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Neuropsychological outcomes following paediatric temporal lobe surgery for epilepsies: Evidence from a systematic review

Alice E. Flint[a,b] , Mitch Waterman[a], Grace Bowmer[b], Gayatri Vadlamani[c], Paul Chumas[d], Matthew C.H.J. Morrall[b]*.

a. Faculty of Medicine and Health, University of Leeds, Leeds, LS2 9JT
b. Paediatric Neuropsychology, E Floor, Martin Wing, Leeds General Infirmary, Great George Street, Leeds, LS1 3EX
c. Paediatric Neurology, F Floor, Martin Wing, Leeds General Infirmary, Great George Street, Leeds, LS1 3EX
d. Department of Neurosurgery, G Floor, Jubilee Wing, Leeds General Infirmary, Great George Street, Leeds, LS1 3EX

*Corresponding author

Email addresses: alice.flint@sssft.nhs.uk (A. Flint), m.g.waterman@leeds.ac.uk (M. Waterman), grace.bowmer@nhs.net (G Bowmer), gayatri.vadlamani@nhs.net (G Vadlamani), p.chumas@nhs.net (P Chumas), m.morrall@nhs.net (M Morrall)

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Highlights

- Most patients remained neuropsychologically stable post-surgery in all domains
- Evidence for increased material-specific memory deficits based on resection side
- Lower pre-surgical ability associated with more positive cognitive outcome
- Limitations of retrieved papers suggest more substantial evidence needed
- Agreement on core outcome measures would permit higher quality evidence

Abstract

Objective: The systematic review aimed to assess the neuropsychological outcomes of temporal lobe resections for epilepsy in children. Additional objectives included determining whether earlier age at surgery leads to better neuropsychological outcomes; the relationships between and predictors of these outcomes.

Methods: Using advanced search terms, a systematic review of electronic databases was conducted, comprising MEDLINE, Embase, PsycINFO, Global Health, Web of Science and CINAHL. Included studies reported on outcome following neurosurgical treatment for epilepsy. Specifically, studies were included if they reported neuropsychological outcomes and were concerned only with temporal lobe resection.

Results: 73 studies met inclusion criteria. For reported neuropsychological outcomes, the majority of participants remained stable after surgery; some declined and some improved. There was some evidence for increased material-specific memory deficits after temporal lobe surgery based on resection side, and more positive cognitive outcome for those with lower pre-surgical ability level.

Significance: Retrieved evidence highlights the need for improvements to quality of methodology and reporting. Appropriately designed prospective multicentre trials should be conducted with adequate follow-up for long-term outcomes to be measured. Core outcome measures should be agreed between centres. This would permit higher quality evidence so that clinicians, young people and their families may

make better informed decisions about whether or not to proceed with surgery and likely post-operative profile.

Keywords: *Paediatric, temporal lobe epilepsy, epilepsy surgery, neuropsychology, cognitive, outcomes*

1. Introduction

Temporal lobe epilepsy (TLE) is the most common cause of partial seizures (Wiebe, 2000). Patients who fail to respond to their first antiepileptic drug (AED) are unlikely to become seizure-free with their second (Kwan & Brodie, 2000). Consequently, there are increasing calls for more rapid referrals of children for neurosurgical assessment (Cross et al., 2006). For children with TLE, resective surgeries of the temporal lobe may vary in the amount of tissue resected and how much of the temporal lobe is preserved. Regions resected are likely to differ slightly for each case of a given procedure, due to inter-child brain differences, presumed aetiology, the extent of abnormalities on imaging, and differences in surgical approach. These factors may introduce variance in outcomes reported (Höller et al., 2015).

Earlier surgical intervention is advocated (Cataltepe & Jallo, 2010) and has been associated with greater reduction in seizure frequency, improved long-term outcomes and reduced risk of SUDEP (Loddenkemper et al, 2007). It is suggested that earlier surgery reduces exposure to damaging seizures during sensitive periods for development (Cross, 2011); therefore, harmful effects of seizures on neuropsychological, social and neurological functioning may potentially be ameliorated earlier. Seizure freedom post-surgery has been associated with improved neurodevelopmental trajectory (Loddenkemper et al, 2007) but this has not been supported universally (Wyllie et al., 1996; Duchowny et al. 1998). There are different rates of each type of surgical procedure and of presenting epilepsies amongst surgical candidates of different age groups, which may also account for differences in outcome (Harvey et al., 2008). Tumour aetiology has been associated with seizure freedom after surgery (Boesebeck et al., 2007; Kossoff et al., 2003). The methodological quality of studies, and the extent to which the many variables are stratified in analyses, needs to be factored into conclusions drawn from results.

Claims for success of paediatric epilepsy surgery tend to be based on seizure outcome, i.e. change in severity and/or frequency of seizures after surgery (Cross, 2011). Non-seizure outcomes after epilepsy surgery are measured seldom, and when this does occur, they are operationalized inadequately, standardised measures are not employed, and studies are limited methodologically. Poor seizure control has

been associated with the development of mental health problems, behavioural difficulties, and cognitive impairment (Ott et al., 2003), and it is suggested that seizure outcome will predict and contribute to improved psychosocial outcomes.

Past reviews have been conducted on paediatric epilepsy surgery outcomes (Sherman et al., 2011; Spencer & Huh, 2008; Tellez-Zenteno et al., 2005; Tellez-Zenteno et al., 2007; Tellez-Zenteno et al., 2010); however, each has methodological limitations and does not specify findings separately for temporal surgical site. A number have reported inadequate search strategies that search too few databases or contain only a narrow range of outcomes (Sherman et al., 2011; Spencer & Huh, 2008; Tellez-Zenteno et al., 2005; Tellez-Zenteno et al., 2007; Tellez-Zenteno et al., 2010). No systematic reviews have been conducted that examine broad neuropsychological outcomes of temporal lobe surgery for epilepsy in childhood.

A systematic review of outcomes using advanced search terms and strategy in neuropsychological domains after temporal lobe surgery for an epilepsy in childhood was performed. It aimed to determine from extracted evidence: the neuropsychological outcomes after temporal lobe epilepsy in childhood; whether earlier age at surgery leads to better neuropsychological outcomes; the relationships between, and predictors of these outcomes.

2. Methods

Study selection was conducted according to guidance from the Preferred Reporting Items for Systematic Reviews (PRISMA) Statement (Liberati et al., 2009) and Centre for Reviews and Dissemination Handbook (Centre for Reviews and Dissemination, 2009). Databases searched were: MEDLINE, HMIC, CINAHL, PsycINFO, EMBASE, Web of Science and Global Health. Search strategies were developed in MEDLINE and then translated to utilise search terms adjusted for each individual database. Grey literature was not included. The final search strategy is appended.

2.1. Inclusion criteria

Participants were children and young people aged <19 years old who underwent surgery for a temporal lobe epilepsy. Where studies described outcomes of surgeries performed on both adults and children, only those permitting disaggregated outcomes for children were included. Child search terms were developed to eliminate reliance on the electronic age limit functions of each database, which may be inaccurate. An existing optimised child search strategy, described by Boluyt et al. (2008), was combined into the developing search strategy, with adaptations to improve sensitivity.

Inclusion criteria were studies with a primary aim of treating an epilepsy that focussed, at least in part, on reporting outcome, or that stated reporting of outcomes as an aim. Included studies reported neuropsychological outcomes and were concerned only with temporal lobe resection. No limits were placed on the study designs that could be included. Search results were limited to English. Applied date limits identified publications from 1st January 1995-2nd April 2016; the search occurred on 2nd April 2015 and auto-alerts retrieved papers for a following year, though no further papers meeting inclusion criteria were identified. Additionally, 1995 represents the time when magnetic resonance imaging became used widely in pre-surgical evaluation for epilepsy surgery (Fried, 1995).

2.2. Quality appraisal

Given the range of the literature, heterogeneity of study samples and outcomes, and the lack of RCTs received, it was deemed important to include all study designs in order to include all relevant data in the review. Most published studies in this area are case series emerging from routine clinical work. In the absence of specific guidance regarding assessment and reporting of quality for uncontrolled case series, appraisal was undertaken according to Oxford Centre for Evidence-Based Medicine (OCEBM Levels of Evidence Working Group, 2011).

2.3. Data extraction

Screening of articles was conducted in accordance with Cochrane (2011) and the Centre for Reviews and Dissemination (2009). Data extraction sheets were devised by AF, MM and MW. AF, MM and MW were involved fully in the development and application of eligibility decisions with quality assurance of extracted data conducted by AF, MM and MW.

Data were extracted into Microsoft Excel (2010) to include study characteristics, outcome data, and conclusions. Study and outcome categories are displayed in Table 1. For each outcome category, fields were established for: outcome measures used; summaries of individual outcome data; group level outcome data and results of outcome predictors.

2.4. Data synthesis

The wide range of methodological variability included in the review meant that extracted data could not be pooled statistically or investigated using meta-analysis due to the risk of introducing bias and producing spurious results (Centre for Reviews and Dissemination, 2009). The wide range of resection types and participant characteristics made data pooling particularly inappropriate. A narrative approach was therefore used to synthesise data. Narrative synthesis was conducted in accordance with the guidance produced by the Economic and Social Research Council (ESRC) (Popay et al., 2006).

3. Results

3.1. Overview of search results

Devised search strategies yielded 4109 papers in MEDLINE, 6080 in Embase, 639 in PsycINFO, 86 in Global Health, 3798 in Web of Science, and 248 in CINAHL. After de-duplication (EndNote, 2015), 8189 publications remained. These were screened in three phases to include the studies reporting neuropsychological outcomes of paediatric temporal lobe resections. Results from each phase of the study selection are displayed in a PRISMA flow chart (Figure 1), with 73 studies meeting inclusion criteria (Table 2).

3.2. Study characteristics

The studies presented neuropsychological outcomes of 1321 children following temporal lobe surgery for epilepsy. Sample sizes within each study varied from single cases (n = 19) to samples of up to 89. Study designs are summarised in Table 3. Length of follow up ranged from 6 months to 27 years and varied between individual participants in the majority of studies. Across the 60 studies that reported mean follow-up duration, the mean duration was 3.21 years. Ninety-six per cent (n = 70) of studies met the criteria for OCEBM Level 4 (Case-series, or case-control studies, or historically controlled studies), with the remainder at Level 3 (non-randomised controlled cohort/follow-up study). Systematic reviews present the possibility of duplicate publications of research results, where the same samples are utilised throughout multiple papers. This is not always explicit and may result in overestimation of effects (Centre for Reviews and Dissemination, 2009). Participants in Skirrow et al. (2011) appear also in Skirrow et al. (2015) with separate research foci.

3.3. Participant characteristics

Participants ranged in age from 3 months to 18 years with the mean age at surgery being 11.9 years. The mean age of seizure onset was 4.7 years and 51% of participants were male. All had intractable temporal lobe epilepsy. Seizure type was

not reported consistently among studies. Many participants had multiple seizure types, and most studies reported outcomes for patients with a variety of seizure presentations. Most studies did not note whether comorbid conditions were present. Within the 30 that did, comorbidities were varied and included physical, social, cognitive and psychological.

3.4. Surgical characteristics

Type of surgery was more thoroughly specified in some papers than others. All included resection of the temporal lobe for the purpose of seizure control. The reported surgeries for all participants across included studies are presented in Figure 2. Across the studies, 650 (49%) children underwent left hemisphere resections, 603 (46%) underwent right sided resections and for 68 (5%) the laterality was not reported. Studies reported conducting a range of pre-surgical assessments for localisation of seizure focus and determination of eloquent cortex before surgery, including: EEG/video EEG in 66 (90%), MRI in 54 (74%), PET in 23 (32%), SPECT in 17 (23%), intracranial EEG in 11 (15%), Wada in 11 (15%), CT in 10 (14%), fMRI in 7 (10%), and MEG with TMS, reported by one (1%) study each. Pre-surgical imaging was not reported in 16 (22%) studies.

3.5. Seizure outcomes

Eighty-nine percent (n = 65/73) of studies reported seizure outcome. Of those that did, most used Engel's (1987) criteria and the remainder described seizure outcome permitting extrapolation to Engel's (1987) criteria. Seizure outcome was reported for 1184 participants: 878 (74%) achieved Engel's Class I outcome (seizure free for at least one year); 64 (5.4%) achieved Class II outcome (almost seizure free) and 242 (20.4%) achieved Class III (worthwhile improvement) or Class IV outcome (no worthwhile improvement). Studies reported a range of neuropsychological outcomes, which are summarised in Figure 3.

3.6. Cognitive outcome

Twenty eight studies (38.4%) reported either IQ or Developmental Quotient (DQ) change data at an individual level, eight studies (11%) presented change data only at group level, and eleven (15%) studies presented IQ change at both the individual and group level. Across those reporting at individual level, 82 (21%) participants improved, 258 (67%) remained stable, and 38 (10%) deteriorated. Eight (2%) participants did not have results for both pre-surgical and follow-up assessments. Of those 19 studies that reported group level outcome, 16 found no statistically significant change in intellectual functioning between baseline and follow-up assessment. No studies reported a significant deterioration in IQ at the group level. Three studies reported significant improvements. Skirrow et al. (2011) found that FSIQ improved significantly by at least 10 points in surgical patients but not matched surgical controls with an epilepsy [$F_{(1, 47)}$=4.8, p=0.033] after a minimum follow-up of six years. Westerveld et al. (2000) showed by repeated-measures ANOVA that for patients with left temporal lobe resections, PIQ improved significantly after surgery (p=0.014) but there was no significant change in VIQ or FSIQ nor any significant change in participants who received right temporal lobe resections. Lewis et al. (1996) reported significantly increased FSIQ in patients with both left and right resections [$F_{(1,22)}$=6.99, p<0.05].

Five studies (6.8%) (Lee et al., 2015; Miranda and Smith, 2001; Roulet-Perez et al., 2010; Skirrow et al., 2011; Westerveld et al., 2000) explored the association between developmental level before surgery with change in IQ after surgery. Roulet-Perez et al. (2010) included only children with delayed development (identified as DQ<72 pre-surgically) and found that participants with a lower pre-surgical DQ experienced greater cognitive gains than those with a higher pre-surgical DQ. Miranda and Smith (2001) found that VIQ increases were predicted by lower pre-surgical VIQ and less favourable VIQ outcome was associated with higher pre-surgical VIQ [ß=-0.379, t=3.342, p=0.002], but no significant association was found between pre- and post-surgical PIQ change. Skirrow et al. (2011) also found that higher preoperative FSIQ negatively predicted positive FSIQ change and lower preoperative IQ was associated with negative FSIQ outcome following surgery [F2,46=8.0, p=0.001, R2=0.26, ß=-0.32]. Similarly, Westerveld et al. (2000) found that higher VIQ at baseline was associated with a negative change score in VIQ and PIQ. Lee et al.

(2015), however, found that pre- and post-operative IQ were not significantly associated.

3.7. Memory outcome

Twenty-eight studies (38.4%) reported memory outcome. Fifteen (20.5%) presented verbal memory outcome at the individual level for 137 children who underwent temporal lobe resection. Across these patients, 23 (17%) improved, 78 (57%) remained stable, 34 (25%) deteriorated and 2 (1%) assessments were not completed at both pre-surgical assessment and follow-up. Eighteen studies presented data at the group level. Eleven studies reported no significant overall change in memory scores. Miserocchi et al. (2013) reported that the percentage of patients with pathological memory scores reduced after surgery, suggesting improved memory function. Jambaqué et al. (2007) reported significant improvements in verbal and working memory tasks, whilst Skirrow (2015) reported significant improvements in visual memory following left temporal lobe surgery and in verbal memory following right temporal lobe surgery. Mosely et al. (2012) reported a significant improvement in verbal memory but no change in visual memory. However, Szabó et al. (1998) presented a significant decline for delayed verbal memory and a non-significant decline on immediate verbal memory. Sinclair et al. (2003) reported no significant change in list learning score but a significant increase in sound symbol associative learning score. Gleissner et al. (2002) demonstrated differences depending on side of surgery: those with left temporal epilepsy showed a significant decline in learning and increased loss after delay, whilst those with right temporal epilepsy showed a significant decline in recognition.

Fourteen studies (19.2%) investigated the effect of side of surgery on memory outcome, and four also investigated the effect of surgical resection volume and anatomical structures on memory outcome (Clusmann et al., 2004; Gleissner et al., 2002; Lah & Smith, 2015; Skirrow et al., 2015). There was an emerging trend to suggest that left sided surgery and greater extent of hippocampal resection predicts deterioration in verbal memory. There was evidence that pre-existing material specific deficits related to the epileptogenic focus were exacerbated after surgery, with left surgical candidates having less favourable verbal memory outcome and

right side surgical candidates having less favourable visual memory outcome (Lewis et al., 1996; Dlugos et al., 1999; Robinson et al., 2000; Gleissner et al., 2002; Meekes et al., 2013; Skirrow et al., 2015), though this effect was not generally found for right sided surgeries. However, not all studies corroborated an effect of side on presented memory outcome (e.g. Bigel & Smith, 2001; Hori et al., 2007; Lah & Smith, 2015; Mabbot & Smith, 2013; Szabo et al., 1998; Vadera et al., 2012; Williams et al., 1998). Three studies found that greater hippocampal resection was associated with poorer verbal memory outcome (Gleissner et al., 2002; Clusmann et al., 2004; Skirrow et al., 2015) and one study found no significant effect of hippocampal resection on memory scores (Lah and Smith, 2015). Four studies reported on the impact of pre-surgical memory scores on post-surgery memory change. Szabo et al. (1998) found that children who performed above the median pre-surgically showed marked decline, whereas those pre-surgically below the median remained stable. Sinclair et al. (2003) demonstrated an interaction between pre-surgical score and laterality: the high-performance group with a left-sided focus tended to recall fewer words after surgery (p=0.06) than before surgery, while the reverse was true for the high-performance group with a right-sided focus and the low-performance group with a left-sided focus. Robinson et al. (2000) found that higher pre-surgical verbal scores or FSIQ were associated with stable scores after surgery, with a number of those who had lower pre-surgical verbal scores improving significantly. For Skirrow et al. (2015), greater improvements in both visual and verbal memory measures were seen for individuals who initially had lower scores.

3.8. Language outcome

Sixteen studies (21.9%) reported language outcomes. Studies measured a number of different aspects of language and the type of language assessments undertaken varied greatly due to the developmental levels and ages of included children. Six studies reported pre- and post-surgical assessment results at the individual level for expressive language. Multiple measures were applied but these examined mainly oral/spoken language. Of 18 patients, 8 (44%) improved, 4 (22%) remained stable, and 2 (11%) deteriorated. From Szabo et al. (1999), one additional patient improved temporarily but later worsened. From De Vos et al. (1995), two patients experienced an expressive decline that subsequently resolved, and one patient had two

surgeries, with decline following the first and maintenance at new baseline following the second. Four studies reported group level expressive language outcomes: one showed no significant change; one showed significant improvement; one showed significant improvement for right- but not left-sided surgeries, and one showed significantly greater delay after surgery. Three studies reported group level outcomes of receptive language: one showed significantly worsened performance; one showed no significant change, whilst one showed stable receptive syntax score but worsened receptive lexicon score. Two studies assessed the effect of temporal lobectomy on reading. Grosmaitre et al. (2004) found that their participant worsened in reading ability by one year of reading age. Lah and Smith (2015) found a significant reduction of reading accuracy post-surgery in a group of 32 patients [$F1, 30=4.20$, $p=.049$], but the effects of laterality and interaction were not significant. No significant effects were found for reading comprehension.

Seven studies (9.6%) investigated the effect of resection side on language outcome after temporal surgery. Four studies found no significant difference between left- and right-sided surgeries in predicting post-surgery change in language scores (Blanchette and Smith, 2002; Clusmann et al., 2004; Jambaqué et al., 2007; Williams et al., 1998), although they reported that left hemisphere surgical candidates generally scored lower than right side candidates at both pre- and post-surgery assessment. Skirrow et al. (2015) found a significant main effect of group [$F2, 44=3.63$, $p=0.004$] on IQ-derived semantic score, with only left temporal lobe resection patients showing significant improvement; however, this effect is evident due to the relatively low overall pre-surgical score of patients who had left-sided resections. Lah and Smith (2015) found a significant interaction of hemisphere and time [$F1,27=4.42$, $p=0.05$] due to significant deterioration in naming score for the left but not the right surgical group; there was no significant interaction for tests of vocabulary, reading, or spelling. De Koning et al. (2009) investigated language development through multiple assessment points before and after resection. Findings indicated delayed development of productive lexicon was increased more by surgery in the language-mediating hemisphere, determined by the intracarotid amytal test (IAT). Relationships with laterality were not found to the same extent in receptive lexicon, receptive syntax or productive syntax, but children with ipsilateral or bilateral language mediation showed a slower development than children

undergoing contralateral surgery. Children with more delayed syntax at pre-surgical assessment had better language development outcome after surgery.

3.9. Attention, processing speed, visuospatial skills, and executive function outcomes

Six studies (8.2%) reported attention and processing speed, two (2.7%) reported executive functioning and one (1.4%) reported visuospatial functioning. Gleissner et al. (2002), Jambaqué et al. (2007), Lendt et al. (1999), and Moseley et al. (2012) demonstrated that participants improved significantly on measures of attention and processing speed at the group level, and Miserocchi et al. (2013) found that the percentage of participants obtaining pathological scores decreased after surgery. Clusmann et al. (2004) reported improvement in attention for left- but not right-sided surgeries. A single case report from Berl et al. (2013) indicated increased difficulties with simple and complex attention tasks following a left temporal lobe resection. The two papers that reported executive function findings indicated different results. Miserocchi et al. (2013) observed a reduction in pathological executive function scores after surgery, whereas Williams et al. (1998) found no significant change in executive function scores at the group level post-surgery. Reported change in visuospatial function (Clusmann et al. 2004) with deteriorated post-surgery visuospatial scores in right-sided patients but increased scores in left-sided patients.

3.10. Quality of life, psychological wellbeing, education/vocation, social and behavioural outcomes

Ten studies (13.7%) reported quality of life (QoL) outcomes. Seven studies reported that surgery was associated with favourable QoL outcome and three studies did not measure QoL pre- and post-surgery or use a non-surgical control group so the effect of surgery was on QoL could not be concluded. Higher QoL was predicted by seizure freedom; however there was considerable variability in methodology and reporting. Nine studies (12.3%) reported mood and mental health outcomes. The results for this domain were highly heterogeneous, making it difficult to draw conclusions. In the study that performed pre-and-post operative psychiatric assessments (McLellan et al., 2005), the majority of participants who previously had a diagnosis improved or

lost their diagnosis at follow-up; however, a minority worsened, and some developed new diagnoses. Seizure freedom appeared to be the only significant predictor of psychological wellbeing. Seven studies (10%) reported educational and vocational outcomes. At long-term follow-up, the majority of participants were reported as participating in education and employment. Fifteen studies (20.5%) reported social and behavioural outcomes. Twelve studies (16.4%) reported individual level behavioural outcomes. Of 98 children, 13 (13%) children showed improved behaviour post-surgery, 73 (74%) showed no change, 9 (9%) deteriorated and 3 (3%) showed behaviours that were qualitatively different. Four studies (5.5%) reported social outcomes and all reported post-surgery improvement.

3.11. Age

The association between age at surgery and intellectual outcome was investigated by eight studies. Miranda and Smith (2001) found that older age at surgery was associated with improved post-surgical VIQ; however, only participants who were seizure free post-surgery were included. By contrast, Jambaqué et al. (2007) found that younger age at surgery was associated with improved FSIQ and VIQ, but the analysis did not attempt to control for condition duration. Westerveld et al. (2000) also found that younger age at surgery was associated with greater positive change in VIQ and in this study age at onset was also entered into the predictive equation. These studies lack control groups of non-surgical age matched children with epilepsy. Gleissner et al. (2002) found no effect of age at surgery on memory and Meekes et al. (2013) found no effect on verbal memory specifically. Skirrow and colleagues (2011), Clussmann et al. (2014) and Lee et al (2015) found that age at surgery was not a significant predictor of post-surgical FSIQ, the former of which utilised age-matched non-surgical controls.

4. Discussion

This systematic review found that for each neuropsychological outcome domain, the majority of young people remained stable after surgery, some improved, and some deteriorated. As this same pattern was found across neuropsychological domains, each domain will not be discussed in detail. These findings are more conservative than some reviews report; for example, Baldeweg and Skirrow (2015) found that half of participants in their included studies showed improved IQ post-surgically. This discrepancy may be because this systematic review focussed only on temporal lobe surgery, whilst others included other surgery, including hemispherectomy, which has been associated with lower risk of reduced cognitive outcome (Baldeweg & Skirrow, 2015; Vining et al., 1997). The studies within this review also utilised heterogeneous neuropsychological outcome measures, which may affect the criteria for improvement.

Only studies of cognitive outcome reported the predictive effect of age at surgery and these studies had mixed results that could not be generalised. Based upon available outcomes, the review was therefore unable to address the question regarding whether earlier age at temporal lobe epilepsy surgery leads to improved neuropsychological outcomes. Studies lacked control groups of non-surgical aged-matched children with epilepsy, and as such, failed to control for the effect of development over the follow-up period, which might be expected to be greater in younger children than older children.

Among the studies that investigated predictive effects of seizure duration, age at onset or age at surgery upon neuropsychological outcome, no clear pattern of predictive effect was demonstrated from available data; however, a number of other participant characteristics that may have a bearing on neuropsychological outcomes are discussed. These include side of surgery and pre-surgical ability level.

Results suggest that left temporal surgery compared to right may be related to poorer verbal memory outcome (Dlugos et al. 1999; Jambaqué et al., 2007; Meekes et al., 2013; Robinson et al., 2000), although not all studies corroborated an effect of side on presented memory outcome (e.g. Bigel & Smith, 2001; Hori et al., 2007; Lah

& Smith, 2015; Mabbot & Smith, 2013; Szabo et al., 1998; Vadera et al., 2012; Williams et al., 1998). Left temporal surgery may also be of relative detriment to language (Lah & Smith, 2015). Those with left TLE generally had poorer language or verbal memory than those with right TLE even before surgery (Blanchette & Smith, 2002; Clusmann et al., 2004; Jambaqué et al., 2007; Williams et al., 1998) but these material specific deficits were increased after surgery (Jambaqué et al., 2007). The effect of side of surgery may have been obscured as many studies reported outcomes according to left and right hemisphere, rather than according to language-dominant and non-dominant hemispheres, which are not always concordant (De Koning et al., 2009).

Many of the studies reporting cognitive outcomes demonstrated that participants with lower pre-surgical baseline scores on assessments achieved greater improvements to post-surgical scores. This is at odds with the cognitive reserve hypothesis, which suggests that those with higher cognitive ability levels have greater neuronal reserves and so are more resilient to the effects of brain damage (Katzman et al., 1988). As Busch et al. (2008) notes, the findings of more positive memory outcomes for lower pre-surgical outcomes align more suitably with the functional adequacy hypothesis (Chelune, 1995), which posits that material-specific post-surgery deficits depend to an extent on the integrity of the ipsilateral hippocampus. This predicts that those with lower pre-surgical memory function will experience less decline; resecting a highly functioning hippocampus is likely to have a greater impact on memory functioning than resecting a hippocampus that is compromised.

The majority of studies returned from the database searches that reported outcomes of paediatric epilepsy surgery did not report any neuropsychological outcomes in their abstracts, instead focussing on seizure outcome. Claims for success of epilepsy surgery are often made on the basis of seizure frequency, and it may be assumed that successful seizure cessation corresponds to positive post-surgery outcome in other realms of life (Baxendale, 2015). Findings from the systematic review indicated that overall, seizure outcome was the most consistent predictor of neuropsychological outcome, with those who achieved seizure freedom demonstrating more positive outcome than those who continued to have seizures on multiple measures. The relationship between seizure outcome and cognitive

outcomes of IQ, memory and language were less clear; potentially the beneficial effects of reduced seizure burden may only become apparent at longer follow-up than was available for most participants.

The relationships between neuropsychological domains are complex. A clear pattern of three outcome groups emerged across outcome domains: one group remained stable (largest proportion), one group improved, and one group deteriorated. This common pattern raises the possibility that the same young people would have fallen into each of these outcome groups across outcome domains, i.e. those who deteriorated in language may also have deteriorated in IQ and mood. Unfortunately, this question could not be addressed by the review, as individual participant data were generally presented separately for each outcome within papers, without reference to participant characteristics, and many of the studies only reported one outcome domain. Additionally, study authors did not always consider causal explanations adequately for their findings beyond the effects of resection. For example, most studies reporting psychological wellbeing outcomes referenced a biological account of mental health outcome after TLE surgery; however, any paediatric surgery may meet a threshold of a traumatic event with long-term effects (Lerwick, 2013).

This review was unable to analyse the effect sizes of post-surgery improvements and deterioration in function because data were generally presented categorically, rather than as individual participant results. Some studies grouped Class III and IV outcomes, potentially losing important information about whether or not seizure frequency improved in those who continued to have persistent seizures after surgery. Pooling of results also frequently combined long-term outcomes with results from recent surgery candidates. Due to this, and the variation in both age at surgery and follow-up assessment time-points in most samples, a potential relationship between surgery and magnitude of change or developmental progress could not be established and investigated. Clear conclusions could not be made about long-term outcomes because studies had variable, and often short, follow-up periods, which ranged from less than one year in many participants to 27 years for one participant (Jarrar et al., 2002). Overall, 40 studies reported an average follow-up period of two years or below, 25 reported an average greater than two years, and for eight studies

the average follow-up period was unclear or not stated. Skirrow et al. (2011) postulate that evidence of cognitive recovery and improvement may necessitate a prolonged follow-up period, as indicated by the number of studies with shorter follow-up that do not find such changes. Without agreed assessment intervals of sufficient duration, analyses of outcome data from studies with variable follow-up intervals would result in unreliable estimates that are difficult to interpret (Centre for Reviews and Dissemination, 2009). There was also a significant variation in sample sizes between the studies. Results should therefore be treated with caution when concluding the existence of an effect.

Participant and surgery characteristics were also sources of potential bias, given their variability. Thirty studies (41%) reported underlying pathologies in children, and these may have existed unreported in others. It should be noted that the underlying pathology has implications for pre-surgical neuropsychological functioning and neurodevelopmental trajectory, and thus may influence neuropsychological performance at both pre- and post-surgical assessments and neuropsychological outcome of surgery (Arzimanoglou et al., 2005). The implications of including structures of the amygdala and hippocampus may be great in terms of the neuropsychological outcomes, due to the role of these structures in mediating fear response (LeDoux, 2003; Yates, 2015) and memory (Bannerman et al., 2008). Failure to report whether or not these structures are included in resections is problematic, as is combining the results of many different resection types. Changes in IQ may be related to factors besides the surgery, such as: neurodevelopmental trajectory; a change in antiepileptic drug use; seizure recurrence; school attendance or the psychosocial challenges of rigorous treatment. From retrieved studies, only three papers utilised a non-surgical control group with an epilepsy. Skirrow et al. (2011; 2015) recruited 11 control participants with an epilepsy. As a group, controls were comparable to the surgical group in terms of age at onset, duration of follow-up and preoperative IQ; however, they were not matched individually. Micallef et al. (2010) recruited 19 individuals with chronic epilepsy as controls. Individuals were matched with surgical participants for age at onset, gender, follow-up time from seizure onset and rate of intellectual disability. Meekes et al. (2013) utilised two age- and gender-matched controls for each participant, resulting in a total of 42 controls;

however, these individuals did not have an epilepsy. No studies that utilised controls employed randomisation or blinding.

Agreeing and providing accurate information about the key outcomes of epilepsy surgery to young people and their families is important to ensure that they are able to accurately weight the potential benefits and possible costs of proceeding with surgery. Due to the complexity and methodological variability of the literature, however, it may be difficult for clinicians to clearly communicate the evidence and its implications. Whilst RCTs in this area may not be feasible, prospectively planned multi-centre follow-up studies with appropriately chosen non-surgical quasi-control participants would allow firmer conclusions to be drawn and thus more substantial evidence-based communication to patients. Studies that include both pre- and post-surgical assessments of outcome are required, so that outcomes can be related to the intervention and the effects of pre-surgical differences between children can be controlled. The emergence of nationally designated children's epilepsy surgery centres in England since 2012, alongside detailed pre- and post-operative assessment, provides an opportunity for prospective follow-up studies.

The studies in this review assessed a wide variety of outcome domains, and for each domain, studies used a wide variety of outcome measures. This makes it difficult to draw conclusions as studies may not be measuring exactly the same abilities with their assessments. A core set of neuropsychological outcome measures would ensure that all relevant outcomes are reported consistently, simplify reporting, and allow data to be better compared between centres. This should include: seizures (Engel's classifications); IQ/developmental level; disability status; quality of life; memory; attention; executive function; visuomotor skills; language; psychological wellbeing/vulnerability; educational attainment; education/vocational outcome; social functioning; behaviour; functional independence and satisfaction with surgery. The specification of the pre-operative evaluation and the particular neuropsychological assessments used should be indicated. Patient-specific factors should also be recorded, to include: aetiology of epilepsy; age at surgery; comorbidities; sex; handedness; site and side of surgery with an agreed time for pre- and post-operative evaluations. This would make possible further systematic reviews with meta-analyses to determine the efficacy of epilepsy surgery for children with particular characteristics or for particular outcome domains. Whilst most young people remain

stable in neuropsychological outcomes or improve post-surgery, some deteriorate. It is important that these individual and surgical predictors of negative outcomes are better understood in order that children at greater risk of post-operative impairment and their families are able to make a better informed decision, with planned access to specialised neurorehabilitation services.

5. Conclusion

Whilst the majority of patients remained neuropsychologically stable following temporal lobe surgery, there was some evidence for increased material-specific memory deficits based on resection side, and a suggestion that lower pre-surgical baseline scores predicted more positive post-surgery cognitive outcome. The findings of the review raise significant questions in this area that require more substantial exploration and more thorough reporting. The development and utilisation of core neuropsychological outcome measures would permit the production of higher quality evidence.

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Conflicts of Interest

No conflicts of interest are declared.

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Table 1. Selected study characteristics and outcome categories

Study characteristics
Aetiology of epilepsy
Age at surgery
Comorbidities
Drop-out rate
Epilepsy syndrome
Length of follow-up
Outcomes measured
Sample size
Sex
Side of surgery
Surgical centre

Outcome categories
Behaviour
Cognitive development
Disability status
Educational functioning
Language
Memory
Mood
Psychiatric disorders
Quality of life
Satisfaction
Social functioning
Vocational functioning

Table 2. Characteristics and results of all studies within systematic review

Study Author, Year	N	Design	Age at surgery: mean (range) (years)	Mean follow-up (range) (years)	Seizure outcomes (Engel Class where reported)	Outcome measures	Level of evidence
Lah & Smith (2015)	40	Case series (U, R)	14.23 (no range; SD 3.36)	1.08 (no range)	24 (60%) seizure free; 16 (40%) not seizure free	CAVLT, CVLT, BNT, Reading accuracy test, reading comprehension, spelling accuracy, EVT, EOWPT,	4
Lee et al. (2015)	20	Case series (U, R)	12.8 (6.5-18.1)	3.6 (2.5-4.83)	14 (70%) Class I; 6 (30%) Class II	Korean WAIS or WISC; Rey-Kim Memory Battery	4
Skirrow et al. (2015)	42[1]	Longitudinal & cross-sectional with chronic epilepsy control group (N=11)	13.8 (SD 2.7, no range)	9 (5-15)	36 (86%) seizure freedom; 18 (42%) remained on medication; 6 (14%) regular seizures	Pre- and Post-Surgery: WMS, CAVLT, vocabulary, comprehension, and information (WAIS/WISC), British Picture Vocabulary scale, category fluency. Post-Surgery only: Doors and People	3
Andresen et al. (2014)	64	Case series (U, R)	11.3 (no range)	0.71 (SD 1.06)	37 (62%) Class I; 21 (25%) Class III; 2 (3%) Class IV	Children's Depression Inventory (CDI), Revised Children's Manifest Anxiety Scale (RCMAS), CBLC	4
Ghatan et al. (2014)	9	Case series (U, R)	12 (1-17)	4.22 (0.5-6.17)	6 (67%) Class IA; 1 (11%) Class IB; 1 (11%) Class IC; 1 (11%) Class IVA	Not reported	4
Grosmaitre et al. (2014)	1	Single case study with healthy control group	16.17	Not reported	Class III	WISC-IV, Batterie d'Efficience Mnesique, Oral-BILO, phonemic & categorical fluency, Depistage des Dyslexies (ODEDYS), L'Alouette, experimental reading task, spelling task	4
Berl et al., (2013)	1	Single case report	7	1	Not reported	WISC-IV, Sentence, story and list learning, spatial memory and faces, attention: "simple measures" and parent questionnaires, teacher and parent report (of educational outcomes)	4
Boronat et al. (2013)	1	Single case report	2.67	1	Class IV	Not reported	4
Meekes et al. (2013)	10	Prospective case series with healthy control group	14.8 (10.4-17.1)	24 months	10 (100%) Class I	WISC (Verbal Comprehension only), Test of Memory and Learning-2 (TOMAL-2), Picture naming and controlled oral word production	4
Miserocchi et al. (2013)	68	Case series (U, R)	8.9 (1-15)	>3	58 (85%) Class I; 2 (3%) Class II; 5 (7.5%) Class III; 3 (4.4%) Class IV	Rey-Osterrieth figure, Corsi span, digit span, list learning, story recall. Executive Functions: attentional matrices trail making, digit span backward, frontal assessment battery, Raven's CPM, phonemic fluency, semantic fluency, naming token test, phonetic fusion,	4

						phonetic segmentation, reading, writing	
Taylor et al. (2013)	1	Single case report	14	2	Seizure free	Not reported	4
Beaton et al. (2012)	10	Case series (U, R)	15.4 (3.6-18)	1.58 (0.67-2.4)	7 (87.5%) Class I; 1 (12.5%) Class II	WPPSI, WIAS-III, WISC-III and WISC-IV, WMS, Children's Memory Scale (CMS), Rey Complex Figure, NEPSY and TEA	4
Moseley et al. (2012)	1	Single case report	11	0.25	Seizure free	Not reported	4
Vadera et al. (2012)	45	Case series (U, R)	11.5 (1.5-18)	5.02 (0.33-12.25)	31 (69%) Class I; 7 (16%) Class II; 4 (9%) Class III; 3 (7%) Class IV	WISC-IV, CMS	4
Bird Lieberman et al. (2011)	1	Single case report	3	12	1 (100%) Class IV	Schooling type	4
Gagliardi et al. (2011)	13	Case series (U, R)	Not reported	0.6-7.9	Not reported	QoL questionnaire given pre- and post-surgery including health, physical, medication, emotional, behavioural, cognitive, social, schooling & environmental aspects	4
Garcia-Fernandez et al. (2011)	13	Case series (U, R)	11.5 (2-16.3)	5.4 (1.5-7.75)	12 (92%) Class I; 1 (8%) Class II	Not reported	4
Lee et al. (2011)	40	Case series (U, R)	ATL: no mean (1-15); Lesionectomy: (6.2 (1-12)	Not reported	Not reported	Not reported	4
Skirrow et al. (2011)	42	Longitudinal & cross-sectional with chronic epilepsy control group (N=11)	13.3 (no range; SD 2.8)	> 5	36 (86%) seizure free	WAIS-III, QOLIE-36-U, given post-surgery only	3
Lee et al. (2010)	19	Case series (U, R)	14.6 (no range; SD 2.8)	2.3 (1.2-3.5)	12 (63.2%) Class I; 5 (26.3%) Class II; 2 (10.5%) Class III	Korean WAIS or WISC, Rey-Kim Memory Battery	4
Muehlebner et al. (2010)	1	Single case report	15	1	Seizure free on AEDs	Not reported	4
Micallef et al. (2010)	20	Prospective cohort study with chronic epilepsy control group	No mean (13.4-21; 75% before 15)	8.2 (0.25-14)	9 (45%) seizure free; 11 (55%) not seizure free	Post-surgery only: Psychological interview using open-ended questions to explore psychosocial functioning and adjustment to epilepsy and treatment; BDI-II; Coopersmith Self-Esteem Inventory - adult form; State-trait anxiety inventory	3
Roulet-Perez et al. (2010)	6	Case series (U, R)	No mean (0.33-4.25)	2-6	5 (83.3%) seizure free; 1 (16.7%) transient relapse	BSID-II, WPPSI-R, WISC-III, calculated DQ	4
Zupanc et al. (2010)	17	Case series (U, R)	10 (0.75-21); whole sample only	Not reported	16 (84.2%) Class I; 2 (10.5%) Class II; 1 (5.3%) Class III	Quality of Life in Childhood Epilepsy, Quality of Life in Epilepsy for Adolescents	4
De Koning et al. (2009)	24	Case series (U, C)	11 (5.8-15.7)	2	22 (92%) Class I; 1	Language Tests for Dutch Children, Verbal	4

					(4%) Class II; 1 (4%) Class IV	comprehension Scale A from Dutch Reynell Developmental Language Scales, Vocabulary and Sentence Production from Schlichting Test of Language Production, Dutch Peabody Picture Vocabulary test	
Leunen et al. (2009)	16	Cross-sectional with healthy controls	R: mean 11.1 (8-15) (SD 3.2) L: 11.5 (SD 2.5)	Not reported; at least 0.5	16 (100%) Class I	Verbal learning: semantic word learning task from Pillon et al 1995. Spatial Learning task, learing pictures from different semantic categories from Bonin et al. Reading accuracy test, reading comprehension, spelling accuracy, EVT, EOWPT	
Mikati et al. (2009)	1	Single case report	7	0.75	Seizure free	Aphasia assessment	4
Benifla et al. (2008)	42	Case series (U, R)	12.5 (0.67-18.8)	12 (10-22)	28 (67%) Class I; 14 (33%) Class III/IV	Telephone interviews with patients or parents (regarding employment or driving outcome)	4
Busch et al. (2008)	3	Case series (U, R)	17	0.9 (0.58-1.83); whole sample only	2 (67%) Class Ia; 1 (33%) Class IV	WMS-III and Memory Assessment Clinics Self-Rating Scale (MACS-S)	4
Cunningham et al. (2007)	1	Single case report	7	1	Class III	Neuropsychological tests not reported; parental report of behaviour	4
Hori et al. (2007)	2	Case series (U, R)	18 and 19	7.83 (5.7-10)	1 (50%) Class Ia, 1 (50%) Class 1b	WAIS-R and WISC, Selective reminding procedure (Japanese version)	4
Jambaqué et al. (2007)	20	Case series (U, R)	12 (7.2-14.6)	1.04 (no range)	20 (100%) Class I	WISC-III, Signoret memory battery, Rey complex figure, The Rivermead Behavioural Memory Test, Coding subtest (attention/working memory), Vocabulary (WAIS), naming test, category verbal fluency	4
Larysz et al. (2007)	1	Case series (U, R)	13	0.5	Class I	Newly developed Polish language QoL questionnaire, pre- and post-surgery	4
Liu et al. (2007)	11	Case series (U, R)	11 (6-15)	14.2 months (9-23 months)	8 (73%) Class I; 2 (18%) Class II; 1 (9%) Class III	WISC-R, WPPSI	4
Adami et al. (2006)	1	Single case report	18	2	Class IV	Clinical psychiatric diagnosis post-surgery (no pre-surgical)	4

Cronel-Ohayon et al. (2006)	1	Single case study with twin control	10	8	Class I	WISC-III. Age 9 pre-surgery: Batterie D'efficience Mnesique. Follow-up: everyday memory questionnaire, digit span, Corsi visuospatial span, Rey's 15 words list, Story recall (CMS), Word pairs (CMS), 15 drawings string, Rey's complex figure test, Questionnaire for auto-biographical past events, vocabulary (WAIS), information (WAIS), Pyramids & Palm trees test, Boston naming test, Questionnaire about personal information, family tree	4
Moser et al. (2006)	1	Single case report	7	0.03	Seizure free	Raven's coloured progressive matrices, VLMT and figural learning and memory test: Diagnosticum für Cerebralschädigung	4
Van Oijen et al. (2006)	34	Case series (U, R)	Not reported	4 (1-9)	25 (73%) Class I; 6 (28%) Class II; 2 (6%) Class III; 1 deceased	WISC-R (Dutch), Revised Amsterdam Kinder Intelligence Test (RAKIT), McCarthy Development Scales, Intelligence Scale for Preschoolers, Bayley Scales of Infant Development (Dutch)	4
Wouters et al. (2006)	1	Single case report	12.42	1	Seizure free	AVLT, CMS, Memory for Faces (NEPSY)	4
Korkman et al. (2005)	23	Case series (U, R)	12.25 (3.5-17.42)	2 years	19 (82%) Class I; 2 (9%) Class II; 2 (9%) Class III	WISC-R, WISC-III, WPPSI-R, WIAS-R (Finnish)	4
McLellan et al. (2005)	60	Case series (U, R)	10.6 (0.6-17.9)	5.16 (2-10)	34 (60%) Class I; 3 (5%) Class II; 9 (16%) Class 3; 11 (19%) Class IV	DSM-IV	4
Clussman et al. (2004)	89	Case series (U, R)	12.7 (1.7-17.9)	1	73 (82%) Class I; 4 (4.5%) Class II; 7 (7.9%) Class III; 5 (5.6%) Class IV	Memory: Digit span, Corsi block design, DCS-R. VLMT. Attention: D2 test of attention, C.1. test, coding, reaction time, Visuospatial visuo-construction and mental rotation, Phonemic fluency, semantic fluency, token test, naming, vocabulary	4
Guimarães et al. (2004)	2	Single case reports	2, 6	0.5	Not reported	Questionnaire including perception of seizures, general health, limitations in daily activities, adverse events of antiepileptic drugs, emotional aspects, cognition, memory, language, motor skills and social relationships, parental report of behavioural	4

						outcomes	
Ozmen et al. (2004)	1	Single case report	12	1	Seizure free	Parental report of behaviour	
Mabbott & Smith (2003)	35	Case series (U, R)	Age at pre-op assessment: 12.2 (R) 12.9 (L) (5.5-16.1)	1.34 (R) 1.24 (L)	Not reported	CAVLT, Rey-Osterrieth Complex figure, face recognition task	4
Nakaji et al. (2003)	2	Single case reports	5.5 and 13.5	1.5	2 (100%) seizure free	Not reported	4
Sinclair et al. (2003)	25	Case series (U, R)	9 (1.5-16)	1	33 (79%) Class I; 5 (11.9%) Class III; 4 (9.5%) Class IV	WPPSI, WISC-III, Rey AVLT, WRAML, Rey AVLT, WRAML, Child Behaviour Checklist	4
Bittar et al. (2002)	3	Case series (U,R)	1 (0.58-1.67)	3 (1.5-4.67) not temporal only	3 (100%) seizure free	Not reported	4
Blanchette & Smith (2002)	10	Case series (R) with frontal lobe resection comparison group	10	4.4 (1.1-7.25)	Not reported	Vocabulary and Verbal IQ (WISC), Reading and Spelling (WRAT), FAS and Categories word fluency, Peabody Picture vocabulary test, token test, test for the reception of grammar	4
Danielsson et al. (2002)	16	Case series (U, R)	11 (3.5-19)	2	7 (44%) Class I; 3 (19%) Class II; 2 (12.5%) Class III; 3 Class IV;(19%) re-operated and not followed up	Conners parent/teacher rating scale. DSM-IV, parent report, neurologist observation	4
Gleissner et al. (2002)	55	Case series (U, R)	13.3 (6-17)	1 (1-1)	38 (69%) seizure free (Class I); 17 (31%) not seizure free (Class not reported)	Attention: letter cancellation test (psychomotor speed). Verbal memory: Verbal Learning and Memory Test (VLMT, German AVLT)	4
Jarrar et al. (2002)	32	Case series (U, R)	14.4 (7-18)	19 (4-27)	17 (53%) Class I. Modified criteria: 19 (59.2%) seizure frequency score 0.4 (excellent), 13 (29.5%) score 5-12	Employment and driving outcome from scripted phone interview or chart review	4
Kuehn et al. (2002)	20	Case series (U, R)	12.9 (no range; SD 3.2)	No mean (5-15 months)	Not reported	WPPSI-R, WISC-III, WAIS-R or WAIS-III., WRAML	4
Bigel et al. (2001)	29	Case series (U, R)	13.27 (6-18)	1.38 (no range)	Not reported	WISC-III, ROCFT, Peabody Picture Vocabulary Test, Story Recall, Trails A	4
Miranda and Smith (2001)	50	Case series (U, R)	13.36 (6.43-18.25)	1.82 (0.04-6.58)	34 (58%) seizure free; 16 (42%) not seizure free	WISC-R/WISC-III or WAIS-R	4
Romanelli et al. (2001)	1	Single case report	2.5	24 months	Class III	Not reported	4
Robinson et al. (2000)	21	Case series (U, R)	Not reported	0.5	11 (65%) Class I; 1 (6%) Class II; 3 (18%) Class III; 2 (12%) Class IV	WISC-III or WIAS-R, Boston Naming, WRAML, WMS-R, logical memory-delayed recall, CVLT, Rey Complex Figure	4
Westerveld et	82	Case series	14.38 (no	1.17 (0.42-	Not reported	WISC-R/WISC-III	4

al. (2000)		(U, R)	range)	5)			
Andermann et al. (1999)	2	Single case reports	8 and 18	4.75 (2.5-7)	1 (50%) Class I; 1 (50%) "seizure frequency reduced by 90%"	DSM-IV diagnosis, suicidality assessment post-surgically (no pre-surgical)	4
Dlugos et al. (1999)	5	Case series (U, R)	13.92 (8.83-18.83)	No mean (0.67-3)	4 (80%) Class I; 1 (20%) Class III	WISC-III or WIAS-R, Woodcock Johnson Test of Cognitive ability, Schooling type	4
Lendt et al. (1999)	20	Case series (R, with healthy control group)	15.1 (R) 12.5 (L) (10-16)	1 (1-1)	14 (70%) seizure free	VLMT, DCS-R, D2 test of attention, Block Design (WAIS), Token test, Written word fluency test	4
Szabó et al. (1999)	4	Case series (U, R)	4.75 (2-8)	1.68 (0.5-3.25)	4 (80%) seizure free; 1 (20%) persistent seizures	Developmental Profile II, Kaufman Assessment Battery for Children, BSID, Stanford-Binet Intelligence Scale-IV , Parent report, Peabody Picture Vocabulary Test	4
Duchowny et al. (1998)	4	Case series (U, R)	21.75 months (12-29 months)	Not reported; at least 1 year	3 (75%) Class I; 1 (25%) Class IV	Not reported	4
Manford et al. (1998)	1	Single case report	13	4	Seizure free	Not reported; parental report of behaviour	4
Szabó et al. (1998)	14	Case series (U, R)	9.4 (7-12)	2.83 (1.92-4)	10 (71%) seizure free; 3 (21%) significantly improved; 1 (7%) worsened	WISC-R or WISC-III, CAVLT, Vineland adaptive behaviour scales - revised, parental report of behaviour	4
Williams et al. (1998)	9	Case series (U, R)	13 (8-15)	2.58 (1.33-4.17)	6 (66.7%) Class I; 2 (22.2%) Class II; 1 (11.1%) Class III	WISC-R/WISC-III, WRAML, Peabody Picture Vocabulary Test, Depression Inventory Scale and Manifest Anxiety Scale, Parent report of educational and vocational outcomes, Child Behaviour Checklist	4
Duncan et al. (1997)	8	Case series (U, R)	12.6 (8-16)	0.08-2	8 (100%) seizure free (Class I)	Not reported	4
Gilliam et al. (1997)	18	Case series (U, R)	9.2 (6-12)	2.7 years (7mo-6yr); whole sample only	13 (72%) seizure free; 3 (17%) some improvement; 2 (11%) no worthwhile improvement (Class IV)	WISC, WPPSI, Child health questionnaire completed by parents (post-surgery only)	4
Keene et al. (1997)	44	Case series (U, R)	13 (SD 4.5; no range)	1-14	24 (55%) Class I; 5 (11%) Class II; 7 (16%) Class III; 8 (18%) Class IV	QOLIE-31	4
Neville et al. (1997)	1	Single case reports (2)	0.83	1 year	2 (100%) seizure free	Not reported	4
Aylett et al. (1996)	1	Single case report	8.33	1.08	Seizures continued post-operatively but controlled	Not reported	4

					via medication		
Lewis et al. (1996)	23	Case series (U, R)	14.5 (up to 17, no range)	4.24 (1-8)	17 (74%) seizure free; 4 (17%) significantly improved; 2 (9%) no significant improvement	WISC or WAIS, WMS, MMPI Social function scale, Educational and employment status at follow-up	4
DeVos et al. (1995)	8	Case series (U, R)	11.9 (5-16)	3.1 (0.33-10.2)	7 (87.5%) seizure free; 1 (12.5%) persistent seizures	WISC-R or WISC-III, VIQ (WISC), Controlled oral word association test, visual naming test, reading decoding test (WRAT), Peabody individual achievement test, Token test	4

U = uncontrolled study
R = retrospective study
[1] = Same participant dataset as utilised in Skirrow et al. (2011)

Study Author, Year	N	Design	Age at surgery: mean (range) (years)	Mean follow-up (range) (years)	Seizure outcomes (Engel Class where reported)	Neuropsychological Domains Measured	Measures	Neuropsychological Outcomes	LoE
Lah & Smith (2015)	40	Case series (U, R)	14.23 (no range; SD 3.36)	1.08 (no range)	24 (60%) seizure free; 16 (40%) not seizure free	Memory; Language	WISC-III; WISC-IV; WAIS-III; WPPSI-III; WASI; CAVLT; CVLT; Boston Naming Test; Reading Accuracy Test; Reading Comprehension; Spelling Accuracy; Expressive Vocabulary Test; Expressive One-Word Picture Vocabulary Test; Woodcock-Johnson-III	Memory: Post-surgically, significant decline in one aspect of semantic memory (Naming) in Left TL patients only. Repeated measures ANOVA showed no significant effect of time or laterality but significant interaction. Language: Post-surgically, significant decline in reading accuracy only in both Right and Left surgeries. No significant changes in memory test scores related to hippocampal resection.	4
Lee et al. (2015)	20	Case series (U, R)	12.8 (6.5-18.1)	3.6 (2.5-4.83)	14 (70%) Class I; 6 (30%) Class II	Cognitive Ability, Memory	Korean WAIS or WISC; Rey-Kim Memory Battery	Cognitive Ability: 7 children had improved FSIQ (more than 5 points) and 6 declined. At the group level, median values of the difference between pre-op and post op IQ were not significant. No significant difference between Right TL and Left TL. Memory: 6 children improved and 7 declined in MQ. At the group level, there was no significant pre/post change.	4
Skirrow et al. (2015)	42[1]	Longitudinal & cross-sectional with chronic epilepsy control group (N=11)	13.8 (SD 2.7, no range)	9 (5-15)	36 (86%) seizure freedom; 18 (42%) remained on medication; 6 (14%) regular seizures	Cognitive Ability, Memory, Language	WISC or WAIS; WMS; British Picture Vocabulary Scale; Category Fluency. Post-Surgery only: Doors and People Test, BPVS-II	Cognitive Ability: significant main interaction of time and group ($F(2,44)=3.63$, $p=0.04$) (LTLE significantly improved post-surgery, and RTLE and non-surgical controls did not $p=0.04$). Semantic memory: Both groups improved post-surgically; however, only LTLE improvement was significant (as initial mean lower). Verbal episodic memory: No main effect of group for story recall post-surgically. Interaction between time and group ($F(2,38)=3.38$, $p=0.04$), was present: post-surgical improvement in RTLE but not in LTLE or controls. In Doors and People Test, RTLE score same as controls whilst LTLE lower (not significantly). Post-surgical hippocampal volume associated with higher verbal memory score (both semantic and episodic measures), particularly after left sided surgery.	3

								Visual episodic memory: No main group effect for design recall scores post-surgically. Significant post-surgical improvement in LTLE on design recall but not in RTLE or controls ($F(2,37)=4.64$, $p=0.02$). Left surgical participants showed a significantly better visual than verbal memory Score on Doors and People task (post hoc paired samples t-test: $t = 4.25$, $p = 0.001$). Greater improvements for individuals with lower pre-operative scores ($r=-0.55$, $p<0.001$). List learning on CAVLT and WMS-R story recall positively associated with seizure freedom. Language: No group differences in category fluency or receptive vocabulary. All groups scored below their chronological age (based on mean score for group).	
Andresen et al. (2014)	64	Case series (U, R)	11.3 (no range)	0.71 (SD 1.06)	37 (62%) Class I; 21 (25%) Class III; 2 (3%) Class IV	Mood, Behaviour	Children's Depression Inventory (CDI); Revised Children's Manifest Anxiety Scale (RCMAS); CBCL	Mood: No significant changes overall. For Left-sided TLE: Anhedonia - 12% declined, 80% stable, 8% improved Social Concerns: 19% declined, 58% stable, 23% improved No data of this nature provided for right-sided TLE Behaviour: No significant change at the group level. For Left-sided TLE: Aggressive behaviour - 9% declined, 88% stable, 3% improved No data of this nature provided for right-sided TLE Effect of group: Frontal lobe surgery demonstrated more significant positive change than TL after surgery, but also worse pre surgical behaviour and mood	4
Ghatan et al. (2014)	9	Case series (U, R)	12 (1-17)	4.22 (0.5-6.17)	6 (67%) Class IA; 1 (11%) Class IB; 1 (11%) Class IC; 1 (11%) Class IVA	Cognitive Ability, Quality of Life, Functional Outcomes	Functional Outcomes: Quality of Life in Epilepsy questionnaires (parental report; post-surgery only) and neuropsychological assessments (not stated)	Functional Outcomes: 6 "markedly improved" and 3 "significantly improved"; however, this was a combination of Quality of Life and Cognitive Ability outcomes, which were neither quantified nor provided separately	4
Grosmaitre et al. (2014)	1	Single case study with healthy control group	16.17	Not reported	Class III	Cognitive Ability, Memory, Language and Literacy	WISC-IV; Batterie d'Efficience Mnesique; Oral-BILO; phonemic & categorical fluency; Depistage des Dyslexies (ODEDYS);	Cognitive Ability: Remained stable Memory: Remained stable Language: Oral language preserved; reading ability started below school level but regressed markedly by a	4

							L'Alouette; experimental reading task; spelling task	year's reading age post-surgery; reading of irregular frequent words and irregular infrequent words decreased post-surgery; spelling largely maintained but reduced for irregular frequent words.	
Berl et al., (2013)	1	Single case report	7	1	Not reported	Cognitive Ability, Memory, Attention, Cognitive/Mental Health Disorder, Educational Outcomes	WISC-IV; Sentence, Story and List Learning; Spatial Memory and Faces; "Simple Measures of Attention"; Parent Questionnaires; Diagnoses; Teacher and Parent Report (of educational outcomes)	Cognitive Ability: Change by <10 on VCI and PCI but improved by 13 on WMI and by 11 on PSI Memory: Largely stable with some improvement in verbal learning Attention: Greater difficulty on simple and complex attention tasks. Parents reported increased difficulty of attention, executive functioning, and self-regulation Cognitive/Mental Health Disorder: Developed GAD and meets most of criteria for ADHD Educational Outcomes: Following surgery, struggling to keep pace with peers, requiring simplification of instructions and more assistance	4
Boronat et al. (2013)	1	Single case report	2.67	1	Class IV	Behaviour	Not reported	Patient demonstrated hyperorality, non-aggressive biting of new objects and people, worsened hyperactivity, constant motion, difficulty sustaining attention, hypersexuality (present pre-op but much increased), polydipsia, and mutism. Diagnosis of Klüver-Bucy syndrome made.	4
Meekes et al. (2013)	10	Prospective case series with healthy control group	14.8 (10.4-17.1)	24 months	10 (100%) Class I	Cognitive Ability (Verbal IQ only), Memory (Verbal only)	WISC (Dutch Edition) (Verbal Comprehension only); Test of Memory and Learning-2 (TOMAL-2, Dutch Edition); Picture Naming; Controlled oral word production	Cognitive Ability (Verbal IQ): no significant change in VIQ [2] Memory (Verbal): 4 L temporal patients significantly decreased VMI relative to prediction; 1 L temporal patient showed non-significant decreases; 2 R temporal patients showed significant decreases; 1 R temporal patient showed a non-significant decrease; 1 R temporal showed non-significant increase.	4
Miserocchi et al. (2013)	68	Case series (U, R)	8.9 (1-15)	>3	58 (85%) Class I; 2 (3%) Class II; 5 (7.5%) Class III; 3 (4.4%) Class IV	Language, Memory, Executive Function	Language: Phonemic fluency; Semantic Fluency; Naming; Token Test Metaphonology Verbal Memory: Digit Span Forward; Word List Recall; Short Story Recall Visuospatial Memory: Corsi Span; Rey-Osterrieth Figure	Follow-up occurred at 36 months. In all cases, patients were lost to follow-up. Language: Overall decrease in the percentage of patients with pathological scores (definition of 'pathological scores' not provided) Memory: Overall decrease in the percentage of patients with pathological scores Executive Function: Overall decrease in the percentage of patients with pathological scores	4

							Recall Executive Function: Rey-Osterrieth Figure Copy; Attentional Matrices; Trail Making; Digit Span Backward; Frontal Assessment Battery; Raven's CPM		
Taylor et al. (2013)	1	Single case report	14	2	Seizure free	Quality of Life	Not reported	Patient's quality of life greatly improved (abstract only)	4
Beaton et al. (2012)	10	Case series (U, R)	15.4 (3.6-18)	1.58 (0.67-2.4)	7 (87.5%) Class I; 1 (12.5%) Class II	Cognitive Ability, Memory	WPPSI; WIAS-III; WISC-III and -IV; WMS; Children's Memory Scale (CMS); Rey Complex Figure Test, NEPSY; Test of Everyday Attention for Children (TEA-CH)	Cognitive Ability: NB: For one patient, scores were not calculated for all domains. Processing Speed Index: 8/9 (89%) showed no change/improved; 3 (33%) improved by more than 1 SD, 1 (11%) declined. Working Memory Index: 7/9 (78%) showed no change; 2 (22%) declined. Verbal Comprehension Index: 9/9 (100%) improved or remained within 1 SD of pre-op scores. Perceptual Reasoning Index: 9/9 (100%) remained within 1 SD of pre-op scores Memory: NB: For two patients, scores were not calculated for all domains. Visual Immediate: 6/8 (75%) showed stability or improvement; 2/8 (25%) declined Visual Delayed: 7/8 (88%) showed stability or improvement; one (12%) showed a significant decline of more than 2 SDs Verbal Immediate: 7/8 (88%) showed stability or improvement; one (12%) showed a decline of more than 1.5 SDs. Verbal Delayed: 7/8 (88%) showed stability or improvement; one (12%) showed a decline of more than 1.5 SDs. Facial Memory: All patients (8/8) remained stable or improved on both immediate and delayed facial memory	4
Moseley et al. (2012)	1	Single case report	11	0.25	Seizure free	Attention, Educational Outcomes	Not reported	Attention: Reported as improved, though still lacking in school Educational Outcomes: Completed homework in a timely manner post-surgery	4
Vadera et al. (2012)	45	Case series (U, R)	11.5 (1.5-18)	5.02 (0.33-12.25)	31 (69%) Class I; 7 (16%) Class II; 4 (9%) Class III; 3 (7%) Class IV	Cognitive Ability, Memory	WISC-IV; CMS	Cognitive Ability: No significant change. Memory: No significant change. No difference in L or R surgery for effect on memory	4
Bird Lieberman et	1	Single case report	3	12	1 (100%) Class IV	Cognitive Ability, Cognitive/Mental	Neuropsychological measures not stated;	Cognitive Ability: Moderately severe cognitive difficulties Cognitive/Mental Health Disorder: Now has ASD	4

al. (2011)						Health Disorder, Schooling	Diagnoses; Schooling type	Schooling: In residential special school	
Gagliardi et al. (2011)	13	Case series (U, R)	Not reported	0.6-7.9	Not reported	Quality of Life	QoL questionnaire given pre- and post-surgery including: health, physical, medication, emotional, behavioural, cognitive, social, schooling & environmental aspects	Almost all participants showed significant improvements to QoL scores. One participant indicated a decreased score, largely due to social, school, and behavioural factors. At the group level, all aspects of QoL improved after surgery (significantly at $p<0.05$ for health, negative effects of AEDs and relationship with parents).	4
Garcia-Fernandez et al. (2011)	13	Case series (U, R)	11.5 (2-16.3)	5.4 (1.5-7.75)	12 (92%) Class I; 1 (8%) Class II	Cognitive Ability	Not reported	Overall group (including extratemporal): no significant deterioration in any cognitive domains; significant post-operative improvement in visual attention, perceptive-auditory skills, line orientation, grammatical comprehension, semantic verbal fluency, verbal learning, recall selective attention, and non-verbal fluency[2]	4
Lee et al. (2011)	40	Case series (U, R)	ATL: no mean (1-15); Lesionectomy: (6.2 (1-12)	Not reported	Not reported	Mood, Behaviour	Not reported	Mood: 2 ATL participants had mood disorders with excessive irritability Behaviour: 2 ATL participants demonstrated neuropsychological complications with normal school life; 2 ATL patients developed aggressive behaviour after operation	4
Skirrow et al. (2011)	42	Longitudinal & cross-sectional with chronic epilepsy control group (N=11)	13.3 (no range; SD 2.8)	> 5	36 (86%) seizure free	Quality of Life, Cognitive Ability	QOLIE-36-U (post-surgery only); WAIS-III	Quality of Life: total quality of life scores higher in surgery group than in non-surgical group. Total quality of life mainly determined by seizure freedom (ß=0.44, p=0.001) (regression included FSIQ, AED use, surgery and seizure status as factors). Cognitive Ability: FSIQ improved at least 10 points in 17 surgery patients (41%) and in one control participant (9%). Only one surgical patient lost at least 13 points (lost 22 points on first procedure then gained 9 after second). Overall, mean FSIQ improved in surgical patients but unchanged for matched non-surgical epilepsy group ($F1,47=4.8$, $p=0.033$). VIQ and PIQ changes dependent on side of surgery (interaction of task by side, $F2, 46=5.1$, $p=0.01$): PIQ improved in both L and R surgery but VIQ only in L surgery. Partial correlations (controlled for age at scan and sex) significant for total grey matter volume and FSIQ. Current AEDs were negative predictors of FSIQ change in regression. Age at onset, duration, number of prior IQ assessments, surgery, and time since last seizure were not significant.	3

Lee et al. (2010)	19	Case series (U, R)	14.6 (no range; SD 2.8)	2.3 (1.2-3.5)	12 (63.2%) Class I; 5 (26.3%) Class II; 2 (10.5%) Class III	Cognitive Ability, Memory	Korean WAIS or WISC; Rey-Kim Memory Battery	Cognitive Ability: 3 children showed decrease more than 10 points in IQ. Overall, IQ values remained almost stable without significant decline. Memory: 1 child declined more than 10 points in MQ. Overall, MQ remained nearly stable with no significant decline	4
Muehlebner et al. (2010)	1	Single case report	15	1	Seizure free on AEDs	Cognitive Ability, Memory	Not reported	Cognitive Ability: Significant improvement of general intellectual performance Memory: Significant improvement in long term memory, serial reproduction and visual-motoric coordination	4
Micallef et al. (2010)	20	Prospective cohort study with chronic epilepsy control group	No mean (13.4-21; 75% before 15)	8.2 (0.25-14)	9 (45%) seizure free; 11 (55%) not seizure free	Quality of Life, Psychological Wellbeing	QOLIE-89; Post-surgery only: Psychological interview using open-ended questions to explore psychosocial functioning and adjustment to epilepsy and treatment; BDI-II; Coopersmith Self-Esteem Inventory - Adult Form; State-Trait Anxiety Inventory	Quality of Life: Those patients who underwent surgery and became seizure free reported quality of life as within the normal range. Those who had surgery but did not become seizure free reported significantly worse overall quality of life than both the former group and non-surgical chronic epilepsy patients. Psychological Wellbeing: 50% of seizure-free surgical patients reported change in perceived identity, which co-occurred with increased overall activity. Depression score in this group was low, although 1 patient developed depression. Self-esteem and anxiety fell within normal limits. The group of patients who had surgery and were not subsequently seizure free (n=8) had poorest outcomes (compared to surgery seizure free, spontaneous remission and chronic epilepsy). Rates of depression higher than chronic epilepsy ($t=2.99$, $d.f=16$, $p<0.01$). 2 had severe depression. 2 developed new depression after surgery. 54% reported increased depression after surgery, compared to 16% increased depression in chronic epilepsy. Self-esteem reported as lower than other groups ($F-4.21$, $d.f.=2,29$, $p<0.05$)	3
Roulet-Perez et al. (2010)	6	Case series (U, R)	No mean (0.33-4.25)	2-6	5 (83.3%) seizure free; 1 (16.7%) transient relapse	Cognitive Ability (DQ & IQ), Behaviour	BSID-II; WPPSI-R; WISC-III; Behavioural measure not reported	Cognitive Ability: 2 (33%) improved, 3 (50%) worsened and 1 (17%) was not evaluable at baseline, only follow-up Behaviour: 1 improved (17%), 2 (33*) unchanged, 3 (50%) qualitatively different	4
Zupanc et al. (2010)	17	Case series (U, R)	10 (0.75-21); whole sample only	Not reported	16 (84.2%) Class I; 2 (10.5%) Class II; 1 (5.3%) Class III	Quality of Life	Quality of Life in Childhood Epilepsy; Quality of Life in Epilepsy for Adolescents	Post-surgery only. QoL in seizure-free individuals significantly higher than in non-seizure free [2]	4
De Koning et	24	Case series (U,	11 (5.8-15.7)	2	22 (92%) Class I;	Language	Language Tests for	No significant change to receptive syntax. Significant	4

al. (2009)		C)			1 (4%) Class II; 1 (4%) Class IV		Dutch Children; Dutch Reynell Developmental Language Scales (Verbal Comprehension Scale A); Schlichting Test of Language Production (Vocabulary and Sentence Production); Dutch Peabody Picture Vocabulary Test	reductions in receptive lexicon, productive lexicon and productive syntax. At 2 year follow-up, receptive lexicon and productive syntax remained stable at the reduced level, whilst productive lexicon continued to demonstrate decline. No differences in L or R surgery, no difference in acquired versus developmental pathology. Patients with large pre-surgical productive syntax delay demonstrated significantly improved development compared to those with a small delay prior to surgery (p<0.05). Delay in productive lexicon decreased more in children in whom language is mediated by the operated hemisphere (p<0.05).	
Leunen et al. (2009)	16	Cross-sectional with healthy controls	R: mean 11.1 (8-15) (SD 3.2) L: 11.5 (SD 2.5)	Not reported; at least 0.5	16 (100%) Class I	Memory	Semantic Word Learning Task; Spatial Learning Task; Reading Accuracy Test, Reading Comprehension, Spelling Accuracy, EVT, EOWPT	No pre-post assessment, only post, and comparison to healthy controls. No significant differences compared to healthy controls on spatial encoding or verbal encoding. Left TL demonstrated lower scores than Right TL and controls in word list learning and recall.	
Mikati et al. (2009)	1	Single case report	7	0.75	Seizure free	Language, Behaviour	Aphasia assessment	Language: Prior to surgery, ignored speech directed to her, was nonresponsive to most commands, could follow few single-step commands. Mental age of 12- to 14-month child. At latest follow-up (9 months post-surgery), expressive speech still at ~12 months, whilst receptive speech, understanding and reception progressed to ~3.5 years. Behaviour: Increased interactivity, calmness, imaginative play, imitation of parental behaviours. Decreased agitation. Beginning to form peer relationships.	4
Benifla et al. (2008)	42	Case series (U, R)	12.5 (0.67-18.8)	12 (10-22)	28 (67%) Class I; 14 (33%) Class III/IV	Vocational Outcome; Driver's Licensure	Telephone interviews with patients or parents (regarding employment or driving outcome)	Employment and School Enrolment: Engel Class I/II = achieved by 24 patients (86%); Engel Class III/IV = achieved by 8 patients (57%). Difference in education/employment status between the two groups is statistically significant. Driver's licensure: Engel Class I/II = 12 of 19 eligible patients (63%) obtained a driver's licence; Engel Class III/IV = 3 of 11 eligible patients (27%) obtained a driver's licence during seizure-free periods.	4
Busch et al. (2008)	3	Case series (U, R)	17	0.9 (0.58-1.83); whole sample only	2 (67%) Class Ia; 1 (33%) Class IV	Memory	WMS-III; Memory Assessment Clinics Self-Rating Scale (MACS-S)	Auditory Delayed: 1 patient significantly improved, 2 no change Visual Delayed: 2 significantly improved, 1 significantly declined.	4

							MACS-S: 2 patients no change, 1 patient significant decline on Ability and Frequency scores, indicating a decline in subjective memory and more frequent memory problems.	
Cunningham et al. (2007)	1	Single case report	7	1	Class III	Cognitive Ability; Attention; Behaviour	Neuropsychological tests not reported; parental report of behaviour	Cognitive Ability: IQ remained stable (low average pre and post); mild improvement in visuoperceptual ability; mild deterioration in reading, otherwise academic skills unchanged Attention: improved Behaviour: reported increase in non-compliant behaviour and emotional lability	4
Hori et al. (2007)	2	Case series (U, R)	18 and 19	7.83 (5.7-10)	1 (50%) Class Ia, 1 (50%) Class 1b	Cognitive Ability	WAIS-R and WISC; Selective reminding procedure (Japanese version)	18 year old: VIQ stable, PIQ and FSIQ improved >10 points after 2 years. Verbal learning stable. 9 year old: Assessed 2 months post-surgery. Improvements in VIQ, PIQ and FSIQ but <10 points. No long-term follow-up data available. No verbal learning data available.	4
Jambaqué et al. (2007)	20	Case series (U, R)	12 (7.2-14.6)	1.04 (no range)	20 (100%) Class I	Cognitive Ability, Memory, Attention	WISC-III; Signoret Memory Battery; Rey Complex Figure Test; The Rivermead Behavioural Memory Test; WAIS (Vocabulary, Coding) Naming Test; Category Verbal Fluency	Cognitive Ability: No significant change (p=0.11 for FSIQ; p=0.10 for PIQ). Younger age at surgery associated with higher improvement of FSIQ (p=0.02), VIQ (p=0.01) and information (p=0.01). Memory: Verbal Memory - 9 children significantly improved, 2 significantly declined, 9 no significant change. Visual Memory - 8 significantly improved, 2 significantly declined, 10 no significant change. Significant improvement for immediate story recall (p=0.03), immediate word list recall (p=0.03), sentence recognition (p=0.02), Verbal Memory Score (p=0.03). Others did not significantly change. All attention/working memory scores showed significant improvement on coding (p=0.007), digit span (p=0.005) and Corsi blocks test (p=0.01). Age at surgery not related to change. Language: only naming showed significant improvement (p=0.03), higher in children with no previous hippocampal damage (p=0.03).	4
Larysz et al. (2007)	1	Case series (U, R)	13	0.5	Class I	Quality of Life	Newly developed Polish language QoL questionnaire, pre- and post-surgery	Child improved	4
Liu et al. (2007)	11	Case series (U, R)	11 (6-15)	14.2 months (9-23 months)	8 (73%) Class I; 2 (18%) Class II; 1 (9%) Class III	Cognitive Ability	WISC-R; WPPSI	8 (73%) improved >10 IQ points, 3 (27%) improved <10 IQ points	4

Adami et al. (2006)	1	Single case report	18	2	Class IV	Cognitive/Mental Health Disorder	Clinical psychiatric diagnosis post-surgery (no pre-surgical)	Developed PTSD post-surgery	4
Cronel-Ohayon et al. (2006)	1	Single case study with twin control	10	8	Class I	Cognitive Ability, Memory	WISC-III; WAIS-R; Wisconsin Card Sorting; Stroop Task; Verbal and Nonverbal Fluency Tasks; Tower of Hanoi; Conners; CMS (French); Everyday Memory Questionnaire (French); Digit Span; Corsi's Visuo-Spatial Span; Rey's 15 Words List; 15 Drawings String; Rey's Complex Figure Test; Questionnaire for Autobiographical Past Events; Pyramids & Palm Trees Test; Boston Naming Test; Questionnaire about Personal Information; Family Tree	Cognitive Ability: Declined at 18 years old as compared to 9 years old pre-surgery; however, remained within the average/low-average range. Vocabulary, Information and Verbal Fluency scores below normal age ranges. Memory: Normal memory functioning pre-surgery. Post-surgery: Reported difficulty learning new facts, interfering with vocational training. Short-term upper range and similar to twin. All CMS subscales within the normal range, with better performance for visual than verbal memory. Memory loss greater and more rapid than twin over longer delays. Reduced semantic memory compared to twin when lexical components involved. Memory for autobiographical and public past events below twin. Lower score than twin brother on memory for past events. Normal range on CMS, but much greater forgetting rate than twin over longer delays: impaired long term consolidation. Reduced semantic memory compared to twin and below normal range. Memory for autobiographical and public past events below twin brother	4
Moser et al. (2006)	1	Single case report	7	0.03	Seizure free	Cognitive Ability, Memory, Behaviour	Raven's Coloured Progressive Matrices; VLMT; Figural Learning; Diagnosticum Für Cerebralschädigung	Cognitive Ability: IQ unchanged Memory: normalised verbal learning and improved figural memory Behaviour: verbalisation and behavioural deficits normalised	4
Van Oijen et al. (2006)	34	Case series (U, R)	Not reported	4 (1-9)	25 (73%) Class I; 6 (28%) Class II; 2 (6%) Class III; 1 deceased	Cognitive Ability	WISC-R (Dutch); Revised Amsterdam Kinder Intelligence Test (RAKIT); McCarthy Development Scales; Stutsman Intelligence Scale for Preschoolers; Bayley Scales of Infant Development (Dutch)	Cognitive Ability: 26/30 (86%) no significant (i.e. >10 points) change in IQ, 2 (7%) deteriorated, 2 (7%) improved	4
Wouters et al. (2006)	1	Single case report	12.42	1	Seizure free	Memory	AVLT; CMS; Memory for Faces (NEPSY); Boson Naming Test	Improvement in memory learning tasks: pre-surgically, 1/4 learning scores were above the 10th centile. Post-surgically 4/4 learning scores above the 10th centile.	4

								Decline in delayed recall tasks: pre-surgically, 3/4 tasks were impaired, 2 only marginally. Post-surgically 4/4 tasks were within the impaired range (*z*« -1.33), 2 only marginally. Working memory deficit intensified: score on non-verbal task remained impaired (*z* = -3.00) and verbal task declined notably into the impaired range (*z* = -1.67). High pre-/post-surgery scores on Boston Naming Test	
Korkman et al. (2005)	23	Case series (U, R)	12.25 (3.5-17.42)	2 years	19 (82%) Class I; 2 (9%) Class II; 2 (9%) Class III	Cognitive Ability	WISC-R; WISC-III; WPPSI-R; WIAS-R (Finnish)	Cognitive Ability: Left temporal patients - 2 significant increase in VIQ/ Performance IQ, 2 significant decrease in VIQ/ performance IQ; Right temporal patients - 2 significant increase in VIQ/ Performance IQ; 17 patients (right and left) no significant change	4
McLellan et al. (2005)	60	Case series (U, R)	10.6 (0.6-17.9)	5.16 (2-10)	34 (60%) Class I; 3 (5%) Class II; 9 (16%) Class 3; 11 (19%) Class IV	Cognitive/Mental Health Disorder	DSM-IV	Pervasive Developmental Disorder: Pre-surgery: 23/60 (60%) Post-surgery: 21/57 (37%) total. 2 lost diagnosis, 11 improved, 7 stable, 3 deteriorated. ADHD: Pre-surgery: 14 (23%). Post-surgery: 13/57 (23%) total. 3 lost diagnosis, 5 improved, 5 stable, 1 deteriorated, 2 developed post-surgically. Oppositional Defiant Disorder/Conduct Disorder: Pre-surgery: 14/60 (23%). Post-surgery: 13/57 (23%) total. 3 lost diagnosis, 2 improved, 4 stable, 5 deteriorated, 2 developed post-surgically. Disruptive Behaviour Disorder (NOS): Pre-surgery: 25/60 (42%). Post-surgery: 25/57 (44%) total. 5 lost diagnosis, 8 improved, 8 stable, 4 deteriorated, 5 developed post-surgically. Emotional Disorder: Pre-surgery: 5/60 (8%). Post-surgery: 12/57 (21%) total. 3 lost diagnosis, 1 stable, 1 deteriorated, 10 developed post-surgically. Eating disorder: Pre-surgery: 1/60 (2%). Post-surgery: 2/57 (4%). 1 lost diagnosis, 1 deteriorated, 1 developed post-surgically (NB: This calculation error is present in paper) Conversion disorder: Pre-surgery: 1/60 (2%). Post-surgery: 1/57 (2%).1 lost diagnosis, 1 developed post-	4

								surgically. Psychosis: Pre-surgery: 0 patients. Post-surgery: 1/57 (2%). 1 developed post-surgically. No clear relationship between seizure free outcome and any psychopathology. AED use was linked to psychosis in one participant but no clear correlation overall. No distinct relationship between outcome and type of surgery. Those with emotional disorders were more likely to have "normal" intelligence (87%) than those without (42%) $p<0.05$.	
Clusmann et al. (2004)	89	Case series (U, R)	12.7 (1.7-17.9)	1	73 (82%) Class I; 4 (4.5%) Class II; 7 (7.9%) Class III; 5 (5.6%) Class IV	Memory, Attention, Visuospatial Ability, Language	Digit Span; Corsi Block Design; DCS-R; VLMT; D2 Test of Attention; C.1. Test; Coding; Reaction Time; Visuo-construction; Mental rotation; Phonemic Fluency; Semantic Fluency; Token Test; Naming; Vocabulary	Memory: Right TLE - no significant group differences according to the type of resection. Left TLE - significantly worse than right TLE 1 year after surgery ($x^2 = 7.3$, $P = 0.026$) and as a trend 3 months after surgery ($x^2 = 4.4$, $P = 0.11$). Attention: Left TLE - no significant gains or losses after 3 months, but significant improvements 1 year post-surgery ($z = -2.2$, $P = 0.031$). Right TLE - significant improvements after 3 months ($z = -2.1$, $P = 0.038$) but not after 1 year. Visuospatial Ability: Right TLE - significantly lower scores 1 year post-op ($x^2 = 5.2$, $P = 0.022$). Left TLE - significant improvements 1 year post-op ($z = -2.4$, P 0.015). Language: Right TLE - significant improvements after 3 months ($z = -2.6$, $P = 0.008$) and 1 year ($z =$ -2.3, $P = 0.02$). Left TLE - no significant gains or losses. A younger age at the time of surgery was not associated with better neuropsychological outcome (all Kendall's $r<0.17$ with $P>0.16$). No effect of seizure outcome. Interaction of side and surgical group. Patients undergoing left sided surgery significantly differed by surgical group, with amygdalohippocampectomies resulting in more deterioration to below average verbal memory scores than anterior temporal lobectomies or lateral lesionectomies. Right sided surgeries did not show this effect	4
Guimarães et al. (2004)	2	Single case reports	2, 6	0.5	Not reported	Quality of Life, Behaviour	Questionnaire (including perception of seizures, general	Quality of Life: Scores in all areas increased or remained stable, aside from: Patient 1: Behaviour/emotional, school, environment. Patient 2: Behaviour/emotional,	4

							health, limitations in daily activities, adverse events of antiepileptic drugs, emotional aspects, cognition, memory, language, motor skills and social relationships); Parental Report of Behavioural Outcomes	cognition, though 4/5 these declines remained within positive ranges ('excellent' to 'very good' or 'very good' to 'good'). Behaviour: Reported behaviour worsened for both children	
Ozmen et al. (2004)	1	Single case report	12	1	Seizure free	Behaviour	Parental report of behaviour	One year post-surgery developed excessive masturbation in inappropriate places, several times per day, causing parental anger. This was treated successfully with psychoeducation. Also demonstrated social withdrawal and aggression.	
Mabbott & Smith (2003)	35	Case series (U, R)	Age at pre-op assessment: 12.2 (R) 12.9 (L) (5.5-16.1)	1.34 (R) 1.24 (L)	Not reported	Memory	CAVLT; Rey-Osterrieth Complex Figure Test; Face Recognition Task	No significant difference between pre-and post-surgery outcomes, temporal and extratemporal surgery, or right and left temporal surgery, for immediate and delayed recall of stories ($F(1,40)<1.60$, $p<0.22$), list learning ($F(1,22<2.86$, $P>0.10$). Mean memory performance fell within the normal range pre-/post-operatively with within-group variance. Visual memory: no change on Rey Complex Figure and no effect of group,)$F(2,37)<1.66$, $P>0.21$). For recognition of unfamiliar faces all groups improved after surgery ($F(1,30)=25.11$, $P<0.001$).	4
Nakaji et al. (2003)	2	Single case reports	5.5 and 13.5	1.5	2 (100%) seizure free	Behaviour	Not reported	Behaviour of both patients showed considerable improvement. Both patients returned to mainstream school.	4
Sinclair et al. (2003)	25	Case series (U, R)	9 (1.5-16)	1	33 (79%) Class I; 5 (11.9%) Class III; 4 (9.5%) Class IV	Cognitive Ability, Memory, Behaviour	WPPSI; WISC-III; Rey AVLT; WRAML; Child Behaviour Checklist	Cognitive Ability: no significant changes in IQ pre-/post-surgery in either older or younger children. Memory: no significant group changes as a result of surgery except a postoperative improvement WRAML Sound Symbol Associative Learning in both older and younger children. For tests of verbal learning/recall, the group with a left temporal seizure focus performed more poorly than the group with a right temporal seizure focus both before and after surgery. The high-performance group with a left-sided focus tended to recall fewer words after surgery ($p=0.06$) than before surgery, while the reverse was true for the high-performance group with a right-sided focus and	4

								the low-performance group with a left-sided focus. Behaviour: No significant pre-/post-operative changes in CBCL scores.	
Bittar et al. (2002)	3	Case series (U,R)	1 (0.58-1.67)	3 (1.5-4.67) not temporal only	3 (100%) seizure free	Cognitive Ability, Quality of Life	Parental report and review of medical notes	Cognitive Ability: 2 unimpaired pre- and post-surgery; 1 regressed after initial surgery and accelerated following reoperation, resulting in mild language and cognitive delay Quality of Life: subjective improvements in cognition, language, communication, level of care, parental anxiety, and reduction in seizure frequency or severity	4
Blanchette & Smith (2002)	10	Case series (R) with frontal lobe resection comparison group	10	4.4 (1.1-7.25)	Not reported	Language	WISC-IV (Vocabulary and Verbal IQ only); WRAT (Reading and Spelling; Word Fluency (FAS and Categories); Peabody Picture vocabulary test; Token Test; Test for the Reception of Grammar (TROG)	5 children who had temporal surgery declined on phonemic fluency, 3 children declined on category fluency No significant difference between frontal and temporal groups before and after surgery Children who had left sided surgery performed less well than those who had right sided surgery on category fluency and token test	4
Danielsson et al. (2002)	16	Case series (U, R)	11 (3.5-19)	2	7 (44%) Class I; 3 (19%) Class II; 2 (12.5%) Class III; 3 Class IV;(19%) re-operated and not followed up	Behaviour	Conners parent/teacher rating scale. DSM-IV, parent report, neurologist observation	2-year follow up data was available from 13 patients as 3 had repeat surgeries. 8/13 experienced positive behaviour changes, 3/13 experienced no change, and 2/13 experienced negative behaviour changes - one developed depression and another showed increased autistic behaviours. No child who became seizure-free deteriorated in behaviour.	4
Gleissner et al. (2002)	55	Case series (U, R)	13.3 (6-17)	1 (1-1)	38 (69%) seizure free (Class I); 17 (31%) not seizure free (Class not reported)	Memory, Attention	Verbal Memory: Verbal Learning and Memory Test (VLMT, German AVLT); Attention: Letter Cancellation Test (Psychomotor Speed)	Memory: Left TLE: Significant decline in learning and in loss after delay at 3 months post-surgery. These recovered after 1 year though not to pre-surgical levels. No significant change in recognition pre/post, though also did not recover to pre-surgical levels. Memory: Right TLE: Significant decline in recognition 3 months post-surgery. This recovered significantly after 1 year though not to pre-surgical levels. No significant changes in learning or loss after delay pre/post. Attention: In both groups, psychomotor speed improved post-surgery. Amygdalohippocampectomy associated with reduced learning capacity and greater loss after delay at follow-up compared to anterior temporal lobe resections, lesionectomies including part of the hippocampus, or pure lesionectomies. Epilepsy	4

								duration was longer in the amygdalohippocampectomy group and this was not controlled for.	
Jarrar et al. (2002)	32	Case series (U, R)	14.4 (7-18)	19 (4-27)	17 (53%) Class I. Modified criteria: 19 (59.2%) seizure frequency score 0.4 (excellent), 13 (29.5%) score 5-12	Vocational/ Educational Outcomes	Employment and Driving Outcome from scripted phone interview or chart review	3/32 (9%) unemployed, 3 (9%) homemakers, 1 (3%) employed part-time, 25 (78%) gainfully employed. 26 (81%) have driving license, 4 (13%) lost driving license, 2 (6%) never had driving license.	4
Kuehn et al. (2002)	20	Case series (U, R)	12.9 (no range; SD 3.2)	No mean (5-15 months)	Not reported	Cognitive Ability, Memory	WPPSI-R, WISC-III, WAIS-R or WAIS-III.; WRAML	Cognitive Ability: no significant change in verbal, performance or full scale IQ in L or R temporal groups; no significant correlation with size of resection and difference between pre and post scores; no significant difference in those with hippocampal resection and those without Memory: in Left TLE patients, no significant difference between pre and post means for verbal and visual memory. Unable to calculate for Right TLE as only 3 participants had measures taken.	4
Bigel and Smith (2001)	29	Case series (U, R)	13.27 (6-18)	1.38 (no range)	Not reported	Cognitive Ability Memory (Delayed)	WISC-III; WRAT (Maths and Reading); ROCFT; Peabody Picture Vocabulary Test; Story Recall; Trails A	Cognitive Ability: No significant differences between pre- and postsurgical performance Memory: No significant differences between pre- and postsurgical performance	4
Miranda and Smith (2001)	50	Case series (U, R)	13.36 (6.43-18.25)	1.82 (0.04-6.58)	34 (58%) seizure free; 16 (42%) not seizure free	Cognitive Ability	WISC-R/WISC-III or WAIS-R	No difference between RTL and LTR with regards to IQ change, and the two groups attained similar patterns of scores across subtests and pre- and post-surgical testing. For all patients, mean VIQ and FSIQ did not change significantly after surgery. Positive change in PIQ small but significant. The majority of patients (36/50; 72%) experienced no significant change in verbal cognitive functioning. 14 (28%) showed significant change in VIQ (7 improved, 7 declined). 33/49 (67%) of patients showed no significant change in PIQ. 12 improved significantly whilst 4 declined significantly. Increases in VIQ score were associated with older age at time of surgery and lower VIQ at preoperative testing.	4
Romanelli et al. (2001)	1	Single case report	2.5	24 months	Class III	Cognitive Ability, Quality Of Life (Parent Report), Speech	Not reported	Cognitive Ability: improved, not quantified Quality of Life: child improved Speech: improved, not quantified	4
Robinson et	21	Case series (U,	Not reported	0.5	11 (65%) Class I;	Cognitive Ability,	WISC-III or WIAS-R;	52% of the patients had stable or improved scores on all	4

al. (2000)		R)			1 (6%) Class II; 3 (18%) Class III; 2 (12%) Class IV	Memory, Behaviour	Boston Naming Test; WRAML; WMS-R (Revised Logical Memory-Delayed Recall); CVLT; Rey Complex Figure; Child Behaviour Checklist	seven cognitive measures. 81% of 21 patients showed significant improvement in scores on at least one of the seven instruments. Cognitive Ability: Overall, pre- and post-operative scores on intelligence tests were not significantly different. One patient had a significant decline in VIQ and another had a significant decline in both PIQ and FSIQ. History of seizures, rather than patient age at seizure onset, had a significant impact on cognition. Memory: 13 patients experienced no decline, 3 declined on naming, 4 declined on rote memory, 5 declined on stories, 3 declined on design. Overall, there was no significant difference pre-/post-surgery on any of the measures. Behaviour: The patients' behavior postoperatively correlated directly with seizure control. Patients with persistent seizures continued to experience psychological and social difficulties. Just one of the six patients with residual seizures demonstrated improvement in behaviour and social skills. Patients who achieved seizure control (Engel Class I) had improved self-confidence and social skills, and decreased anxiety.	
Westerveld et al. (2000)	82	Case series (U, R)	14.38 (no range)	1.17 (0.42-5)	Not reported	Cognitive Ability	WISC-R/WISC-III	Significant change defined as 2xSE of test. 67 (82%) did not significantly change in VIQ, 8 (10%) declined, 7 (9%) improved. PIQ: 67 (82%) no change, 2 deteriorated, 3 improved. Repeated-measures ANOVA showed left TL attained higher PIQ after surgery than at baseline, (p=0.014). However, no significant change in any type of IQ for right TL. Younger patient age at surgery associated with greater positive change in VIQ (R^2=0.198; p<0.005). Higher baseline VIQ and longer duration of follow up together account for 12% of PIQ outcome (R^2=0.121; p=0.03). No other significant predictors.	4
Andermann et al. (1999)	2	Single case reports	8 and 18	4.75 (2.5-7)	1 (50%) Class I; 1 (50%) "seizure frequency reduced by 90%"	Cognitive/Mental Health Disorder	DSM-IV diagnosis, suicidality assessment (post-surgical only)	8 year-old: initial post-op improvements in behaviour, alertness and social interactions. Subsequent auditory hallucinations, depression and suicidal ideation, thoughts of violence against sister. DSM-IV diagnosis of psychotic disorder due to brain disease with hallucinations and depressive features. 18 year-old: Developed post-op paranoid psychosis and	4

								depressive symptoms, and made a suicide attempt. Recovered from psychosis within 3 months but depression persisted. DSM-IV diagnosis of delusional disorder due to brain disease with paranoid and depressive features.	
Dlugos et al. (1999)	8	Case series (U, R)	13.92 (8.83-18.83)	No mean (0.67-3)	4 (80%) Class I; 1 (20%) Class III	Cognitive Ability, Memory, Education	WISC-III or WIAS-R; WIAT; Woodcock Johnson Test of Cognitive Ability; CVLT; Wide Range Assessment of Memory and Learning (Visual Memory subtest); Education: Not stated	Cognitive Ability: In Right TL, none of the 3 patients demonstrated significant pre/post changes. In Left TL, one patient (of 5) demonstrated significantly decreased VIQ (difference of over 1 SD) whilst one demonstrated significantly increased PIQ. No significant changes in FSIQ. Memory: No significant changes in Right TL. In L TL, 4/5 patients (where the results of the 5th were not interpretable) deteriorated more than 1 SD on Verbal Learning, 2 decreased (>1 SD) on Visual Memory, 1 decreased (>1 SD) on Reading Comprehension and 1 increased (>1 SD) on Reading Comprehension. Education: 4 of 5 L TL group required educational adaptations after surgery. 1 did not and is attending community college. No data for R TL.	4
Lendt et al. (1999)	20	Case series (R, with healthy control group)	15.1 (R) 12.5 (L) (10-16)	1 (1-1)	14 (70%) seizure free	Attention, Memory, Language	VLMT (German AVLT); DCS-R; D2 Test of Attention; WAIS (Block Design only); Token Test, Written Word Fluency Test	Attention: At the group level, significant increase in attention. Memory: significant change found in 9 patients: 5 improved and 4 deteriorated. None of the children with losses were seizure-free post-surgery. Language: Those who were preoperatively impaired showed improved language performance after surgery. At the whole group level, Token Test score significantly decreased post-surgically and remained this way at 12 months.	4
Szabó et al. (1999)	5	Case series (U, R)	4.75 (2-8)	1.68 (0.5-3.25)	4 (80%) seizure free; 1 (20%) persistent seizures	Cognitive Ability, Language, Behaviour, Cognitive/Mental Health Disorder	Developmental Profile II; Kaufman Assessment Battery for Children; BSID; Stanford-Binet Intelligence Scale-IV - Parent report; Peabody Picture Vocabulary Test; DSM-IV; Vineland adaptive behaviour scales-revised - parental report	Cognitive Ability: 3 (60%) improved, 1 (20%) unchanged, 1 (20%) deteriorated Language: 3 (60%) improved, 2 (40%) deteriorated (1 of whom initially improved then deteriorated). Behaviour: 4 (80%) improved, 1 (20%) worsened Cognitive/Mental Health Disorder: All demonstrated PDD before and after.	4
Duchowny et	4	Case series (U,	21.75 months	Not reported; at	3 (75%) Class I; 1	Developmental and	Not reported	No pre- and post-surgery outcomes reported; only	4

al. (1998)		R)	(12-29 months)	least 1 year	(25%) Class IV	Social Outcome		sparse comments on some individuals	
Manford et al. (1998)	1	Single case report	13	4	Seizure free	Cognitive Ability, Educational Outcomes, Behaviour	Not reported; parental report of behaviour	Cognitive Ability: PIQ slightly decreased to 125 Educational Functioning: Substantial improvement Behaviour: Improved socialisation, engagement in hobbies	4
Szabó et al. (1998)	14	Case series (U, R)	9.4 (7-12)	2.83 (1.92-4)	10 (71%) seizure free; 3 (21%) significantly improved; 1 (7%) worsened	Cognitive Ability, Memory	WISC-R or WISC-III; CAVLT; Vineland Adaptive Behaviour Scales - Revised; Parental Report of Behaviour	Cognitive Ability: FSIQ, VIQ and PIQ all within low average range and did not change significantly after surgery. Memory: non-significant pre-/post-surgery decline on immediate memory. Significant pre-/post-surgery decline on delayed trial ($F(8,1)=28.7$, $p=0.001$). Interaction between baseline memory performance level and test session was significant $F(1,0)=5.19$, $p=0.049$. Children who performed above median pre-surgery showed marked decline, whereas those pre-surgically below median remained stable. No significant interaction between side of resection and immediate memory.	4
Williams et al. (1998)	9	Case series (U, R)	13 (8-15)	2.58 (1.33-4.17)	6 (66.7%) Class I; 2 (22.2%) Class II; 1 (11.1%) Class III	Cognitive Ability, Memory, Language, Mood, Behaviour, Social Interactions Motor Speed, Behaviour, Anxiety	WISC-R/WISC-III; WRAML; Peabody Picture Vocabulary Test; Depression Inventory Scale and Manifest Anxiety Scale; Parent Report of Educational and Vocational Outcomes; Child Behaviour Checklist (activity, social, school scales)	Cognitive Ability: No significant increases in FSIQ, PIQ, VIQ. No significant changes in reading, spelling, maths from WRAT-R. Memory: Non-significant increases in visual memory and verbal memory indices. Language (vocabulary): Non-significant increase Mood: Non-significant decrease in anxiety and depression Behaviour: Significant improvements in internalising ($t=2.33$, $p<0.05$), thought problems ($t=4.36$; $p<0.002$) and aggression ($t=2.31$; $p<0.05$). Social problems approached significance. School performance was perceived to decline. Social Interactions: Parents observed improvements in social relationships and activities	4
Duncan et al. (1997)	8	Case series (U, R)	12.6 (8-16)	0.08-2	8 (100%) seizure free (Class I)	Speech, Language	Not specified	No child sustained a post-operative speech or language deficit	4
Gilliam et al. (1997)	18	Case series (U, R)	9.2 (6-12)	2.7 years (7mo-6yr); whole sample only	13 (72%) seizure free; 3 (17%) some improvement; 2 (11%) no worthwhile	Cognitive Ability, Quality of Life	WISC, WPPSI, Child Health Questionnaire (parental report; post-surgery only)	Cognitive Ability: 7 (39%) did not have both pre- and post- surgery IQ scores. Declines of 10 or more points were seen in 2 patients for Verbal IQ and 1 patient for Performance IQ. Increases of 10 or more points were seen in 1 patient for Verbal IQ and 3 patients for Performance IQ. The mean difference between pre- and	4

					improvement (Class IV)			post-operative IQ scores across overall group (not solely temporal) was not significant[2] Quality of Life: Overall group significantly lower than non-surgical controls on physical function, behaviour, general health, self-esteem, emotion impact on parent and time impact on parent[2]	
Keene et al. (1997)	44	Case series (U, R)	13 (SD 4.5; no range)	1-14	24 (55%) Class I; 5 (11%) Class II; 7 (16%) Class III; 8 (18%) Class IV	Quality of Life (post-surgery)	QOLIE-31	Post-surgery only. QoL in seizure-free individuals significantly higher than in non-seizure free [2]	4
Neville et al. (1997)	1	Single case reports (2)	0.83	1 year	2 (100%) seizure free	Cognitive Ability and Development	Not reported	Frequency and quality of eye contact improved. Patient began to anticipate in action songs, babble became inflected, vocalised for her bottle, using referential eye gaze in support. Raised arms to be picked up, imitative skills observed at 5 months had returned, developing more appropriate use of toys and more eye contact. Communication remained largely motoric and understanding remained situational.	4
Aylett et al. (1996)	1	Single case report	8.33	1.08	Seizures continued post-operatively but controlled via medication	Cognitive/Mental Health Disorder, Social Interaction	Not reported	Thirteen months after surgery it was reported that the following occurred: vacant episodes of hyperventilation, lacking in spontaneous communication, able to respond to some commands and could only speak name, not responsive to painful stimuli. This occurred at any time of day and lasting up to 2 hours The patient also lost friends, and demonstrated social regression and worsening behaviour	4
Lewis et al. (1996)	23	Case series (U, R)	14.5 (up to 17, no range)	4.24 (1-8)	17 (74%) seizure free; 4 (17%) significantly improved; 2 (9%) no significant improvement	Cognitive Ability, Memory, Cognitive/Mental Health Disorder, Educational and Vocational Outcomes, Social Interaction	WISC or WAIS; WMS; Minnesota Multiphasic Personality Inventory; Educational and employment status (at follow-up); Social Function Interviews (post-operatively)	Cognitive Ability: Significant increase in FSIQ post-surgery (mean 82.78 vs 86.30, $F1,22=6.99$, $p<0.05$). VIQ and PIQ not significantly different but trend towards improvement. Memory: No significant change post-surgery Cognitive/Mental Health Disorder: significant post-surgery increases on hyperchondriasis ($F1,8=9.23$, $p<0.05$), psychasthenia ($F1,8=9.02$, $p<0.05$), schizophrenia ($F1,8=11.53$, $p<0.01$) and hypomania ($F1,8=20.74$, $p<0.01$). Educational and Vocational Outcomes: 10/23 were still in high school (6 employed part time), 9/23 graduated from high school (5 full-time employed, 9 employed part-time, 3 unemployed), 2/23 had attended only grade school, 2/23 were in college.	4

								Social Interaction: All reported social improvement after operation. Significant improvements in family relations (F1,22=10.03, *p*<0.01), peer relations (F1,22=31.12, *p*<0.0001), leisure activities (F1,22=67.23, *p*<0.0001), job/school performance (F1, 22=23.15, *p*<0.0001), personal satisfaction (F1,22=26.19, *p*<0.0001), and adaption to illness (F1,22=15.00, *p*<0.001).	
DeVos et al. (1995)	9	Case series (U, R)	11.9 (5-16)	3.1 (0.33-10.2)	7 (87.5%) seizure free; 1 (12.5%) persistent seizures	Cognitive Ability, Language	WISC-R or WISC-III; VIQ (WISC); Controlled Oral Word Association Test; Visual Naming Test; WRAT (Reading Recognition); Peabody Individual Achievement Test, Token Test	Cognitive Ability IQ: 1 improved (>10 points), 5 unchanged, 2 no results PIQ: 1 improved (>10 points), 4 unchanged, 1 declined (>10 points), 2 no results VIQ: 1 improved (>10 points), 5 unchanged, 2 no results Language 4 improved, 2 unchanged, 2 temporarily worsened but resolved One patient had two surgeries. A decline of more than 10 points was evident in FSIQ and VIQ after the first surgery, in addition to impaired object naming. Following the second surgery, VIQ and FSIQ remained unchanged and object naming was improved.	4

LoE = Levels of Evidence
U = Uncontrolled Study
R = Retrospective Study
[1] = Same participant dataset as utilised in Skirrow et al. (2011)
[2] = Disaggregated data for temporal lobe patients is not presented

Table 3. Designs of Included Studies

Study Design	No. (%) of Studies
Uncontrolled retrospective case series	45 (62%)
Case reports	20 (27%)
Longitudinal case series data with cross-sectional data from comparison with chronic epilepsy controls	3 (4%)
Longitudinal case series data with cross-sectional data from a comparison group of healthy young people	2 (3%)
Single case study with healthy control group	1 (1%)
Single case study with child's twin as control participant	1 (1%)
Prospective cohort study with chronic epilepsy control group	1 (1%)

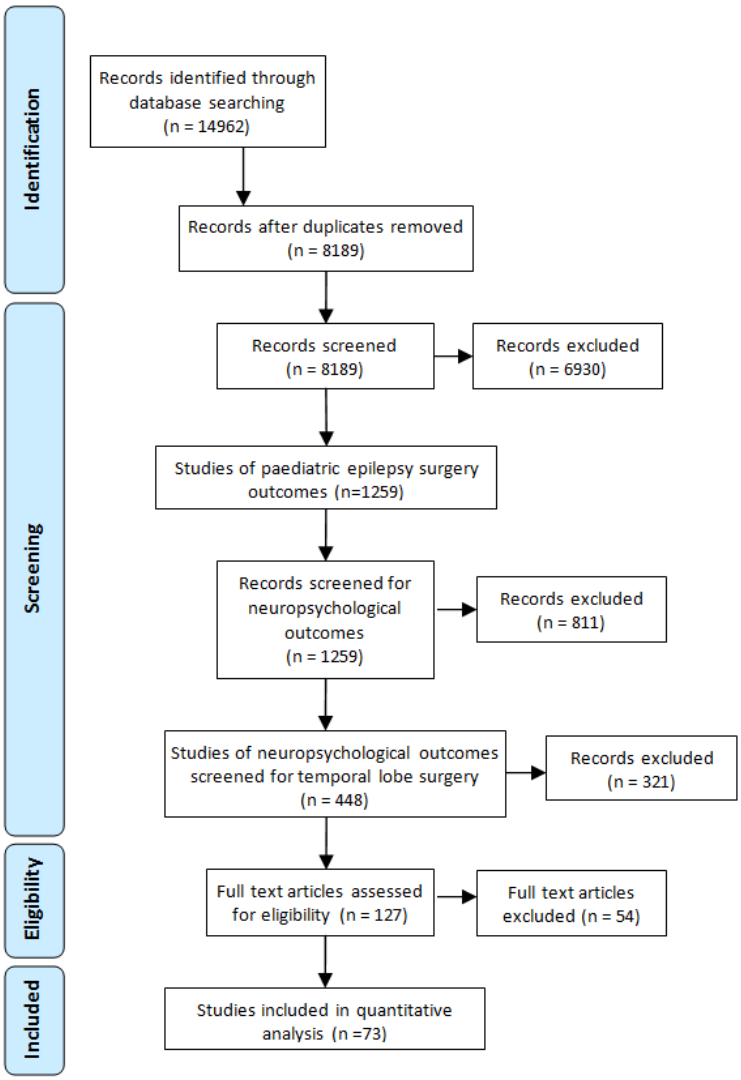

Figure 1. PRISMA diagram of study selection process

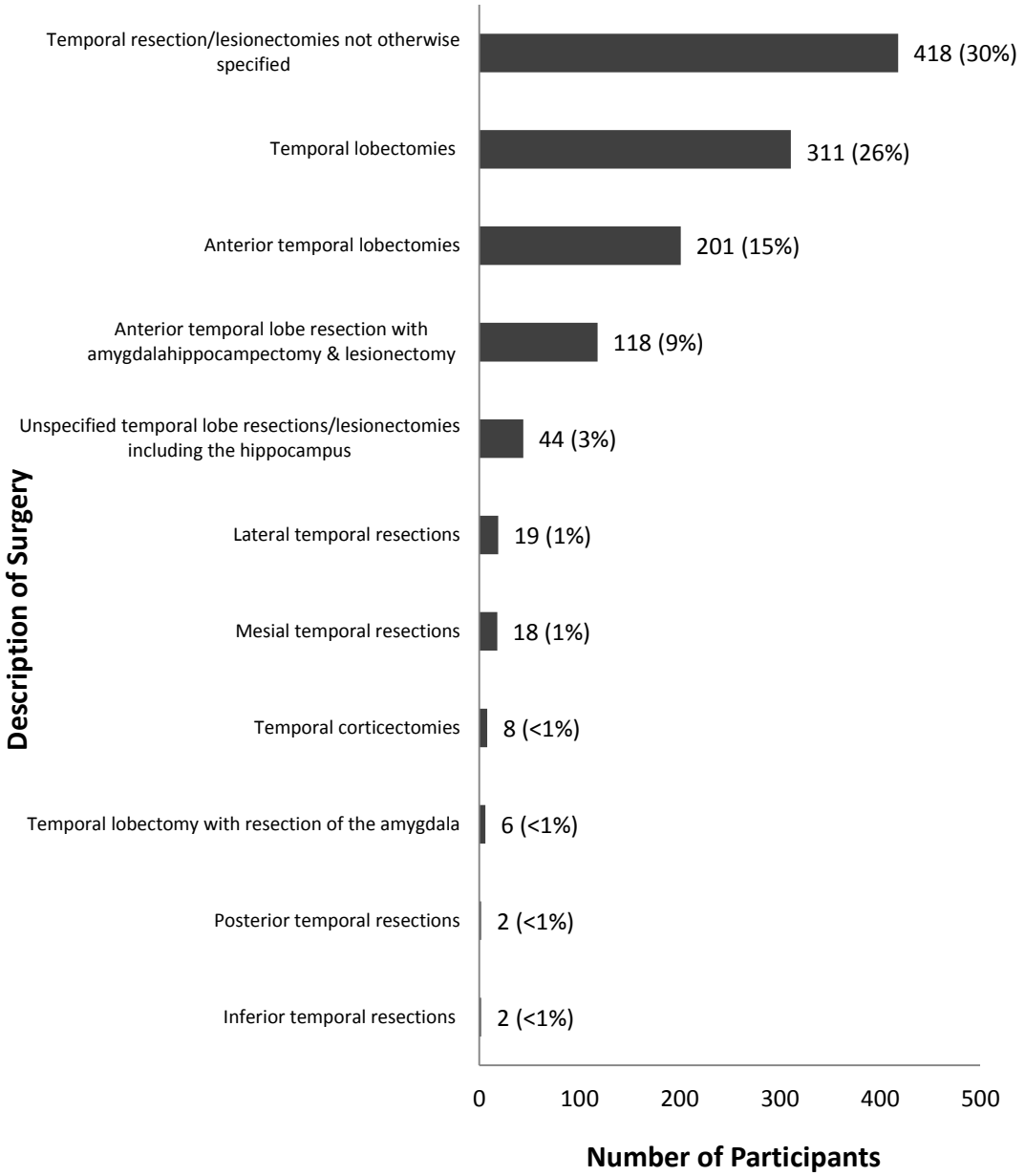

Figure 2. Type of temporal lobe surgery described for each participant

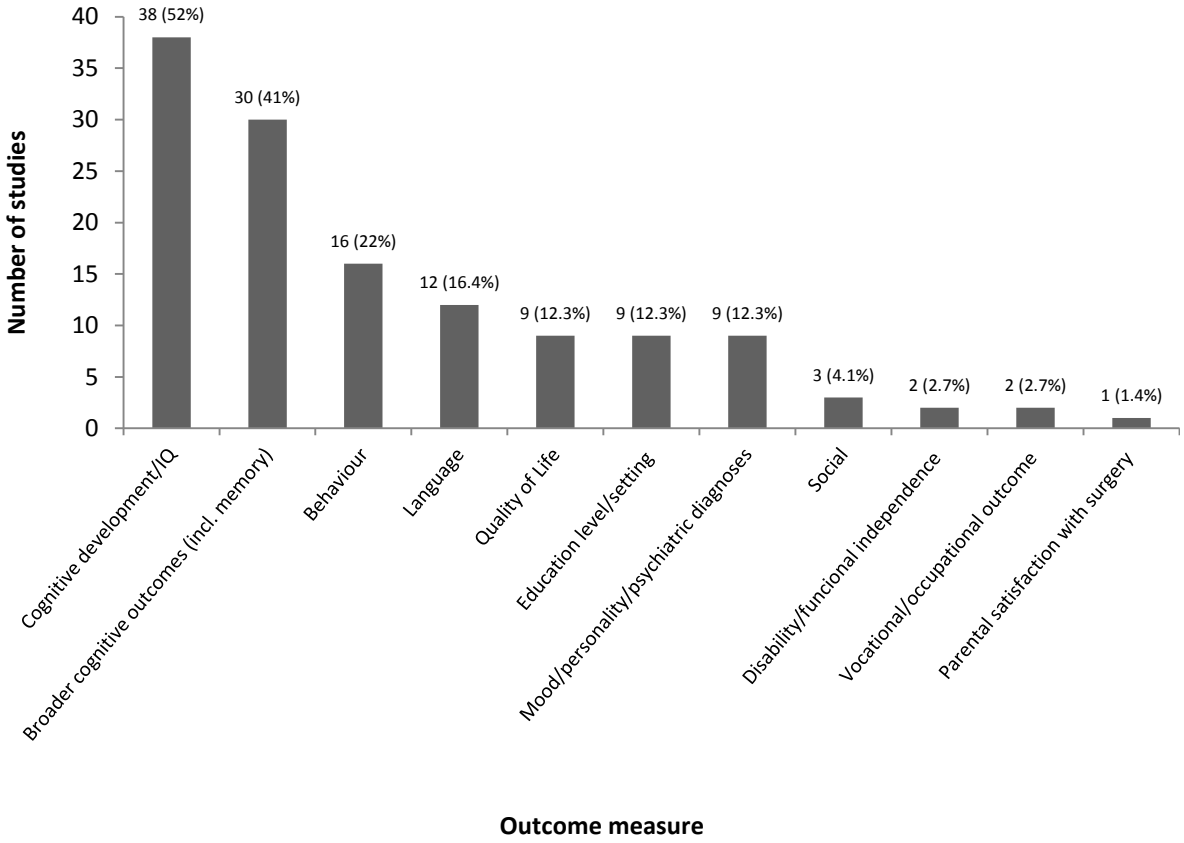

Figure 3. Neuropsychological outcomes reported by included studies