
University of Glasgow

# Sleep and Forgetting in Children with Genetic Generalised Epilepsy

Major Research Project
&
Clinical Research Portfolio

*VOLUME I*
*(Volume II bound separately)*

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*Submitted in partial fulfilment of the requirements for the degree of Doctorate in Clinical Psychology*

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# CONTENTS

**VOLUME 1**

**ACKNOWLEDGEMENTS** ..... **5**

**CHAPTER 1: SYSTEMATIC REVIEW** ..... **6**

*Psychosocial interventions for children and young people with epilepsy: A Systematic Review of the Literature*

Abstract ..... 7
1. Introduction ..... 8
2. Method ..... 11
3. Results ..... 13
4. Discussion ..... 30
References ..... 35

**CHAPTER 2: MAJOR RESEARCH PROJECT** ..... **40**

*Sleep and Forgetting in Children with Genetic Generalised Epilepsy*

Plain English Summary ..... 41
Abstract ..... 42
1. Introduction ..... 43
2. Methods ..... 46
3. Results ..... 51
4. Discussion ..... 59
References ..... 64

**CHAPTER 3: ADVANCED CLINICAL PRACTICE I: REFLECTIVE ACCOUNT** ..... **67**

*Different dynamics: experience of participating in a service user drama group*

(Abstract only, for full account see Volume II)

Abstract ..... 68

**CHAPTER 4: ADVANCED CLINICAL PRACTICE II: REFLECTIVE ACCOUNT** ..... **69**

*A 10 year longitudinal study: my changing perception of research in psychology*

(Abstract only, for full account see Volume II)

Abstract ..... 70

**APPENDICES** ..... **71**

***Appendix 1.1*** *Epilepsy and Behavior Guide for Authors* ..... *71*
***Appendix 1.2*** *Crowe Critical Appraisal Tool* ..... *82*
***Appendix 1.3*** *Agreed Quality Ratings for all Included Articles* ..... *84*
***Appendix 1.4*** *References for Table 1 Study Outcome Measures* ..... *85*
***Appendix 2.1*** *Letter granting ethical approval by the North of Scotland Research Ethics Committee* ..... *89*

***Appendix 2.2*** *Letter of acknowledgement of minor amendment by the North of Scotland Research Ethics Committee.....93*
***Appendix 2.3*** *Letter granting site and management approval by the NHS Greater Glasgow and Clyde Research and Development Department.....95*
***Appendix 2.4*** *Letter granting site and management approval by the NHS Lothian Research and Development Department.....97*
***Appendix 2.5*** *Participant Invitation Letter.....98*
***Appendix 2.6*** *Participant Opt-in Form .....99*
***Appendix 2.7*** *Child Information Sheet (Age 9-12).....100*
***Appendix 2.8*** *Child Information Sheet (Age13-16).....102*
***Appendix 2.9*** *Parent Information Sheet.....104*
***Appendix 2.10*** *Child Assent Form.....107*
***Appendix 2.11*** *Child Consent Form .....108*
***Appendix 2.12*** *Parent Consent Form.....109*
***Appendix 2.13*** *Major Research Proposal .....110*

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## SYSTEMATIC REVIEW

# Psychosocial interventions for children and young people with epilepsy: A Systematic Review of the Literature

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*Prepared in accordance with the instructions to authors for Epilepsy and Behavior (see Appendix 1.1)*

**Abstract**

*Background*

Despite the recognition that psychosocial interventions can improve quality of life and mental health, there continues to be a lack of clarity and guidance around effective psychosocial interventions for children and young people with epilepsy. This review utilises specific quality criteria to systematically identify and appraise the evidence for the effectiveness of psychosocial interventions for children and young people with epilepsy.

*Methods*

A systematic search of six electronic databases was conducted using predefined eligibility criteria. The reference lists of previous review papers were also manually searched. Seventeen studies met the inclusion and exclusion criteria. A quality appraisal checklist, the 'Crowe Critical Appraisal Tool' (CCAT) [1] was applied to the included articles and effect sizes were calculated when not provided in the papers.

*Results*

Methodological quality of the majority of studies included was moderate, with only three studies rated as high quality. Meta-analysis was not conducted as the studies used heterogeneous methodologies and lacked consistency in outcome measures. Limited evidence was found for interventions improving epilepsy knowledge, quality of life and psychological outcomes.

*Conclusions*

Psychosocial interventions may provide clinical benefit although further research is needed to clarify the most effective treatment components, delivery methods and measurement of intervention outcomes. The existing evidence base for children and young people is limited by methodological issues such as the use of small samples, inadequate power and a lack of controlled studies.

*Keywords:* psychosocial; intervention; treatment; epilepsy; children; adolescents
*Word Count:* 8,689

## 1. Introduction

Epilepsy is the most common neurological disorder in children under 18 years of age in the UK [2] and is defined by the presence of recurrent seizures, resulting from abnormal electrical activity in the nerve cells of the cerebral cortex. Approximately 63,400 children and young people aged 18 years and under in the UK have a diagnosis of epilepsy and take anti-epileptic drugs (AED), equivalent to approximately 1 in 220 children [3].

Epilepsy is known to be associated with a range of psychosocial difficulties and cognitive deficits. Baker et al. [4] highlighted that although strong correlations have been found between epilepsy and depression in adolescents, mental health problems are under-diagnosed and undertreated in this population. Children with epilepsy have been found to be almost five times more likely to have behavioural problems than healthy controls [5]. Dunn et al. [6] reported younger age at onset of seizures, a lower socioeconomic status and family stress as predictors of behavioural problems in children and young people with epilepsy (CYPE). Neuropsychological assessment and parental questionnaires within the first year of diagnosis have demonstrated that significantly more children with epilepsy require special educational assistance than matched classmate controls [7]. Children with epilepsy also obtained worse scores in behavioural and cognitive domains.

Given the potential for psychosocial difficulties related to epilepsy, the impact on quality of life (QoL) has been researched. In adult studies, depression and anxiety were found to explain more variance in QoL than seizure control/frequency or demographic variables [8, 9]. In Baker et al.'s [10] international questionnaire study, more than one third of CYPE who responded expected the condition to hinder their lives in the future, with 36% keeping their epilepsy a secret from others from fear of being treated differently. Taylor et al. [11] found that when compared to healthy children and children with asthma, children with newly diagnosed epilepsy had significantly poorer QoL across multiple domains. QoL was significantly poorer in children with new-onset epilepsy. It also noted that parents of children with epilepsy reported reduced QoL. They suggest that QoL could be improved in adolescents with newly diagnosed epilepsy through psychosocial interventions focussed on increasing self-esteem [11]. Involvement of parents in these

interventions was also advocated to maintain healthy and positive parent-child relationships. The literature indicates that both psychosocial and seizure factors impact on the wellbeing of CYPE, and that cognitive and academic functioning and psychosocial adjustment can be negatively impacted by epilepsy, underlining the need for early

Dunn et al. [6] found that children with a more positive response and attitude towards illness and increased sense of control over their epilepsy reduced their risk of developing behavioural problems, depression and poor self-concept. Oostrom et al. [7] reported that epilepsy syndrome, use of AED and seizure control were not significantly related to the cognitive or behavioural findings. Rather, the child's pre-diagnostic learning and behavioural histories and the parents' ability to continue their habitual parenting post-epilepsy diagnosis were associated with cognitive and behavioural functioning [12]. However, Hermann et al. [13] found that inadequate seizure control (frequency and severity) was the best predictor of behavioural problems in 6-11 year old children. Much of the literature has used self and carer-reported QoL via standardised questionnaires, but some have used qualitative techniques to develop a better understanding of the issues and concerns directly expressed by CYPE [14, 15]. These studies have used the young people's own perspectives to develop a biopsychosocial model of the impact of epilepsy on the lives of young people and have been used to develop psychosocial interventions.

The recent NICE guideline on the management of epilepsy promotes the consideration of the physical, psychological and social needs of CYPE by healthcare professionals, highlighting that particular attention should be paid to their relationships with family and friends, and at school [16]. It is recommended that CYPE should be given information on general issues with epilepsy, ranging from treatment options to the impact on lifestyle e.g. effects of sleep deprivation [16].

Within the last fifteen years, research developing psychosocial interventions for CYPE has increased, with the majority using group educational programs and cognitive and behavioural interventions. Several literature reviews have been carried out in this area in the past ten years but often they do not meet the requirements of a *systematic* review [17-19]. The focus of most has been on adult populations, although two do include child and adolescent studies [20, 21]. A more recent Cochrane systematic review examined the

effectiveness of specialist service models for children with epilepsy and their families [22]. Although the Cochrane paper reviewed some of the studies that will be included in the current review, it focussed on comparing the effectiveness of specialist teams/individuals in the care of children with epilepsy with usual care services and only included controlled studies. It was therefore considered timely to review the literature on psychosocial interventions for CYPE, incorporating a wider range of methodologies and also including studies published since 2010. This systematic review aims to synthesise and analyse the research that investigates psychosocial interventions for CYPE. In addition to a summary of study findings, it will critically assess the quality of the evidence. An evaluation of the literature will help determine the effectiveness of interventions for CYPE and may help to develop guidelines on their use.

For the purpose of this review a psychosocial intervention is defined as a therapeutic intervention without a pharmacalogical component focusing on psychological, relational and social functioning. They can include formal psychological interventions e.g. CBT and health education-based programmes, as well as those with an emphasis on developing social interaction skills. Interventions with a physical exercise content can also be considered under this definition if the aims are related to improving psychosocial wellbeing through physical activity and the associated physical and social benefits.

*1.1 Research Aims*

1. To establish if there is any evidence for the efficacy of psychosocial interventions for CYPE.

2. To identify specific treatment components or methods of delivery that may increase the efficacy of these interventions.

3. To identify intervention goals and how these measured.

## 2. Method

The PRISMA statement [23] was used as guidance for the undertaking and reporting of this systematic review.

### *2.1 Search Strategy*

The following electronic databases were systematically searched on 28th November 2014 to identify studies: CINAHL, PsychInfo, Psychology & Behavioral Sciences Collection (via EBSCO host); Embase, Medline (via OVID online); and Web of Science (via Web of Knowledge).

The following search terms were used, both as key words and as Medical Subject Headings (MeSH), creating four search strings (using the Boolean operators 'OR' to combine searches within strings and 'AND' to combine search strings).

> *Exp* Epilepsy OR Epilep*
>
> AND
>
> Psychosocial OR Psychoeducation* OR Psycholog* OR Psychotherap* OR *Exp* Psychotherapy
>
> AND
>
> Interven* OR Treat* OR Therap*
>
> *signifies truncations or possible extra letters in the term to be included within the search. 'Exp' indicates the term was exploded.

Searches were limited to those published in English with human subjects. An age limit was not set as this could have excluded some studies meeting inclusion criteria. Hand searches were also carried out on reference lists of 7 review papers in addition to the electronic search [17-22, 24]. Duplicate entries were removed. Where more than one paper reported on the same participant sample within the same follow-up timeframe, all papers were selected for inclusion. The following selection criteria were applied. Inclusion criteria: (1) Studies published in English from any country; (2) Studies published in peer

reviewed journals; (3) Studies published between 1989 and 2014; (4) Studies describing original data; (5) Studies including children and young people aged 0-19 years with a diagnosis of any type of epilepsy[1]. Exclusion criteria: (1) Drug/animal studies; (2) Studies including participants without an epilepsy diagnosis; (3) Studies including participants with learning disabilities; (4) Studies including children and adolescents within an adult population (5) Studies with a ketogenic diet as the sole content. The following categories of article were also excluded: case studies, qualitative studies, book sections, systematic reviews, literature reviews, meta-analyses, dissertations, conference presentations/abstracts, guidelines, and commentaries.

*2.2 Quality Assessment*

The Crowe Critical Appraisal Tool [CCAT, version 1.4] [1] was used to assess the quality of included studies (Appendix 1.2). The CCAT was developed from a critical review of existing critical appraisal tools and based on general research methods theory and reporting guidelines. It was specifically designed for systematic reviews which want to include information from a variety of quantitative and qualitative health research designs. The CCAT can be used to assess the quality of the reporting of the research in addition to comprehensively assessing the research studies. The results obtained from using the CCAT have undergone evaluation for validity and reliability testing to verify those results. A user guide is provided to be used along with the CCAT to maintain reliability. The CCAT contains 22 items within 8 categories which are rated on a scale of 'Present', 'Absent' or Not Applicable'. A score out of 5 is given for each category with 40 being the maximum achievable total score. Scores were converted into percentages and as the CCAT does not include qualitative descriptions of scores, the following categories were assigned to allow for comparison: Poor Quality (≤50%); Acceptable Quality (51-74%); High Quality (≥75%).

[1] In the UK child and adolescent health services typically provide care for children up to age 18 (or age 16 in some paediatric hospital settings). The age of adolescence is currently debated in regards to brain and social development, with some now arguing it continues into a person's twenties [52, 53]. However, it was decided that this review would use the World Health Organization and UNICEF's definition of adolescence of any person between ages 10 and 19 years. A participant age range from 0-19 years was therefore set [54].

## 3. Results

### *3.1 Search Results*

The study selection process is detailed in Figure 1. Electronic searches initially returned 3177 articles reduced to 2231 once duplicate articles were removed. These 2231 articles were examined on the basis of title and abstract according to the inclusion and exclusion criteria, which led to the rejection of 2160 articles. Full text journal articles were sourced for the remaining 71 articles, along with 11 additional articles identified through seven review papers [17-22, 24]. This resulted in the exclusion of a further 59 articles. Two studies were reported across two articles [25-28] and two across three [29-34], resulting in a total of 17 studies, reported in 23 articles eligible for inclusion in this review.

### *3.2 Quality Rating Results*

All 17 studies were rated by the author and an independent reviewer using the CCAT quality rating scale. Full agreement was achieved on the majority of papers (14 out of 17; 82%) initially. Disagreements were resolved by discussion leading to 100% inter-rater agreement. Ratings of study quality for each paper are provided in Appendix 1.3. Only three studies were rated as high quality [32-36], three were poor quality [37-39] and the rest were of acceptable quality [25-31, 40-47].

### *3.3 Data Extraction*

Table 1 presents a summary of the relevant information from all 17 studies. This includes sample characteristics, design, intervention delivery method, outcome measures used, data analysis, the key significant findings of the studies and calculated effect sizes.

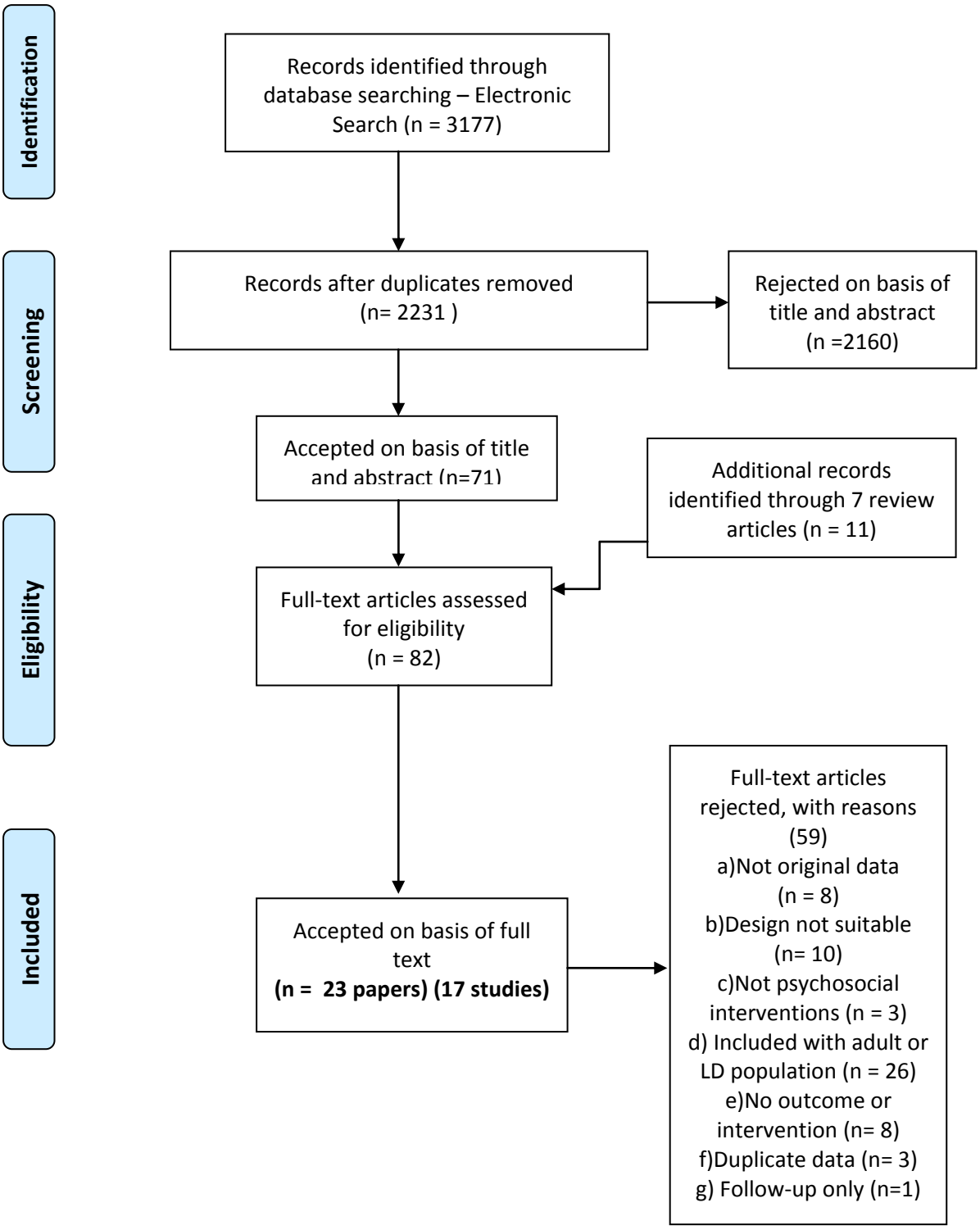


Figure 1: Flow diagram of study selection process

*3.3.1 Sample size*

With the exception of two studies [25, 26, 35] all of the papers had sample sizes <100 participants. Only one study [35] explicitly reported a power calculation. Twelve of the studies had sample sizes of 30 or fewer participants, demonstrating the challenges of recruiting large samples to psychosocial intervention studies. Such small samples meant

that many of the studies called for replication of their research with larger samples to establish the validity and generalisability of their findings. The design of many of the studies also restricted the strength of the conclusions that could be drawn from the outcomes. Only seven of the seventeen studies included control groups [25, 26, 29, 30, 31, 35, 36, 43, 44, 47], two of which were not randomised [29, 30, 31 35].

*3.3.2 Effect size*

Notably, only two studies [29, 30, 31, 35] in this review reported effect sizes and even in these cases they were not calculated for every outcome. Effect sizes were therefore calculated for papers providing the required data (means and standard deviations) (Table 1). Cohen's d [48] was used for studies which had a sample size of 30 participants or more [29, 30, 31, 35, 40, 42, 47] and for those with less [27-29, 32-34, 36-38, 41, 43, 45], Hedge's g was used to calculate effect size to provide a more accurate estimate [49]. Hedges' g is a variation of Cohen's d that corrects for and is less susceptible to potential sources of bias due to small sample sizes [50]. The magnitude of Hedges' g may be interpreted using Cohen's convention as small (0.2), medium (0.5), and large (0.8) [48]. Effect sizes could not be calculated for two studies with insufficient data [25, 26, 44] and only partially for another article [47].

**Table 1** Summary of Studies

| **Study** | **Sample** | **Design** | **Intervention Delivery** | **Outcome Measures** a See appendix 1.4 for full outcome measures and references | **Analysis** | **Main Findings – significant results and Effect Sizes** * Effect sizes not reported in paper, calculated where possible. |
|---|---|---|---|---|---|---|
| Austin et al. (2002) 'Be Seizure Smart' | 9 children aged 7-13 years in 10 families (8 mothers, 2 fathers, 1 grandmother, 4 siblings).<br><br>Epilepsy duration: >2months, <12months.<br><br>USA. | One group, pre-test/post-test (2 weeks prior to intervention and 2 week follow-up). | Five family tailored educational telephone interviews plus postal information delivered by a nurse over 3-4 months. | Authors-designed parent and child questionnaires (general concerns, fears of epilepsy, seizure management, epilepsy knowledge).<br>PCS.<br>CATIS.<br>APGAR. | Paired t-tests. | *<br>Significantly lower epilepsy concerns (g =0.15) and less need for information (g =0.76) and significantly higher general knowledge about epilepsy (g=1.60) and better family functioning (g=0.95) from baseline to 2 week follow-up.<br><br>Parents: Significantly greater knowledge about seizures (g=0.62) and significantly less need for information (g=1.79) and support (g=1.25) from baseline to 2 week follow up. |
| Blocher et al. (2012, 2013) & Jones et al. | 15 children aged 8-13 years. | One group, pre-test/post-test (baseline, | Manualised computer assisted CBT delivered in | SCARED.<br>MASC.<br>CDI. | Repeated-measures one-way ANOVAS. | *<br>Significant reduction in anxiety SCARED-C (g=0.88), |

| | | | | | | |
|---|---|---|---|---|---|---|
| (2014) 'Camp Cope-A-Lot' | Epilepsy duration:> 6 months.<br><br>Met DSM-IV criteria for an anxiety disorder.<br><br>USA. | final session and 3 month follow up). | presence of therapist in a medical centre.12 weekly 50-60 minute sessions. Parents met with child's therapist for 4 sessions and at follow up. | CBCL.<br>PH-1. | | MASC (g=0.70), depression CDI (g=0.54), and problem behaviours CBCL (g=0.38) from baseline to 3 month follow up. |
| Conant et al. (2008) Karate program | 11 children aged 8-16 years (data only available for 9).<br><br>Epilepsy duration:<br>> 1year.<br><br>USA. | One group, pre-test/post-test (week 1 and final session). | Group karate program for 10 weekly 1 hour sessions. | PH1.<br>QOLCE.<br>PSI/SF. | Wilcoxon signed-rank test. | *<br>Significant increase in memory subscale of parent's perception of child's QoL (g=0.76) from between week 1 and week 10 of intervention. |
| Carbone et al. (2014) Group CBT | 34 adolescents aged 13-17 years.<br><br>Epilepsy duration: not specified. | One group, pre-test/post-test (baseline, final session and 4 month follow up). | Group CBT delivered by social workers and one study author. Either one-day 6 hour workshop or 6 weekly 1 hour sessions of online | SDQ. | Repeated-measures ANOVA for child SDQ scores. Paired t-tests for parent SDQ scores. | *<br>Intervention delivery methods (workshop and online) were analysed together due to small sample size.<br><br>Adolescents reported a |

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|---|---|---|---|---|---|---|
| | USA. | | group via videoconferencing and instant messaging. | | | significant increase in pro-social behaviour (d=2.37) from baseline to 4 month follow up.<br><br>Parents scores significantly improved from baseline to 4 month follow up in: total difficulties (d=1.94), impact (d=4.50), peer problems (d=2.22) and pro-social behaviour (d=2.05). |
| Eom et al. (2014) Exercise therapy | 10 children aged 8-12 years.<br><br>Epilepsy duration: not specified.<br><br>Republic of Korea. | One group, pre-test/post-test (baseline and final session). | Exercise group intervention, 3 hour sessions twice weekly for 5 weeks, delivered by an exercise therapist plus home practice. Separate parents exercise education programme. | WISC-III<br>CAT<br>CCTT<br>CDI-K<br>RCMAS<br>K-QOLCE<br>K-CBCL | Wilcoxon signed rank test. | *<br>Significant improvement in visual (g=0.87) and auditory attention (g=0.47) on the CAT, executive function index CCTT2 (g=0.92), internalizing behaviour problems (g=1.85) and social problems (g=0.37) on the CBCL, and well-being (mood) (g=0.55) on the K-QOLCE from baseline to week five. |
| Frizzell et al. (2011) Education intervention | 30 adolescents aged 12-19 years. | One group, pre-test/post-test (baseline and 1 month | Education based, 1 individual 2 hour session and 1 group 2 hour | Self-knowledge of epilepsy<br>AKEQ<br>SSES-C | Paired t-tests. | *<br>Significant improvement in self-knowledge (d= 2.60), general epilepsy knowledge |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Epilepsy duration: >12 months.<br><br>Australia. | follow up). | session 1-3 months later. | CATIS<br>RSES | | AKEQ (d=1.77), attitude towards illness CATIS (d=0.33) and self-efficacy SSES-C (d=0.42) from baseline to 1 month follow up. |
| Glueckauf et al. (2002)Family counselling | 22 adolescents aged 12-19 years and 21 mothers, 15 fathers.<br><br>5 in video-conferencing group, 4 in speakerphone group, 6 in office group and 7 wait list control group.<br><br>Epilepsy duration: not specified.<br><br>USA. | RCT - 3 arm (baseline, 1 week post-intervention and 6 month follow-up). | Family counselling delivered via either video-conferencing, speakerphone or face-to-face. 6 fortnightly 90-120 minute sessions. | ISS<br>IFS<br>ICS<br>SSRS<br>WAI<br>Proportion of outside assignments completed<br>Number of missed appointments. | MANOVA followed by univariate ANOVA<br>ANOVA and $Chi^2$ test. | *<br>Data for wait list control group not reported<br><br>Significant reduction in problem severity ISS (g=2.07) and frequency IFS (g=1.53) from baseline to 6 month follow up for all 3 intervention groups combined.<br><br>Significant improvements in parental report of pro-social behaviour from baseline to 1 week post-intervention were not maintained at 6 month follow up for all 3 intervention groups combined. |
| Jantzen et al. | 135 8-16 year | Pre-test/post- | Group psycho- | EKP-G | Repeated- | ES reported. |

| | | | | | | |
|---|---|---|---|---|---|---|
| (2009) 'Flip & Flap' | olds. 65 in intervention group (IG) plus 72 parents. 70 Controls (WCG) plus 72 parents.<br><br>Epilepsy duration: not specified.<br><br>Germany. | test non-randomised control group (baseline and 6 month follow up).<br><br>Control group 6 months before intervention and just before receiving intervention. | educational programme for either 2 days (14 hours) or 2.5 days (16 hours). Separate groups for children (8-11years), adolescents (12-16 years) and parents. Delivered by a doctor and psychologist for parents and delivered by various health care professionals/social workers to children.<br><br>Waiting list control group. | EKP 27<br>HRQOL<br>ZUF-8<br>Parental report of child self-management skills<br>Parental epilepsy-related worries<br>Disclosure of epilepsy to others | measures<br>Univariate ANOVA, $Chi^2$-test, Mann-Whitney test and t-test. | Significant time-by-group effect of increased self-management skills (d=0.6) and decreased direct carer control (d=0.7) and increased independence in their child's social activities (d=0.8) for IG compared with WCG.<br><br>Significant time-by-group effect of increase in QoL on social exclusion scale (d=0.3).<br><br>Significant time-by-group effect for parental report of decrease in epilepsy-related worries (d = 0.5).<br><br>Significant increase in epilepsy knowledge for children, adolescents and parents from baseline to 6 month follow up in treatment group compared to control group (d = 0.6–1.4). |
| Lewis et al. (1990, | 236 children aged 7-14. 123 | Pre-test/post-test control | Family educational programme. 4 | Harter's Self Competency | $Chi^2$ test. | * Data not available to calculate ES. |

| | | | | | | |
|---|---|---|---|---|---|---|
| 1991)Educational programme | in treatment group 113 in control. 365 Parents attended separately.<br><br>Epilepsy duration: not specified<br><br>Chile. | group (baseline and 5 month follow up). | weekly 90 minute sessions of child groups delivered by teacher and parent groups by a social worker.<br><br>Control group attended three 2 hour sessions of lectures delivered by a physician covering same content as intervention group. | Scale<br>Interview on medical, social history, knowledge of epilepsy and self-competency. | | Treatment group demonstrated a significant increase in half of the epilepsy knowledge items at 5 month follow up and compared to control group.<br><br>Significant decrease in parental anxiety compared to controls at 5 month follow up. |
| Martinovic et al. (2006) CBT for depression | 30 adolescents aged 13-19 years with sub-threshold depression assigned to intervention (CBI) or TAU groups.<br><br>Epilepsy duration<br>≤ 12 months. | RCT (baseline and 6 and 9 month follow ups). | Individual Cognitive behavioural intervention (CBI) administered by two of study authors for 8 fortnightly sessions then 4 monthly sessions.<br><br>TAU was therapeutic counselling without | BDI<br>HAMD<br>CES-D<br>QOLIE-31 | Repeated-measures ANOVA, Pearson correlation, $Chi^2$ test, Wald Wolfowitz run test. | *<br>Significant in reduction in depression BDI (g=0.85) CES-D (g=0.69) and increase in QoL QOLIE-31 (g=-1.79) in CBI group compared to TAU group at 9 month follow up. |

| | | | | | | |
|---|---|---|---|---|---|---|
| | Serbia. | | CBI. | | | |
| Modi et al. (2013) Education intervention | 8 children aged 2-12 years assigned to intervention or TAU groups.<br>19 in 'near perfect adherence group'<br>Plus families.<br><br>Epilepsy duration: ≤ 7 months<br><br>USA. | RCT pilot (baseline and final session). | Family education and problem solving skills intervention for 4 fortnightly sessions, ranging over 3-4 months. | MEMS'TrackCap' FAQ | Descriptive statistics and qualitative data from questionnaires. | *Data not available to calculate ES.<br><br>2 families had large improvements in AED adherence rates but had low baseline rates. |
| Rau et al. (2006), Wohlrab et al. (2007) & Pfafflin et al. (2012) FAMOSES | 50 children aged 7-13 years, and 103 parents were assigned to intervention or waiting list control group.<br><br>Epilepsy duration: | Pre-test/post-test non-randomised control group (baseline and 3 month follow up and 5 year follow up with parents only). | Education programme for 7 60-90 minute sessions for children and 6 sessions for parents, delivered by a physician and psychologist. Delivered either 1 | KINDL<br>School attendance<br>Seizure frequency<br>Specifically designed questionnaire on epilepsy knowledge, | MANOVA<br>ANOVA<br>Wilcoxon signed rank test. | ES reported.<br><br>Significant improvements reported by children in social restrictions in daily life for intervention group compared to controls at 3 month follow up (d=-0.58)<br><br>Significant improvements |

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| | Not specified<br><br>Germany. | | session per day in inpatient settings, and weekly or over a weekend for outpatients. | coping, adaptation, restrictions in daily living, anxiety | | reported by parents in the intervention group compared to control group at 3 month follow up in the following areas: epilepsy knowledge (d=1.20); adaptation (d=0.46); epilepsy-related anxiety (d=-0.29); attendance to rules (d=-0.42) and seizure management (d=0.41) |
| Shore at al. (2008) SEE Program | 11 Children aged 13-18 years in 13 families.<br><br>Epilepsy duration: not specified<br><br>USA. | One group, pre-test/post-test (baseline and 1 month and 6 months follow ups). | Parent and child education sessions. Two 8 hour sessions over a weekend delivered by program developer (not author of paper). | CHQ<br>MAACL<br>CDI<br>PCS<br>Parent response to illness scale<br>SSES<br>Knowledge related to epilepsy scale | T-tests, Repeated-measures ANCOVA | *<br>Significant improvement in child self-report of QoL from baseline to 6 month follow up on the following domains: Mental health (g=0.69); behaviour (g=0.59); self-esteem (g=0.78) and in depression scores CDI (g=0.69).<br><br>There were also significant improvements in parental report of child's QoL. |
| Snead et al. (2004) 'Taking Charge of Epilepsy' | 7 adolescents aged 13-18 years and at least one | One group, pre-test/post-test (baseline and final | Group psychoeducation intervention for 6 weekly 1-hour | QOLIE-AD-48<br>CDI<br>RCMAS | Paired t-test, $Chi^2$ test, descriptive qualitative | *<br>No quantitative results reached significance. |

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| | parent.<br><br>Epilepsy duration:<br>>1 seizure in last 24 months<br><br>USA. | session). | sessions delivered by clinical psychology interns. Separate adolescent and parent groups. | | data. | |
| Stafstrom et al. (2012) Art therapy | 16 children aged 7-18 years.<br><br>Epilepsy duration:<br>>6 months<br><br>USA. | One group, pre-test/post-test (baseline and no details provided of post-test). | Art therapy focus groups. Four 90 minute groups over 1 month | CATIS | Not stated, presumed t-test. | *<br>No quantitative results reached significance. |
| Tieffenberg et al. (2000) 'Acindes' | 99 children aged 7-12 years, 54 in treatment group, 45 in control group plus parents.<br><br>Epilepsy duration:<br>> 5 months<br><br>Argentina | Randomised field trial – pre-test/-post-test control group (baseline and 6 and 12 month follow ups). | Group play-based educational intervention with separate sessions for children and parents. 5 weekly 2 hour meetings followed by a reinforcement meeting 2-6 months later, facilitated by | CHLCS<br>Parent and Child Survey – sociocultural<br>School Absenteeism<br>Clinical Variables. | Duncan test of multiple comparisons, Mann-Whitney U test, Wilcoxon signed rank test, Probability of Gain test. | *<br>Significant increase in children's internal locus of control, significant decrease in school absenteeism, seizures (d= -0.08) and emergency hospital visits (d=-1.32) from baseline to 12 month follow up. |

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| | | | teachers. | | | |
| Wagner et al. (2010, 2011) COPE | 9 children aged 10-15 years and 9 parents.<br><br>Epilepsy duration:> 6 months.<br><br>USA. | One group, pre-test/post-test (maximum of 2 weeks prior to intervention and final session). | CBT based groups over 8 weekly 1 hour sessions or 2 four hour sessions. Child groups conducted by paediatric psychologist and parent groups by social worker. | CDI<br>SSES-C<br>CATIS<br>HSC<br>SSSS<br>ESES<br>CHIC<br>PIP | T-tests and Wilcoxon Signed rank test. | *<br>Significant improvement in children's knowledge of epilepsy (g=0.61), self-efficacy in seizure management (g=0.53) and parent's perception of support seeking from children (g=0.67) pre- to post-intervention. |

### *3.4 High Quality Studies*

#### *3.4.1 Intervention goals and outcome measures*

Among the three high quality studies, two focussed on reducing anxiety and depression [32-34, 36] and the other sought to increase epilepsy knowledge and coping strategies [35]. Specifically, Martinovic et al. [36] aimed to prevent depression in 'at risk' adolescents with epilepsy while Blocher et al. [32-34] primarily focussed on the reduction of anxiety but also examined symptoms of depression and behavioural problems. All three studies used standardised outcome measures directly related to their aims and used in clinical practice. Jantzen et al. [35] also developed their own measurement scales specifically for the study.

#### *3.4.2 Treatment components and methods of delivery*

Only Jantzen et al. [35] included parents in the full intervention, which ran simultaneous group psycho-educational programmes for parents and CYPE. The programme was researched with CYPE and parents and validated in a pilot using techniques based on family and behavioural therapy. It used an interactive story-telling method, tailored to age group, with education about epilepsy, emotions and self-management. Parents were partially involved in the cognitive behavioural therapy (CBT) intervention used by Blocher et al. [32-34]. They met with their child's therapist for four sessions and at follow up to discuss progress, receive a summary of the intervention material covered and contribute to developing their child's exposure hierarchy. Parents were not involved in any aspect of the CBT intervention in the Martinovic et al. [36] study. Both CBT interventions were delivered individually to the CYPE and incorporated key components of CBT such as: relaxation; identifying thoughts, feelings and cognitive errors; and problem solving, with exposure tasks tailored to anxiety [32-34] and activity scheduling to depression [36]. Additionally, Blocher et al. [32-34] used manualised computer video demonstrations delivered by the therapist.

#### *3.4.3 Effectiveness of Interventions*

Effect sizes were moderate-large for improvements in epilepsy knowledge and self-management skills for the intervention compared to control group in the study by Jantzen et al. [35]. Although there were improvements in QoL for CYPE over time, effect sizes

were small and only significantly better than the control group on one dimension. There was a significant time-by-group effect for parental report of decrease in epilepsy-related worries with a moderate effect size. Martinovic et al.'s [36] study had only 15 participants in each group but found a significant reduction in depression symptoms on two outcome scales and improvement in QoL for the intervention group compared to controls at 9 month follow up, all with large effect sizes. Blocher et al. [32-34] did not use a control group but found a significant reduction in anxiety (large ES), depression (medium ES) and problem behaviours (small ES) at 3-month follow up.

### *3.5 Acceptable Quality Studies*

#### *3.5.1 Intervention goals and outcome measures*

Studies of an acceptable quality had the following intervention goals: enhance levels of pro-social functioning [40]; improve neurocognitive, emotional and behavioural functioning and QoL [41]; increase epilepsy knowledge and improve self-esteem, seizure self-efficacy and attitudes towards epilepsy [42]; increase adherence to AEDs [44]; increase children's knowledge, perceptions of competency and skills in seizure management [25, 26]; improve QoL, management of seizures, and health care utilisation of families [45]; improve QoL and psychosocial functioning [46]; enhance coping skills, self-efficacy, self-management and promote resilience [27, 28]; improve social skills, treatment adherence and reduce social, educational and family difficulties [43]; improve knowledge, coping, treatment outcomes and adaptation [29-31]; and increase child chronic illness self-management skills (epilepsy and asthma) [47]. Studies used a wide range of outcome measures (Table 2 and Appendix 1.4). The majority used a combination of standardised validated psychosocial measures, purpose-designed questionnaires and qualitative data. Only one study used an objective measure of medication adherence [44] and only one study examined neurocognitive outcomes [41]. Two studies measured seizure frequency through parental report [37, 38].

#### *3.5.2 Treatment components and methods of delivery*

Nine of the eleven acceptable quality studies included parents/family directly in the interventions. Six of these ran separate sessions for CYPE and parents/family [25-31, 41,

46, 47] whilst in three, families attended all sessions together [43-45]. One had no parental involvement [42] and the other provided parents with an intervention manual but they were not directly involved [40]. Seven of the studies implemented educational interventions [25, 26, 29-31, 42, 44-47], two CBT interventions [27, 28, 40], one family counselling [33] and another, an exercise programme [41]. Small sample size did not allow for comparison of different delivery methods of CBT (in-person one-day 6 hour workshop or 1 hour 6 weekly sessions online) in the Carbone et al. [40] study.

*3.5.3 Effectiveness of Interventions*

Of the education-based interventions, Lewis et al. [25, 26] had the largest sample size but data was not available to calculate ES. Rather than using a standardised tool to measure epilepsy knowledge, they used open ended interview questions in which there was a significant improvement on half the items for intervention group compared to controls at 5-month follow up. Tieffenberg et al. [47] also had a relatively large sample size but again it was not possible to calculate ES for all outcomes. Their intervention was not epilepsy specific but was for children with chronic illnesses. At 12-month follow up there were significant improvements in seizure frequency, emergency hospital visits, and school absenteeism but not in parent's epilepsy knowledge, parental anxiety or number of routine medical consultations. Rau et al. [29-31] found 'social restrictions' was the only area of significant improvement, with a moderate ES, for CYPE in the intervention group compared to controls at 3-month follow up. There were no significant differences in clinical outcomes (e.g. seizure frequency and medication tolerability) or epilepsy knowledge for children but for parents there were significant improvements in the intervention group compared to controls in epilepsy knowledge (large ES), seizure management, adaptation (moderate ES) and epilepsy related anxiety (small ES). Although there was significant improvement in the main outcome of QoL (and also in depressed mood) in one study with moderate effect sizes, there was no significant change to CYPE's knowledge about epilepsy as may have been expected from an educational programme [39]. Snead et al. [46] had the smallest sample size (7) and perhaps due to this found no significant results. Frizzell et al. [42] found large ES for significant improvements in self and epilepsy knowledge but there was no improvement on one of the main outcomes, self-esteem. Feedback on the intervention from focus groups was positive. Although

Modi et al. [44] found their intervention to be feasible and acceptable to families, improvements in medication adherence was only reported in percentages and the study did not provide sufficient data for results to be interpreted fully.

Carbone et al. [40] used group CBT and found no significant changes in behaviours from baseline to 4-month follow up other than an increase in pro-social behaviour (large ES). Better outcomes were reported by parents over time but at baseline their scores were lower than adolescents. The authors helpfully considered the characteristics of individuals who may benefit most from the intervention e.g. children whose parents had a lower level of education and socio-economic status. Wagner et al.'s [27, 28] (2010) CBT intervention study found significant improvements across various outcomes but the sample size was only 9 and they had eleven outcome measures, increasing the likelihood of a type II error. Glueckauf et al. [43] found their family counselling intervention to be effective when delivered via three different means (video-conferencing, speaker phone and in person) at 6 month follow up in significantly improving problem severity and frequency within families with a large effect size. However, the study had a small sample size, reducing statistical power and improvements in parental measures were not maintained at 6-month follow up.

Eom et al.'s [41] exercise intervention found significant improvements in cognitive and behavioural domains with small and large effect sizes respectively. However, these results should be interpreted with caution due to only having a sample size of 10. Mean depression scores were below clinical significance at both pre and post intervention, with no significant change in depression or anxiety scores.

*3.6 Poor Quality Studies*

Poor quality studies will not be discussed in detail due to the weaknesses in their design. Austin et al. [37] aimed to improve epilepsy knowledge, attitudes and family functioning based on individual family needs through family educational phone sessions. Although they produced promising results, the intervention was tailored to individual families, meaning it lacked consistency and would be difficult to replicate. Conant et al. [38] aimed

to increase social confidence, self-concept and QoL in CYPE and reduce parental anxiety through a 10-week group karate programme. However, their only significant finding between pre and post intervention was in the memory subscale of parent's perception of child's QoL with a moderate effect size. There was no follow up past last session. Stafstrom et al. [39] (2012) used art therapy to attempt to enhance self-image in CYPE but this was not measured at follow-up.

## 4. Discussion

### *4.1 Main Outcomes*

In terms of interventions focused on improving mental health, one high quality study [36] provides evidence for a significant reduction in depression and improvement in QoL, with large effect sizes maintained at 9-month follow up. Another found that at 3-month follow up there were significant reductions in anxiety and depression symptoms with moderate-large effect sizes and in problem behaviours with a small effect size [32-34]. However, the second study did not use a control group, reducing confidence that improvements were related principally to the intervention. An education-based intervention found improvements in QoL and depression scores but not in epilepsy knowledge [45]. However, the sample size was small; limiting what can be drawn from these findings. Of the two acceptable quality CBT interventions, Carbone et al. [40] reported an improvement in pro-social behaviour for adolescents and Wagner et al. [27, 28] found improvements in self-efficacy for seizure management knowledge of epilepsy in children. Both studies also reported improvements reported by parents, such as an increase in child coping skills. However, again, there were no control groups and the sample size for one study [27, 28] was particularly small. More positively, a family counselling RCT found a significant reduction in problem severity and frequency (in problems in family functioning such as child anti-social behaviour) with large effect sizes, maintained at 6-month follow up. However, parent improvements were not maintained [43].

The literature also provides evidence for the efficacy of psychosocial interventions for improving epilepsy knowledge and self-management skills in CYPE and parents [35].

These are target areas recommended in the NICE guideline [16]. As recommended by previous research [6] four studies focussed on self-efficacy [25-27, 42, 47]. Improvements in epilepsy knowledge were found with large effect sizes in another study but there was no control group, moderating the conclusion that the intervention led to changes [42]. Improvements in parents' epilepsy knowledge, seizure management and parental restrictions with small-moderate effect sizes were found in one study but for CYPE there were only minimal improvements in one aspect of QoL at 3-month follow up [29-31]. Of the acceptable quality education-based studies, those with the largest participant samples and control groups suffered from methodological flaws, such as failure to use outcome measures related to mental health or QoL [25, 26, 47], and failure to use a treatment comparison group [47]. These prevent definitive conclusions being drawn with regard to changes in epilepsy knowledge. The only study to examine cognitive domains found significant improvements after an exercise intervention but had no control group and a small sample [41]. Similarly, a study focussed on medication adherence had the same design flaws in addition to insufficient data analysis [44].

*4.2 Future Research*

Whilst the evidence base is limited, there is some evidence for the effectiveness of psychosocial interventions for improving mood outcomes for CYPE. When considering treatment components, CBT had more reliable evidence for improving these outcomes than education-based interventions but it is not possible to make a direct comparison. The limited evidence suggests it is not necessary to have direct parent involvement in these interventions for improvements in mood to occur. It may be that it is enough to have parents involved indirectly through progress meetings and having knowledge of the intervention content. Both high quality CBT intervention studies delivered the therapy individually, whereas the moderate quality studies ran group interventions. The studies with more of a focus on increasing epilepsy knowledge and management were most often delivered in groups. The positive outcomes from these studies suggest this is a cost-effective way to administer education-focussed interventions for CYPE and their families. It is unfortunate that some of the studies with a superior design (RCT) or larger samples failed to use standardised outcome measures or carry out data analysis beyond

descriptive statistics. There is a need for further good quality RCTs with other treatment comparison groups. Future research could contain different treatment arms, for example, comparing group with individual one-to-one interventions or with parent and child groups, in order to evaluate effective treatment components for this population. It may also be that different age groups benefit from different interventions, warranting further investigation.

Furthermore, only one study included a twelve-month follow up [41]. Ten of the studies had a follow up period of one month or more, five with six months or more. Future research should utilise longer-term follow up periods to establish if improvements in psychosocial functioning are sustained. However, it is also worth considering what extent of improvement should be expected in relation to the intensity and level of delivery of any psychosocial intervention. In some studies it was unclear who administered the interventions but the majority used a wide range of health and social care professionals. In one study teachers facilitated the educational groups [47]. It would be helpful to know what level of training and qualifications are optimally required to deliver the interventions effectively. For example, some interventions may require medical staff and clinical psychologists to deliver the interventions while in others training and supervision could be provided to other professionals to facilitate the intervention.

As the majority of studies in this review did, it is important for future research to include self-report outcome measures completed by both CYPE and their parents/carers. It is important that research takes account of the potential bias associated with child versus proxy reported outcomes, as often there are discrepancies on psychosocial measures [51]. Objective outcome measures such as medication adherence, hospital visits and neuropsychological tests were less frequently used in the studies included in this review. Using both subjective and objective measures would help increase the validity of findings. Given the evidence for cognitive deficits in CYPE [7], it is surprising only one study in this review examined cognitive outcomes and further research is clearly required along with the use of educational outcome measures such as school performance or teacher report. This could help to determine whether psychosocial interventions can impact on academic attainment and cognitive skills. The conflicting evidence [7, 13] regarding the influence of

seizure frequency and severity on psychosocial outcomes, such as mood, social functioning and QoL also requires further consideration in well-designed studies.

*4.3 Strengths and Limitations*

While there have been previous reviews which have looked at psychosocial interventions for epilepsy, few have used formal systematic review criteria or they have considered adult and child studies together. One systematic review of care delivery and self-management strategies for CYPE does have a similar scope to the current review [22]. However, since half of the studies in the current review were published after their paper, it was thought timely to review the literature once more. As the CCAT [1] is an all-encompassing tool, unlike the review mentioned above, the current systematic review was not limited to only true experimental studies. Incorporating data from across research designs into a single review provides a wider range of intervention options and ideas for readers to draw upon. This could aid the selection of treatment components, methods of delivery and outcome measurements based on the resources available to services. The inclusion of a wider range of study designs was appropriate in this area since it is often not possible for psychosocial studies to include randomised control groups and long-term follow up periods due to funding and ethical restrictions. The CCAT also allowed for the incorporation of evaluation of papers based on their reporting, in the overall assessment of studies.

The age range of CYPE in these studies ranged from 7 to 19 years and the minimum epilepsy duration ranged from 2 to 12 months. It may be useful for future reviews to focus on the influence of these factors, specifically as early intervention is promoted for psychosocial wellbeing. It should be noted that studies which included participants with a learning disability were excluded from the current review. Given that epilepsy is common in the learning disability population, the generalisability of the current findings are restricted and this area requires greater attention. Furthermore, the review did not consider intervention effects on different types of epilepsy and other factors such as epilepsy duration. This was primarily due to varying levels of reporting of these factors in previous studies. Nevertheless, this is an area that merits examination. The current

review did not carry out a meta-analysis of the studies due to the heterogeneity of methodologies and outcome measures used. The current review therefore lacks the benefits that a meta-analysis provides, such as overcoming small sample sizes of individual studies and increased precision in estimating effects.

### *4.4 Conclusions*

In conclusion, there were some promising findings produced from the studies in this review with regard to the effectiveness of psychosocial interventions in increasing epilepsy knowledge and self-management, and in improving QoL and psychological symptoms such as anxiety and low mood. The evidence indicates that both CBT based and educational interventions are effective to an extent but findings were not unanimous across all studies. The differences in the quality of these studies could explain these inconsistencies. No single treatment components can be identified as superior at present. Further research with larger samples, control groups and objective outcome measures is required.

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## MAJOR RESEARCH PROJECT

# Sleep and Forgetting in Children with Genetic Generalised Epilepsy

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*Prepared in accordance with the instructions to authors for Epilepsy and Behavior (see Appendix 1.1)*

## Plain English Summary

### Background

Problems with sleep and memory are common in children with epilepsy. Previous studies have shown that many people with epilepsy forget information they have learned at a faster rate than people without epilepsy. This is a recent finding and therefore little is known about the factors that influence rate of forgetting. As there is a well-established relationship between sleep and memory abilities, the present study aimed to investigate if there is an association between rate of forgetting and sleep in children with epilepsy. It also investigated the relationship between learning efficiency (i.e. how often information is presented before it is learnt) and sleep.

### Questions addressed by this study

1. Is poorer sleep quality and duration associated with a higher rate of forgetting over time in children with epilepsy?
2. Is poorer sleep quality and duration associated with poorer 'learning efficiency'?

### How this was done

Nineteen children with epilepsy were asked to memorise stories and a list of words from a standardised neuropsychological memory test. They were then asked to repeat the stories and word list 30 minutes after learning them and then again, one week later. Their recognition for the information was also tested at these time points. During this week-long period their sleep duration and quality was measured through use of an actiwatch (a small watch-like device recording rest and activity patterns) and children and their parents completed a sleep diary. Parents also completed two questionnaires about their children's sleep and memory over the week-long period. Children completed a questionnaire about their sleep.

### Results and Conclusions

The data showed no relationship between sleep duration or sleep efficiency and rate of forgetting. The results provided some evidence that children who took longer to get to sleep had a higher rate of forgetting for recalling and recognising previously learned information. Results relating to sleep and learning efficiency were mixed, therefore little can be concluded about the relationship between them. These mixed results are due to the small sample size. Further research is required to learn more about the exact nature of the relationship between sleep and rate of forgetting in children with epilepsy.

**Abstract**

*Objective*

Given the well-established association between epilepsy and sleep disturbance and the evidence suggesting the importance of sleep in memory consolidation, there is reason to investigate the relationship between sleep and rate of forgetting in children with epilepsy. This study aimed to investigate the relationship between sleep and forgetting in children with Genetic Generalised Epilepsy (GGE).

*Methods*

Participants were 19 children with GGE (9-15 years old). Actigraphy, sleep diaries and standardised questionnaires were used to measure sleep over a week long period. Rate of forgetting was measured using neuropsychological tests at the beginning and end of the study week. Spearman's correlation analysis was used to determine if poorer sleep was associated with poorer initial learning and rate of forgetting in verbal memory recall and recognition.

*Results*

No association was found between sleep efficiency or duration and rate of forgetting. Measures of sleep disturbance were mixed, with sleep onset latency found to be associated with rate of forgetting on the Word Lists test. However, increased wake after sleep onset was associated with decreased rate of forgetting.

*Conclusions*

Whilst there was limited evidence of a relationship between some actigraphic sleep parameters and rate of forgetting for verbal information, the results were mixed and likely biased by the small sample size. There is need for further research with a larger sample to establish the nature of the relationship between sleep and rate of forgetting in children with GGE.

*Keywords:* Sleep; Forgetting; Memory Consolidation; Children; Epilepsy

*Word Count:* 7,797

## 1. Introduction

The phenomenon of accelerated long-term forgetting (ALF), in which newly acquired memories are intact after short delays but fade over days to weeks, has become an increasingly prominent area of epilepsy and cognition research. ALF has recently been established to occur more often in both adult and paediatric epilepsy populations compared to healthy controls [1, 2]. However, little is currently known about the factors that influence ALF. Given the well-established association between epilepsy and sleep disturbance [3-5] and the evidence suggesting the importance of sleep in memory consolidation [6, 7] there is reason to investigate the relationship between ALF and sleep in children with epilepsy (CWE).

First identified in adults with temporal lobe epilepsy (TLE) [8], the mechanisms that underlie ALF are debated with most attention given to theories of consolidation. Research into ALF suggests that the temporal gradient required for new information to be successfully consolidated into long-term memory is extended beyond minutes and the process could potentially take days, weeks or longer [8]. The exact time course and mechanisms of memory consolidation remain unclear. It is speculated that the process of consolidation involves an interaction between the hippocampus and neocortex [9, 10], areas that often suffer neuronal damage from seizure disorders [10]. However, recent neuroimaging studies found no relationship between structural anatomical damage and ALF [11, 12]. This may suggest that ALF is a consequence of subclinical epileptiform activity disrupting interactions between the mesial temporal lobe (MTL) and the neocortex. Indeed, in a review of ALF case reports and group studies, it was concluded that ALF posed a challenge to current theoretical models of memory [1].

Three studies to date have demonstrated ALF in paediatric epilepsy populations. Two found that children with idiopathic generalised epilepsy (IGE) demonstrated ALF for verbal information compared to matched controls after a one-week delay, but no effect for non-verbal information [13, 14]. Davidson et al. [13] found that CWE required a greater number of learning trials to reach a learning criterion compared with controls, whereas Shepley et al. [14] found no difference. In both studies ALF was demonstrated

for verbal recall but not for recognition, suggesting that difficulties in retrieving successfully stored information characterised ALF. However, Gascoigne et al.'s [15] study was consistent with the consolidation hypothesis. Similarly, they found children with IGE recalled fewer words than controls after a week, but not a thirty-minute delay. They found no significant difference between the epilepsy group and controls in the number of initial learning trials and also found deficits in recognition over a delay in the IGE group. Although there is debate between the studies regarding the mechanisms underlying ALF, they all evidence that CWE experience deficits in new learning.

Sleep dependent memory consolidation is the process whereby memory traces are preferentially consolidated during sleep as opposed to wakefulness, leading to an improved performance after a retention interval including a sleep phase [6]. Non-rapid eye movement (NREM) has been shown to have a role in the consolidation of both verbal and nonverbal declarative memories in healthy children, as demonstrated by improvement in performance after sleep compared to a period of wakefulness [16]. Diekelmann et al. [17] also provide a review of studies in the area of sleep-dependent memory consolidation. Children with high amounts of slow-wave-sleep (SWS) post-learning had distinctly enhanced declarative memories. Ashworth et al. [18] used actigraphy and novel learning tasks to investigate sleep-dependent memory consolidation in typically-developing children. No change in recall performance was found after a wake period but recall scores improved significantly following a period of sleep, regardless of whether initial training took place in the morning or evening. Of note, the average wake period (10hrs 25mins) was shorter than the average sleep period (13hrs 14mins). In adult epilepsy populations, evidence for the role of sleep on memory function is mixed [19-21]. A recent review of the relationship between sleep and the effect on cognitive functioning in CWE highlighted the influence of sleep disruption on the neurophysiological and neurochemical mechanisms important for the memory–learning process [22]. It was concluded that improvement in the long-term cognitive–behavioural prognosis of CWE requires good sleep quality as well as good seizure control.

Two recent studies have examined the relationship between memory consolidation and sleep in CWE. Sud et al. [23] aimed to determine whether CWE were better able to

consolidate memories after a sleep versus a wake period. Participants were presented with word lists over five learning trials and recall was tested immediately and again after a delay. Each participant was tested twice, after a period of wakefulness and after a period of sleep, with conditions counterbalanced among participants. The length of the wake and sleep delay intervals were matched for each child. It was found that recall was significantly better after sleep compared to a period of wakefulness in 7/10 participants but this sleep-memory relationship was not demonstrated in the group analysis. Due to the small sample and good sleep efficiency of the group, consideration of how poor sleep may impact on consolidation was restricted. Gaeler et al. [24] found overnight recall performance on declarative memory tasks to be lower in CWE than in control children, further confirming ALF in CWE. Higher spike–wave index (SWI) during NREM sleep (as measured by polysomnography (PSG) and electroencephalography (EEG)) was associated with poorer performance in the nonverbal task but not the verbal task. They concluded that interictalepileptiform discharges (IED) could disrupt sleep memory consolidation.

Although the above studies have investigated whether sleep improves memory consolidation in CWE, they compared sleep and wake periods with recall over periods no longer than twenty-four hours. The current study extends this investigation by analysing the relationship between sleep parameters and rate of forgetting over a week long period in children with GGE. Determining whether there is a relationship between sleep parameters and rate of forgetting could inform how learning could be improved in CWE, and may also identify those children most at risk of education attainment problems. In turn, this could encourage and inform future research in designing effective psychological and educational interventions.

*1.1 Aim*

To investigate the relationship between behavioural sleep disturbance and rate of forgetting in children with GGE.

*1.2 Hypotheses*

1) There will be a positive correlation between children's ‘sleep efficiency’ (and 'total sleep time') and their percentage recall between thirty minutes and one week.

2) There will be a negative correlation between sleep disruption ('sleep onset latency' and 'wake after sleep onset') and percentage recall between thirty minutes and one week.

3) There will be a negative correlation between the ‘number of learning trials it takes to learn the minimum criterion’ for the verbal memory tests and ‘sleep efficiency’/ ‘total sleep time’.

4) There will be a positive correlation between ‘number of learning trials to minimum learning criterion’ for the verbal memory tests and sleep disruption ('sleep onset latency' and 'wake after sleep onset').

## 2. Methods

A cross-sectional correlational research design was used to explore the relationship between ALF and sleep parameters.

### *2.1 Ethical Approval*

Ethical approval was granted by the North of Scotland Research Ethics Committee (Appendices 2.1 & 2.2). Site approval was awarded by NHS Greater Glasgow and Clyde Research and Development Department and NHS Lothian Research and Development Department (Appendices 2.3 & 2.4).

### *2.2 Justification of Sample Size*

As there were no correlational studies looking at sleep and ALF in children with epilepsy, studies with related constructs in adults were used to derive an estimate of the sample size required for adequate statistical power. Deak et al. [19] found a moderately strong correlation between delayed recall on a selective reminding word list test and slow wave sleep ($r = 0.64$) in adults with temporal lobe epilepsy. Similarly, Clemens et al. [25] found moderately strong positive correlations between delayed recall on a verbal memory test and sleep stage 2 spindle activity measured by EEG ($r = 0.73$, $r = 0.66$, $r = .54$, $r = 0.52$).

Schabus et al. [26] also found a moderately strong positive correlation between sleep stage 2 spindle activity and delayed recall for a word-pair test in young adults (r = 0.63). On this basis, a large effect size (r = 0.50) was assumed for the current study, with the power set at .80 and alpha at .05 [27]. A power calculation using G*Power [28] provided a sample size estimate of 29 for the main hypothesis.

*2.3 Participants*

Recruitment took place between January and June 2015 at the Royal Hospital for Sick Children (RHSC) Glasgow and RHSC Edinburgh. Inclusion criteria included children aged between 9 and 16 years with a diagnosis of GGE, according to ILEA criteria [29] and fluency in English. Exclusion criteria included: 1) learning disability (i.e. IQ of less than 70); 2) presence of another major health or physical condition; 3) history of a neurological disorder other than epilepsy; 4) history of head injury; 5) history of a specific sleep disorder; and 6) history of major psychiatric disorder. Twenty-eight children receiving care at the epilepsy clinics and identified as meeting criteria were invited to participate by their consultant neurologist or specialist nurse. Potential participants and their parents were provided with written information about the study (Appendices 2.5-2.9) and then either contacted the researcher directly or provided written consent to their clinician for the researcher to contact them. Nineteen families (68% of potential participants contacted) consented to participate and were included in final analysis. Written informed consent was obtained from all children and their parent prior to participation (Appendices 2.10-2.12).

*2.4 Procedure*

Participants attended two appointments, one week apart, at either RHSC Glasgow or RHSC Edinburgh. During the first appointment children completed neuropsychological tests and a questionnaire with the researcher, while parents completed a proxy questionnaire independently. The tests were administered in quiet clinic rooms and breaks were provided during testing where required. Participants and parents were provided with guidance on the use of the actiwatch and on the completion of sleep and

seizure diaries, all of which were taken home for one week. Information on epilepsy/seizure variables, medication, memory and sleep was also collected from participants/parents. At the second appointment, neuropsychological tests were re-administered with children, parents completed a second questionnaire and data from the actiwatch, sleep and seizure diaries was collected. The first appointment typically lasted one hour and the second fifteen minutes.

### *2.5 Measures*

#### *2.5.1 Demographic Information*

Socio-economic status (SES) was rated using the Scottish Index of Multiple Deprivation (SIMD) [30] on the basis of postcode. The SIMD estimates deprivation in small geographical areas across Scotland with scores ranked from most to least deprived and then split into 10 deprivation deciles.

#### *2.5.2 The Wechsler Abbreviated Scale of Intelligence (WASI) [31]*

The two subtest form of the WASI was administered to ensure participants met the minimum IQ inclusion criterion. The vocabulary and matrix reasoning subtests provide a brief, reliable measure of cognitive ability, suitable for use in clinical and research settings.

#### *2.5.3 The Children's Memory Scale (CMS) [32]*

The Stories and Word Lists subtests were used to assess participants' verbal memory. The Stories test involved reading two short stories to the participant, who was then asked to repeat them verbatim. Participants were required to learn each story to a level of 90% accuracy (learning criterion). During the Word List test, participants were read a list of 14 unrelated words and then immediately asked to recall as many words as possible. Participants were then selectively reminded of words they omitted on the previous trial and again asked to recall the entire list. Selective reminding of missed items was provided until participants reached 85% accuracy, allowing for 2 words to be missed from the recall list. Both tests had a maximum of ten consecutive learning trials. Following the last learning trial, participants' recall and recognition of the material was tested after a 30-

minute delay and then again after a 1-week delay. Children were asked to recall the stories as best they could and as many of the words from the list as possible. Recognition for Stories was tested using thirty true or false questions and for Word Lists through the identification of the original 14 words from a list of 42 words read to them containing target and distractor words. Children were instructed not to rehearse or write down the material during the 1-week delay.

*2.5.4 The Observer Memory Questionnaire - Parent Form (OMQ-PF) [33]*

This 27-item questionnaire provided a subjective parental-report of their child's everyday memory abilities, with a higher score being optimal. The OMQ-PF was significantly correlated with immediate and delayed recall on standardised neuropsychological tests in a sample of CWE.

*2.5.6 Actigraphy using Actiwatch 2 (Philips Respironics)*

Actigraphy was used as an objective measure of sleep between the two recall/recognition time points (30-minutes and 1-week). The Actiwatch is a nonintrusive watch-like device, which provides information on sleep/wake cycles in the participants' natural sleep environment. It records and monitors movement for one-minute epochs through a wristwatch microprocessor link and provides estimates of sleep and nap times based on periods of wrist immobility. Acebo et al. [34] recommend that studies aiming to gather five nights of actigraph data for children and adolescents should record for at least one full week to ensure a reliable measurement is obtained. The actiwatch was worn on the non-dominant wrist continuously for seven nights. Data was downloaded to a computer for calculation of sleep outcomes using Philips Respironics Actiware Software version 6.0.2, set to a medium default setting. From this, the following objective measures were obtained according to the manufacturer's predefined algorithms: Time in Bed (TIB); Total Sleep Time (TST - total night-time sleep); Sleep Onset Latency (SOL - time required for sleep initiation following ''lights out''); Wake After Sleep Onset (WASO - total time spent awake after first sleep initiation); Sleep Efficiency (SE - percentage of time spent in bed asleep). Actigraphy data were then checked against sleep diary estimates for each participant, as recommended by Acebo et al. [34], and adjusted accordingly.

*2.5.7 Sleep Diaries*

Children and their parents were asked to complete sleep diaries recording bed, "lights-out", wakening and rise times, daytime naps and watch removal (e.g. for swimming) over the seven nights of participation, in parallel with actigraphy monitoring. Sleep diaries not only provide a subjective report of sleep but can help provide corroboration of actigraphy data and assist with the interpretation of ambiguous actigraphy data, for example by discriminating between naps and periods of inactivity.

*2.5.8 The Children's Sleep Habits Questionnaire (CSHQ)* [35]

The CSHQ provided a subjective parental-report of their child's sleep over the participation week. Frequency ratings for 33 items of the most common sleep problems are scored on a 3-point scale and the parent can indicate whether or not a behaviour is problematic. A higher score is indicative of more disturbed sleep and a cut-off score of 41 indicates sleep disturbances with a sensitivity of 0.80 and specificity of 0.72 [35].

*2.5.9 Sleep Self Report (SSR)* [36]

This 26-item questionnaire provided a subjective child-report of frequency of sleep behaviours, rated on a 3-point scale. The SSR was designed to assess sleep domains similar to those of the CSHQ, with a higher score indicating more sleep problems. The SSR was completed independently or with the assistance of the researcher depending on age and ability of child.

*2.5.10 Seizure Diaries*

Parents recorded seizure frequency over the participation week along with information on average seizure frequency, epilepsy onset, status and medication.

*2.6 Data Analysis*

SPSS statistics (version 19) was used to analyse the data. Participant characteristics were explored using descriptive statistics. To determine the rate of forgetting over time, the percentage recalled and recognised between 30-minutes and 1-week was calculated for each participant using the following calculation: *(1-week score/30-minute score) x100*. A

lower percentage recalled from 30-minutes to 1-week indicates a higher rate of forgetting. Bland-Altman analysis was used to assess the level of agreement between actigraphy and sleep diary measures. A range of agreement was defined as mean bias ±1.96 SD. A Bland-Altman analysis has been accepted as the standard statistical approach to assess the agreement between two methods of clinical measurement [37, 38]. After examining distributions of data for normality, associations between measures of forgetting, sleep, IQ and age were examined using Spearman's rho. Wilcoxon signed ranks tests and linear regressions were undertaken as secondary exploratory analysis to further investigate relationships between variables.

## 3. Results

### *3.1 Demographic Variables*

Data from 19 participants (14 females, 5 males) were collected and analysed. The study did not reach the desired sample size of 29 to achieve a statistical power of 0.80. Participants ranged in age from 9 to 15.5 years (Mdn = 11.3, IQR = 10.3, 13.0). Socio-economic status decile rank ranged from 1 to 9 (Mdn = 5, IQR = 2, 6) [30]. Almost half of the sample (47%) lived within the category of the 30% most deprived areas in Scotland. As the group was heterogeneous, clinical characteristics for individual participants are provided in Table 1. WASI full scale IQ ranged from 75 to 118 (Mdn = 88, IQR = 85, 100). 17/19 (90%) participants were treated with antiepileptic drugs and 79% had an epilepsy duration of 12 months or more. Seizure types experienced by the group included: absence only (47%); tonic clonic (16%) and mixed in 37%. 3/19 participants (15%) were seizure free for two years or more (remitted epilepsy). During the study week, 9/19 participants (47%) had one or more seizures.

**Table 1**
Clinical Characteristics

| Gender | Age (Years. Months) | Full Scale IQ | Epilepsy Duration (Months) | Epilepsy Syndrome* | Seizure Type* | No. seizures during study week | Average Seizure Frequency | AED |
|---|---|---|---|---|---|---|---|---|
| F | 15.5 | 101 | 96 | JME | A,B | 0 | Monthly | Lamotrigine/ Topiramate |
| F | 11.9 | 86 | 19 | JAE | A,B | 4A, 1B | Weekly | Sodium valporate/ Zonisamide |
| M | 9.8 | 77 | 60 | FS-Plus | A | 3A | Weekly | Sodium Valproate |
| F | 10.9 | 83 | 7 | EM | B | > 40A | Daily | Ethosuximide |
| F | 10.8 | 88 | 6 | JME | A,B | 1B | Monthly | Levetiracetam |
| M | 12.1 | 88 | 111 | AE | A,B | 0 | Seizure free ≥ 2 years | Lamotrigine |
| M | 11.2 | 118 | 8 | CAE | A | 0 | Weekly | None |
| F | 9.0 | 113 | 30 | CAE | A | 4A | Weekly | Ethosuximide |
| F | 9.4 | 111 | 22 | FAE | A | 1A | Weekly | Lamotrigine/ Ethosuximide |
| F | 11.2 | 79 | 86 | CAE | A | 0 | Seizure free ≥ 2 years | Ethosuximide |
| F | 12.9 | 94 | 13 | JAE | A | 1A | 1 or 2 annually | Sodium Valporate |
| F | 9.8 | 86 | 28 | JAE | A | 0 | 1 or 2 annually | Sodium Valporate |
| M | 14.6 | 88 | 77 | U-GGE | A, B | 0 | Seizure free = 1 year | Sodium Valporate |
| M | 9.6 | 89 | 14 | CAE | A, B | 0 | Weekly | Sodium Valporate |
| F | 13.4 | 99 | 22 | JME | B | 0 | 1 or 2 annually | Levetiracetam |
| F | 11.3 | 103 | 96 | CAE | A | 0 | Seizure free = 1 year | Ethosuximide |
| F | 14.5 | 75 | 6 | JME | B | 1B | Monthly | Levetiracetam |
| F | 13.11 | 86 | 94 | AE | A | 0 | Seizure free ≥ 2 years | None |
| F | 12.1 | 83 | 54 | U-GGE | A | >7A | Daily | Sodium Valporate |

*JME (Juvenile myoclonic epilepsy); JAE (Juvenile absence epilepsy); FS-Plus (Febrile seizure plus); EM (Eyelid myoclonia with absences); CAE (Childhood absence epilepsy); FAE (Familial Absence Epilepsy); U-GGE (Unspecified Genetic Generalised Epilepsy) AE (Absence epilepsy); A (Absence Seizure), B (Tonic Clonic Seizure)

*3.2 Recall, Recognition and Rate of Forgetting*

Distributions of the frequency of sleep and memory measures were examined using boxplots, and were not normally distributed. Therefore, these variables are described using the median along with interquartile range (Table 2). Spearman's rho correlations (rs) were used to analyse the associations between the number of learning trials to criterion for the Stories and Word List tests and the recall and recognition scores (Table 3). There was a significant negative correlation between the Stories number of learning trials to criterion and 30-minute recall (rs = - 0.63, $p$ <0.01), with a large effect size but an association was not evident in any of the other recall or recognition outcomes. For Word Lists number of learning trials to criterion, there was a significant negative correlation with 30-minute recall (rs = -0.58, $p$ <0.01), with a large effect size. These relationships indicated an association between an increase in learning trials and decrease in recall at 30 minutes on Stories and Word Lists. For Word Lists only, there was evidence of a significant positive relationship between learning trials and % recalled from 30-Minutes to 1-Week (rs = 0.51, $p$ <0.05), with a large effect size. A Wilcoxon signed ranks test was carried out to compare the median recall rates of forgetting on the Stories and Word Lists test. Of the 19 participants, 13 performed better on the Stories test compared to the Word Lists test while 1 participant showed no difference and 5 performed worse on the Stories compared to Word Lists. A Wilcoxon signed-rank test determined that Stories % recalled from 30-minutes to 1-week (Mdn = 79.09, IQR = 70.43, 92.27) was statistically significantly higher than Word Lists % Recalled from 30-minutes to 1-week (Mdn = 60, IQR = 47.73, 80.36), z = -1.982, p = 0.048.

Scores for parents of the current sample on the OMQ (M = 85, SD = 21.82) ranged from 56 to 126, and OMQ did not correlate with any of the CMS outcomes. In a 2008 study [33], a sample of healthy children (n = 376, M = 107.26, SD = 13) and a sample of children with TLE (n = 44, M = 93.48, SD = 23.04) were compared. The mean OMQ seen in the current sample is lower than both of these groups.

**Table 2**

Children's Memory Scale and Observer Memory Questionnaire Descriptive Statistics

| | Stories | | | Word Lists | | |
|---|---|---|---|---|---|---|
| **Children's Memory Scale** | **Median (IQR)** | **Mean (SD)** | **Range** | **Median (IQR)** | **Mean (SD)** | **Range** |
| Number of Learning Trials to Criterion | 7.00 (6.00, 8.00) | 8.26 (4.19) | 4.00 - 20.00 | 6.00 (5.00, 10.00) | 7.05 (2.46) | 4.00 - 10.00 |
| Last Learning Trial * | 91.46 (90.79, 95.12) | 92.9 (2.69) | 90.24 - 98.94 | 12.00 (12.00, 12.00) | 12.26 (0.56) | 12.00 - 14.00 |
| 30-Minute Recall * | 76.83 (73.17, 86.29) | 76.73 (12.00) | 47.90 - 92.68 | 8.00 (7.00, 10.00) | 8.26 (2.35) | 2.00 - 12.00 |
| 1-Week Recall * | 60.97 (55.22, 71.34) | 58.89 (21.37) | 0.00 - 86.00 | 6.00 (4.00, 6.00) | 4.79 (2.59) | 0.00 - 10.00 |
| % Recalled from 30-Minutes to 1-Week | 79.09 (70.43, 92.27) | 76.10 (27.94) | 0.00 - 114.94 | 60.00 (47.73, 80.36) | 64.06 (45.15) | 0.00 - 200.00 |
| 30-Minute Recognition Score ** | 28.00 (27.00, 28.50) | 27.53 (1.84) | 23.00 - 30.00 | 41.00 (40.00, 42.00) | 41.00 (1.20) | 38.00 - 42.00 |
| 1-Week Recognition Score ** | 27.00 (26.00, 27.10) | 26.79 (1.32) | 24.00 - 29.00 | 36.00 (34.00, 37.50) | 35.89 (3.74) | 27.00 - 42.00 |
| % Recognition from 30-Minutes to 1-Week | 96.55 (94.81, 101.85) | 97.67 (7.04) | 85.71 - 113.04 | 87.5 (83.13, 91.49) | 87.45 (7.80) | 71.05 - 100.00 |
| **Observer Memory Questionnaire** | 78.00 (73.00, 100.00) | 85.00 (21.82) | 49.00 - 126.00 | | | |

* % recall for Stories, raw score out of 14 for Word Lists; **out of 30 for stories, out of 42 for Word Lists

**Table 3**
CMS Spearman's Correlations for Number of Learning Trials

| | Stories No. of Learning Trials to Criterion | | Word Lists No. of Learning Trials to Criterion |
|---|---|---|---|
| **Stories 30-Minute Recall** | rs = -0.63** | **WL 30-Minute Recall** | rs = -0.58** |
| **Stories 1-Week Recall** | rs = -0.34 | **WL 1-Week Recall** | rs = 0.15 |
| **Stories % Recalled from 30-Minutes to 1-Week** | rs = -0.03 | **Word Lists % Recalled from 30-Minutes to 1-Week** | rs = 0.51* |
| **Stories 30-Minute Recognition** | rs = -0.30 | **WL 30-Minute Recognition** | rs = 0.21 |
| **Stories 1-Week Recognition** | rs = -0.04 | **WL 1-Week Recognition** | rs = -0.02 |
| **Stories % Recognition from 30-Minutes to 1-Week** | rs = 0.28 | **Word Lists % Recognition from 30-Minutes to 1-Week** | rs = -0.07 |

** p* <0.05; ***p* <0.01

*3.4 Sleep*

Descriptive statistics for actigraphy, sleep diary and sleep questionnaire measures are displayed in Table 4. The actigraphy outcomes (Time in Bed, Total Sleep Time, Sleep Onset Latency, Wake After Sleep Onset and Sleep Efficiency) were calculated from 7 nights of data from all but two participants, where 6 nights was used. This was due to actiwatch battery drainage in one case and extreme disagreement between the sleep diary and actigraph in the other. Agreement between participants' self-report sleep diaries and the objective actigraphy measure of sleep was explored using Bland-Altman analysis. Although participants reported their TIB and TST to be longer and their SE to be higher than was objectively measured by actigraphy, the Bland-Altman plots of sleep diary and actigraphy did not show evidence of any systematic differences, indicating an acceptable level of agreement for these two measures. Twelve parents (63%) scored their children above the cut-off score of 41 on the CSHQ, indicating they have sleep disturbance. Thirteen parents (68%) indicated that sleep behaviours were problematic. On the SSR, a higher score (where the maximum possible is 69) indicates disturbed sleep or more problematic sleep behaviour, with scores in the current sample ranging from 24 to 58. Six children (32%) indicated that they have trouble sleeping. The current sample had a higher mean score (n = 19, M = 37.58, SD = 7.22) compared to a healthy cohort (n = 24, M = 18.62, SD = 3.28) observed in a study looking at SSR in healthy children and children with

ADHD [36]. Spearman rho correlations were used to explore the association between self and parent reported sleep quality (SSR and CSHQ) and actigraphy outcomes (Table 5). The correlations between sleep efficiency as measured by actigraphy and the SSR and CSHQ indicate the presence of a relationship, which may be more evident given a larger sample.

**Table 4**
Actigraphy Descriptive Statistics

| | Median (IQR) | Mean (SD) | Range |
|---|---|---|---|
| **Actigraphy Sleep Analysis** | | | |
| *Time in Bed (hr:min)* | 09:38 (09:02, 10:02) | 09:27 (01:05) | 06:54 - 11:13 |
| *Total Sleep Time (hr:min)* | 07:59 (07:21, 08:22 ) | 07:53 (00:48) | 06:09 - 09:05 |
| *Sleep Onset Latency (hr:min)* | 00:12 (00:09, 00:19) | 00:20 (00:22) | 00:04 - 01:21 |
| *Wake After Sleep Onset (hr:min)* | 00:48 (00:37, 00:57) | 00:50 (00:18) | 00:22 - 01:26 |
| *Sleep Efficiency (%)* | 85.31 (81.39, 87.29) | 84.52 (4.37) | 75.18 - 92.26 |
| **Sleep Diary - Subjective Report** | | | |
| *Time in Bed (hr:min)* | 10:22 (09:44, 10:52) | 10:20 (00:52) | 09.01 - 11.47 |
| *Total Sleep Time (hr:min)* | 09:12 (08:30, 09:50) | 09:20 (00:52) | 08.16 - 11.11 |
| *Sleep Efficiency (%)* | 91.41 (88.94, 93.17) | 90.37 (4.13) | 80.54 - 95.79 |
| **Sleep Self Report (Total Score)** | 36.00 (34.00, 41.50) | 37.58 (7.22) | 24.00 - 58.00 |
| **Children's Sleep Habits Questionnaire (Total Score)** | 45.00 (39.50, 48.50) | 45.47 (10.30) | 33.00 - 73.00 |

*3.5 Associations between Rate of forgetting and Sleep*

Relationships between rate of forgetting, number of learning trials and actigraphy outcomes (SE, TST, SOL, WASO) were explored using Spearman's rho correlations and are displayed in Table 5. There was no evidence of significant relationships between SE or TST and any of the CMS variables. A significant negative relationship was found between SOL and Word Lists % Recalled from 30-Minutes to 1-Week (rs = -0.47, $p$ <0.05). A significant negative relationship was found between SOL and Word Lists % Recognition from 30-Minutes to 1-Week (rs = -0.66, $p$ <0.01); an increase in SOL was significantly correlated with a decrease in WL % Recalled and Recognised from 30-Minutes to 1-Week. There was a mild positive relationship between WASO and Word Lists number of learning trials to criterion (rs = 0.44, $p$ <0.05); indicating that an increase in WASO was associated with an increase in learning trials.

One correlation revealed an unexpected finding. There was a significant positive correlation between WASO and Word Lists % Recalled from 30-Minutes to 1-Week (rs = 0.48, $p$ <0.05). This indicated that an increase in WASO was associated with an increase in Word Lists % Recalled from 30-Minutes to 1-Week.

**Table 5**
Rate of Forgetting and Sleep Spearman's Correlations

| n=19 | **Sleep Efficiency** | **Total Sleep Time** | **Sleep Onset Latency** | **Wake After Sleep Onset** |
|---|---|---|---|---|
| **Sleep Self Report** | rs = 0.36 | rs = 0.12 | rs = -0.24 | rs = 0.09 |
| **Children's Sleep Habits Questionnaire** | rs= 0.28 | rs = -0.13 | rs = -0.21 | rs = -0.21 |
| **No. of learning trials to criterion** | rs = 0.01 | rs = 0.16 | rs = 0.01 | rs = -0.11 |
| **Stories % Recalled from 30-Minutes to 1-Week** | rs = -0.16 | rs = 0.10 | rs = -0.31 | rs = 0.45 |
| **Stories % Recognition from 30-Minutes to 1-Week** | rs = 0.10 | rs = 0.24 | rs = -0.17 | rs = 0.17 |
| **No. of learning trials to criterion** | rs = 0.04 | rs = 0.23 | rs = -0.44 | rs = 0.44* |
| **Word Lists % Recalled from 30-Minutes to 1-Week** | rs = 0.09 | rs = 0.35 | rs = -0.47* | rs = 0.48* |
| **Word Lists % Recognition from 30-Minutes to 1-Week** | rs = 0.25 | rs = -0.01 | rs = -0.66** | rs = 0.23 |

*$p$ <0.05; **$p$ <0.01

*3.6 Regression Analysis*

Based on the correlation results between CMS and actigraphy outcomes, variables with the strongest relationships were explored further with linear regression analysis. Residual plots were used to verify the assumptions of linear regression, and revealed no problems. Regression analysis was carried out using the rate of forgetting on Word Lists % scores from 30-Minutes to 1-Week as response variables and SOL as a predictor variable, while adjusting for baseline, IQ, age and number of learning trials in separate models (see Table 6). SOL, adjusted for baseline (30-minute recall score) and age, significantly predicted Word Lists % Recalled from 30-minutes to 1-week, $F(3, 15) = 8.488$, $p < 0.001$. Adjusted $R^2$

= 0.555 shows that SOL, adjusted for baseline and age together, explain 55.5% of the total variability in Word Lists % Recall from 30-minutes to 1-week. In the current sample, as SOL increased by 1 minute, Word Lists % Recalled from 30-minutes to 1-week significantly ($p$ = 0.004) decreased by 1.49% on average, after adjusting for baseline and age. In the wider population of similar patients, this decrease is likely to be between 0.57 and 2.42% (95% C.I). While this was the strongest relationship, SOL adjusted for the following variables: baseline; baseline and IQ together; and baseline and number of learning trials together, was also associated with both Word Lists % Recalled and Recognised from 30-minutes to 1-week.

**Table 6**
Regression Analysis

| Response Variable | Predictor Variable | *B* | 95% CI | P-value |
|---|---|---|---|---|
| **Word Lists % Recalled from 30-Minutes to 1-Week** | SOL, adjusted for baseline | -1.26 | (-1.96, -0.57) | 0.001 |
| | SOL, multivariable* | -1.20 | (-1.94, -0.45) | 0.004 |
| | SOL, multivariable** | -1.47 | (-2.29, -0.66) | 0.002 |
| | SOL, multivariable*** | -1.49 | (-2.42, -0.57) | 0.004 |
| **Word Lists % Recognition from 30-Minutes to 1-Week** | SOL, adjusted for baseline | -0.22 | (-0.36, -0.08) | 0.004 |
| | SOL, multivariable* | -0.20 | (-0.35, -0.05) | 0.011 |
| | SOL, multivariable** | -0.26 | (-0.38, -0.14) | <0.001 |
| | SOL, multivariable*** | -0.29 | (-0.45, -0.12) | 0.002 |

B = unstandardised regression coefficient; *Multivariable model is adjusted for baseline score at 30-minutes and IQ; **Multivariable model is adjusted for baseline (30-minute delay score) and number of learning trials; **Multivariable model is adjusted for baseline (30-minute delay score) and age

As a secondary analysis, associations between SOL and Stories % Recalled and Recognised from 30-minutes to 1-week were examined. Due to the small sample size and the potential issue of multiple testing, this analysis is exploratory and should be interpreted with caution. Therefore, general associations are described but p-values are not provided. In separate multivariable models, adjusting for baseline, IQ and number of learning trials, SOL was found to be associated with Stories % Recalled from 30-minutes to 1-week. This effect was not found for Stories % Recognition score. Adjusting for age as well as baseline, SOL showed no evidence of association with either Stories % Recall or Recognition.

## 4. Discussion

The present study aimed to investigate whether there was evidence of a relationship between sleep and rate of forgetting in children with GGE, using actigraphy and neuropsychological memory tests as outcome measures. The study was not able to achieve statistical power within the timeframe provided, and therefore results presented have to be considered with caution but will be discussed in relation to the hypotheses and relevant theory.

### *4.1 Main Findings*

Contrary to the first hypothesis, there was no evidence of linear relationships between SE or TST and rate of forgetting on either the Stories or Word Lists memory tests. This finding is consistent with Ashworth et al [18] who found no statistically significant correlation between SE or TST and initial or delayed recall in typically developing children. Similarly, Fitzgerald et al [21] found that SE was not related to the percentage of information lost between 30-minutes and 1-day on a word memory test. However, unlike Ashworth et al. [18], the current study did find relationships between SOL, WASO and rate of forgetting. Evidence for a relationship between sleep disturbance and rate of forgetting was mixed. Higher levels of SOL were associated with a higher rate of forgetting for recall and recognition on the Word Lists test, with a moderate to large effect size. SOL was found to be a predictive factor for rate of forgetting on the Word Lists test, with a large effect size. On the Stories test, no linear relationships were found with SOL in the correlation analysis. However, exploratory regression analysis revealed SOL to be a predictive factor for rate of forgetting for recall on the Stories tests, when baseline, IQ and number of learning trials were controlled for, with a moderate effect size.

These results provide some evidence that children with GGE who take longer to transition from wakefulness to sleep have a higher rate of forgetting for recalling and recognising previously learned verbal information. This finding is consistent with other studies suggesting that learning and memory consolidation can take place over extended periods, and sleep disruption plays a fundamental role in these neurophysiological and neurochemical processes [22].

However, contrary to our second hypothesis, higher levels of WASO were associated with a lower rate of forgetting for recall on the Word Lists test, with a moderate effect size. Due to the small heterogeneous sample, it is suspected the latter result is due to bias. Replication with a larger sample would be required to confirm this was not typical of the wider population. The findings examining the relationship between sleep and forgetting suffer from the same limitations as previous studies failing to demonstrate group effects due to small sample size [23].

In relation to the number of learning trials to reach criterion, there was no evidence of significant correlations with SE, TST or SOL. For sleep disturbance, there was an association between higher levels of WASO and a higher number of learning trials required on the Word Lists test, with a moderate effect size. These results suggest there is no significant relationship between sleep and learning efficiency for these particular tests.

Children were found to have a higher rate of forgetting on the Word Lists test compared to the Stories test. This difference in performance may be related to the different methods of learning on each test, i.e. repeated presentations and rehearsal of Stories until criterion was met and selective reminding on Word Lists until criterion was met. With the first method, repeated presentations of the stories could have potentially resulted in the material being over-learnt, meaning that forgetting was possibly masked by ceiling effects in the current sample [2]. Presenting only non-remembered items at each trial during selective reminding on Word Lists may have avoided this. There is also more context in the Stories test to trigger a 'recall cascade', as opposed to the unrelated words in the list learning. Interestingly, more efficient learners recalled more at 30-minutes on both the Stories and Word Lists tests but did not maintain this at 1-week. On the Word Lists test only an increase in number of learning trials was associated with a lower rate of forgetting.

A comparison of group means indicated that the current sample had poorer memory than a healthy sample and TLE sample, as measured by subjective parental report [33]. This may indicate a self-selection bias of the sample, as parents who felt their children had

more memory difficulties or were concerned about their child's memory may have been more likely to participate than those without concerns. It is also of note that our participants had a median IQ of 88, falling within the lower end of the average range, with 12/19 with an IQ ≤89 falling within the low average range [31]. This is in contrast to other AF studies using CYP e.g. Davidson et al [13] had an epilepsy group mean IQ of 99, whilst Gascoigne et al [15] had an epilepsy group mean IQ of 102. Over half of parents reported that their children had sleep disturbance above the cut-off score on the CSHQ and indicated problematic sleep behaviours. A higher group mean of children's self-report of sleep on the SSR was found in the current sample, compared to a healthy sample [36]. This indicates that the children in the current sample perceive themselves to have poorer sleep than this population.

*4.2 Clinical Implications*

The present study provides evidence that there is an acceptable level of agreement between sleep diaries completed by children and parents and actigraphy for measuring time in bed, total sleep time and sleep efficiency. This is a helpful finding as clinically objective sleep measures such as actigraphy are often not available when implementing sleep interventions and sleep diaries have to be relied upon for a baseline and follow up measure of sleep. It should be noted that self-reported estimates from the sleep diaries were greater than the actigraphy outcomes. Over-estimation of sleep efficiency in adolescents is likely to be the result of disregarding the amount of time spent awake in bed. This finding is consistent with the existing literature [39]. Nevertheless, sleep diaries could be a cost effective alternative to actigraphy and polysomnography for larger samples.

*4.3 Limitations*

Results from the present study and the conclusions drawn from these should be interpreted with caution for several reasons. The sample size is modest and did not meet the predicted numbers based on the power calculation. It may be that due to the complex nature of the seizure disorders, impact on intellectual abilities and other confounding

variables inherent in using clinical samples such as that used in the present study, examination of sleep and learning requires significantly larger samples to detect what may be modest effects.

The current study contributes to the early stages of exploring the factors related to forgetting in children with GGE. However, due to the execution of multiple correlations and regression analysis with an underpowered sample, the results can only be interpreted tentatively.

While actigraphy has been previously validated against PSG [40], it is not considered the gold-standard technique for assessment of sleep. However, actigraphy is more cost-effective than PSG and as it is less invasive, it can allow for individuals to sleep more comfortably and naturally in a familiar environment as opposed to a hospital, as is usually required when using PSG.

### *4.4 Future Research*

Future research utilising a much larger sample size would enable use of further regression analysis that could explore in more detail the relative contribution of different variables and move closer to determining causal factors in forgetting in children with GGE. Given the heterogeneity of the current sample, researchers may wish to consider using a higher IQ cut-off score such as +- 1sd from the population norm, and use designs enabling seizure severity/frequency to be more accurately factored into the analyses. Future research should consider the advantage of using a research design including a healthy control group matched for age, IQ, SES and learning efficiency as suggested in a recent review [2]. This would allow for a comparison of rate of forgetting and sleep parameters in addition to exploring the relationship between the two.

### *4.5 Conclusion*

In conclusion, while limited evidence is provided that sleep disturbance is associated with rate of forgetting in children with GGE, there was no evidence of an association between

sleep efficiency or sleep duration and rate of forgetting. More research is necessary to determine if these findings apply to the wider population or whether they are influenced by the small sample. Research that incorporates a control group is required before conclusions can be made with confidence regarding whether having epilepsy impacts on the relationship between sleep and rate of forgetting.

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## ADVANCED CLINICAL PRACTICE I: REFLECTIVE ACCOUNT

# Different dynamics: experience of participating in a service user drama group

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**Abstract**

In order to enhance or develop clinical practice, reflective practice involves applying knowledge gained through one's own experience. This reflective account focuses on the thoughts and feelings I experienced while participating in a service user drama group on placement. I then go on to discuss how it impacted on my individual work with clients. I draw upon Gibbs' model of reflection (1988) to guide my reflections but rather than use this as a prescriptive structure, I follow a more natural train of thought. I refer to past experiences which have influenced my current practice, in addition to supervision and personal study and reading. The group experience prompted me to think more widely about boundaries and power dynamics in therapy and how my understanding of these has changed over time. Finally I discuss the process of writing this reflective account and areas I think I need to develop to further my learning. It has provided me with an opportunity to think about my own practice and to develop insight into my ways of working, impacting on my professional development.

## ADVANCED CLINICAL PRACTICE II: REFLECTIVE ACCOUNT

# A 10 year longitudinal study: my changing perception of research in psychology

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**Abstract**

Reflection on professional development over time is an essential undertaking of the reflective scientist-practitioner. The following reflective account documents my experiences of research since beginning my study of psychology. I then consider the potential ways research could feature in my career as a clinical psychologist in the future and how this relates to professional guidelines and job roles. I use Rolfe, Freshwater and Jasper's (2001) reflective model to structure my discussion of my thoughts and feelings around the role of research in clinical psychology. To conclude I reflect of the process of writing this reflective account and the purpose of reflective practice.

# APPENDICES

**Appendix 1.1** Epilepsy and Behavior Guide for Authors

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The electronic text should be prepared in a way very similar to that of conventional manuscripts (see also the Guide to Publishing with Elsevier: http://www.elsevier.com/guidepublication). Note that source files of figures, tables and text graphics will be required whether or not you embed your figures in the text. See also the section on Electronic artwork. To avoid unnecessary errors you are strongly advised to use the 'spell-check' and 'grammar-check' functions of your word processor.

### *Article structure*
AUTHOR INFORMATION PACK 21 Feb 2015 www.elsevier.com/locate/yebeh 7
*Subdivision - numbered sections*
Divide your article into clearly defined and numbered sections. Subsections should be numbered 1.1 (then 1.1.1, 1.1.2, ...), 1.2, etc. (the abstract is not included in section numbering). Use this numbering also for internal cross-referencing: do not just refer to 'the text'. Any subsection may be given a brief heading. Each heading should appear on its own separate line.
*Introduction*
State the objectives of the work and provide an adequate background, avoiding a detailed literature survey or a summary of the results.
*Material and methods*
Provide sufficient detail to allow the work to be reproduced. Methods already published should be indicated by a reference: only relevant modifications should be described.
*Results*

Results should be clear and concise.
*Discussion*
The **Discussion** section should explore the significance of the results of the work, not repeat them.
**Results** and **Discussion** should be separate and may be organized into subheadings. Avoid extensive citations and discussion of published literature.
*Conclusions*
The main conclusions of the study may be presented in a short Conclusions section, which may stand alone or form a subsection of a Discussion or Results and Discussion section.

## Essential title page information

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• ***Corresponding author.*** Clearly indicate who will handle correspondence at all stages of refereeing and publication, also post-publication. **Ensure that the e-mail address is given and that contact details are kept up to date by the corresponding author.**
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Please note that proprietary names for drugs should *not* be used in the article title.

## Abstract

A concise and factual abstract is required. The abstract should state briefly the purpose of the research, the principal results and major conclusions. An abstract is often presented separately from the article, so it must be able to stand alone. For this reason, References should be avoided, but if essential, then cite the author(s) and year(s). Also, non-standard or uncommon abbreviations should be avoided, but if essential they must be defined at their first mention in the abstract itself.

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Immediately after the abstract, provide a maximum of 6 keywords, using American spelling and avoiding general and plural terms and multiple concepts (avoid, for example, 'and', 'of'). Be sparing with abbreviations: only abbreviations firmly established in the field may be eligible. These keywords will be used for indexing purposes.

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Define abbreviations that are not standard in this field in a footnote to be placed on the first page of the article. Such abbreviations that are unavoidable in the abstract must be defined at their first mention there, as well as in the footnote. Ensure consistency of abbreviations throughout the article.

### Acknowledgements
Collate acknowledgements in a separate section at the end of the article before the references and do not, therefore, include them on the title page, as a footnote to the title or otherwise. List here those individuals who provided help during the research (e.g., providing language help, writing assistance
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*Citation in text*
Please ensure that every reference cited in the text is also present in the reference list (and vice versa). Any references cited in the abstract must be given in full. Unpublished results and personal communications are not recommended in the reference list, but may be mentioned in the text. If these references are included in the reference list they should follow the standard reference style of the journal and should include a substitution of the publication date with either 'Unpublished results' or 'Personal communication'. Citation of a reference as 'in press' implies that the item has been accepted for publication.
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*References in a special issue*
Please ensure that the words 'this issue' are added to any references in the list (and any citations in the text) to other articles in the same Special Issue.
*Reference style*
*Text:* Indicate references by number(s) in square brackets in line with the text. The actual authors can be referred to, but the reference number(s) must always be given.
*List:* Number the references (numbers in square brackets) in the list in the order in which they appear in the text.
*Examples:*
Reference to a journal publication:
[1] Van der Geer J, Hanraads JAJ, Lupton RA. The art of writing a scientific article. J Sci Commun 2010;163:51–9.
Reference to a book:
[2] Strunk Jr W, White EB. The elements of style. 4th ed. New York: Longman; 2000.
Reference to a chapter in an edited book:
[3] Mettam GR, Adams LB. How to prepare an electronic version of your article. In: Jones BS, Smith RZ, editors. Introduction to the electronic age, New York: E Publishing Inc; 2009, p. 281–304.

Note shortened form for last page number. e.g., 51–9, and that for more than 6 authors the first 6 should be listed followed by 'et al.' For further details you are referred to 'Uniform Requirements for Manuscripts submitted to Biomedical Journals' (J Am Med Assoc 1997;277:927–34) (see also http://www.nlm.nih.gov/bsd/uniform_requirements.html).
*Journal abbreviations source*
Journal names should be abbreviated according to the List of Title Word Abbreviations:

http://www.issn.org/services/online-services/access-to-the-ltwa/.

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Please supply 'stills' with your files: you can choose any frame from the video or animation or make a separate image. These will be used instead of standard icons and will personalize the link to your video data. For more detailed instructions please visit our video instruction pages at http://www.elsevier.com/artworkinstructions. Note: since video and animation cannot be embedded in the print version of the journal, please provide text for both the electronic and the print version for the portions of the article that refer to this content.

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2D projected views; and download the data. The viewer supports both single (.nii) and dual (.hdr and .img) NIfTI file formats. Recommended size of a single uncompressed dataset is 100 MB or less. Multiple datasets can be submitted. Each dataset will have to be zipped and uploaded to the online submission system via the '3D neuroimaging data' submission category. Please provide a short informative description for each dataset by filling in the 'Description' field when uploading a dataset.

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**Appendix 1.2** Crowe Critical Appraisal Tool

**Crowe Critical Appraisal Tool (CCAT) Form** (v1.4) Reference Reviewer

This form must be used in conjunction with the CCAT User Guide (v1.4); otherwise validity and reliability may be severely compromised.

**Citation**

| | Year |
|---|---|
| | |

**Research design** (add if not listed)

| | | |
|---|---|---|
| ❑ Not research | | Article \| Editorial \| Report \| Opinion \| Guideline \| Pamphlet \| ... |
| ❑ Historical | | ... |
| ❑ Qualitative | | Narrative \| Phenomenology \| Ethnography \| Grounded theory \| Narrative case study \| ... |
| ❑ Descriptive, Exploratory, Observational | | A. Cross-sectional \| Longitudinal \| Retrospective \| Prospective \| Correlational \| Predictive \| ... |
| | | B. Cohort \| Case-control \| Survey \| Developmental \| Normative \| Case study \| ... |
| Experimental | ❑ True experiment | Pre-test/post-test control group \| Solomon four-group \| Post-test only control group \| Randomised two-factor \| Placebo controlled trial \| ... |
| | ❑ Quasi-experiment | Post-test only \| Non-equivalent control group \| Counter balanced *(cross-over)* \| Multiple time series \| Separate sample pre-test post-test [no Control] [Control] \| ... |
| | ❑ Single system | One-shot experimental *(case study)* \| Simple time series \| One group pre-test/post-test \| Interactive \| Multiple baseline \| Within subjects *(Equivalent time, repeated measures, multiple treatment)* \| ... |
| ❑ Mixed Methods | | Action research \| Sequential \| Concurrent \| Transformative \| ... |
| ❑ Synthesis | | Systematic review \| Critical review \| Thematic synthesis \| Meta-ethnography \| Narrative synthesis \| ... |
| ❑ Other | | ... |

**Variables and analysis**

| Intervention(s), Treatment(s), Exposure(s) | Outcome(s), Output(s), Predictor(s), Measure(s) | Data analysis method(s) |
|---|---|---|
| | | |

**Sampling**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Total size | | Group 1 | | Group 2 | | Group 3 | | Group 4 | | Control | |
| Population, sample, setting | | | | | | | | | |

**Data collection** (add if not listed)

| | | | |
|---|---|---|---|
| Audit/Review | a) Primary \| Secondary \| ...<br>b) Authoritative \| Partisan \| Antagonist \| ...<br>c) Literature \| Systematic \| ... | Interview | a) Formal \| Informal \| ...<br>b) Structured \| Semi-structured \| Unstructured \| ...<br>c) One-on-one \| Group \| Multiple \| Self-administered \| ... |
| Observation | a) Participant \| Non-participant \| ...<br>b) Structured \| Semi-structured \| Unstructured \| ...<br>c) Covert \| Candid \| ... | Testing | a) Standardised \| Norm-ref \| Criterion-ref \| Ipsative \| ...<br>b) Objective \| Subjective \| ...<br>c) One-on-one \| Group \| Self-administered \| ... |

**Scores**

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Preliminaries | | Design | | Data Collection | | Results | | Total [/40] | |
| Introduction | | Sampling | | Ethical Matters | | Discussion | | Total [%] | |

**General notes**

Appraise research on the merits of the research design used, not against other research designs.

| Category<br>Item | Item descriptors<br>[☑ Present; ☒ Absent; ■ Not applicable] | Description<br>[Important information for each item] | Score<br>[0–5] |
|---|---|---|---|
| **1. Preliminaries** | | | |
| Title | 1. Includes study aims ❑ and design ❑ | | |
| Abstract<br>(assess last) | 1. Key information ❑<br>2. Balanced ❑ and informative ❑ | | |
| Text<br>(assess last) | 1. Sufficient detail others could reproduce ❑<br>2. Clear/concise writing ❑, table(s) ❑, diagram(s) ❑, figure(s) ❑ | | |
| | | **Preliminaries [/5]** | |
| **2. Introduction** | | | |
| Background | 1. Summary of current knowledge ❑<br>2. Specific problem(s) addressed ❑ and reason(s) for addressing ❑ | | |
| Objective | 1. Primary objective(s), hypothesis(es), or aim(s) ❑<br>2. Secondary question(s) ❑ | | |
| | **Is it worth continuing?** | **Introduction [/5]** | |
| **3. Design** | | | |
| Research design | 1. Research design(s) chosen ❑ and why ❑<br>2. Suitability of research design(s) ❑ | | |
| Intervention,<br>Treatment, Exposure | 1. Intervention(s)/treatment(s)/exposure(s) chosen ❑ and why ❑<br>2. Precise details of the intervention(s)/treatment(s)/exposure(s) ❑ for each group ❑<br>3. Intervention(s)/treatment(s)/exposure(s) valid ❑ and reliable ❑ | | |
| Outcome, Output,<br>Predictor, Measure | 1. Outcome(s)/output(s)/predictor(s)/measure(s) chosen ❑ and why ❑<br>2. Clearly define outcome(s)/output(s)/predictor(s)/measure(s) ❑<br>3. Outcome(s)/output(s)/predictor(s)/measure(s) valid ❑ and reliable ❑ | | |
| Bias, etc | 1. Potential bias ❑, confounding variables ❑, effect modifiers ❑, interactions ❑<br>2. Sequence generation ❑, group allocation ❑, group balance ❑, and by whom ❑<br>3. Equivalent treatment of participants/cases/groups ❑ | | |
| | **Is it worth continuing?** | **Design [/5]** | |
| **4. Sampling** | | | |
| Sampling method | 1. Sampling method(s) chosen ❑ and why ❑<br>2. Suitability of sampling method ❑ | | |
| Sample size | 1. Sample size ❑, how chosen ❑, and why ❑<br>2. Suitability of sample size ❑ | | |
| Sampling protocol | 1. Target/actual/sample population(s): description ❑ and suitability ❑<br>2. Participants/cases/groups: inclusion ❑ and exclusion ❑ criteria<br>3. Recruitment of participants/cases/groups ❑ | | |
| | **Is it worth continuing?** | **Sampling [/5]** | |
| **5. Data collection** | | | |
| Collection method | 1. Collection method(s) chosen ❑ and why ❑<br>2. Suitability of collection method(s) ❑ | | |
| Collection protocol | 1. Include date(s) ❑, location(s) ❑, setting(s) ❑, personnel ❑, materials ❑, processes ❑<br>2. Method(s) to ensure/enhance quality of measurement/instrumentation ❑<br>3. Manage non-participation ❑, withdrawal ❑, incomplete/lost data ❑ | | |
| | **Is it worth continuing?** | **Data collection [/5]** | |
| **6. Ethical matters** | | | |
| Participant ethics | 1. Informed consent ❑, equity ❑<br>2. Privacy ❑, confidentiality/anonymity ❑ | | |
| Researcher ethics | 1. Ethical approval ❑, funding ❑, conflict(s) of interest ❑<br>2. Subjectivities ❑, relationship(s) with participants/cases ❑ | | |
| | **Is it worth continuing?** | **Ethical matters [/5]** | |
| **7. Results** | | | |
| Analysis, Integration,<br>Interpretation method | 1. A.I.I. method(s) for primary outcome(s)/output(s)/predictor(s) chosen ❑ and why ❑<br>2. Additional A.I.I. methods (e.g. subgroup analysis) chosen ❑ and why ❑<br>3. Suitability of analysis/integration/interpretation method(s) ❑ | | |
| Essential analysis | 1. Flow of participants/cases/groups through each stage of research ❑<br>2. Demographic and other characteristics of participants/cases/groups ❑<br>3. Analyse raw data ❑, response rate ❑, non-participation/withdrawal/incomplete/lost data ❑ | | |
| Outcome, Output,<br>Predictor analysis | 1. Summary of results ❑ and precision ❑ for each outcome/output/predictor/measure<br>2. Consideration of benefits/harms ❑, unexpected results ❑, problems/failures ❑<br>3. Description of outlying data (e.g. diverse cases, adverse effects, minor themes) ❑ | | |
| | | **Results [/5]** | |
| **8. Discussion** | | | |
| Interpretation | 1. Interpretation of results in the context of current evidence ❑ and objectives ❑<br>2. Draw inferences consistent with the strength of the data ❑<br>3. Consideration of alternative explanations for observed results ❑<br>4. Account for bias ❑, confounding/effect modifiers/interactions/imprecision ❑ | | |
| Generalisation | 1. Consideration of overall practical usefulness of the study ❑<br>2. Description of generalisability (external validity) of the study ❑ | | |
| Concluding remarks | 1. Highlight study's particular strengths ❑<br>2. Suggest steps that may improve future results (e.g. limitations) ❑<br>3. Suggest further studies ❑ | | |
| | | **Discussion [/5]** | |
| **9. Total** | | | |
| Total score | 1. Add all scores for categories 1–8 | | |
| | | **Total [/40]** | |

**Appendix 1.3** Agreed Quality Ratings for all Included Articles

| Study | Preliminaries | Introduction | Design | Sampling | Data Collection | Ethical Matters | Results | Discussion | Total /40 | Total % |
|---|---|---|---|---|---|---|---|---|---|---|
| Austin et al. (2002) | 4 | 5 | 2 | 0 | 4 | 2 | 1 | 2 | 20 | 50 |
| Blocher et al. (2013) | 4 | 5 | 3 | 3 | 4 | 5 | 4 | 5 | 33 | 82.5 |
| Conant et al. (2008) | 4 | 5 | 2 | 1 | 2 | 1 | 2 | 2 | 19 | 47.5 |
| Carbone et al. (2014) | 4 | 4 | 3 | 3 | 2 | 3 | 3 | 4 | 26 | 65 |
| Eom et al. (2014) | 4 | 4 | 3 | 1 | 3 | 2 | 2 | 5 | 24 | 60 |
| Frizzel et al. (2011) | 4 | 4 | 2 | 1 | 2 | 3 | 4 | 4 | 24 | 60 |
| Glueckauf et al. 2002 | 2 | 5 | 3 | 1 | 4 | 1 | 4 | 4 | 24 | 60 |
| Jantzen et al. (2009) | 4 | 5 | 3 | 5 | 5 | 3 | 5 | 2 | 31 | 77.5 |
| Lewis et al. (1990, 1991) | 5 | 5 | 4 | 3 | 2 | 2 | 2 | 3 | 26 | 65 |
| Martinovic et al. (2006) | 4 | 4 | 4 | 3 | 4 | 3 | 4 | 5 | 31 | 77.5 |
| Modi et al. (2013) | 4 | 5 | 3 | 2 | 3 | 5 | 3 | 3 | 28 | 70 |
| Rau et al. (2006) | 4 | 5 | 3 | 2 | 2 | 1 | 4 | 4 | 25 | 62.5 |
| Shore et al. (2008) | 2 | 4 | 3 | 3 | 3 | 4 | 3 | 5 | 27 | 67.5 |
| Snead et al. (2004) | 4 | 5 | 2 | 1 | 3 | 2 | 3 | 3 | 23 | 57.5 |
| Stafstrom et al. (2012) | 3 | 5 | 1 | 1 | 4 | 3 | 1 | 2 | 20 | 50 |
| Tiffenberg et al. (2000) | 5 | 4 | 2 | 2 | 4 | 2 | 2 | 3 | 24 | 60 |
| Wagner et al. 2010 | 4 | 4 | 2 | 4 | 3 | 3 | 3 | 4 | 27 | 67.5 |

**Appendix 1.4** References for Table 1 Study Outcome Measures

**AKEQ** - The Adolescents' Knowledge of Epilepsy Questionnaire (Baker GA, Spector S, McGrath Y, Soteriou H. Impact of epilepsy in adolescence: a UK controlled study. Epilepsy Behav 2005; 6: 556–62.)

**APGAR** - Measure of family functioning (Smilkstein G, Ashworth C, Montano, D. Validity and reliability of the family APGAR as a test of family function. The Journal of family practice 1982;15: 303-11.)

**BDI** - Beck Depression Inventory (Beck AT, Ward CH, Mendelson M. An inventory for measuring depression. Arch Gen Psychiatry 1961;4: 861–71.)

**CATIS** - Child Attitude Toward Illness Scale (Austin JK, Huberty TJ. Development of the child attitude toward illness scale. Journal of Pediatric Psychology1993;18: 467–80.)

**CBCL** - Child Behavior Checklist (Achenbach TM, Rescorla LA. Manual for the ASEBA school-age forms and profiles. Burlington, VT: University of Vermont, Research Center for Children, Youth, & Families; 2001.)

**CDI** - Child Depression Inventory (Kovacs M. Children's depression inventory (CDI) manual. New York: Multi-Health Systems, Inc; 1992.)

**CDI-K** - Children's Depression Inventory, Korean Version (Kim EK, Yang JW, Chung YS, Hong SD, Kim JH. Factor structure of the Children's Depression Inventory (CDI) in children and adolescent. Korean Journal of Clinical Psychology 2005;24: 693–707.)

**CAT** - Comprehensive Attention Test (Yoo H, Lee J S HK, Park EH, Jung J, Kim BN, et al. Standardization of the Comprehensive Attention Test for the Korean children and adolescents. Journal of Korean Academic Child and Adolescent Psychiatry 2009;20: 68–75.)

**CCTT** - Children's Color Trails Test (Llorente AM, Voigt RG, Williams J, Frailey JK, Satz P, D'Elia LF. Children's Color Trails Test 1 & 2: test–retest reliability and factorial validity. Clinical Neuropsychology 2009;23: 645–60.)

**CHLCS** – Child Health Locus of Control Scale (Parcel CS, Meyer MP. Development of an instrument to measure children's health locus of control. Health Educ Monogr 1978;6: 149-59.

**CHQ** - Child Health Questionnaire (Landgraf JM, Abetz L, Ware JE. The Child Health Questionnaire (CHQ): A user's manual. Boston: New England Medical Centre; 1999.)

**CES-D** - Centre for Epidemiological Study on Depression Scale (Radloff LS. TheCES-Dscale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977;1: 385–401.)

**CHIC** - Coping Health Inventory for Children (Austin JK, Patterson JM, Huberty TJ. Development of the Coping Health Inventory for Children. J Pediatr Nurs 1991;6: 166–74.)

**EKP-G** - Parents-Epilepsy Knowledge Profile (Jantzen S, Muller-Godeffroy E, Hallfahrt-Krisl T, Aksu F, Pust B, Kohl B, Redlich A, Sperner J, Thyen U. FLIP&FLAP-a training programme for children and adolescents with epilepsy, and their parents. Seizure 2009;18: 478-86.)

**EKP-27** - Parents epilepsy-related worries questionnaire (Jantzen S, Muller-Godeffroy E, Hallfahrt-Krisl T, Aksu F, Pust B, Kohl B, Redlich A, Sperner J, Thyen U. FLIP&FLAP-a training programme for children and adolescents with epilepsy, and their parents. Seizure l2009;18: 478-86.)

**ESES** - Epilepsy Self-Efficacy Scale (DiIorio C, Faherty B, Manteuffel B, Hoeffer B, Hilbert GA. Self-efficacy and social support in self-management of epilepsy. West J Nurs Res 1992;14: 292–307.)

**FAQ** - Feasibility-Acceptability Questionnaire on Adherence Intervention (Modi AC, Guilfoyle SM, Rausch J. Preliminary Feasibility, Acceptability, and Efficacy of an Innovative Adherence Intervention for Children with newly Diagnosed Epilepsy. Journal of Paediatric Psychology 2013: 1-12.)

**HAMD** - Hamilton Depression Scale (Hamilton M. Development of a rating scale for primary depressive illness. Br J Doc Clin Psychol 1967;6:278–96.)

**Harter's Self Competency Scale** (Harter S. The perceived competence scale for children. Child Dev 1982;53:87-97.)

**HRQOL** - Health Related Quality of Life (Baars RM, Atherton CI, Koopman HM, Bullinger M, Power M. The European DISABKIDS project: development of seven condition-specific modules to measure health related quality of life in children and adolescents. Health and Quality of Life Outcomes 2005; 3:70.)

**HSC** - Hopelessness Scale for Children (Kazdin AE, French NH, Unis AS, Esveldt-Dawson K, Sherick RB. Hopelessness, depression, and suicidal intent among psychiatrically disturbed inpatient children. J Consult Clin Psychol 1983;51: 504–10.)

**ISS, IFS, ICS** - The family and disability assessment manual (Glueckauf RL, Webb P, Papandria-Long M, Rasmussen JL, Markand O, Farlow M. The Family and Disability Assessment System: Consistency and accuracy of judgments across coders and measures. Rehab Psychol 1992;37: 291–304)

**KINDL** - Health-Related Quality of Life Questionnaire (Ravens-Sieberer U, Bullinger M. Assessing health related quality of life in chronically ill children with the German KINDL: first psychometric and content-analytical results. Quality of Life Research 1998;4: 7)

**Knowledge Related to Epilepsy Scale** (Helgeson DC, Mittan R, Tan SY, Chayasirisobhon S. Sepulveda Epilepsy Education: the efficacy of a psychoeducational treatment program in treating medical and psychosocial aspects of epilepsy. Epilepsia 1990;31: 75–82.)

**K-CBCL** - Korea-Child Behaviour Checklist (Oh KJ, Lee HR. Development of Korean version of Child Behavior Checklist (K-CBCL).Seoul: Korean Research Foundation; 1997)

**K-QOLCE** - Quality of Life in Childhood Epilepsy (Lim KH, Kim HD. Validation of a Korean version of the Quality of Life in Childhood Epilepsy Questionnaire (K-QOLCE). Journal of Korean Epilepsy Society 2002;6: 32–44.)

**MAACL** - Multiple Affect Adjective Checklist (Zuckerman M, Lubin B. Multiple Affect Adjective Checklist Revised Manual. San Diego: Edits; 1965)

**MASC** - Multidimensional Anxiety Scale for Children (March JS, Parker JDA, Sullivan K, Stallings P. The Multidimensional Anxiety Scale for Children (MASC): factor structure, reliability, and validity. Journal of the American Academy of Child Adolescent Psychiatry 1997;36(4): 554–65.)

**MEMS 'TrackCap'** - Medication Event Monitoring System (Aardex group, Sion, Switzerland)

**Parent Response to Illness Scale** (Austin JK, Dunn D, Huster G, Rose D. Development of scales to measure psychosocial care needs of children with seizures and their parents. J Neurosci Nurs 1998;30: 155–60.)

**PCS** - Psychosocial Care Scale - Parent and Child Report. (Austin JK, Dunn D, Huster GA, Rose DF. Development of scales to measure psychosocial care needs of children with seizures and their parents. J Neurosci Nurs 1998;30(3): 155–160.)

**PH-1** - Piers-Harris Children's Self Concept Scale (Piers EVH, Piers-Harris DS, editors. Children's self-concept scale-second edition manual. 2nd ed. Los Angeles: Western Psychological Services; 2002)

**PIP** – Pediatric Inventory for Parents (Streisand R, Branieck S, Tercyak KP, Kazak AE. Childhood illness-related parenting stress: the Pediatric Inventory for Parents. J Pediatr Psychol 2001;26: 155–62.)

**PSI** - Parenting Stress Index (Abidin RR.Parenting stress index (4th ed.). Lutz, FL: PAR; 2012.)

**QOLCE** - Quality of Life in Childhood Epilepsy Scale (Talarska D. The usefulness of Quality of Life Childhood Epilepsy (QOLCE) questionnaire in evaluating the quality of life of children with epilepsy. Advances in medical science 2007;52(1): 191-3.)

**QOLIE-AD-48** - Quality of Life Inventory for Adolescents with Epilepsy (Cramer JA, Westbrook L, Devinsky O, Perrine K, Glassman M, Camfield C. Development of a quality of life inventory for adolescents: the QOLIE-AD-48. Epilepsia 1999;40: 1114–21.)

**QOLIE-31** - Quality of Life in epilepsy inventory (Cramer JA, Perrine K, Devinsky O, Bryant-Comstock L, Meador K, Hermann B. Development and cross-cultural translations of 31-item Quality of Life in Epilepsy Inventory (QUOLIE-31). Epilepsia 1998;39: 81–8.)

**RCMAS** - Revised children's manifest anxiety scale, Korean version (Chio JS, Cho SC. Reliability and validity of Revised Children's Manifest Anxiety Scale. Korean Journal of Neuropsychiatric Association 1989;14: 150–7.)

**RSES** - The Rosenberg Self-Esteem Scale (Rosenberg M. Society and the Adolescent Self-Image. Princeton: Princeton University Press; 1965)

**SCARED** - Screen for Child Anxiety Related Emotional Disorders (Birmaher B, Khetarpal S, Brent D, Cully M, Balach L, Kaufman J, Neer SM. The Screen for Child Anxiety Related Emotional Disorders (SCARED): scale construction and psychometric characteristics. Journal of the American Academy of Child Adolescent Psychiatry 1997;36(4): 545–53.)

**SDQ** - Strengths and Difficulties Questionnaire (Goodman R, Renfrew D, Mullick M. Predicting type of psychiatric disorder from Strengths and Difficulties Questionnaire (SDQ) scores in child mental health clinics in London and Dhaka. European Child Adolescent Psychiatry 2000;9: 129–34.)

**SSES** - Seizure self-efficacy scale (Caplin D, Austin J, Dunn D, Shen J, Perkins S. Development of a self-efficacy scale for children and adolescents with epilepsy. Child Health Care 2002;31: 295–309.)

**SSES-C** – The State Self Esteem Scale (Heatherton, T.F. and Polivy, J. Development and Validation of a Scale for Measuring State Self-Esteem. Journal of Personality and Social Psychology 60: 895-910)

**SSRS** - Social Skills Rating System (Gresham FM, Elliott SN. Social skills rating system manual. Circle Pines: American Guidance Service; 1990)

**SSSS**- Seizure Social Severity Scale (Austin JK, Dunn DW, Perkins SM, Shen J. Youth with epilepsy: development of a model of children's attitudes toward their condition. Child Health Care 2006;35: 123–40.)

**WAI** - Working Alliance Inventory (Horvath AO, Greenberg LS (1989). Development and validation of the Working Alliance Inventory. Journal of Counseling Psychology 1989;36: 223-33.)

**WISC-III** - Wechsler Intelligence Scale (Kwak K, Choi HP, Kim C. A study for the standardization of the Korean Wechsler Intelligence Scale—Third Edition (WISC-III). Korean Journal of Developmental Psychology 2002;15: 19–33.)

**ZUF-8** - Client Satisfaction Questionnaire, German Version (Schmidt J, Nubling R. ZUF-8. Fragebogen zur Messung der Patientenzufriedenheit. In: Brahler E, Schumacher J, Strauß B, editors. Diagnostische Verfahren in der Psychotherapie. Gottingen: Hogrefe; 2002. p. 392–6)

**Appendix 2.1** Letter granting ethical approval by the North of Scotland Research Ethics Committee

Further Information Favourable Opinion letter re-submitted – 21 October 14 – Corrected documents version & Date in documents table

**NRES Committees - North of Scotland**
Summerfield House
2 Eday Road
Aberdeen
AB15 6RE

Telephone: 01224 558458
Facsimile: 01224 558609
Email: nosres@nhs.net

NHS Grampian

10 October 2014

Dr Liam Dorris
Fraser of Allander Neurosciences Unit
Royal Hospital For Sick Children
Yorkhill Hospital
Dalnair Street
GLASGOW
G3 8SJ

Dear Dr Dorris

| | |
|---|---|
| **Study title:** | **Accelerated long-term forgetting and behavioural sleep disruption in children with Genetic Generalised Epilepsy (GGE).** |
| **REC reference:** | **14/NS/1054** |
| **IRAS project ID:** | **156692** |

Thank you for the letter dated 8 October 2014 from Fiona Corrigan, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Alternate Vice-Chair.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details. Publication will be no earlier than three months from the date of this opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to make a request to postpone publication, please contact the REC Manager, Mrs Carol Irvine, nosres@nhs.net.

**Confirmation of ethical opinion**

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

**Conditions of the favourable opinion**

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Further Information Favourable Opinion letter re-submitted – 21 October 14 – Corrected documents version & Date in documents table

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

**It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).**

**Ethical review of research sites**

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

**Approved documents**

The final list of documents reviewed and approved by the Committee is as follows:

| *Document* | *Version* | *Date* |
|---|---|---|
| Covering letter on headed paper | 1 | 3 September 2014 |
| GP/consultant information sheets or letters: Clinician letter | 2 | 15 August 2014 |
| IRAS Checklist XML: Checklist 10102014 | | 10 October 2014 |
| Opt in Form Glasgow | 1 | 15 August 2014 |
| Opt in Form Edinburgh | 1 | 15 August 2014 |
| Letters of invitation to participant: Glasgow | 3 | 6 October 2014 |
| Letters of invitation to participant: Edinburgh | 3 | 6 October 2014 |
| *Document* | *Version* | *Date* |

Further Information Favourable Opinion letter re-submitted – 21 October 14 – Corrected documents version & Date in documents table

| | | |
|---|---|---|
| Non-validated questionnaire: Seizure Diary Glasgow | 1 | 1 September 2014 |
| Non-validated questionnaire: Seizure Diary Edinburgh | 1 | 1 September 2014 |
| Non-validated questionnaire: Sleep Diary Glasgow | 1 | 1 September 2014 |
| Non-validated questionnaire: Sleep Diary Edinburgh | 1 | 1 September 2014 |
| MRP Draft Proposal - clean | | 23 February 2014 |
| MRP Draft Proposal - tracked | | 7 January 2014 |
| Response to Provisional Opinion | 1 | 8 October 2014 |
| University of Glasgow Approval Letter | | 30 June 2014 |
| MRP Feedback | | 20 May 2014 |
| Participant Consent Form: Parent - Glasgow | 2 | 02 September 2014 |
| Participant Consent Form: Parent - Edinburgh | 2 | 02 September 2014 |
| Participant Consent Form: Assent Form Glasgow | 2 | 8 October 2014 |
| Participant Consent Form: Assent Form Edinburgh | 2 | 8 October 2014 |
| Participant Consent Form: YP Consent Glasgow | 2 | 02 September 2014 |
| Participant Consent Form YP Consent Edinburgh | 2 | 02 September 2014 |
| Participant Information Sheet (PIS): Parent - Glasgow | 3 | 6 October 2014 |
| Participant Information Sheet (PIS): Parent - Edinburgh | 3 | 6 October 2014 |
| Participant Information Sheet (PIS): Child - 9-12 - Glasgow | 1 | 8 October 2014 |
| Participant Information Sheet (PIS): Child - 9-12 - Edinburgh | 1 | 8 October 2014 |
| Participant Information Sheet (PIS): 13-16 - Glasgow | 1 | 6 October 2014 |
| Participant Information Sheet (PIS): 13-16 - Edinburgh | 1 | 6 October 2014 |
| REC Application Form: REC Form 04092014 | 156692/662 313/1/41 | 4 September 2014 |
| Research protocol or project proposal | 3 | 15 August 2014 |
| Summary CV for Chief Investigator (CI): Liam Dorris | 1 | 9 September 2014 |
| Summary CV for student: Fiona Corrigan | 1 | 2 September 2014 |
| Summary CV for supervisor (student research): Liam Dorris | 1 | 3 September 2014 |
| Validated questionnaire: WASI | 1 | 2 September 2014 |
| Validated questionnaire: Children's Sleep Habits | 1 | 2 September 2014 |
| Validated questionnaire: Children's Memory Scale | 1 | 2 September 2014 |
| Validated questionnaire: Sleep Self Report | 1 | 1 September 2014 |
| Validated questionnaire: Observer Memory Questionnaire | 1 | 2 September 2014 |

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

**After ethical review**

Reporting requirements

Further Information Favourable Opinion letter re-submitted – 21 October 14 – Corrected documents version & Date in documents table

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The HRA website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

**User Feedback**

The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

**HRA Training**

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

| **14/NS/1054** | **Please quote this number on all correspondence** |
|---|---|

With the Committee's best wishes for the success of this project.

Yours sincerely

[redacted]

**pp'd on behalf of**
**Mrs Sue Harrison**
**Alternate Vice-Chair**

Enclosures: "After ethical review – guidance for researchers" SL-AR2

Copy to: Ms Emma-Jane Gault
Ms Joanne McGarry, NHS Greater Glasgow and Clyde

**Appendix 2.2** Letter of acknowledgement of minor amendment by the North of Scotland Research Ethics Committee

**NRES Committees – North of Scotland**
Summerfield House
2 Eday Road
Aberdeen
AB15 6RE

Telephone: 01224 558474
Facsimile: 01224 558609
Email: nosres@nhs.net

NHS Grampian

29 October 2014

Dr Liam Dorris
Fraser of Allander Neurosciences Unit
Royal Hospital For Sick Children
Yorkhill Hospital
Dalnair Street
GLASGOW
G3 8SJ

Dear Dr Dorris

| | |
|---|---|
| **Study title:** | **Accelerated long-term forgetting and behavioural sleep disruption in children with Genetic Generalised Epilepsy (GGE).** |
| **REC reference:** | **14/NS/1054** |
| **Amendment number:** | **AM01** |
| **Amendment date:** | **27 October 2014** |
| **IRAS project ID:** | **156692** |

Thank you for your letter of 27 October 2014, notifying the Committee of the above amendment.

The amendment has been considered by the Ethics Co-ordinator.

The Committee does not consider this to be a "substantial amendment" as defined in the Standard Operating Procedures for Research Ethics Committees. The amendment does not therefore require an ethical opinion from the Committee and may be implemented immediately, provided that it does not affect the approval for the research given by the R&D office for the relevant NHS care organisation.

**Documents received**

The documents received were as follows:

| Document | Version | Date |
|---|---|---|
| Invitation Letter – Edinburgh | 4 | 27 October 2014 |
| Invitation Letter – Glasgow | 4 | 27 October 2014 |
| Notice of Minor Amendment | AM01 | 27 October 2014 |
| Opt in Form – Glasgow | 2 | 27 October 2014 |

| | | |
|---|---|---|
| Opt in Form – Edinburgh | 2 | 27 October 2014 |
| 9-12 Child Info Sheet – Glasgow | 2 | 27 October 2014 |
| 9-12 Child Info Sheet – Edinburgh | 2 | 27 October 2014 |
| 13-16 Child Info Sheet – Glasgow | 2 | 27 October 2014 |
| Parent Info Sheet – Glasgow | 4 | 27 October 2014 |
| 13-16 Child Info Sheet – Edinburgh | 2 | 27 October 2014 |
| Parent Info Sheet – Edinburgh | 4 | 27 October 2014 |

**Statement of compliance**

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

**14/NS/1054: Please quote this number on all correspondence**

Yours sincerely

[redacted]

**Lisa Shearer**
**Assistant Co-ordinator**

Copy to: NHS Greater Glasgow and Clyde

**Appendix 2.3** Letter granting site and management approval by the NHS Greater Glasgow and Clyde Research and Development Department

**Coordinator: Joanne McGarry**
**Telephone Number: 0141 211 2142**
**E-Mail: Joanne.McGarry@ggc.scot.nhs.uk**
**Website: www.nhsggc.org.uk/r&d**

**R&D Management Office**
**Western Infirmary**
**Tennent Institute**
**1st Floor 38 Church Street**
**Glasgow, G11 6NT,**

23/10/2014

Dr Liam Dorris
NHS Greater Glasgow and Clyde
Fraser of Allander Neurosciences Unit
Royal Hospital for Sick Children
Yorkhill
Glasgow, G3 8SJ

## NHS GG&C Board Approval

Dear Dr Dorris,

| | |
|---|---|
| **Study Title:** | Accelerated long-term forgetting and behavioural sleep disruption in children with Genetic Generalised Epilepsy (GGE) |
| **Principal Investigator:** | Dr Liam Dorris |
| **GG&C HB site** | Royal Hospital for Sick Children |
| **Sponsor** | NHS GG&C |
| **R&D reference:** | GN14KH456 |
| **REC reference:** | 14/NS/1054 |
| **Protocol no:** (including version and date) | V3 Date: 15/08/14 |

I am pleased to confirm that Greater Glasgow & Clyde Health Board is now able to grant **Approval** for the above study.

**Conditions of Approval**

1. **For Clinical Trials** as defined by the Medicines for Human Use Clinical Trial Regulations, 2004
   a. During the life span of the study GGHB requires the following information relating to this site
      i. Notification of any potential serious breaches.
      ii. Notification of any regulatory inspections.

It is your responsibility to ensure that all staff involved in the study at this site have the appropriate GCP training according to the GGHB GCP policy (www.nhsggc.org.uk/content/default.asp?page=s1411), evidence of such training to be filed in the site file.

2. **For all studies** the following information is required during their lifespan.

a. Recruitment Numbers on a quarterly basis
b. Any change of staff named on the original SSI form
c. Any amendments – Substantial or Non Substantial
d. Notification of Trial/study end including final recruitment figures
e. Final Report & Copies of Publications/Abstracts

**Please add this approval to your study file as this letter may be subject to audit and monitoring.**

Your personal information will be held on a secure national web-based NHS database.

I wish you every success with this research study

Yours sincerely,

[redacted]

Joanne McGarry
**Research Co-ordinator**

**Cc:** F. Corrigan, NHSGG&C; NRSPCC.

**Appendix 2.4** Letter granting site and management approval by the NHS Lothian Research and Development Department

University Hospitals Division

NHS Lothian

**Queen's Medical Research Institute**
**47 Little France Crescent, Edinburgh, EH16 4TJ**

FM/NM/approval

05 November 2014

**Research & Development**
**Room E1.12**
**Tel: 0131 242 3330**

**Email:**
**R&DOffice@nhslothian.scot.nhs.uk**

**Director: Professor David E Newby**

Dr Ailsa McLellan
Edinburgh Sick Children's Hospital
9 Sciennes Road
Edinburgh
EH9 1LF

Dear Dr McLellan

**Lothian R&D Project No:** 2014/0363

**Title of Research:** Accelerated long-term forgetting and behavioural sleep disruption in children with Genetic Generalised Epilepsy (GGE)

**REC No:** 14/NS/1054

**Participant Information Sheet:**
9-12 years version 2 dated 27 October 2014
Parent version 4 dated 27 October 2014
13-16 years version 2 dated 27 October 2014

**Protocol:**
Version 3 dated 15 August 2014

**Consent Form:**
Assent version 2 date 8 October 2014
Young Person version 2 dated 2 September 2014
Parent version 2 dated 2 September 2014

I am pleased to inform you that this study has been approved for NHS Lothian and you may proceed with your research, subject to the conditions below. This letter provides Site Specific approval for NHS Lothian.

We note that this project includes a researcher who will require a Clinical Research Access letter from NHS Lothian. The individual concerned (Fiona Corrigan) should contact our offices with a view to applying for the necessary documentation. Please note all final paperwork will have to be signed and returned to our R&D offices before the researcher can commence work on the project.
Please note that the NHS Lothian R&D Office must be informed if there are any changes to the study such as amendments to the protocol, recruitment, funding, personnel or resource input required of NHS Lothian.

Substantial amendments to the protocol will require approval from the ethics committee which approved your study and the MHRA where applicable.

Please inform this office when recruitment has closed and when the study has been completed.

I wish you every success with your study.

Yours sincerely

[redacted]

Ms Fiona McArdle
Deputy R&D Director

STA034

**Appendix 2.5** Participant Invitation Letter

Dear Parent/Guardian and Child,

**Invitation to Participate in Research Study: Learning and sleep in children and young people with epilepsy.**

As you know, I am part of a team of people who are involved in your child's ongoing care. As your healthcare professional I would like to inform you of some new research that is being carried out.

We are interested in studying the relationship between sleep and learning. We know that many young people with epilepsy can have sleep problems and therefore want to look at whether this can affect their learning during the day. We are asking everyone who comes to the Epilepsy Clinic at the Royal Hospital for Sick Children to consider taking part in a research study being carried out by Fiona Corrigan as part of her Doctorate in Clinical Psychology. This research may help us to gain knowledge on how children with epilepsy's learning could be improved.

Before you and your child make up your mind, it is important for you both to understand what we are asking them to do and why. Please find enclosed an information sheet to tell you all about the study. Please read it and ask your child to read it as well.

The study involves arranging two appointments with Fiona for your child to complete some tasks related to their memory. It would also involve measurement of your child's sleep over a week long period using a small device like a wrist watch. When your child attends they will have time to find out more about the study and ask more questions before taking part. If your child decides they don't want to take part, then they can say no and they won't be asked anything else.

Asking your child to take part in this study does not mean we think they have a problem with their memory or sleep. We are asking everyone who comes to clinics and they can say "no" if they don't want to take part.

If they decide they want to take part after reading the information sheet, you can either return the form in the enclosed envelope to Fiona Corrigan, Institute of Health and Wellbeing, University of Glasgow, 1st floor, Administration Building, Gartnavel Royal Hospital, 1055 Great Western Road, Glasgow, G12 0XH or call Fiona Corrigan on XXXXor email at f.corrigan.1@research.gla.ac.uk

If you want to ask anything else about the study you can call or email Fiona using the above contact details.

Thank you for reading this.

Yours sincerely, {Insert Name here} Consultant Paediatric Neurologist

**Appendix 2.6** Participant Opt-in Form

**Learning and sleep in children and young people with epilepsy**

I have read the information sheets dated 15/08/14 (Version 1 Child and Version 2 Parent) and I would like to participate in this study.

Name of child:_____

Name of parent/carer:_____

Signed:_____

Please contact me to arrange an appointment by:

Email: my email address is:_____

Phone: my telephone number is:_____

Post: my address is:_____

_____

_____

Return Details:

Fiona Corrigan,
Institute of Health and Wellbeing,
University of Glasgow,
1st floor, Administration Building,
Gartnavel Royal Hospital,
1055 Great Western Road,
Glasgow, G12 0XH

or call Fiona Corrigan on XXXX

or email at f.corrigan.1@research.gla.ac.uk

**Appendix 2.7** Child Information Sheet (Age 9-12)

**Participant Information Sheet**

**(To be shown and read by parent/carer if required)**

**Learning and sleep in children and young people with epilepsy.** Researcher: Fiona Corrigan

My name is Fiona Corrigan and I am a Trainee Clinical Psychologist at the University of Glasgow. I am doing a project on epilepsy, sleep and learning and I am inviting you to take part in it. Before you decide you need to understand why the project is being done and what you would need to do.

**1. Why is this project being done?**

I want to find out if there is a connection between learning and sleep in children with epilepsy.
It may help doctors understand more about the difficulties that children with epilepsy might have.

**2. Why me?**

All children aged between 9 and 16 years that have epilepsy and go to the Royal Hospital for Sick Children (RHSC) (Glasgow or Edinburgh) have been asked to take part.

**3. Do I have to take part?**

No you do not, it is up to you. If you don't want to take part, just say no.


**4. What will happen?**

If you would like to take part, then you and I would meet together for two appointments at the at the hospital you normally go to. Your Mum, Dad or carer can come with you.

When we meet, I will ask you some questions about your sleep and we will do some learning tasks together. Between our two appointments I will ask you to wear a special watch like the one in the picture below. This is called an "actiwatch" and it will tell me how much sleep you are getting. You will be involved in the study for 8 days in total.

**5. Will my answers be private?**

I will write down your answers to the tasks but everything you say will be kept private and only people working on the study will be allowed to see it. Information in the report will not have your name on it.

**6. What if I don't want to do the research anymore?**

If you decide that you don't want to take part even after we have started then that is okay. We can stop at any time for a break and you can leave with your parent/carer when you decide you want to leave. This will not affect the care you are getting from any doctors or nurses at the hospital.

**7. What happens to what the researchers find out?**

The results will be written up in a report and might go in a book or magazine about epilepsy that doctors read.

If you would like to take part or have any questions then please ask your parent/carer to get in touch with me on: Tel: 07934157344, Email: f.corrigan.1@research.gla.ac.uk. Alternatively they can contact: Dr Liam Dorris, Chief Research Investigator and Consultant Paediatric Neuropsychologist, Fraser of Allander Neurosciences Unit (Tel: 0141 201 0863)

**Appendix 2.8** Child Information Sheet (Age13-16)

**Participant Information Sheet: Learning and sleep in children and young people with epilepsy.** Researcher: Fiona Corrigan

My name is Fiona Corrigan. I am a Trainee Clinical Psychologist at the University of Glasgow. I would like to ask you to take part in my research project. This project is about sleep and memory in children and young people who have epilepsy. It may help doctors understand more about the difficulties that children with epilepsy might have. Please speak to your parents or guardians about this project. If you have any questions you can also ask me.

**What is this project for?** Some children with epilepsy find it harder to remember information over long periods of time and might forget things more easily. Sleep is also something that can be affected by epilepsy. I want to find out if there is a connection between forgetting information and sleep in children with epilepsy.

**Why have I been asked to take part?** All children aged between 9 and 16 years that have epilepsy and go to the Royal Hospital for Sick Children (RHSC) (Glasgow or Edinburgh) have been asked to take part.

**Do I have to take part?** No. Talk it over with your parent or guardian and decide if you want to take part or not. You can pull out at any time and don't have to say why. This will not affect the treatment you are getting from any doctors or nurses.

**If I agree to take part, what will happen next?** I will arrange to meet with you and your parent/guardian twice at the RHSC (Glasgow or Edinburgh).

**What will I have to do?** When we meet up I will make sure that you want to take part and ask you to sign a form to say you understand what taking part will involve. I will then ask you to do some tasks related to your memory and ask you some questions about your sleep. I will then give you an Actiwatch, which looks like a normal watch (as shown in photo) that you wear on your wrist, and show you how to use it to measure your sleep at home. You will wear the watch all day and night for seven days, it is waterproof but you can take it off while bathing if you want to. This meeting will take about 1 hour. I will also give your parents or guardians a questionnaire with questions about your sleep and memory. I will then meet with you at the hospital a week later to collect the Actiwatch and ask you some more questions. This should take about 15 minutes. You will be involvedin the study for 8 days in total.

**Will my answers be private?** All the information you give me will be kept private and only people working on the study will be allowed to see it. Information in the report will not have your name on it.

**What will happen to the results?** The results will be written up in a report and might be published in a book or magazine about epilepsy that doctors read. You can get a copy of a brief summary from me (Fiona Corrigan).

**Thank you very much for reading this leaflet.**

For More Information Please Contact:

• Fiona Corrigan, Trainee Clinical Psychologist, Department of Psychological Medicine, Gartnavel Royal Hospital (Tel: 07934157344, Email: f.corrigan.1@research.gla.ac.uk)

• Dr Liam Dorris, Chief Research Investigator and Consultant Paediatric Neuropsychologist, Fraser of Allander Neurosciences Unit (Tel: 0141 201 0863)

**Appendix 2.9** Parent Information Sheet

**Parent/ Guardian Information Sheet**

**Learning and sleep in children and young people with epilepsy.**
Researcher: Fiona Corrigan

My name is Fiona Corrigan and I am a final year Trainee Clinical Psychologist at the University of Glasgow. As part of my training I am carrying out research looking at the relationship between memory and sleep in children and young people with epilepsy. This kind of research will hopefully improve our knowledge of the effects of epilepsy on children's learning.

You and your child are being invited to take part in this study. This leaflet provides information about the study. If anything is not clear or you have any questions please do not hesitate to contact me (my contact details are at the end of the leaflet). I have enclosed a child information sheet and would be grateful if you would read through this with your child.

**What is the purpose of this research?** It has been found that some children with epilepsy forget information at a faster rate than those without epilepsy. Epilepsy can also have an effect on sleep. We would like to know whether there is a relationship between this type of forgetting and sleep in children and young people with epilepsy. This research will add to our knowledge of the factors that influence memory and learning in children with epilepsy. In turn, this could lead to the development of interventions that could improve their learning.

**Why have we been chosen to take part?** Children aged between 9 and 16 years old who have epilepsy and attend the Royal Hospital for Sick Children (Glasgow or Edinburgh) are being invited to take part in the study.

**Do I have to take part?** No, it is up to you and your child whether or not you want to take part. If you decide to take part you are both free to withdraw at any time without giving a reason. A decision to withdraw or not to take part will not affect any on-going care.

**What will happen if my child and I agree to take part?**
If your child decides to take part you can contact me by phone, email or by returning the slip enclosed, in the stamped addressed envelope provided. Once you have indicated you and your child would like to participate I will contact you to arrange a suitable time and place to meet your child at Royal Hospital for Sick Children, Glasgow or Edinburgh. Before you and your child begin I will ask you to complete an Assent/Consent Form. I ask that you come along with your child to this meeting and I will issue you with the parent-completed questionnaires at the first appointment.

**What will my child have to do?** Taking part will involve two visits to the hospital. When I first meet your child I will explain what is involved to them and check that they are willing to take part. I will ask them to complete some short tasks to confirm we can proceed with the rest of the questions. I will then ask your child to complete two tasks related to their memory and ask them some questions. While your child is taking part, I will ask you to complete two parent questionnaires. These ask about your child's sleep and memory. These questionnaires should take no longer than 20 minutes to complete. I will then explain to you and your child how to use the Actiwatch which is a wristwatch-like device that will record their sleep over a week long period. The watch is worn continuously and is water-resistent.. It records and monitors movement, providing an estimate of sleep times based on periods of immobility. Actigraphy provides objective information on sleep-wake cycles in the participant's natural sleep environment.I will also give your child a questionnaire about their sleep to complete at home, which should take no longer than 10 minutes. This appointment should last approximately 1 hour in total. I will ask you to return for a second short appointment with your child one week later. During this I will collect the Actiwatch and ask your child to complete some tasks related to their memory. This will take approximately 15 minutes. You and your child's participation in the study will begin at your first appointment and will end at your second appointment, eight days later.

**Are there risks or benefits to taking part?** There are no risks to taking part. Your child will not be asked to take any medication or take part in any medical procedures. The information you and your child provide us with will help us to understand more about memory and sleep in children with epilepsy. The clinician who invited you to take part in the research may be informed of any relevant findings from the questionnaires.

**Will my taking part in the study be kept private?** All information collected from you and your child will be kept strictly confidential. Any information about them that is reported in the research will have all identifiable information like their name and address removed. Only the researchers (myself, Dr Liam Dorris (Chief Research Investigator) and Andrew Morley (Respiratory Physiologist)) will have access to the information gathered as well as representatives of the study Sponsor, NHS GG&C, who may access information to make sure the study is being conducted properly. All information will be stored in locked filing cabinets and a securely encrypted computer. As the initial tasks and memory tasks that your child will complete are routine clinical assessments, they will be stored securely in your child's clinical case notes and only be seen by NHS clinicians involved in their medical care. Case notes will not be accessed by the research team.

**What will happen to the results of the study?** It is intended that the results will be published in my Doctoral thesis and a journal that specialises in epilepsy research. You can obtain a copy of a lay summary by contacting me (Fiona Corrigan).

**Will the study help my child?**
This research could increase our understanding of how children with epilepsy learn and whether they might need extra educational support, for example, during

exams when there are more demands to learn new information. The medical and healthcare team could also benefit from understanding more about how having epilepsy can affect the education and learning of your child which may influence treatment and support decisions.

**Will my child be paid for taking part?**
No. Sorry, we cannot offer any payment or travel expenses.

**Who has reviewed this study?**
This study has been reviewed by the University of Glasgow, NHS Greater Glasgow and Clyde Research and Development Department and the North of Scotland Research Ethics Committee.

**For Further Information Please Contact:**

1) Fiona Corrigan, Trainee Clinical Psychologist, Department of Psychological Medicine, Gartnavel Royal Hospital (Tel: 07934157344, Email: f.corrigan.1@research.gla.ac.uk)

2) Dr Liam Dorris, Consultant Paediatric Neuropsychologist, Fraser of Allander Neurosciences Unit (Tel: 0141 201 0863)

If you would like to speak to someone impartial you can also contact Dr Helen Broome on 0141 201 0863 She is a Clinical Psychologist and researcher who works in Glasgow University but is not directly involved in thisresearch. She will be able to answer any questions you have.

**Thank you very much for taking the time to read this leaflet.**

**Appendix 2.10** Child Assent Form

**ASSENT FORM FOR CHILDREN**
**(To be completed by the child and their parent/carer)**

**Learning and sleep in children and young people with epilepsy.**

**Please circle Yes or No:**

Someone explained to me what the project is about. **Yes/No**

I read and understood the information sheet and the explanation given to me. **Yes/No**


I asked the researcher questions about the study if I didn't know what something meant. **Yes/No**

I know that I don't have to take part in the project and that I can stop anytime I want to. **Yes/No**


I know that I will have to wear a special watch for a week to measure my sleep. **Yes/No**

I know that my answers will be put into the study but no-one will know it was me because my name will not be in the study. **Yes/No**


I would like to take part in this study. **Yes/No**

**If <u>any</u> answers are 'no' or you don't want to take part, don't sign your name!**

If you <u>do</u> want to take part, you can sign your name below

Your name _____

Signature _____

Date _____

The person who explained this project to you needs to sign too:

Print Name _____

Signature _____

Date _____

**Thank you for your help!**

**Appendix 2.11** Child Consent Form

## Young Person's Consent Form

### Learning and sleep in children and young people with epilepsy

Institute of Health and Wellbeing, University of Glasgow, 1st floor, Administration Building, Gartnavel Royal Hospital, 1055 Great Western Road, Glasgow, G12 0XH

The purpose of this form is to make sure that you are happy to take part in the research and that you know exactly what this involves. Thank you for agreeing to take part in our study investigating the relationship between memory and sleep in children with epilepsy.

**Subject number:**

**Please initial the BOX**

| | |
|---|---|
| I confirm that I have read the information sheet dated 15/08/14 (Version 1) for the above study. | ☐ |
| I have had a chance to discuss this study and ask questions. | ☐ |
| I am happy with the answers given to all of my questions. | ☐ |
| I have been told enough about the study | ☐ |
| I agree for the data I provide to be recorded on a computer and made anonymous, so that no one can tell it was me. | ☐ |
| I understand that this information will be kept securely so that only the research team and the people organising the study can see it. | ☐ |
| I agree for my data to be used in the final report, as long as it is anonymous | ☐ |
| I understand that my neurologist will be informed of my participation and any relevant findings from my participation. | ☐ |
| **I understand that my participation is voluntary I am free to say no to taking part in this study at any time without having to give a reason and without affecting future medical care or legal rights** | ☐ |
| I agree to take part in the above study | ☐ |

| | | |
|---|---|---|
| ---------- | ---------- | ---------- |
| Name of Patient | Date | Signature |
| ---------- | ---------- | ---------- |
| Name of Person taking consent | Date | Signature |

*1 copy to the patient, 1 copy to the researcher, 1 Original for the patients' notes*

**Appendix 2.12** Parent Consent Form

# Parent/Guardian Consent Form

## Learning and sleep in children and young people with epilepsy

Institute of Health and Wellbeing, University of Glasgow, 1st floor, Administration Building, Gartnavel Royal Hospital, 1055 Great Western Road, Glasgow, G12 0XH

Thank you for agreeing to take part in our study. The purpose of this form is to make sure that you and your child are happy to take part in the research and that you know exactly what this involves.

Please initial box

1. I confirm that my child and I have read and understood the information sheet dated 15/08/14 (Version 2) for the above study. We have had the opportunity to ask questions about the study and we are happy with the answers provided. ☐

2. I understand that my participation and my child's is voluntary and that we are free to withdraw at any time without giving a reason, without any medical care or rights being affected. ☐

3. I confirm that my child and I agree for the data we provide to be recorded on a computer or stored securely in a locked filing cabinet and made anonymous. ☐

4. I understand that my child's medical records and data may be looked at by representatives of the study Sponsor for audit purposes. ☐

5. I understand that my child's neurologist will be informed of participation and any relevant findings from my child's participation. They will be provided with some research task responses to store in your child's clinical case notes. ☐

6. I agree for my data to be used in the final report, as long as it is anonymous. ☐

7. I agree to myself and my child taking part in the above study, and my child agrees to take part. ☐

PLEASE COMPLETE:

Name of Parent/Guardian……..Date……
Signature……

Name of Child.....……

Name of Researcher……Date……..
Signature……

1 copy to be retained by parent/carer and 1 copy to be retained by researcher

**Appendix 2.13** Major Research Proposal


## Abstract

Background: The phenomenon of accelerated long-term forgetting (ALF), in which newly acquired memories are intact after short delays but fade over days to weeks has recently been recognised in the paediatric epilepsy population. Given the well-established association between epilepsy and sleep disturbance and the evidence suggesting the importance of sleep in memory consolidation there is reason to investigate the relationship between ALF and sleep in children with epilepsy.

Aims: This study aims to replicate previous findings and demonstrate the ALF phenomenon in children with Genetic Generalised Epilepsy (GGE). It will also investigate the relationship between ALF and behavioural sleep disturbance.

Methods: Neuropsychological tests to assess ALF and objective and subjective measures of sleep will be used to explore the relationship between ALF and sleep. Correlation analysis will be used to determine whether poorer sleep is related to poorer initial learning and verbal memory recall.

Applications: Findings from this study may improve our understanding of the ALF phenomenon and potentially underline the need for management of sleep problems in improving the learning of children with GGE.


## Introduction

Clinically it has been observed that there is often a discrepancy between epilepsy patients' subjective report of memory abilities and their performance on neuropsychological tests of memory. An area researched in relation to this is the phenomenon of accelerated long-term forgetting (ALF), in which newly acquired memories are intact after short delays but fade over days to weeks. Relatively few group studies have been carried out in this area, and even fewer within the paediatric epilepsy population.

Davidson, Dorris, O'Regan and Zuberi (2007) investigated whether children with idiopathic generalised epilepsy (IGE) demonstrated ALF for verbal and non-verbal information compared to matched controls after a one-week delay. Children with IGE required a greater number of learning trials to reach a learning criterion and displayed a significantly increased rate of forgetting compared with controls. Results indicated that poorer initial learning efficiency only impacted negatively on access to stored verbal information at the greater delay of one week, as there was no group difference at thirty-minute delay. The authors concluded that the IGE group's poorer recall at one week (i.e. ALF) was due to a problem with memory retrieval for verbal information rather than poor retention. Findings were not consistent with the consolidation theory i.e. that failure of consolidation leads to a failure of long term (neocortical) storage. Davidson et al.'s study serves to evidence that ALF exists in children with IGE.

A similar study was carried out in 2012 by Gascoigne et al. Findings supported Davidson et al.'s (2007) results; children with IGE were found to recall fewer words

than controls after a week-long delay, but not thirty-minute delay. Conversely, their results were not explained by reduced learning efficiency as in the above study as there was no significant difference between the epilepsy group and controls in number of initial learning trials. Their findings were consistent with the consolidation theory. Although there is discrepancy between the two studies regarding the mechanisms underlying ALF, they are in agreement that it occurs in children with IGE.

Most other research in the area has been undertaken with adults with temporal lobe epilepsy including the first report of ALF by Blake, Wroe, Breen and McCarthy (2000). Other studies have investigated the relationship between seizures, neuropathology and ALF (Muhlert et al. 2011; Mameniskiene, Jatuzis, Kaubrys & Budrys, 2006; Wilkinson et al., 2012). Whilst it is relatively uncontentious that a lifetime of temporal lobe seizures may affect learning and memory, the demonstration of these cognitive deficits in children with other epilepsy syndromes may have a significant role in planning education.

Given the well-established association between epilepsy and sleep disturbance (Bazil, 2003; Becker, Fennell & Carney, 2003; Beran Plunket & Holland, 1999) and the evidence suggesting the importance of sleep in memory consolidation (Stickgold & Walker, 2007; Walker & Stickgold, 2004) there is reason to investigate the relationship between ALF and sleep in children with epilepsy. It is possible that sleep disturbance commonly experienced by children with epilepsy may affect their learning and explicit recall. Fitzgerald, Mohamed, Ricci, Thayer and Miller (2013a) discussed sleep as a potential contributing factor to ALF in epilepsy but highlighted that the limited existing evidence has produced mixed results. Fitzgerald, Thayer, Mohamed and Miller (2013b) tested recall for word and design lists at different delays, while patients with epilepsy underwent five days on continuous ambulatory EEG. Daytime naps were associated with better retention. Self-report of everyday memory functioning was related to recall at longer delays but not at thirty minutes, emphasising that standardised memory tests may fail to capture long-term recall abilities accurately.

Walker and Stickgold (2004) reviewed the substantial body of evidence on sleep-dependent learning and memory consolidation. Evidence is contradictory for the role of sleep in processing simple, emotion-free declarative memories, such as unrelated word pairs. A selective reminding test and actigraphy were used in a study by Deak, Stickgold, Pietras, Nelson and Bubrick (2011) examining how sleep impacts on the memory function of adults with TLE. People with TLE displayed greater forgetting compared to controls over twelve hours of daytime wakefulness but not over a similar period of sleep. The small sample size should be noted, along with the finding that there was no significant difference between TLE and control group on the objective or subjective measures of sleep. Slow wave sleep (SWS) was correlated with overnight performance change on the selective reminding test. Diekelmann, Wilhelm and Born (2009) also provide a review of studies in the area of sleep-dependent memory consolidation. Regarding children, those with high amounts of SWS post-learning had distinctly enhanced declarative memories.

A review of the relationship between sleep and the effect on cognitive functioning in children with epilepsy discussed the influence of sleep disruption on seizures

and the neurophysiological and neurochemical mechanisms important for the memory–learning process (Parisi et al., 2010). It was concluded that improvement in the long-term cognitive–behavioural prognosis of children with epilepsy requires good sleep quality as well as good seizure control.

Ashworth, Hill, Karmiloff-Smith and Dimitriou (2013) used actigraphy and novel learning tasks to investigate sleep-dependent memory consolidation in typically-developing children. Recall performance improved significantly following a period of sleep but there was no change in score after a wake period. There was no statistically significant correlation between sleep quality or duration and initial or delayed task performance. All participants' sleep was within the normal range, perhaps explaining why they did not find a relationship between sleep quality/duration and performance on the learning tasks. Ashworth et al. (2013) suggest that future research compares memory consolidation and baseline performance in good and poor sleepers.

One study to date has examined the relationship between memory consolidation and sleep in children with epilepsy. Sud et al. (2014) aimed to determine whether children with epilepsy were better able to consolidate memories after a sleep versus a wake period as has been demonstrated in typically developing children. Participants were presented word lists over five learning trials and recall was tested immediately and again after an average eleven hour delay. It was found that recall was significantly better after sleep, with results demonstrating a significant difference between memory consolidation and sleep versus wake trials for the majority of participants. However, this result was not found in the group analysis. Sud et al. (2014) used a small sample of children with epilepsy who had good sleep efficiency, which calls for further research to address these factors.

Although the above two studies have investigated whether sleep improves memory consolidation in children, they compared sleep and wake periods with recall over periods no longer than twenty-four hours. The current proposed study will extend this investigation by analysing the relationship between sleep and ALF over a week long period in children with GGE.

## Aim

This study aims to further investigate the phenomenon of ALF in children with Genetic Generalised Epilepsy (GGE).

## Hypotheses

1)There will be a significant negative correlation between the number of learning trials it takes to learn the minimum criterion for the Stories and Word Lists tests and sleep efficiency.

2) There will be a significant positive correlation between children's sleep efficiency and their recall for Stories and Word Lists tests after a delay of one week.

Participants

This study will include twenty-seven children with GGE. GGE is the new terminology developed by the International League against Epilepsy that has replaced the disorders previously known as idiopathic generalised epilepsy (IGE) (Berg & Scheffer, 2011).

Inclusion criteria include children and adolescents between the ages of 9-16 years who have a diagnosis of GGE and who speak English fluently. This age range was chosen as this is the age range the Children's Memory Scale (CMS) is standardised for. Exclusion criteria include: 1) individuals with a learning disability i.e. Full Scale IQ less than 70; 2) the presence of another major health or physical condition; 3) history of a neurological disorder other than epilepsy; 4) history of head injury 5) history of a specific sleep disorder and 6) history of psychiatric disorder.

Recruitment

All children with GGE who present at the epilepsy clinic or EEG department at the Fraser of Allander Neurosciences Unit at the Royal Hospital for Sick Children (who meet the inclusion criteria) will be identified by their Consultant Neurologist. If a potential participant is identified by the clinician at their first appointment with the service, information regarding the study will be handed to the young person and their parents/carer at their appointment. Study information will also be posted to all parents/carers of potential participants who attend for continuing care that are identified as meeting the inclusion criteria.

Should they wish to participate, families will be asked to contact the main researcher either by returning the opt-in slip included with their invitation or by emailing or phoning. They will also indicate how they would prefer to be contacted to arrange a convenient time for the young person to attend for participation. Informed consent will be obtained from the young person and their parent/carer.

If possible, research appointments will be scheduled for the same day as the young person’s next returning appointment to the clinic.

From discussion with staff in the department, there is a large cohort of children with GGE who attend the epilepsy clinic. Davidson et al. (2007) were able to recruit their sample of twenty-one participants from the same site in a six-month period. If numbers were not available from RHSC Glasgow, it may be possible to supplement with recruitment from Edinburgh RHSC.

Sample Size Justification

An estimate of the sample size required for adequate statistical power was derived based on a study by Ashworth et al. (2013). This study was chosen as its design most closely resembles the one that will be used in the current study. From the results from the verbal memory task, it was calculated that there was a medium effect size (d=0.47). On this basis a medium effect size (d=0.50) was assumed, with the error value set at 0.05 and power at 0.80, for a power calculation (Cohen,

1992). The aim for recruitment is therefore to assess twenty-seven children with GGE.

Measures

The Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999) will be used to measure IQ to ensure participants meet the inclusion criteria. In general, each subtest takes approximately 5 minutes to administer and the time taken to administer the entire battery is approximately 20 minutes.

The Children's Memory Scale (CMS) (Cohen, 1997) is a battery of nine subtests which assess children's memory abilities. The Stories and Word Lists subtests will be used to assess participants' verbal memory. The Stories test involves two short stories being read to the participant, who is then asked to repeat them verbatim. The stories will be administered in the same order to each participant. There are two sets of stories; use is dependent on the child's age, either the 9-12 or 13-16 age groups. Participants will be required to learn two short stories to a level of 90% accuracy (learning criterion), as set by Davidson et al. (2007). There will be a minimum of two learning trials, and up to a maximum of ten. Children who do not achieve the learning criterion within the maximum will be excluded from the study. Word Lists involve reading a list of 14 unrelated words to the participant who is then asked to recall as many items as possible. Items that have been missed are then repeated, and the participant again tries to recall the entire study list. Selective reminding of missed items will be provided for a maximum of ten learning trials until participants have reached 90% accuracy. Following the last learning trial, the participants' recall and recognition of the material will be tested after a thirty minute delay and then again after a one week delay. The recall and recognition scores for both stories will be combined to provide an overall score of recall and recognition respectively. The age appropriate versions of the subtests have different maximum total scores; therefore the delayed recall scores will be converted into z-scores to enable comparisons between the different versions. The CMS will take approximately 10-25 minutes to administer (depending on how many trial to criterion are required).

Actigraphy will be used as an objective measure of participants' sleep. The actigraph is a nonintrusive device that records and monitors movement for one-minute epochs through a wristwatch microprocessor link. It provides estimates of sleep and nap times based on periods of wrist immobility. Acebo et al. (1999) recommended that studies aiming to gather five nights of actigraph data for children and adolescents should record for at least one full week to ensure a reliable measurement is obtained. Five nights is adequate as a measure of sleep onset latency, number of awakenings, nocturnal restlessness and sleep efficiency. Participants will be set up with an actiwatch and given a sleep diary to complete when they complete the initial neuropsychological tests. This will take approximately 15 minutes.

Seizure frequency, epilepsy status and epilepsy medication will be recorded over the testing period. This would require parents to provide this information.

The Children's Sleep Habits Questionnaire (CSHQ) (Owens, Spirito & McGuinn, 2000) will be used as a subjective parental report of sleep. Participants will also

complete the Sleep Self Report (SSR) (Owens, Maxim, Nobile, McGuinn, & Msall, 2000). The Observer Memory Questionnaire - Parent Form (OMQ-PF) (Gonzalez et al., 2008) will be used as a subjective parental report of memory. These will each take 5-10 minutes to complete.

Design

A correlational design will be used to explore the relationship between ALF and sleep parameters.

Procedures

The WASI and subtests from the CMS will be administered. Recall and recognition will be assessed at a delay of thirty minutes after the last learning trial. During this delay participants and their parent/carer will be provided with information on how to use the actiwatches and complete the questionnaires. Participants will also be given a short break. Recall and recognition on the CMS will be tested again, seven days later. Actiwatches will be used to record sleep between the two recall/recognition time points (thirty minutes and seven days). Parents will complete sleep diaries, the CSHQ and OMQ-PF and participants will complete SSR for their return appointments. The CMS will take approximately 10 minutes and the main researcher will gather the actiwatch equipment and questionnaires and answer any questions the participants may have. The total time of the first appointment is estimated to be 60 minutes and 15 minutes for the return appointment.

Data Analysis

SPSS will be used for data analysis. Associations between variables will be examined using Pearson's correlation for normally distributed variables and Spearman's for non-normally distributed variables. Actiwatch data will be downloaded to a computer for analysis using the relevant software.

Settings and equipment

The study will take place at the Fraser of Allander Neurosciences Unit RHSC. There are approximately five actiwatches available from RHSC which could be used at any one time.

Health and Safety Issues

The study will be conducted within staffed settings during working hours. The researcher will comply with health and safety procedures of the department. The researcher will be present at all times and will remain vigilant to levels of client distress. Breaks will be provided as required by the participant. Participants will be informed that they can withdraw from the study at any time.

Ethical Issues

Ethical approval for this study will be sought from the NHS West of Scotland Research Ethics Service, the NHS GG&C R&D department, and from Glasgow

University Ethics Committee. Written consent will be obtained from participants and their parent/carer. Participants will be informed that they are free to leave the study at any point and that this will not affect any clinical treatment that they receive. Data will be coded and stored in accordance to NHS policies to ensure confidentiality.

## Financial Issues

The overall cost of the study is estimated to be £213.86.

## Timetable

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| Full Proposal for examination | **April 2014** |
| Ethics and R&D submission | **June 2014** |
| Participant recruitment | **October 2014-May 2015** |
| Data analysis | **May 2015** |
| Penultimate draft (final paper) | **June 2015** |
| Final draft | **July 2015** |

## Practical Applications

The findings from this study will enhance our understanding of the ALF phenomenon in children with epilepsy. Determining whether sleep influences ALF in children with epilepsy will have practical applications for their learning. As children with epilepsy are known to perform poorer academically than their typically developing peers, any knowledge of how their learning could be improved is helpful. Data gathered can be used to design appropriate and effective psychological and educational interventions for children with epilepsy. The findings will encourage and inform future research in this area.

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