aetiology were precluded from this intervention. Those in the surgery group (n=14) underwent MST as proposed by Morrell et al.,[1] with transections in the posterior temporal region going into the sylvian fissure where necessary as indicated by spiking on intraoperative electrocorticography, until resolution of discharges. In order to control for the severity of the presenting condition, only children with drug-resistant

LKS or ESES related regression who underwent pre-surgical investigations for possible MST were included in the non-surgery group (n=21). Data were a combination of clinical note review and research follow-up.

Neurodevelopmental assessment procedures

Due to the nature of clinical data collected over time and also the wide variability in ages and ability levels of the population, a combination of language and cognitive assessment scores (completed by speech and language therapists and clinical psychologists respectively) were used and the assessments used prior to surgery and at follow-up sometimes varied (see appendix 1 for full list of assessments). Language scores focused on oral language skills and were calculated based on a total standard score (including performance on expressive and receptive language subtests), where this was unavailable language quotients based on both expressive and receptive language levels were calculated (language age equivalent score/ chronological age x 100). Non-verbal scores were standardised scores from Wechsler scales of intelligence (performance or perceptual reasoning indices), unless children were unable to access age appropriate measures, in which case developmental quotients were calculated. Language and non-verbal ability were categorised into ability ranges based on the ICD-10 cut-offs for cognitive impairment. [21]

In addition to the available clinical data, at follow-up parents were interviewed with the Vineland Adaptive Behaviour Scales-II (VABS-II) [24] as a measure of adaptive skills in communication, daily living skills and socialisation. As the language assessments focused on oral language skills and a proportion of the sample are proficient in sign language, the VABS-II communication scale questions were adapted based on the individual's best mode of communication (either signed or oral). The Pediatric Quality of Life Inventory (PedsQL™)[25] was used as a measure of quality of life at follow-up. The self-report version was used when the young person was able to complete a questionnaire, otherwise the parent-

report version was used. A telephone interview was also carried out to collect information on medical, educational, and psychosocial outcomes.

Additional surgeries and complications

One surgical patient underwent a combined right temporal lobectomy as well as MST. He developed a post-operative extradural haematoma that required surgical removal and experienced residual left-sided weakness. This patient continued to have drug resistant seizures and underwent corpus callosotomy, aimed at reducing drop seizures, nine years following MST surgery. Another surgical patient experienced a CSF leak from his wound six weeks following MST that was managed conservatively. One surgical patient underwent a revision of the MST 14 months after the initial surgery as ESES had returned with no improvement in language. There were no other complications associated with MST and there were no other additional surgical procedures.

Statistical Analysis

Pre-surgical differences in language and non-verbal skills were investigated, using Fisher's exact, Chi-square, and Mann Whitney U tests. Post-surgical differences between groups in seizure outcome, medication, neurocognitive assessment, adaptive functioning, sign language outcomes, behavioural improvement, special education outcomes and quality of life were investigated. Group differences in demographic, neurocognitive and adaptive functioning were tested using Mann Whitney U tests for continuous outcomes and Fisher exact tests or Chi-Square for categorical outcomes. Forward step-wise multi-variable linear regression analyses were used to identify predictors of quality of life. Quality of life data were normally distributed and there were similar variances between groups in order to meet the statistical assumptions of linear regression analyses. Associations between quality of life outcomes and VABS-II domains were investigated using Pearson's correlations.

RESULTS

Of the total sample of 35 patients, 14 underwent MST. Patients in the non-surgical group did not proceed with surgery due to lack of clear localisation of epileptiform activity (n=9), language ability considered to be too good (n=3), parental decision (n=2) and observed improvements (n=7; the pre-surgical evaluation for this historical cohort often took over a year, giving time for natural recovery to occur).

Group matching and pre-surgical investigations of neurocognitive ability

When language categories were assessed, there was a statistically significant difference between the surgery and non-surgery groups on baseline testing, with the surgery group showing lower scores; however there were no differences between the two groups on non-verbal functioning. There was also a significant difference in age at time of pre-surgical assessment with younger children more likely to undergo surgery although there was no group difference in the age of presentation of language regression. A significant difference in laterality of discharges was also observed between the two groups at baseline, with non-lateralising cases in the non-surgery group, but not in the surgery group, evidence of a lateralised focus being a requirement for surgery. There were more children in the surgery group who were considered to have difficulties in attention and hyperactivity at baseline but this did not reach significance.

Thirty-two participants had available data at short-term follow-up (less than five years following baseline investigations). For those who did not have available data after this time frame, short-term follow-up data were also taken to be their last available outcome only if data collection occurred more than 18 months following the baseline assessment.

Neurocognitive outcome

There was a large degree of variability within both groups for both language and non-verbal functioning (see appendix 2 for selected individual case examples and appendix 3 for individual descriptions of whole sample). Group-wise, there were no significant differences in seizure or ESES outcomes between the surgery and non-surgery groups at follow-up. There were also no significant group differences in general language functioning, communicative ability, and non-verbal categories. An improvement in language category was seen for 3/13 of the surgery group and 7/20 of the non-surgery group, no change in category was observed for 7/13 of the surgery group and 10/20 of the non-surgery group, while deterioration in language category was found for 3/13 of the surgery group and 3/20 of the non-surgery group. There were no significant difference in changes in language categories over time between groups (p=.714). Of the children with language ability in the average range across both groups at follow-up (n=5), all had a classical LKS presentation, one underwent MST, none had evidence of continuing seizures, and all of them had their final follow-up longer than five years after baseline assessment.

There were no significant differences between groups in quality-of-life scores or in the parent-reported domains of communication, daily living, and socialisation skills on the VABS-II (Fig. 1) at follow-up. Stepwise regression analyses across groups, showed that seizures at follow-up (β=-.78) and a younger age at regression (β=.27) were the strongest predictors of poorer reported quality of life ($F_{2,23}$ = 26.2, p=<.001, R^2= .714). Variables that did not significantly predict quality of life were excluded; these variables were ASD and ADHD symptomatology at baseline, laterality of discharges, language category at baseline, diagnosis (LKS v ERR), group (surgery v non-surgery) and time to follow-up. Further analysis revealed a positive correlation between quality of life and VABS-II scores for communication (r=.691, p=<.001), daily living (r=.799, p=<.001), and socialization (r=.646, p =<.001).

Figure 1. Surgery and non-surgery group means on (A) adaptive functioning subdomains of the VABS-II and (B) Peds-Ql domains (95% confidence intervals)

DISCUSSION

This study aimed to investigate potential differences in the long-term outcome of patients with LKS and ESES related regression following MST in the temporal lobe compared to a non-surgery group of similar patients who were also considered for MST but did not proceed to surgery. We have shown that at long-term follow-up the surgery and non-surgery groups showed no significant differences on any measure. Parent-reported quality of life at follow-up was mainly predicted by continuing seizures and a younger age at regression, which is consistent with the findings of other follow-up studies of childhood epilepsy disorders. [26]

The outcome results do not support the conclusion drawn by Grote et al.[18] that MST may support restoration of language abilities in children with LKS. The language ability seen in some children within our surgery group were not dissimilar from those seen in the non-surgery group. The proportion of patients showing improvement or deterioration in language ability over time was similar for both groups, suggesting that there was no demonstrable effect of MST in comparison to the group who did not have surgery. However, whilst the surgical patients do not outperform the non-surgery group in any particular domain at follow-up, a potential benefit in the surgical group who had a more severe language presentation at baseline cannot be excluded. The current findings in the classic LKS group are consistent with other reports of improvements in language and behaviour during the recovery phase of the condition, but with some degree of language impairment of varying severity in most at longer term follow-up. [12,27]

There was great inter- and intra-individual variability in language and non-verbal functioning within both groups across time points. This can be explained by the nature of LKS and other ESES related regression where fluctuations in ability during the active phase are commonly observed. Greater caution is therefore required when interpreting individual scores at specific time points, particularly during the active phase. The variability in individual patient outcomes is in line with previous research findings.[12] It is also important to note that whilst oral language difficulties are a core presentation of LKS, the condition can have a wide reaching impact and some children and young people are able to compensate well using sign language.[28] Thus, reliance on oral language outcome measures alone may be misleading in terms of actual functioning and quality of life. Due to the varied and fluctuating nature of this disorder, it is difficult to predict the trajectory of development during or after the active phase of the disorder. The variability of outcomes is demonstrated by sample cases as summarised in appendix 2.

This study had several limitations, including the relatively small sample size and the nature of clinical data collected at varying ages and timepoints, and so results need to be interpreted with caution. Nevertheless, the rarity of this heterogeneous population who experience symptoms severe enough to be considered for MST means that the data on the patients presented span two decades. As these longitudinal data span many years, the psychometric tests used at follow-up were not always the same version or the same task, which may have resulted in systematic changes in assessment scores. However, unlike previous studies of MST in LKS, a non-surgery comparison group was included in this study in order to attempt to control for the effect of these potential confounds. The non-surgery group differed in some aspects, including higher language levels at baseline. This in part reflects the language criteria for surgery employed by our centre, but is also the result of some patients not proceeding to surgery as they were showing signs of improvement. This

may have been a corollary of the length of time taken to complete the evaluation process and indirectly led to the surgery group being more severe. The non-surgery group also differed from the surgery group in laterality of discharges, with non-lateralising cases in the non-surgery group, but not in the surgery group as a unilateral focus was a requirement of surgery. This may reflect currently unknown differences in aetiology such as genetic causes or subtle differences in brain structure.

In conclusion, this study finds no statistically significant differences between groups at long-term follow-up. Due to the limited power in the study, the extent to which these findings can be interpreted is limited. However, overall the findings indicate that there is insufficient evidence that MST in LKS and ESES related regression produces substantial benefits over and above the recovery seen in patients who do not receive surgery.

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Disclosure

The authors have no conflict of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

References

1. Morrell F, Whisler WW, Bleck TP. Multiple subpial transection: a new approach to the surgical treatment of focal epilepsy. *J Neurosurg* 1989; 70: 231-239.

2. Obeid M, Wyllie E, Rahi A, et al. Approach to epilepsy surgery: state of the art. Part II: Approach to specific epilepsy syndromes and etiologies. *Europ J Paediat Neurol* 2009; 13:115-127.

3. Hufnagel A, Zetner J, Fernandez G, et al. Multiple subpial transection for control of epileptic seizures: effectiveness and safety. *Epilepsia* 1997; 38: 678-688.

4. Schramm J, Aliashkevich AF, Grunwald T. Multiple subpial transections: outcome and complications in 20 patients who did not undergo resection. *J Neurosurg* 2002; 97: 39-47.

5. Sawhney IM, Robertson IJ, Polkey CE, et al. Multiple subpial transection: a review of 21 cases. *J Neurol Neurosurg Psychiatry* 1995; 58: 344–349.

6. Wyler AR. Recent advances in epilepsy surgery: temporal lobectomy and multiple subpial transections. *Neurosurgery* 1997; 41: 1294–301.

7. Ntsambi-Eba G, Vaz G, Docquier MA, et al. Patients with refractory epilepsy treated using a modified multiple subpial transection technique. *Neurosurgery* 2013; 72: 890–897.

8. Blount JP, Langburt W, Otsubo H, et al. Multiple subpial transections in he treatment of pediatric epilepsy. *J Neurosurg* 2004; 100: 118-124.

9. Landau WM, Kleffner FR. Syndrome of acquired aphasia with convulsive disorder in children. *Neurology* 1957; 7: 523-523.

10. Smith M, Hoeppner TJ. Epileptic encephalopathy of late childhood: Landau-Kleffner syndrome and the syndrome of continuous spikes and waves during slow-wave sleep. *J Clin Neurophysiol* 2003; 20: 462.

11. Morrell T, Whisler F, Smith WW, et al. Landau-Kleffner syndrome: Treatment with subpial intracortical transection. *Brain* 1995; 118: 1529-1546.

12. Robinson RO, Baird G, Robinson G, et al. Landau-Kleffner syndrome: course and correlates with outcome. *Dev Med Child Neurol* 2001; 43: 243-247.

13. Gillberg C. The ESSENCE in child psychiatry: Early symptomatic syndromes eliciting neurodevelopmental clinical examinations. *Res Dev Disabil* 2010; 31: 1543-1551.

14. Deonna T, Roulet-Perez E. Epilepsy and autistic spectrum disorders. In Trimble M, Schmitz B (Ed) The Neuropsychiatry of Epilepsy. New York: Cambridge University Press, 2011:24-29

15. Metz-Lutz MN, Filippini M. Neuropsychological findings in rolandic epilepsy and Landau-Kleffner Syndrome. *Epilepsia* 2006; 47: 71-75.

16. Duran MHC, Guimarães CA, Medeiros LL, et al. Landau-Kleffner syndrome: long-term follow-up. *Brain Dev* 2009; 31: 58-63.

17. Bishop DVM. Age of onset and outcome in 'acquired aphasia with convulsive disorder' (Landau-Kleffner Syndrome). *Dev Med Child Neurol* 1985; 27: 705-712.

18. Grote CL, Van Slyke P, Hoeppner JAB. Language outcome following multiple subpial transection for Landau-Kleffner syndrome. *Brain* 1999; 122: 561-566.

19. Irwin K, Lees J, Polkey C, et al. Multiple subpial transection in Landau-Kleffner syndrome. *Dev Med Child Neurol* 2001; 43: 248-252.

20. Massa R, de Saint-Martin A, Hirsch E, et al. Landau-Kleffner syndrome: sleep EEG characteristics at onset. *Clin Neurophysiol* 2000; 111 (Suppl. 2): 87-93.

21. World Health Organisation. ICD-10 classification of mental and behavioural disorders: Clinical description and diagnostic guidelines. Geneva; World Health Organisation; 1992.

22.Stefanatos, G. Changing perspectives on Landau-Kleffner syndrome. The Clinical Neuropsychologist 2011; 25(6): 963-988.

23. Paetau R. Magnetoencephalography in Landau-Kleffner syndrome. *Epilepsia* 2009; 50: 51-54.

24. Perry A, Flanagan HE, Dunn Geier J, et al. Brief report: the Vineland Adaptive Behavior Scales in young children with autism spectrum disorders at different cognitive levels. *J Autism Dev Disord* 2009; 39: 1066-1078.

25. Varni JW, Seid M, Kurtin PS. PedsQL (TM) 4.0: Reliability and validity of the Pediatric Quality of Life Inventory (TM) version 4.0 Generic Core Scales in healthy and patient populations. *Medical care* 2001; 39: 800.

26. Sabaz M, Lawson JA, Cairns DR, et al. The impact of epilepsy surgery on quality of life in children. *Neurology* 2006; 66: 557-561.

27. Caraballo RH, Cejas N, Chamorro N, et al. Landau-Kleffner syndrome: A study of 29 patients. *Seizure* 2014; 23:98-104.

28. Deonna T, Prelaz-Girod AC, Mayor-Dubois, C, et al. Sign language in Landau Kleffner syndrome. *Epilepsia* 2009; 50: 77–82.

29. Semel E, Wiig EH, Secord WA. Clinical Evaluation of Language Fundamentals IV (Rev. ed.). TX: The Psychological Corporation; 2003.

30. Semel E, Wiig EH, Secord WA. Clinical Evaluation of Language Fundamentals IV. TX: The Psychological Corporation; 1995.

31. Wiig EH, Secord W, Semel E. Clinical evaluation of language fundamentals–Preschool. San Antonio, TX: The Psychological Corporation; 1992.

32. Wiig EH, Secord W, Semel EM. CELF Preschool 2: Clinical Evaluation of Language Fundamentals-Preschool. San Antonio, TX: The Psychological Corporation; 2004.

33. Bishop DVM. Test for reception of grammar: TROG-2. London: The Psychologcial Corporation; 2003.

34. Reynell J, Gruber C. Reynell developmental language scales. LA: Western Psychological Services; 1990.

35. Wechsler D. WISC-IV: Administration and scoring manual. San Antonio, TX: The Psychological Corporation; 2003.

36. Wechsler D. Wechsler Preschool and Primary Scale of intelligence third edition: San Antonio, TX: Harcourt Assessment, Inc; 2002.

37. Arthur G. Arthur adaption of the Leiter International Performance Scale. Washington, DC: The Psychological Service Center Press; 1952

38. Elliott CD, Murray DJ, Pearson LS. British ability scales. Windsor, UK: Nfer Nelson; 1983

39. Griffiths R. The Griffiths scales of mental development: Extended scales. High Wycombe: Test Agency; 1970.

40. Neville BG, Harkness WFJ, Cross JH, et al. Surgical treatment of severe autistic regression in childhood epilepsy. *Pediat Neurol* 1997; 16: 137-140.

Table 1. Patient characteristics for the surgery and non-surgery groups at baseline

Variable	Surgery n=14		Non-surgery n=21		P-value
Male, n (%)	11	(78.6)	12	(57.1)	.28
Age at regression in years	3.58	(1.3)	4.19	(2.2)	.65
Age at pre-surgical investigation in years	6.23	(1.4)	7.51	(1.9)	.03
Time to Surgery in years	3.4	(1.48)		-	-
LKS diagnosis, n (%)	11	(78.6)	15	(71.4)	.71
Baseline language level					.01
Profound	10		7		
Severe	4		8		
Moderate	0		2		
Mild	0		3		
Borderline	0		1		
Baseline non-verbal level					.91
Profound	2		1		
Severe	2		2		
Moderate	0		3		
Mild	2		2		

Borderline	0		4		
Low Average	3		0		
Average	2		8		
High Average	3		0		
Superior	0		1		
Behavioural problems, n (%)	12	(85.7)	14	(66.7)	.26
Overt seizures, n (%)	9	(64.3)	17	(81.0)	.43
Laterality of discharges [a]					.004
Left lateralising, n (%)	8	(57.1)	7	(33.3)	-
Right lateralising, n (%)	6	(42.9)	3	(14.3)	-
Non-lateralising, n (%)	0	(0)	11	(52.4)	-
ASD symptomology					.24
ASD, n (%)	5	(35.7)	3	(14.3)	-
ASD traits, n (%)	5	(35.7)	7	(33.3)	-
No ASD, n (%)	4	(28.6)	11	(52.4)	-
ADHD symptomatology					.06
ADHD, n (%)	3	(21.4)	5	(23.8)	-
ADHD traits, n (%)	6	(42.9)	2	(9.5)	-
No ADHD, n (%)	5	(35.7)	14	(66.7)	-

Values given as Mean (SD) unless otherwise stated

ASD = Autism Spectrum Disorder; ADHD = Attention Deficit Hyperactivity Disorder

[a] Based on MHST/MEG investigations

Table 2. Patient characteristics for the surgery and non-surgery groups at last available outcome

Variable	Surgery n=14	Non-surgery n=21	P-value
Age last available outcome	12.6 (4.9)	14.17 (4.1)	.16
Time to last available outcome	6.35 (2.9)	6.6 (3.1)	.60
Overt Seizures, n (%)	4 (28.6)	7 (33.3)	.53
Continued ESES (N=32), n (%)	7 (50.0)	5 (23.8)	.15
On anticonvulsants, n (%)	7 (50.0)	10 (45.5)	.89
Vineland II adaptive functioning	57.92 (28.4)	61.08 (21.9)	.65

(n=25)					
Language Level					.14
Profound	11		6		
Severe	0		5		
Moderate	0		2		
Mild	2		3		
Borderline	0		0		
Low Average	0		2		
Average	0		2		
High Average	1		0		
Non-verbal Level					.95
Profound	4		3		
Severe	0		2		
Moderate	1		2		
Mild	1		0		
Borderline	0		1		
Low Average	1		4		
Average	6		6		
High Average	1		0		
Superior	0		1		
Behaviour improvement, n (%)	9	(64.3)	10	(45.5)	.33

PedsQl (n=25)	62.92	(27.7)	61.62	(22.4)	.81
Level of independence					.75
Independent/mild needs, n (%)	4	(28.6)	7	(33.3)	
Moderate additional needs, n (%)	5	(35.7)	5	(22.7)	
Fully dependent, n (%)	5	(35.7)	9	(40.9)	
Communication					.41
Good functional speech, n (%)	3	(21.4)	9	(40.9)	
Single words/phrases, n (%)	5	(35.7)	8	(36.4)	
Functional sign language, n (%)	4	(28.6)	3	(13.6)	
Little communication, n (%)	2	(14.3)	1	(4.5)	

Values given as Mean (SD) unless otherwise stated.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Table S1. Validated measures used to acquire language and non-verbal scores

Data S1. Case Summaries

Table S2. Individual demographic and clinical variables