A Longitudinal Study of Cognitive Development and Mental Health in Maltreated Children Entering Foster Care & Clinical Research Portfolio

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THE EFFECTS OF MALTREATMENT IN CHILDHOOD ON NEUROCOGNITIVE FUNCTIONING IN ADULTHOOD: SYSTEMATIC REVIEW

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ABSTRACT

Background: Childhood maltreatment (CM) is associated with a number of adverse outcomes in adulthood. Over the last two decades there has been an increasing number of studies investigating the relationship between CM and neurocognitive functioning in adulthood. This review synthesises research that have explored this association.

Methods: Fifteen eligible research studies were identified based on pre-determined inclusion and exclusion criteria. These were synthesised and described, and the quality of the studies were appraised using the Quality Assessment Tool.

Results: The results suggest that although individuals with CM score lower on many neurocognitive measures, some of these deficits can be accounted for by pre-existing factors such as childhood IQ and family socio-economical status.

Conclusions: CM should be considered as an individual risk factor alongside other important social and environmental risk factors, including cognitive ability in childhood, to understand the collative impact of early life experiences on neurocognitive functioning in adulthood.

Keywords: Childhood maltreatment, cognitive function, memory, executive function, adulthood outcomes.

INTRODUCTION

Childhood Maltreatment

The impact of childhood experiences on later physical and psychosocial functioning is widely acknowledged, and emerging evidence from the Adverse Childhood Experiences study (ACEs) continues to highlight the impact of early adversities on outcomes in adulthood (Felitti et al., 1998; McLaughlin, 2016).

Childhood maltreatment (CM), defined as exposure to neglect, emotional, physical, and/or sexual abuse (Barnett et al., 1993), can have significant consequences for the young person's development and the life they go on to lead. Exposure to maltreatment during the early years can disrupt opportunities for a typical pathway of neurocognitive development and increase susceptibility to poorer outcomes. Outcome research on survivors of CM indicates high prevalence of mental health and neurocognitive problems (Norman et al., 2012; Felitti et al., 1998; Teicher et al., 2016). Although an individual's development and emotional responses to their experiences are differentially susceptible (Belsky & Pluess, 2009), research in this area suggests that CM can lead to neural alterations and changes in the stress response system, and potentially compromise a person's psychosocial and neurocognitive functioning (Pechtel & Pizzagalli, 2011; Gunnar & Quevedo, 2007; Perry et al., 1995).

Childhood Maltreatment and the Developing Brain

The brain develops in a hierarchical manner, and early exposure to CM leads to disruptions in brain development that has downstream effects derailing normal development (Gogtay & Thompson, 2010). Research demonstrates structural and functional changes in the brain as a result of CM (Weber & Reynolds, 2004; Wilson et al., 2011).

Childhood Maltreatment and Neurocognition

The complex cortical structures that develop during childhood are responsible for neurocognitive processes such as formation of memories, attentional control, working memory, inhibition, impulse control, problem-solving, and emotional processing (Schoenberg & Scott, 2011). These important neuropsychological processes can influence how well a person is able to function in their everyday

life. Studies investigating the impact of CM on neurocognition suggest a devastating effect on these processes.

In their review, Irigaray and colleagues (2012) highlighted CM as a risk factor for both short and long-term cognitive difficulties in childhood and adulthood. The authors concluded that CM has a harmful effect on cognition even after controlling for potential confounds. Their review provided a good snapshot of the impact of CM on neurocognitive functioning in both children and adults; however, since then, there has been more recent research in the last decade exploring the relationship between CM and cognition. Malarbi and colleagues (2017) recently provided an update of the evidence for neurocognitive functioning in childhood. They found greater cognitive deficits in maltreated children than controls, with more profound difficulties in those with a post-traumatic stress disorder. An update of the evidence base for adult survivors of CM remains.

Rationale for the Current Review

The review by Irigaray and colleagues (2012) largely comprised of small and predominantly female samples, and reported outcomes mainly for individuals with experiences of sexual abuse or physical neglect. The authors stated the need for larger samples and longitudinal studies to gain a better perspective of the impact of CM on adult neurocognitive functioning. Since then, the wider recognition of ACEs has paved the way for the publication of longitudinal prospective cohort studies and other research exploring the topic of CM and neurocognition.

In light of these new emerging evidence, the current review aims to critically examine the evidence base as it currently stands for the relationship between CM and neurocognition. The specific aim of this review was to investigate the impact of CM on neurocognitive functioning in adulthood.

METHODS

The current review followed PRISMA guidelines. Initially, a literature scoping exercise was conducted to determine the feasibility and utility of undertaking this review. The searches were undertaken on Embase, MEDLINE, and PsychINFO databases. Subject headings (MeSH or thesaurus terms) and appropriate search terms were generated based on the literature outlined above and in consultation with the librarians. These were then used in each database to identify related indexing terms.

The literature scoping exercise produced a large volume of studies, and many carried out in the last decade, suggesting that the current review was viable. This exercise also indicated much research focusing on the cognitive outcomes of individuals with Borderline Personality Disorder, and Schizophrenia, in the context of CM, as well as research exploring trauma-specific cognitions. As a result, studies with such stringent participant inclusion criteria and/or specific measure of cognition were excluded from this review.

Search Strategy

The primary source of original studies was electronic database searches, followed by exploring onward citations of the included studies. A Google Scholar search was also completed for thoroughness.

Electronic Databases

The following databases were searched electronically: Embase, MEDLINE, and PsychINFO. Search terms and subject headings used in the literature scoping exercise were used to yield the results. Although subject identifiers were not identical across databases due to variations in their indices, the same keyword terms were utilized across databases. The search terms used related to neurocognitive functioning (outcome) in adults (population) with experiences of CM (exposure).

Table 1 provides details of the terms searched in titles, abstracts and keywords of all databases (Steps 1-3) and the subsequent steps carried out to narrow the search results (Steps 4-5). Due to the large volume of studies retrieved one final

step (Step 6) was undertaken to narrow the results to studies with adult subjects only. Table 2 provides details of the databases searched and their final results prior to removal of duplicates on Endnote.

Table 1. Database search strategy

STEP	SEARCH TERMS	
1	Database MESH Terms OR [child* OR infan* OR ((child* OR infan*) N3 (develop*))]	Childhood
2	Database MeSH Terms OR [(child* N3(abuse* OR neglect* OR mistreat* OR maltreat*)] OR [sex* N3(abuse*)] OR [physical* N3(abuse OR neglect* OR violen*)] OR [emotion* N3(abuse* OR neglect*)]	Maltreatment
3	Database MeSH Terms OR [cognit* N3(function* OR assess* OR impair*)] OR [cognit* OR executive function* OR decision making OR problem solving OR attention OR memory OR language OR percept* OR thinking]	Cognition
4	1 AND 2 AND 3	
5	Limit 4 to: Not Qualitative Studies, Not Books, Not Case Studies, Not Animal Studies, In English Language.	
6	5 AND exp adult/	Adults

Table 2. Databases searched and results

DATABASE	DATE SEARCHED	INTERFACE	SEARCH RESULTS
EMBASE	05/01/2018	Ovid	694
MEDLINE	05/01/2018	Ovid	171
PsychINFO	05/01/2018	EBSCOhost	578

Forward Citation

The reference lists of included studies were hand searched, and Web of Science was used to find articles citing the included studies. This generated two additional results considered suitable for inclusion. Google Scholar was searched using the terms 'Childhood Maltreatment' AND 'Cognitive Functioning'. The majority of

results generated had already been considered as part of the systematic review process. This served as a quality check indicating good coverage of literature from database searches. Two additional studies were identified through this and included in the review.

Eligibility Criteria

The following inclusion and exclusion criteria were applied to the generated results. There was no restriction placed on date of publication.

Inclusion criteria:

- Articles in English (written or translated)
- Adult population (age 18+)
- Participants with experiences of CM
- Reporting neurocognitive outcomes using standardized and validated instruments
- Statistical analysis of the relationship between CM and neurocognition

Exclusion criteria:

- Participants with neurological or other conditions such as active substance misuse which may have confounded cognitive findings
- Studies with samples of individuals with Schizophrenia, and/or Borderline Personality Disorder Systematic, or studies exploring trauma specific memories as the main outcome measure, due to the large number of studies retrieved
- Qualitative research
- Book chapters
- Case studies
- Duplicate studies

Screening Process

In total, 37 full texts were reviewed from database searches, of which 11 met the inclusion criteria, and 4 additional studies were discovered through other search methods as outlined above (See Figure 1). The eligibility of these studies were discussed and confirmed with the academic supervisor, and were all subsequently included in the review. The included studies then underwent data extraction and quality appraisal.

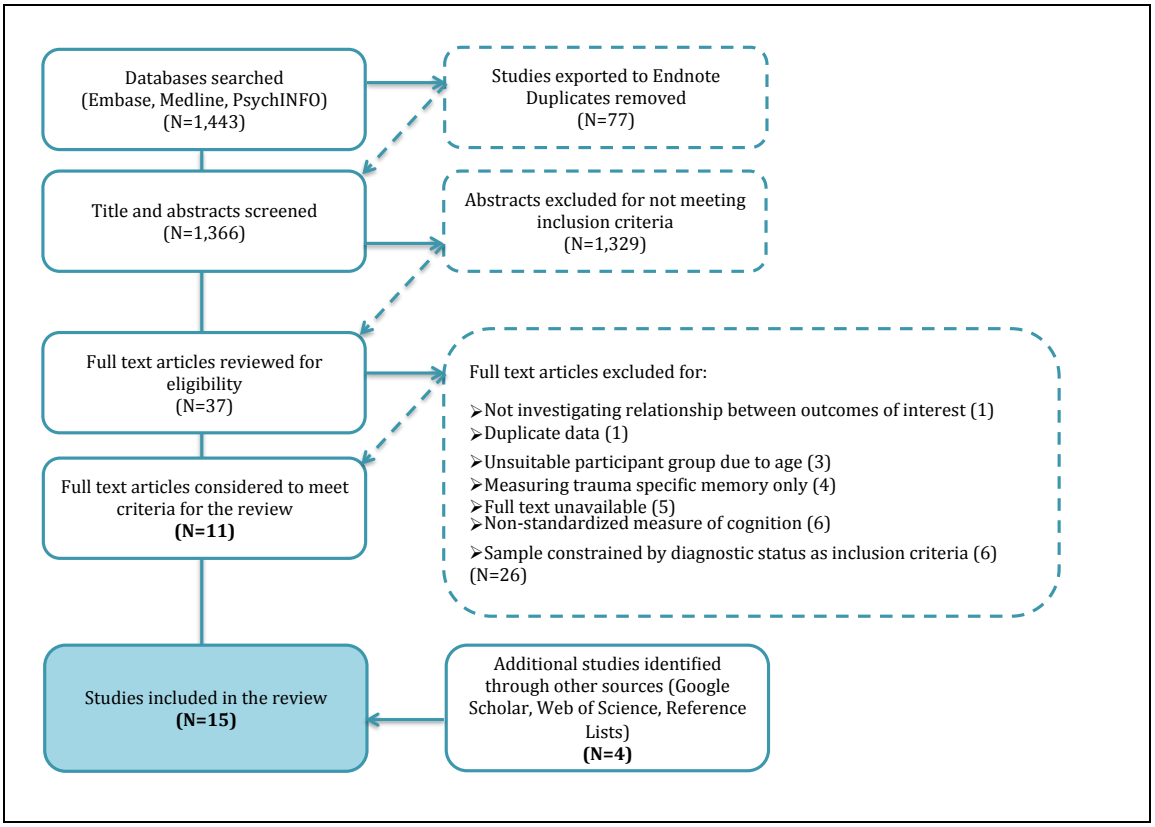

Figure 1. Flowchart of reviewing process

Data Extraction

Information describing outcomes on the relationship between CM and cognition were extracted from the studies. A narrative synthesis approach (Popay et al., 2006) was undertaken due to variability in the designs and/or measures used, making it difficult to conduct a meta-analysis of the findings.

Quality Appraisal

The majority of studies included were observational or cross-sectional studies. A recommended tool for assessing the quality of such studies is the Quality Assessment Tool (QAT) for Observational Cohort and Cross-Sectional Studies (Wardle & Steel, 2015), developed by the National Institutes of Health. The QAT rates the extent to which the results of a study can be attributed to the effects of the exposures being studied, based on fourteen questions. The studies were rated as Good, Fair, or Poor in quality, based on their overall appraisal against the QAT (See Appendix 2). To ascertain inter-rater reliability, an independent reviewer (Trainee Clinical Psychologist) rated a third of the articles (33%), selected randomly using Random.org.

RESULTS

The Studies

The fifteen articles included in the review and their collated results are outlined below. Table 3 provides a summary of the study design, its quality rating, sample characteristics, assessment measures and key findings.

Study Characteristics

The studies included in this review were published in the last two decades, with the majority being relatively new. One of the papers reported findings from two separate studies (Danese et al, 2017). The two studies outlined by Danese and colleagues (2017) and the other fourteen studies were carried out across different counties including: Brazil (1), China (1), New Zealand (1), Puerto-Rico (1), UK (2), and USA (10). These included cross-sectional (10), longitudinal prospective (3), longitudinal survey (1), and prospective-cohort (1) designs.

Quality Appraisal of Studies

Using the QAT, all studies were rated as 'Good' (See Table 3). The full scores for each study are presented in Appendix 3. Inter-rater agreement was high (87%) and discrepancies were resolved through discussion.

Study Participants

A total of 24,577 individuals (excluding controls) were included across studies. Participant ages ranged from 18-50 years, and age at the time of exposure to CM ranged from birth to 17 years. Gender distribution was 33% male and 67% female. Four studies consisted of female only samples. Twelve studies had a control comparison group, and three did not. Control groups either consisted of healthy participants, or individuals referred to as not having CM.

Study Outcome Measures

CM was measured using a range of different methods across studies, including: reviewing legal records (2); direct questioning (4) and self-report questionnaires (9). The questionnaires used are outlined in Table 3. Cognitive assessment measures also varied across studies, with some consistency in the use of Wechsler measures of intelligence and memory, and other domain specific measures (See Table 3).

Table 3. Study characteristics and key findings

STUDY		SAMPLE					MALTREATMENT	COGNITION	RESULTS	
Author, Year, Country	**Design, Quality rating**	**Age of CM**	**Sample Size**	**Age M(SD)**	**Gender**	**Control Group**	**Measurement (Types)**	**Domain (Instruments)**	**Key findings**	**After Controlling for Confounds**
Bremner 1995 USA	Cross-Sectional Study, Good	N/R	21	39.7 (7.1)	M:71% F:29%	N=20 Age & Gender Matched	ETI (Physical, sexual abuse)	IQ (WAIS-R); Memory (WMS; WAIS-R; SRT)	Significantly poorer performance for verbal episodic memory tasks, but not visual memory or IQ. Verbal memory associated with severity of abuse.	N/A
Stein 1999 USA	Cross-Sectional Study, Good	≤14	22	32.6 (6.0)	F:100%	N=20 Age & Gender Matched	Phone screening (CSA)	Memory (WAIS-R subtests); Memory and Verbal Learning (CVLT); Visual memory (BVRT); EF and Attention (TMT A B)	No difference in WAIS-R. No significant differences on any memory indexes, EF or attention.	N/A
Navalta 2006 USA	Cross-Sectional Study, Good	≤15	26	20 (N/R)	F:100%	N=19 Age: 19.40 (N/R) F:100%	TAQ (CSA Only, other types excluded)	Short-term Verbal and Visual, and Global Memory (MAS)	No differences in short-term verbal memory. IwCM scored higher in visual and global memory. Increasing duration of abuse related to increasing impairments in all scores.	N/A
Currie 2010 USA	Longitudinal Prospective Study, Good	≤11	358	41.1 (3.6)	M:45% F:55%	Matched pairs	Official records (Physical, sexual abuse, neglect)	IQ (Quick Test)	IwCM had significantly lower IQ. IwCM on lower income and with less skilled jobs. Impact more profound in female survivors.	Results as reported. Confounds: age, race, gender, family SES.
Gould 2012 USA	Cross-Sectional Study, Good	<13	60	30.2 (7.38)	M:55% F:45%	N=33 Age: 29.15 (7.88) M:80% F:20%	CTQ (Physical, sexual, emotional abuse, neglect)	Memory, Attention, Reasoning and Planning Abilities (All CANTAB)	IwCM showed more deficits in visual memory, EF and emotional processing. Neglect related to emotional processing and processing speed deficits.	N/A

Table 3. *Continued*

STUDY		SAMPLE					MALTREATMENT	COGNITION	RESULTS	
Author, Year, Country	**Design, Quality rating**	**Age of CM**	**Sample Size**	**Age M(SD)**	**Gender**	**Control Group**	**Measurement (Types)**	**Domain (Instruments)**	**Key findings**	**After Controlling for Confounds**
Lavallo 2013 USA	Cross-Sectional Study, Good	<15	386	Range: 18-30	M:42% F:58%	None	Questioning based on PTSD Scale. (N/R)	Mental Age (SILS); WM (SCWT); Impulsive Decision Making (DDQ)	Composite adversity predicted lower mental age scores. Increasing adversity related to poorer WM performance, and greater impulsivity. Preference for smaller immediate rewards in favor of larger future rewards.	Results as reported. Confounds: age, gender, education, race, depression history.
Nikulina 2013 USA	Prospective cohort design, Good	≤11	451	41 (N/R)	M:47% F:53%	N=341 Age & Gender Matched	Court Case Records (Overall CM, physical, sexual abuse, neglect)	IQ(Quick Test); EF (TMT A B); Non-Verbal reasoning (WAIS-II subtest)	CM and neglect predicted poorer EF and non-verbal reasoning, but physical and sexual abuse did not.	Results became non-significant after controlling for IQ. Confounds: Age, gender, race, IQ.
Viola 2013 Brazil	Cross Sectional Study, Good	N/R	37 All: CD	31.5 (7.8)	F:100%	N=48 All: CD Age: 28.9 (8.7) F:100%	CTQ-SF (Physical abuse, neglect)	EF (SCWT, TMT B, WAIS-II subtests); WM (WAIS-III subtest, nBACK); Verbal Fluency (Verbal fluency task); Decision Making (IGT)	IwCM performed worse on all cognitive tasks except decision-making.	N/A
Rivera-Velez 2014 Puerto Rico	Cross-Sectional Study, Good	N/R	12	29.31(4 .64)	F:100%	N=12 Age & Gender Matched	PCSASS (CSA)	Executive Function (WAIS-III subtests, TMT A, B); Attention and Concentration; (WAIS-III subtest); Short and Long-term Memory (WMS-III); Visual Memory (WMS-III, RAVLT)	IwCM showed poorer short-term and long-term visual and verbal memory, and EF. Some differences reached significance. No significant difference in attention.	N/A

Table 3. *Continued*

STUDY		SAMPLE					MALTREATMENT	COGNITION	RESULTS	
Author, Year, Country	**Design, Quality rating**	**Age of CM**	**Sample Size**	**Age M(SD)**	**Gender**	**Control Group**	**Measurement (Types)**	**Domain (Instruments)**	**Key findings**	**After Controlling for Confounds**
Dunn 2016 USA	Longitudinal Survey, Good	0-17	10,788	Range: 24-32	M:49% F:51%	None	Self-Report (Physical, sexual abuse)	Short-term Memory (RAVLT); WM (WAIS-III adapted task)	No difference in short-term memory between IwCM and IwoCM. WM better in those exposed to physical abuse during childhood, and worse in those exposed to sexual abuse during adolescence. SES exerted greater impact on cognition than CM.	Results as reported. Confounds: age, gender, race, family SES.
Geoffroy 2016 UK	Longitudinal Prospective Study, Good	≤7	8,928	50yrs	N/R	None	Direct questioning (Physical, sexual, psychological abuse, witnessing abuse, neglect)	Memory (Immediate and delayed word tests); Verbal Fluency (Verbal Fluency Test); Processing Speed (Letter Cancellation Test)	Cognition negatively associated with neglect, sexual abuse and witnessing abuse. Association between neglect and lower qualifications. No other associations.	Significance remained only for neglect. Confounds: Family SES.
Daly 2017 USA	Cross-Sectional Study, Good	N/R	66	20.36 (1.38)	M:26% F:74%	N=44 Age: 20.42 (1.28) M:32% F:68%	CTQ-SF (N/R)	IQ(WASI); EF (BRIEF-A, D-KEFS, Tower Test)	No differences in IQ. IwCM indicated problems with cognitive inhibition, switching, and metacognition. Differences approached significance for semantic and phonetic fluency. Severity of CM associated with poorer inhibition, switching and phonetic fluency.	Results as reported. Confounds: IQ, depression and anxiety symptoms.
Lu 2017 China	Cross-Sectional Study, Good	N/R	24	21.5 (3.98)	M:37% F:62%	N=24 Age & Gender Matched	CTQ (N/R)	EF (WCST; SCWT; TMT A B)	IwCM exhibited impaired EF relative to controls.	N/A

Table 3. *Continued*

STUDY		SAMPLE					MALTREATMENT	COGNITION	RESULTS	
Author, Year, Country	**Design, Quality rating**	**Age of CM**	**Sample Size**	**Age M(SD)**	**Gender**	**Control Group**	**Measurement (Types)**	**Domain (Instruments)**	**Key findings**	**After Controlling for Confounds**
Saleh 2017 USA	Cross-Sectional Study, Good	3-11	129 64: MDD 65: wMDD	32.4 (9.42)	M:36% F:64%	None	ELSQ (N/R)	EF (COWA, TMT-B, VF, SCWT); Processing Speed (WAIS-IV subtests, TMT A, SCWT); Episodic Memory (WAIS-IV subtests, BVRT, RAVLT); WM (WAIS-IV subtests)	IwCM indicated significantly poorer WM and processing speed relative to IwoCM. No difference in EF or episodic memory. No variations between depressed and non-depressed groups.	Only processing speed remained significant. Confounds: age, gender, and education.
Danese 2017 Study 1: Moffitt 2002 UK	Reporting two Longitudinal Prospective Studies, Good	≤12	2,232	18.40 (0.36)	M:47% F:53%	None	CTQ	IQ (WAIS-IV); EF (WAIS-IV); Processing Speed (CANTAB)	Significantly lower IQ, poorer EF and processing speed relative to IwoCM.	Differences no longer significant. Confounds: Childhood IQ and family SES.
Study 2: Poulton 2015 New Zealand		≤10	1,037	38yrs	N/R	None	CTQ	IQ (WAIS-IV); EF; (WAIS-IV and WMS-III subtests, CANTAB, TMT B); Processing Speed (WAIS-IV subtests, WMS-III, CANTAB, RAVLT); Memory (RAVLT); Perceptual reasoning (WAIS-IV subtests); Verbal comprehension (WAIS-IV subtests)	Significantly poorer IQ, and cognitive outcomes in all domains.	Differences no longer significant. Confounds: Childhood IQ, maternal IQ, and family SES.

BRIEF-A – Behaviour Rating Inventory of Executive Function, Adult; **BVRT**-Benton Visual Retention Task-Form; **CANTAB**-Cambridge Neuropsychological Test Automated Battery; **CD**-Cocaine Dependent; **CSA**-Childhood Sexual Abuse; **CVLT**-California Verbal Learning Test; **CM**-Childhood Maltreatment; **COWA**-Controlled Oral Word Association Test; **CTQ**-Childhood Trauma Questionnaire; **CTQ-SF**-Childhood Trauma Questionnaire-Short Form; **DDQ**-Delay discounting questionnaire; **D-KEFS**- Delis-Kaplan Executive Function System; **ETI**-Early Trauma Inventory; **ELSQ**-Early Life Stress Questionnaire; **EF**-Executive Function; **F**-Female; **IGT**-Iowa Gambling Task; **IQ**-Intelligent Quotient; **IwCM**-Individuals with experiences of Childhood Maltreatment; **IwoCM**-Individuals without experience of Childhood Maltreatment; **M**-Male; **MAS**-Memory Assessment Scale; **MMD**-Major Depressive Disorder; **N/A**-Not Applicable; **N/R**-Not Reported; **PASAT**-Paced Auditory Serial Addition Test; **PCSASS**-Physical and Childhood Sexual Abuse Short-Form; **PTSD**-Post Traumatic Stress Disorder; **QR**-Quality Rating; **RAVLT**-Rey Auditory Verbal Learning Test; **SES**-Socio-Economical Status; **SCWT**-Stroop Colour-Word Test; **SD**-Standard Deviation; **SILS**-Shipley Institute for Living Scale; **SRT**–Selective Reminding Tests; **TAQ**– Traumatic Antecedents Questionnaire; **TMT A B**–Trial Making Test A, B; **WAIS**-Wechsler Adult Intelligence Scale; **WASI**-Wechsler Abbreviated Scale of Intelligence; **WMS**-Wechsler Memory Scale; **wMMD**- without Major Depressive Disorder; **WM**-Working Memory.

Key Findings

Studies in this review looked at intelligence quotient (IQ) and specific neurocognitive abilities of individuals with experiences of CM (IwCM). Their results indicate poorer outcomes in IwCM but also highlight that other important factors such as family socio-economical status (SES) and childhood IQ could be contributing to the observed outcomes in adulthood.

CM and IQ

Five studies looked at IQ in adult survivors of CM, and showed mixed results. Whilst two report no differences (Daly et al., 2017, Bremner et al., 1995), others provide evidence for significantly poorer IQ in IwCM relative to controls (Currie et al., 2010; Danese et al., 2017). In some studies the reported differences attenuated after confounding variables including family socio-economical status (SES) (Currie et al., 2010) and pre-existing childhood IQ were considered (Danese et al., 2017). Elsewhere, Lavallo and colleagues (2013) showed a negative association between greater childhood adversity, including CM, and IQ.

CM and Memory

Ten studies investigated the impact of CM on memory. Two explored outcomes for global memory compared to controls, with one reporting no difference (Stein et al., 1999) and the other reporting better memory in Childhood Sexual Abuse (CSA) survivors (Navalta et al., 2006). Others looking at verbal and visual memory present mixed results. Relative to controls, some report significantly poorer visual and verbal memory (Rivera-Velez et al., 2014), or only verbal (Gould et al., 2012; Bremner et al., 1995) or visual memory (Navalta et al., 2006), whilst others describe no differences in visual (Bremner et al., 1995), or verbal memory (Saleh et al., 2017; Dunn et al., 2016). Navalta and colleagues (2006) reported an association between duration of CSA and poorer verbal, visual and global memory, and Bremner and colleagues (1995) showed an association between verbal memory and severity of CSA and physical abuse. Longitudinal studies following children into adulthood report poorer immediate and delayed (Geoffroy et al., 2016), and verbal memory (Danese et al., 2017) in comparison to controls. The effect for verbal memory attenuated after childhood IQ and family SES were considered.

Four studies looked specifically at working memory (WM). These reported poorer outcomes in IwCM compared to controls (Saleh et al., 2017, Lavallo et al., 2013; Viola et al., 2013), which remained despite controlling for age and years of education in one study (Lavallo et al., 2013). Relative to controls, Dunn and colleagues (2016) reported better WM in IwCM first exposed to physical abuse in late childhood, and poorer WM in those exposed to sexual abuse during adolescence.

CM and Executive Function

Ten studies investigated executive function (EF). Relative to controls, two studies reported no difference (Stein et al., 1999; Saleh et al., 2017), and eight showed significantly poorer EF (Currie et al., 2010; Danese et al., 2017; Daly et al., 2017; Rivera-Velez, et al., 2014; Viola et al., 2013; Lu et al., 2017; Gould et al., 2012; Nikulina et al., 2013). The reported differences in these studies remained after controlling for IQ in adulthood (Nikulina et al., 2013; Daly et al., 2017), but reduced after considering family SES and childhood IQ (Currie et al., 2010; Danese et al., 2017).

Looking at specific aspects of EF, Daly and colleagues (2017) described difficulties with metacognition, cognitive inhibition and switching in IwCM compared to controls. Increasing severity of maltreatment was also significantly associated with more inhibition and switching problems. Exploration of variations between maltreatment types indicated an association between poorer EF and neglect (Lu et al., 2017; Nikulina et al., 2013), but not physical abuse (Nukulina et al., 2013), and with sexual abuse in one (Rivera-Velez et al., 2014) but not another study (Nikulina, et al., 2013).

CM and Other Neurocognitive Domains

Other cognitive domains sparsely assessed include verbal fluency, processing speed, perceptual reasoning, attention, and decision-making.

Evidence for verbal comprehension/fluency is mixed. Geoffroy and colleagues (2016) associated CM with poorer verbal fluency. Daly and colleagues (2016) found no difference between IwCM and controls, despite an association between CM and phonetic fluency. Others reported poorer outcomes in IwCM relative to controls (Viola et al., 2013; Danese et al., 2017), which remained despite considering confounding factors in one of the studies (Viola et al., 2013). Nikulina and colleagues (2013) explored variations between maltreatment types after controlling for IQ in adulthood, and found that overall CM and neglect predicted poorer verbal reasoning, but physical and sexual abuse did not.

Three studies reported outcomes for processing speed. Two showed slower processing speed in IwCM compared to controls (Danese et al., 2017; Geoffroy et al., 2016), which remained even after controlling for family SES and childhood IQ in one study (Geoffroy et al., 2016). Saleh and colleagues (2017) found an association between poorer processing speed and increasing duration of abuse. Two studies explored decision-making using different assessment measures (See Table 3). Relative to controls, one reported no difference (Viola et al., 2013), whilst the other showed greater impulsivity (Lavallo et al., 2013).

Elsewhere, one study reported outcomes from the perceptual reasoning index of Wechsler Adult Intelligence Scale (Danese et al., 2017), and found poorer perceptual reasoning compared to controls, which reduced after family SES and childhood IQ were considered. Similarly, one study investigated attention in survivors of CSA using the Trials Making Test, and found no difference relative to controls (Stein et al., 1999).

DISCUSSION

In light of new and emerging evidence adding to our scientific understanding of the long-term implications of CM, this review aimed to explore the current evidence base for the impact of CM on neurocognitive function in adulthood. Fifteen studies were included in this review of which twelve were published in the last decade alone.

Key Findings

The results of this review demonstrate that despite some evidence for poorer neurocognition in the maltreated population, the deficits are not necessarily due to the experience of CM alone.

CM and IQ

Studies in this review suggest that CM elevates the risk of poorer IQ in adulthood, but that the relationship is not necessarily causal. In line with previous research, they suggest that the pathway to lower IQ in adulthood may be multifactorial, and that upstream risk factors such as low SES may be increasing vulnerability to CM (Paxson & Waldfogel, 2002), and combined with other outcomes such as poor schooling and lower childhood IQ (Breslau et al., 2001) subsequently contribute to poorer IQ in adulthood. It was difficult to establish the magnitude of the effects found due to limited information relating to average scores being reported.

CM and Specific Neurocognitive Domains

Memory is one of the most researched cognitive domains in the context of CM but with no conclusive findings. One study indicating better global memory in IwCM relative to controls (Navalta et al., 2006) consisted of a small sample of female CSA survivors with strict exclusion of other forms of CM, making it unrepresentative of the maltreated population. Similarly whilst deficits in verbal and visual memory are described, there are great inconsistencies across studies, possibly due to variations in sample characteristics.

In contrast, there is a more consistent evidence base for the impact of CM on WM and EF. These indicate poorer WM and EF ability in IwCM, which in some cases persists despite controlling for relevant confounds such as childhood IQ and family SES. Studies looking at specific EF abilities suggest greater difficulties in ability to switch between tasks or to sustain focus and inhibit certain responses. The poorer WM ability can be explained through the increased stress response in survivors of CM, which involves brain regions also involved in the control of WM function. Similarly, the ability to selectively respond to a stimulus is an important cognitive skill for regulating emotions and behaviours. Since children exposed to CM might endure highly stressful situations with limited resources, they become more susceptible to experiencing problems with switching and inhibition as adults.

The only other cognitive domain with some research evidence is processing speed. Studies exploring this indicate poorer outcomes in CM survivors. Impact of CM on other cognitive domains is not very well established. The only study reporting poorer decision-making ability was conducted with a sample of maltreated individuals with past substance dependence, therefore limiting the generalizability of its findings. Studies looking at verbal comprehension or fluency describe mixed results, and research into attention or perceptual reasoning is limited.

Type and Timing of CM and Neurocognitive Impact

Survivors of CM often experience more than one type of maltreatment making it difficult to explore the impact of different CM types. However neglect during childhood has been shown to predict poorer verbal reasoning and EF. Attentive care giving is important for the development of language and affect-regulation skills during early years of life (Landry et al., 2006), which is often absent in the context of neglect and therefore likely to result in these difficulties.

Some also suggest that age of first exposure to maltreatment potentially plays an important role in determining the extent of impact. Exposure to abuse in late childhood has been associated with better WM, and during adolescence with poorer WM. Cognitive capabilities or appraisal of experiences is more sophisticated in adolescents than children, therefore making adolescence a potentially sensitive period for the manifestation of the effects of exposure to CM on neurocognition function (Mothes et al., 2015).

Strengths & Limitations

Current Evidence Base

Clinicians and researchers have explored the predicted association between CM and cognition in a number of different ways. The status of the current evidence base has both strengths and limitations.

Firstly, over the recent years, many studies including longitudinal studies have emerged exploring cognition in adult survivors of CM. This movement towards understanding the long-term implications of CM can potentially pave the way to preventative measures being implemented. Secondly, the emerging studies provide outcomes for larger samples, making their results more reliable. All studies included in this review were rated to be of good quality based on the QAT. Thirdly, most studies consider important confounding variables providing more information on the temporal relationship of associated factors. Fourthly, some studies have explored the impact of severity, duration, and timing of CM on cognitive outcomes. Finally, although it is difficult to separate different forms of CM as they often co-exist, some studies have started to make distinctions where it has been possible. These processes add more detail to the complex picture of the impact of CM.

Despite these progressive developments however, there are a number of limitations present. Inconsistent results across studies suggest the possibility of low effect size, which the studies do not provide information on. Although most studies have similar aims, they lack homogeneity across samples and measures, making the generalizability of their results questionable. The process of establishing CM is largely variable across the studies, with some authors using self-report measures and others reviewing official legal records. This creates the potential risk of having participants with very different experiences grouped as IwCM. Additionally, different cognitive tools are utilised for measuring cognition, possibly due to clinician preferences or resource availability. Some consensus as to what measures are most suitable for measuring CM and more sensitive to picking up potentially present cognitive deficits in this population would eliminate some of the discrepancies currently present.

Current Systematic Review

This review provides a good account of the current evidence base and has a number of strengths. Firstly, the method adopted has required screening of a reasonable body of literature, and has resulted in a systematic approach to collating and synthesizing different studies. Secondly, inclusion of standardized cognitive measures was set to limit the review to studies with a higher level of quality. This was reflected in the 'Good' quality rating of all fifteen studies, with high inter-rater agreement. The QAT used for rating the quality of the studies was selected on the grounds of its suitability for cross-sectional and observational (longitudinal) studies. Finally, the majority of the studies are enhancements of previous research that have occurred in the last decade alone and were lacking at the time of the previous systematic review by Irigaray and colleagues (2013) exploring this topic.

However the current review also has a number of limitations. Firstly, albeit there was a large number of studies retrieved looking at cognition in participants identified as IwCM and a severe mental illness at the screening stage, their exclusion may have altered the reported outcomes. Secondly, although the studies included in this review supposedly explored cognition following CM, the definition of CM and age at which it first occurred varied hugely between different studies. Finally, the quality-rating tool used was recommended for the type of studies included in this review, however it did not consider some important items such as the method of statistical analysis, and therefore ratings provided should be considered in the context of the questions covered by the tool.

Recommendations for Future Research

Exposure to CM is a possible risk factor for poorer outcomes in some aspects of neurocognition in adulthood, which can be explained to some extent by other factors that increase the risk of CM in the first place, such as low SES or childhood IQ (Paxson & Waldfogel, 2002). Future research should explore the quality of life

of CM survivors, to determine the extent to which the presence of any cognitive deficits may be impacting their everyday functioning. Variations in individual susceptibility and responses to maltreating experiences should also be considered to highlight individual differences that increase vulnerability or promote resilience in response to varying doses of adversity. This review also highlighted a number of ongoing longitudinal prospective cohort studies with data on cognitive outcomes in childhood as well as adulthood in a population that is generally hard to reach. Future research could extend the results of the current review by exploring the relationship between cognitive outcomes in childhood and adulthood, and to see if this relationship is amenable to appropriate interventions. Future studies should also specify the magnitude of any effects found more clearly.

Recommendations for Clinical Practice

The long-term impact of CM should be explicitly addressed to normalize any experiences of difficulties, when working with CM survivors. The possibility of potential cognitive deficits that could hinder engagement or benefits from intervention should be readily considered and every effort should be made to use compensatory strategies to facilitate engagement or optimize usefulness of treatment as necessary. IwCM should also be supported to learn and use compensatory cognitive and emotional regulation strategies to increase their resources for managing difficult situations.

Conclusions

The results of this review suggest that IwCM are at a greater risk of experiencing cognitive deficits in adulthood; however, CM should be considered as an individual risk factor alongside other important social and environmental risk factors to understand the collative impact of early life experiences on neurocognition in adulthood. The results also suggest that young age at the time of maltreatment or reduced duration of abuse may buffer the adverse impact of early life stress on development. Reducing CM is paramount, and these findings further indicate the damaging impact of early life experience on development.

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CHAPTER 2: MAJOR RESEARCH PROJECT

A LONGITUDINAL STUDY OF COGNITIVE DEVELOPMENT AND MENTAL HEALTH IN MALTREATED CHILDREN ENTERING FOSTER CARE

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PLAIN ENGLISH SUMMARY

Background: Children entering care as a result of parental maltreatment can experience problems with cognition and mental health. Research has shown that children with experiences of maltreatment placed into institutions show great improvements in cognitive ability once they are taken into care. However, little is known about the cognitive development of children in foster care, and the relationship between their mental health when they enter care and their cognition later on.

Aims: This study aimed to better understand how children's cognition changes in the first few years of life and how much their mental health when they enter care influences their cognitive development.

Methods: Thirty-two children in foster care were assessed on three occasions to measure their mental health and monitor their cognitive development over 30 months.

Results: The results showed that children's cognitive ability does improve when they are taken to a place of greater safety; however, the developments are very small. The child's age at the time of entering care may be an important factor in determining how much cognitive development occurs. The results did not show a relationship between mental health and cognitive outcomes.

Conclusions: The results of this study emphasize the possible benefits of placing children exposed to maltreatment to a place of greater safety as early as possible to support the development of their cognitive skills.

ABSTRACT

Background: Childhood maltreatment has repeatedly been associated with poorer mental health and cognitive outcomes. Although there is evidence that maltreated children in institutions can make cognitive gains following entry-to-care, especially when entering care at a younger age, the potential for developmental catch-up is not known amongst children in foster care. Similarly, despite the established presence of poorer mental health and cognitive outcomes in this population, the relationship between mental health and cognitive development is not well understood.

Aims: This study aimed to explore the rate of cognitive development over time in a sample of maltreated children in foster care, and to investigate the relationship between mental health at entry-to-care and later cognitive function.

Methods: The sample consisted of thirty-two maltreated children, recruited for the on-going Best Services Trial. Assessments of mental health and cognition were administered following entry-to-care, and cognitive assessments were repeated after 15 and 30 months.

Results: The results suggested that childhood maltreatment is a possible risk factor for poorer cognition and that there is scope for developmental catch-up following entry-to-care, particularly for younger children. Mental health at entry-to-care did not influence subsequent cognitive ability.

Conclusions: The findings of this study highlight the potential benefits of early placement of maltreated children to a place of greater safety, in aid of supporting their cognitive development.

INTRODUCTION

It is widely accepted that early childhood experiences play a pivotal role in shaping a person's development and how they go on to operate in the world. Over the last two decades there has been a growing body of evidence demonstrating the enduring negative impact of childhood maltreatment (CM) on a range of health and mental health outcomes. CM defined as exposure to neglect, emotional, physical, and/or sexual abuse (Barnett et al., 1993), has been associated with high prevalence of psychological problems, including mental health and cognitive difficulties (Norman et al., 2012; Teicher & Samson, 2013; Gould et al., 2012; Felitti et al., 1998; Teicher et al., 2016).

Whilst any causal relationship between CM and cognitive deficits is disputed, with some arguing that cognitive problems can precede CM (Danese et al., 2017), the majority of research conducted identifies CM as a risk factor for poorer cognitive outcomes (Veltman & Browne, 2001; Malarbi et al., 2017; Irigaray et al., 2013). In a review of child maltreatment studies, Veltman & Browne (2001) reported that 75% of 65 studies found cognitive and/or intellectual delay in maltreated cohorts. Two systematic reviews looking specifically at cognition in child and adult survivors of CM also describe cognitive problems (Malarbi et al., 2017; Irigaray et al., 2013).

One of the dominant current theoretical frameworks used in services for maltreated children is Attachment Theory. This framework considers a child's access to a responsive primary attachment figure during the critical first two years of life as the catalyst promoting the infant's psychological wellbeing by developing capacities for managing stress (Bowlby, 1982), and encouraging cognitive growth (Ding et al., 2014). Exposure to CM can therefore interfere with pathways for emotional regulation and cognitive development resulting in subsequent difficulties.

From a neurosciences perspective, CM is associated with brain changes affecting a person's sensitivity to stress. Repeated maltreatment over-stimulates the developing limbic system responsible for managing stress responses (van der Kolk & Greenberg, 1987) and so brain regions with high levels of stress hormone receptor density become overactive and more vulnerable to stress induced alterations (Teicher et al., 2003). Whilst the altered stress tolerance capacity and increased sensitivity to hyper-arousal responses may initially help the child cope with unpredictable and difficult environments, it can later increase their vulnerability to mental health problems (Teicher et al., 2016). The experience of emotional difficulties can subsequently compromise cognitive functioning due to dysfunctional cognitive processes (de Haan et al., 2017) and changes in information processing capacity (Triverdi, 2006).

Although the precise incidence of child maltreatment is not known, children who are looked-after and accommodated by local authorities experience higher known exposure to this type of harm. There are currently over 93,000 children in care across the UK, over 60% of whom have been placed in care due to maltreatment (National Society for the Prevention of Cruelty to Children, 2015). Research with maltreated children in care suggests that although they show poorer cognitive outcomes when entering care, some may subsequently developmentally 'catch-up' to their peers (Rutter, 1998; Nelson et al., 2007; Ames et al., 1997; Smyke et al., 2009; O'Connor et al., 2000). Nelson and colleagues (2007) demonstrated cognitive recovery in maltreated children in institutions, with the cognitive 'gains' coinciding with entering care.

Follow-up studies of adopted children from institutions have also demonstrated improvements in social, emotional, and cognitive outcomes (Tizard, 1977; Rutter, 1998). Researchers looking at variations between children adopted before and after the age of two from institutions suggest that although improvements are found in both groups, younger children demonstrate more rapid and complete developmental catch-up (Rutter, 1998; Ames et al., 1997; Dennis, 1973). Others have linked poorer cognition in children in foster care with increasing placement instability (Proctor et al., 2011). These findings indicate that there may be a sensitive phase for early placement into care to increase the extent of cognitive gains (referred to as cognitive recovery) possible. This is in line with developmental theories, which suggest that children are more sensitive to their experiences in the first few years of life (Fahlberg, 1991; Piaget, 1953).

Despite these advances in understanding the possible impact of CM on cognition, and the scope for cognitive 'recovery', particularly in children placed in care before the age of two, the majority of existing research evidence comes from studies using retrospective measures of CM, or looking at cognitive outcomes in maltreated children in institutionalised settings. Institutions are often the context of extreme emotional and cognitive deprivation (Zeanah et al., 2003), and therefore likely to confound the relationship observed between CM and subsequent outcomes.

To our knowledge there has not been any exploration of cognitive outcomes in children placed directly into foster care following their removal from the maltreating environment. Thus, little is known about the rate of cognitive development during the early years of life in this population. Similarly, whilst poorer mental health and cognitive outcomes have been documented in survivors of CM, there has been no direct exploration of the relationship between the two. Since maltreated children entering care can experience a significant adjustment process, their mental health at entry is likely to impact their cognitive functioning. Experience of CM and cognitive deficits in this population can have critical implications for lifelong functioning and therefore need to be addressed. Given

that some parents of children exposed to CM have shown capacity to change and provide a nurturing home environment for their children (Ward et al., 2012), an improved understanding of the possible benefits of early placement of children into care and the trajectory of their subsequent development will add to the cost-benefit analysis against the prolonged placement of children in the familial context where further maltreatment may be likely.

The proposed study provides a unique opportunity to bridge this gap in understanding by using longitudinal data from a cohort of children placed in foster care. This study explored changes in the cognitive profile of maltreated children entering foster care in the first few years of life, with follow-up over 30 months, alongside the impact of their mental health at entry-to-care on their later cognitive functioning. This study will utilize data collected for the target population from the Best Services Trial (BeST^2), an ongoing randomised control trial exploring a mental health intervention for infants compared to an enhanced treatment as usual program. Children in the trial complete a thorough assessment at three intervals over 30 months covering various aspects of their neurodevelopment.

AIMS AND HYPOTHESES

PART 1: Rate of Cognitive Development Over Time

Aim: To investigate the rate of cognitive development in maltreated children over 30 months after entering foster care.

Hypothesis: There will be an improvement indicated by a recovery of cognitive development rates by 30 months.

PART 2: Relationship Between Mental Health and Cognition

Aim: To investigate the relationship between mental health outcomes at baseline and cognition 30 months after entering foster care.

Hypothesis: Poorer mental health outcomes at baseline will be associated with poorer cognition later on.

METHODS

Design

This was a longitudinal cohort study looking at cognition and mental health outcomes of maltreated children entering foster care at three time-points.

Participants

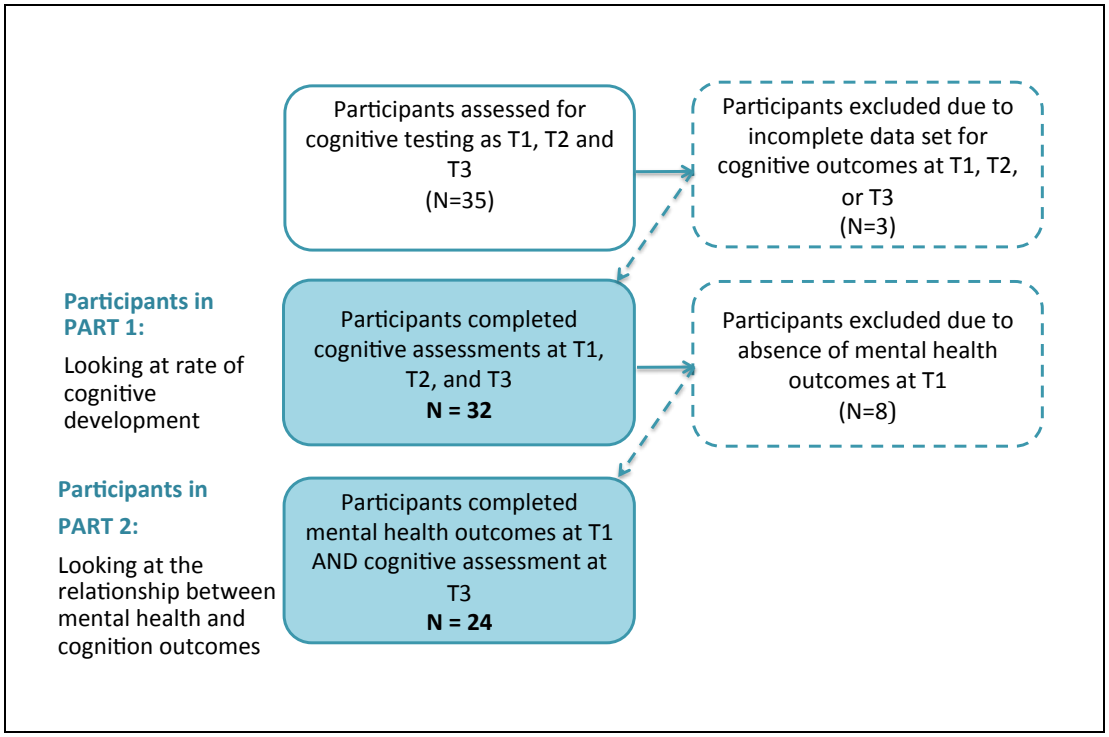
The sample consisted of thirty-five children taking part in the BeST?, an on-going randomised control trial investigating an intervention for infant mental health in Glasgow City. Participants completed assessments at three time-points: T1 (within 10 weeks from entry-to-care); T2 (after 15 months) and T3 (after 30 months). All participants with available data were included in this study.

Inclusion and exclusion criteria

Participants included in the trial met the following inclusion criteria: entering care during the first five years of life; entering care on the grounds of maltreatment; parents contactable and available to take part. Figure 1 shows the study inclusion flowchart for Parts 1 (rate of cognitive development) and 2 (relationship between mental health and cognition). The participants included in this study will have met the following additional criteria for Parts 1 and 2 of the study:

PART 1: Completed cognitive assessments at T1, T2, and T3
PART 2: Completed mental health outcomes at T1 and completed cognitive assessment at T3

Figure 1. Flowchart of study participants



From the thirty-five children in this study, thirty-two (91%) had complete data sets with no missing data at all three time-points. Data for these children were used in the first part of the study investigating rate of cognitive development over time.

Twenty-four of the thirty-five participants (69%) assessed at all three time-points had completed mental health outcomes at T1 and cognitive outcomes at T3. Data for these children were used in the second part of the study exploring the relationship between mental health and cognition.

Recruitment procedure

Recruitment for BeST? started in December 2011 and is ongoing. The BeST? Trial Study Recruitment Co-ordinator, a social worker embedded within the family placement service in Glasgow, identified all children entering foster care due to child protection concerns. The children's parents were provided information about BeST?, and those expressing an interest were subsequently approached by a research assistant for participation. The BeST? has ethical approval from the West of Scotland Research Ethics Committee. For the purposes of this study, the researcher was granted access to the data for research by the trial project coordinator (Appendix 4) and the NHS Greater Glasgow & Clyde Research & Development Department (Appendix 5).

Measures

The primary outcome measures included assessment of mental health and cognitive outcomes.

Measures of mental health:

Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997): A widely used screening measure for emotional and behavioural problems in children and adolescents. It has four subscales assessing emotional symptoms; conduct problems; hyperactivity/inattention; and peer relationship problems. These subscale scores are combined to generate a total difficulties score indicating presence of difficulties that are: close to average, slightly raised, high, or very high. The scale has an additional subscale assessing pro-social behaviour. SDQ has been validated for use with a wide age range by various studies (Goodman, 2001).

Development and Wellbeing Assessment (DAWBA) (Goodman et al., 2000): A categorical measure of psychiatric diagnosis in children and adolescents. It collects information from interviews, questionnaires and ratings through multiple sources and generates six possible diagnoses with an associated probability score for each. DAWBA has strong evidence for validity and reliability (Getward & Meltzer, 2000; Goodman et al., 2000).

Measures of cognitive functioning:

Age appropriate and developmentally relevant assessment tools were used to assess cognition at each time point, resulting in some variation in the tools used across time-points according to the child's chronological age at assessment.

Bayley Scales of Infant and Toddler Development (BSID-III) (Bayley, 2006): A comprehensive assessment tool for children measuring five key developmental domains: cognition, language, social-emotional, motor and adaptive behaviour. The scale generates a developmental quotient (DQ) to indicate a child's level of cognition. The BSID-III is recommended for use with children between 1 to 42 months old. All children under the age of 30 months were assessed using the BSID-III. At baseline, 12 children (38%) were assessed using BSID-III.

Wechsler Preschool and Primary Scale of Intelligence (WPPSI-III) (Wechsler, 1967): A commonly used measure of cognition in children that provides composite scores indicating intellectual functioning in verbal and performance domains, and a full scale intelligence quotient (IQ) for general intellectual ability. It is recommended for use with children between 30 to 91 months old. All children above the age of 30 months were assessed using the WPPSI-III. This included 20 (62%) children at baseline, and all children at T2 and T3.

Research suggests that BSID-III has a strong predictive validity for WPPSI-III (Bode et al., 2014), and both scales offer standardisation using Z Scores (see below), lending support for their use to make comparisons in scores over time.

Research procedure

Due to the longitudinal nature of this study, existing data collected as part of BeST[?] was extracted from a central database. This included outcomes for mental health (SDQ, DAWBA), and cognitive measures (BSID-III, WPPSI-III) at all three time-points.

Data analysis

Data were tested for normality of distribution by visually inspecting histograms and box-pots and considering the Shapiro-Wilk test of normality. Where assumptions of a normal distribution and homogeneity of variance were violated, non-parametric tests were used. A repeated measures approach was undertaken to investigate the rate of cognitive development longitudinally, and a linear multiple regression analysis was used to look at the relationship between mental health and cognitive outcomes. Data analysis was carried out using IBM SPSS, version 22.

RESULTS

PART 1: Rate of Cognitive Development Over Time

Thirty-two participants (53% male, 47% female) were included in this part of the study (See Table 1 for details). The participant's DQ/IQ scores from the BSID-III/WPPSI-III were used as the measure of their cognition and referred to as their full-scale intelligence quotient (FSIQ). To allow comparison of the participant's cognitive scores with normative data, the raw cognitive scores were transformed into Z-scores and summed to provide a composite score. The assumptions of normality for the cognitive data were not met, possibly due to the small sample size, and so rate of cognitive development over time was investigated using a within groups non-parametric Friedman test.

The results indicated that children's cognitive scores remained relatively similar and did not vary significantly across time-points: $\chi 2(2, N= 32) = 3.376$, $p = 0.185$. The Kendall's coefficient of concordance was used to calculate the effect size for the Friedman test (Tomczak & Tomczak, 2014). This indicated a small effect (Kendall's W: = 0.053). Descriptive exploration of mean scores indicated some variation (See Table 1), and post-hoc pairwise comparisons using Wilcoxon signed-ranks tests with a Bonferroni correction applied, showed that there was a significant difference in mean cognitive scores between T1 and T2 ($p< 0.01$), but not T1 and T3, or T2 and T3 (both $p> 0.01$) (See Figure 2).

Table 1. Demographic and clinical details of participants in Part 1

	Time 1	Time 2	Time 3
N	32	32	32
Age (months)	36.94 ± 14.28	51.72 ± 16.10	63.56 ± 13.71
FSIQ	86.21 ± 15.79	91.47 ± 16.01	90.31 ± 19.30
FSIQ - Classification	Low Average	Average	Average

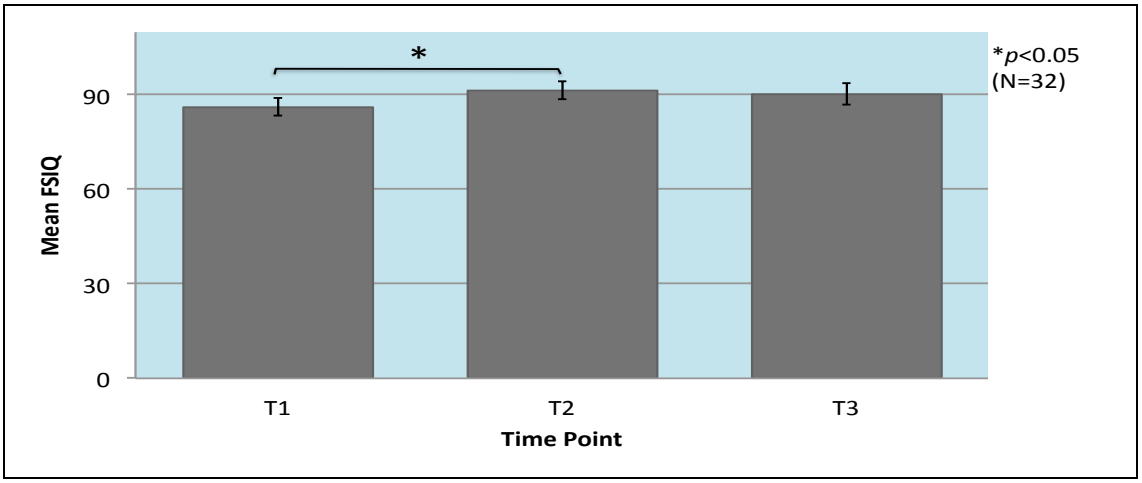


Figure 2. Mean FSIQ and standard error of the mean (error bars) at each time-point

Inspection of the individual data points indicated that although majority of the children showed cognitive gains at T2, their scores had reversed at T3 resembling their baseline cognitive scores (See Figure 3).

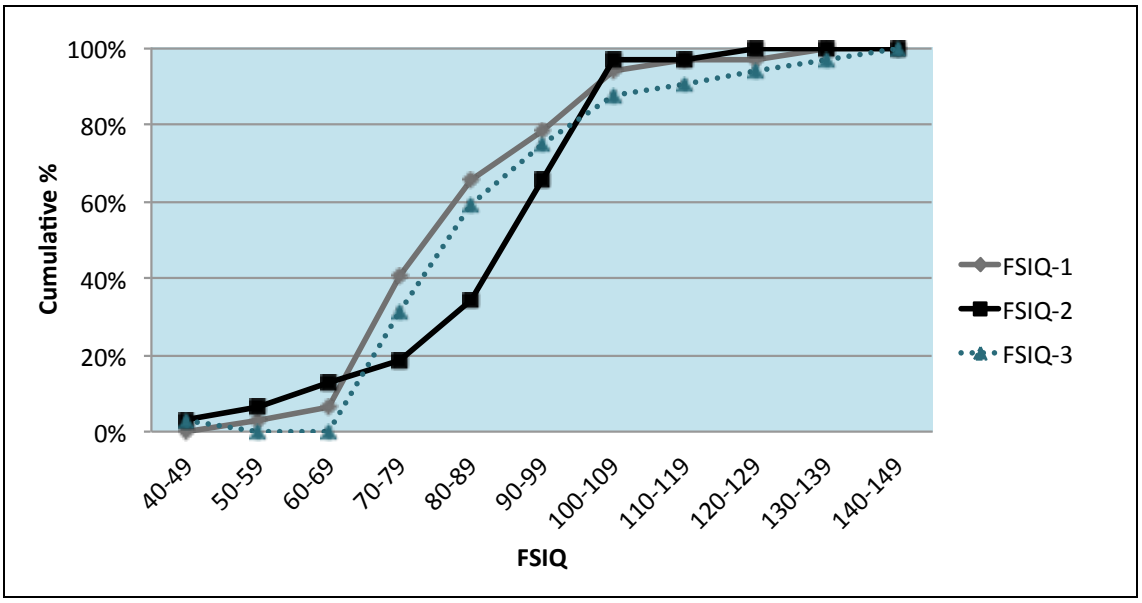


Figure 3. FSIQ for individual participants across all three time-points

Given the variation in cognitive scores over time, an additional post-hoc analysis was carried out to investigate the impact of age at entry-to-care on the trajectory of cognitive development. Thus, the participants were divided into two groups: entry-to-care before 2 years of age (below 2) and at 2 years of age and beyond (above 2). Table 2 illustrates cognitive scores for the two groups at each time-point. Independent t-tests applied showed that there was a significant difference between the groups at T2 ($p<0.05$) but not at T1 or T3 (both $p>0.05$) (See Figure 4).

Table 2. Mean FSIQ for participants in groups below and above 2 years of age over-time

		Time 1	**Time 2**	**Time 3**
Below 2 (N=9)	FSIQ	85.56 ± 8.08	97.67 ± 8.90	93.33 ± 17.55
	Classification	Low Average	Average	Average
Above 2 (N=23)	FSIQ	86.48 ± 18.09	89.04 ± 17.62	89.13 ± 20.20
	Classification	Low Average	Low Average	Low Average
	p	0.062	0.027*	0.914

*$p<.05$

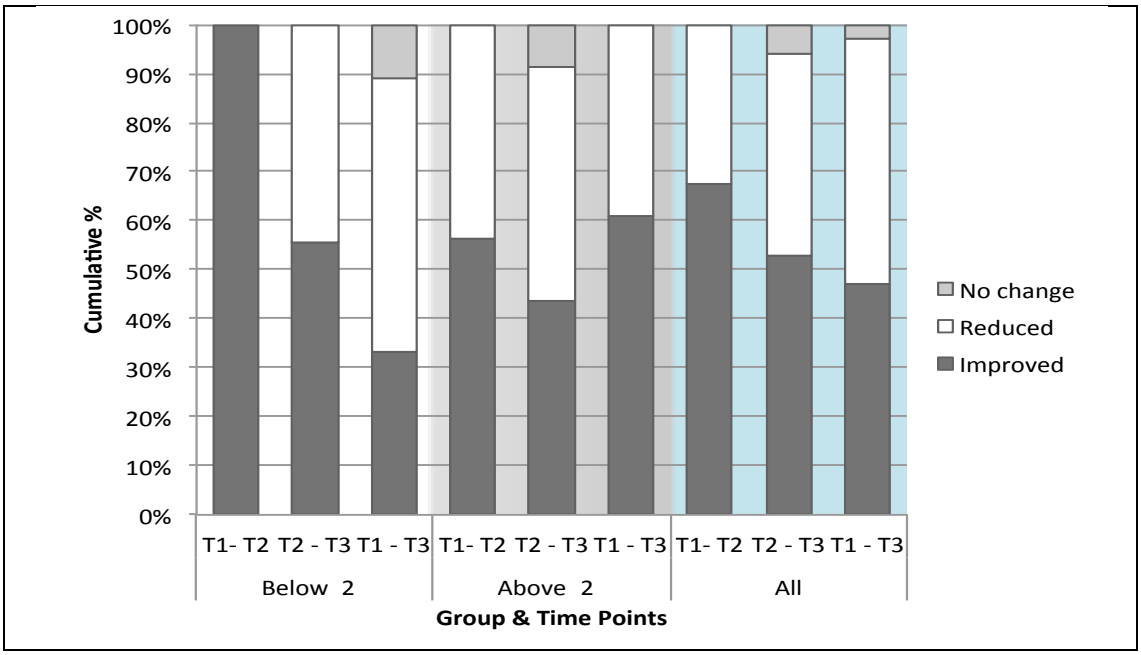


Figure 4. Percentages of participants showing change in FSIQ between time-points

In light of the changes in cognition found between baseline and the final follow-up, the children's placement stability was explored to see if increasing number of placement changes over the reporting period was related to the rate of cognitive change. From those children showing improvements between T1 and T3 (N=19, 59%) 15 had no placement changes, and 4 had one placement change. In comparison, from the children who showed poorer cognition at T3 compared to baseline (N=12, 38%), 6 had no changes, 4 had one, and 2 had two placement changes. In addition 1 (3%) participant showed no cognitive change over time, and had no placement changes.

PART 2: Relationship between Mental Health and Cognition

Twenty-four participants (50% male, 50% female) were included in this part of the study exploring the relationship between mental health at baseline and cognition at 30 months (See Table 3 for details).

Table 3. Demographic and clinical details of participants in Part 2

	Time 1	**Time 3**
Age (months)	42.00 ± 12.00	68.00 ± 12.00
FSIQ	85.80 ± 18.00	89.20 ± 19.80
FSIQ - Classification	Low Average	Low Average
SDQ	14.50 ± 8.20	
SDQ - Interpretation	Slightly Raised	
DAWBA	Yes: 14 (58%) No: 10 (42%)	

SDQ: Strength & Difficulties Questionnaire;
DAWBA: Development and Wellbeing Assessment

Descriptive results of children's mental health at baseline indicated that just over half of the children had a mental health diagnosis based on DAWBA predictions, and despite a large range on their SDQ total difficulties (1-33), their average difficulties score was only slightly raised (See Figure 3).

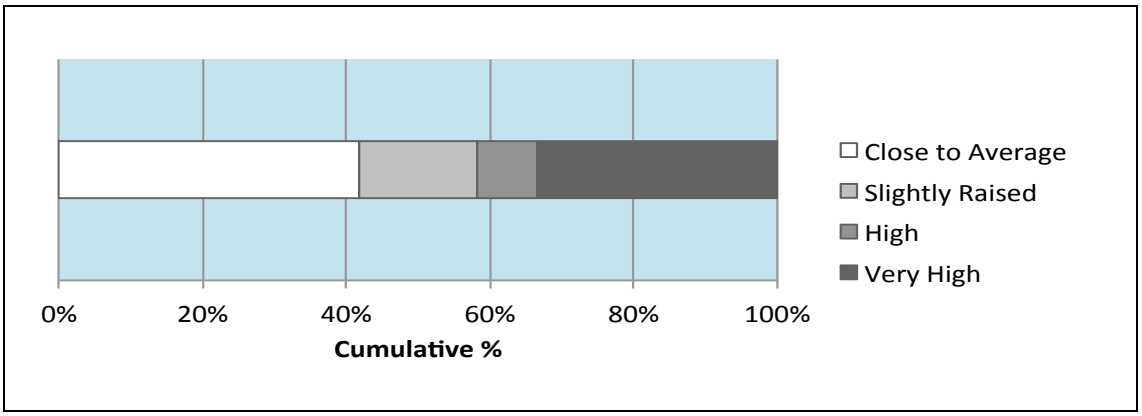


Figure 5. Degrees of difficulty on the SDQ at baseline for participants in Part 2

A multiple regression analysis was used to look at the relationship between mental health at baseline and later cognition. The DAWBA algorithm and SDQ total difficulties at T1 were used as the predictor variables and FSIQ at T3 was used as the outcome variable. Given that cognition at T1 would influence cognition at T3, it was included as an additional predictor variable. The data met assumptions for normality and there was no significant multicolinearity between the predictor variables, despite significant correlations between some predictor variables (See Table 4).

Table 4. Correlations between predictor variables at baseline

	FSIQ	**SDQ**	**DAWBA**
FSIQ	1		
SDQ	-.155*	1	
DAWBA	-.109	.631**	1

SDQ: Strength & Difficulties Questionnaire;
DAWBA: Development and Wellbeing Assessment
*p< 0.05; **p<0.01

Using the enter method, a significant model emerged: $F(3,20) = 10.547$, $p<0.05$, explaining 55% of the variance in cognition at T3 (Adjusted R2 = .555). Cognition at baseline was the only significant predictor of cognition at follow-up ($\beta=0.86$, $p<0.01$), while SDQ and DAWBA outcomes were not significant ($\beta=0.34$, $p>0.01$; $\beta=-.23$, $p>0.01$, respectively). Using G*Power, the post hoc calculation of effect size for the multiple regression analysis was large ($f^2 = 0.79$).

DISCUSSION

Key Findings

This study provides the first longitudinal data on mental health and cognitive outcomes for maltreated children entering foster care in Scotland. The aim of the present study was twofold: Firstly, to investigate the rate of cognitive development following entry to foster-care. Secondly, to establish whether mental health outcomes at entry-to-care could predict later cognitive outcomes.

Rate of Cognitive Development Over Time

In the context of previous research suggesting that children entering care after experiences of CM can developmentally 'catch-up' to their peers, it was hypothesized that there would be an improvement in the childrens cognition following entry-to-care. The results of this study indicated that there was no overall statistically significant change in children's cognition over time, possibly due to the small sample size.

A trend indicating some improvement in mean cognitive scores was observed over time as the children's mean IQ moved from the low average range relative to normative data at baseline, into the average range at follow-up assessments. However, these scores were very close to classification boundaries and did not indicate significant change. Thus this trend would suggest that children exposed to CM exhibit lower than average cognitive ability, and that their scores resemble that of other children their age once they are removed from the maltreating environment, without significant additional cognitive development. The changes noted in our sample are much smaller than that of prior research with children in institutions. These studies identify CM as a risk factor for poorer cognition, and early placement of the child in care as a protective factor for greater cognitive recovery (Tizard, 1977; Rutter, 1998; Nelson et al., 2007; Ames et al., 1997; Smyke et al., 2009; O'Connor et al., 2000).

It is possible that the non-significant rate of change identified in our study is due to the small sample size and likelihood of a Type II error; however, the difference in the extent of developmental catch-up between the results of our study and that of prior research is likely to be due to variations in the populations studied. This is reflected in the milder cognitive deficits present at baseline in our sample compared to children reared in institutionalised settings who may have been exposed to additional deprivation. Similarly, other factors from non-optimal rearing environments may also contribute to poorer cognition, beyond CM alone, such as maternal IQ and family socio-economical status (Danese et al., 2017). Alternatively, it may be that the effects found in our sample are relatively small and unstable due to the timescale of this study and that longer follow-up is required for the cumulative benefits of placement into care to have an effect.

In addition to this main finding, further exploration of the data indicated two other intriguing results. Firstly, exploration of differences between time-points indicated statistically significant cognitive development at 15 months, but not at 30 months following entry-to-care. Although the improvements observed at 15 months were possibly due to the use of different scales between T1 and T2 for some of the children, these were not maintained at 30 months, suggesting a non-linear pattern of development. To identify possible causes for this pattern, the impact of placement changes was explored, as increasing placement changes have previously been related to poorer cognition in maltreated children in foster care (Proctor et al., 2011). However, exploration of this in our sample did not reveal any meaningful patterns. It is possible that this pattern of change may be related to the effects of environmental impoverishment that the children are removed from, and the advantages of greater cognitive stimulation received whilst in foster care initially that then begins to subside by 30 months. Prior research with non-maltreated populations suggests continuous and stable development of IQ during the first two years of life (Blaga et al., 2009) and less so later in childhood (Moffitt et al., 1993).

Since our findings are the first longitudinal study of children in foster care, it was not possible to compare the emerging patterns with other research. Assessment of cognition over a longer period is warranted to determine whether this non-linear pattern continues beyond 30 months. Thus, any inferences about the generalizability of this finding should be made with caution. Alternatively, according to findings of Danese and colleagues (2017), for some children cognitive deficits precede maltreatment and therefore the relationship between CM and cognition may be bidirectional, which would explain the non-linear pattern of development observed.

Secondly, given that prior research of institutionalized children suggests age at entry-to-care plays a role in the trajectory of cognitive 'recovery' (Rutter, 1998; Ames et al., 1997; Dennis, 1973), we aimed to explore this in our sample of children in foster care. We compared children entering care before the age of 2 years with those entering care at 2 years of age and above. These comparisons indicated that younger children exhibited greater cognitive gains and higher average scores at both follow-ups, with statistically significant differences at 15 months. In line with previous research, this finding suggests that although improvements in cognitive outcomes are noted for all children (Tizard, 1977), those entering care at a younger age show more rapid and complete 'recovery' compared to older children (Rutter, 1998).

Whilst the increases in the younger group's cognitive scores over time may be partly attributed to the use of different measurements, since all of the children in the younger group were assessed using the BSID-III at baseline and WPPSI-III at follow-ups, the higher average scores compared to those entering care later

suggests that early placement into care is potentially protective against greater cognitive deficits. This difference can be understood in the context of children's cognitive and emotional development at different ages (Fahlberg, 1991; Piaget, 1953). According to developmental theories, children begin to experience social emotions such as shame or sympathy (Fahlberg, 1991), and develop cognitively through use of skills such as language (Piaget, 1953), from around the age of two. As such, our data fit with the suggestion that children entering care before the age of 2 years are more likely to show cognitive gains compared to slightly older children whose developmental capacity has already been somewhat compromised by being in a maltreating environment at a time where they are more sensitive to developing cognitively through their interactions.

Taken together, our findings may offer some partial support for the view that early placement of children in foster care is likely to be of benefit in promoting their cognitive development and consequently their future functioning and preventing longer term harm,.

Relationship between Mental Health and Cognition

To our knowledge, this is the first study to directly investigate the relationship between mental health and subsequent cognition in this population. Using a multiple regression analysis, we looked to see if children's cognitive and mental health outcomes at the time of entry-to-care could predict cognition later on. The results indicated that cognition at baseline was the greatest and only significant predictor of subsequent cognition, while mental health outcomes did not significantly influence cognition at a later time.

Although mental health problems were present in our sample of maltreated children, they were less profound than previous accounts of mental health difficulties in other studies with insitutionalised children. This is possibly related to the added deprivation that children in institutions are likely to encounter. In our sample, just over half of the children were predicted to have a mental health problem on the DAWBA and rated to show difficulties beyond average on the SDQ at baseline. It is therefore not surprising that the children's mental health status at entry-to-care did not predict their cognition later on. However, the presence of difficulties as rated on the SDQ was correlated with the children's cognitive scores at baseline and therefore may have had an indirect effect on the trajectory of their cognitive development.

Study Strengths and Limitations

We explored outcomes in children who entered foster care after being removed from the maltreating home environment and thus the outcomes are likely to be a better reflection of the impact of CM alone. Additionally, the study offers longitudinal cognitive data using validated and age specific instruments in a population that is otherwise hard to recruit for research. Albeit, the findings are

based on a small sample size and thus the results should be interpreted with caution as important significant changes may have gone undetected, the descriptive results offer useful information about the rate of change in cognition.

The small sample size in this study restricted the number and nature of statistical analysis possible and limited the inclusion of more potential confounds. Due to the small number of participants with missing data and the redundant nature of incomplete cognitive data, it was not possible to make comparisons between children with and those without complete datasets. Access to a larger pool of children available for participation is likely to result in a larger sample size, and therefore greater statistical power. Due to the time-bound nature of the current study, it was not possible to include more participants. The BeST$^{?}$ continues to assess more children, which will result in larger sample sizes in future studies.

An additional study limitation, albeit an unavoidable one, was the variability in cognitive measures used. Whilst the predictability of IQ using DQ after 24months is good, it only predicts a small part of childhood IQ during the first year of life (Dorris, 2017). Similarly, exploration of subscale level variations in cognition was not possible due to the use of different assessment tools. Although it is not currently possible to assess cognition in children of different ages using a common measure, differences in assessment may have contributed to some degree of variation in the reported outcomes. Future studies could explore cognition on more than one occasion during the period of development where the same cognitive measures can be administered. This will also be helpful in understanding the trajectory of cognitive development over shorter intervals.

Clinical Implications

The outcomes of this study have important clinical implications. Given the compromised development of children exposed to CM, professionals involved in safeguarding of these children are encouraged to prioritise the needs of the child against the parent's capacity to change for prolonging their stay at home. It may be that with appropriate support and intervention, some parents are capable of addressing difficulties which mitigate the risk of CM and can provide a nurturing home for their children; however, the timescale needed for the parents to show sufficient changes should be given great consideration to ensure the timely placement of children for the best developmental recovery possible. Those working with maltreated children and making decisions about their placement should therefore have a good awareness of the neurodevelopmental consequences of CM on the child, and the importance of timely intervention. They should also facilitate access to cognitively stimulating activities to promote children's cognitive development.

Future Directions

The findings of this study suggest that although children show some upward movement towards an average range of cognitive functioning (consistent with the extant literature), a longer follow-up period shows a non-linear pattern of recovery. Future research is needed in larger samples, and with assessment of cognition over a longer period, to confirm the detection and stability of this pattern. Similar follow-up assessments of children known to have experienced CM, and not solely relying on retrospective self-report measures, into adolescence and adulthood will also extend our understanding of the trajectory and impact on cognition in this population.

Conclusion

This study highlights the importance of early intervention in improving outcomes for maltreated children and suggests that there may be a sensitive period during which fewer cognitive deficits can be observed if the child is removed from the maltreating environment. Although the children's mental health outcomes at the time of entering care did not predict their subsequent cognitive functioning, they were related to baseline cognitive outcomes that best predicted subsequent cognition.

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APPENDICES

Appendix 1. Author Guidelines – Infant Mental Health Journal

Author Guidelines

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Appendix 2. The Quality Appraisal Tool

National Heart, Lung, and Blood Institute

Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies

Criteria	Yes	No	Other (CD, NR, NA)*
1. Was the research question or objective in this paper clearly stated?			
2. Was the study population clearly specified and defined?			
3. Was the participation rate of eligible persons at least 50%?			
4. Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants?			
5. Was a sample size justification, power description, or variance and effect estimates provided?			
6. For the analyses in this paper, were the exposure(s) of interest measured prior to the outcome(s) being measured?			
7. Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed?			
8. For exposures that can vary in amount or level, did the study examine different levels of the exposure as related to the outcome (e.g., categories of exposure, or exposure measured as continuous variable)?			
9. Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
10. Was the exposure(s) assessed more than once over time?			
11. Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants?			
12. Were the outcome assessors blinded to the exposure status of participants?			
13. Was loss to follow-up after baseline 20% or less?			
14. Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome(s)?			

Quality Rating (Good, Fair, or Poor) (see guidance)
Rater #1 initials:
Rater #2 initials:
Additional Comments (If POOR, please state why):

*CD, cannot determine; NA, not applicable; NR, not reported

Guidance for Assessing the Quality of Observational Cohort and Cross-Sectional Studies

The guidance document below is organized by question number from the tool for quality assessment of observational cohort and cross-sectional studies.

Question 1. Research question

Did the authors describe their goal in conducting this research? Is it easy to understand what they were looking to find? This issue is important for any scientific paper of any type. Higher quality scientific research explicitly defines a research question.

Questions 2 and 3. Study population

Did the authors describe the group of people from which the study participants were selected or recruited, using demographics, location, and time period? If you were to conduct this study again, would you know who to recruit, from where, and from what time period? Is the cohort population free of the outcomes of interest at the time they were recruited?

An example would be men over 40 years old with type 2 diabetes who began seeking medical care at Phoenix Good Samaritan Hospital between January 1, 1990 and December 31, 1994. In this example, the population is clearly described as: (1) who (men over 40 years old with type 2 diabetes); (2) where (Phoenix Good Samaritan Hospital); and (3) when (between January 1, 1990 and December 31, 1994). Another example is women ages 34 to 59 years of age in 1980 who were in the nursing profession and had no known coronary disease, stroke, cancer, hypercholesterolemia, or diabetes, and were recruited from the 11 most populous States, with contact information obtained from State nursing boards.

In cohort studies, it is crucial that the population at baseline is free of the outcome of interest. For example, the nurses' population above would be an appropriate group in which to study incident coronary disease. This information is usually found either in descriptions of population recruitment, definitions of variables, or inclusion/exclusion criteria.

You may need to look at prior papers on methods in order to make the assessment for this question. Those papers are usually in the reference list.

If fewer than 50% of eligible persons participated in the study, then there is concern that the study population does not adequately represent the target population. This increases the risk of bias.

Question 4. Groups recruited from the same population and uniform eligibility criteria

Were the inclusion and exclusion criteria developed prior to recruitment or selection of the study population? Were the same underlying criteria used for all of the subjects involved? This issue is related to the description of the study population, above, and you may find the information for both of these questions in the same section of the paper.

Most cohort studies begin with the selection of the cohort; participants in this cohort are then measured or evaluated to determine their exposure status. However, some cohort studies may recruit or select exposed participants in a different time or place than unexposed participants, especially retrospective cohort studies–which is when data are obtained from the past (retrospectively), but the analysis examines exposures prior to outcomes. For example, one research question could be whether diabetic men with clinical depression are at higher risk for cardiovascular disease than those without clinical depression. So, diabetic men with depression might be selected from a mental health clinic, while diabetic men without depression might be selected from an internal medicine or endocrinology clinic. This study recruits groups from different clinic populations, so this example would get a "no."

However, the women nurses described in the question above were selected based on the same inclusion/exclusion criteria, so that example would get a "yes."

Question 5. Sample size justification

Did the authors present their reasons for selecting or recruiting the number of people included or analyzed? Do they note or discuss the statistical power of the study? This question is about whether or not the study had enough participants to detect an association if one truly existed.

A paragraph in the methods section of the article may explain the sample size needed to detect a hypothesized difference in outcomes. You may also find a discussion of power in the discussion section (such as the study had 85 percent power to detect a 20 percent increase in the rate of an outcome of interest, with a 2-sided alpha of 0.05). Sometimes estimates of variance and/or estimates of effect size are given, instead of sample size calculations. In any of these cases, the answer would be "yes."

However, observational cohort studies often do not report anything about power or sample sizes because the analyses are exploratory in nature. In this case, the answer would be "no." This is not a "fatal flaw." It just may indicate that attention was not paid to whether the study was sufficiently sized to answer a prespecified question–i.e., it may have been an exploratory, hypothesis-generating study.

Question 6. Exposure assessed prior to outcome measurement

This question is important because, in order to determine whether an exposure causes an outcome, the exposure must come before the outcome.

For some prospective cohort studies, the investigator enrolls the cohort and then determines the exposure status of various members of the cohort (large epidemiological studies like Framingham used this approach). However, for other cohort studies, the cohort is selected based on its exposure status, as in the example above of depressed diabetic men (the exposure being depression). Other examples include a cohort identified by its exposure to fluoridated drinking water and then compared to a cohort living in an area without fluoridated water, or a cohort of military personnel exposed to combat in the Gulf War compared to a cohort of military personnel not deployed in a combat zone.

With either of these types of cohort studies, the cohort is followed forward in time (i.e., prospectively) to assess the outcomes that occurred in the exposed members compared to nonexposed members of the cohort. Therefore, you begin the study in the present by looking at groups that were exposed (or not) to some biological or behavioral factor, intervention, etc., and then you follow them forward in time to examine outcomes. If a cohort study is conducted properly, the answer to this question should be "yes," since the exposure status of members of the cohort was determined at the beginning of the study before the outcomes occurred.

For retrospective cohort studies, the same principal applies. The difference is that, rather than identifying a cohort in the present and following them forward in time, the investigators go back in time (i.e., retrospectively) and select a cohort based on their exposure status in the past and then follow them forward to assess the outcomes that occurred in the exposed and nonexposed cohort members. Because in retrospective cohort studies the exposure and outcomes may have already occurred (it depends on how long they follow the cohort), it is important to make sure that the exposure preceded the outcome.

Sometimes cross-sectional studies are conducted (or cross-sectional analyses of cohort-study data), where the exposures and outcomes are measured during the same timeframe. As a result, cross-sectional analyses provide weaker evidence than regular cohort studies regarding a potential causal relationship between exposures and outcomes. For cross-sectional analyses, the answer to Question 6 should be "no."

Question 7. Sufficient timeframe to see an effect

Did the study allow enough time for a sufficient number of outcomes to occur or be observed, or enough time for an exposure to have a biological effect on an outcome? In the examples given above, if clinical depression has a biological effect on increasing risk for CVD, such an effect may take years. In the other example, if higher dietary sodium increases BP, a short timeframe may be sufficient to assess its association with BP, but a longer timeframe would be needed to examine its association with heart attacks.

The issue of timeframe is important to enable meaningful analysis of the relationships between exposures and outcomes to be conducted. This often requires at least several years, especially when looking at health outcomes, but it depends on the research question and outcomes being examined.

Cross-sectional analyses allow no time to see an effect, since the exposures and outcomes are assessed at the same time, so those would get a "no" response.

Question 8. Different levels of the exposure of interest

If the exposure can be defined as a range (examples: drug dosage, amount of physical activity, amount of sodium consumed), were multiple categories of that exposure assessed? (for example, for drugs: not on the medication, on a low dose, medium dose, high dose; for dietary sodium, higher than average U.S. consumption, lower than recommended consumption, between the two). Sometimes discrete categories of exposure are not used, but instead exposures are measured as continuous variables (for example, mg/day of dietary sodium or BP values).

In any case, studying different levels of exposure (where possible) enables investigators to assess trends or dose-response relationships between exposures and outcomes–e.g., the higher the exposure, the greater the rate of the health outcome. The presence of trends or dose-response relationships lends credibility to the hypothesis of causality between exposure and outcome.

For some exposures, however, this question may not be applicable (e.g., the exposure may be a dichotomous variable like living in a rural setting versus an urban setting, or vaccinated/not vaccinated with a one-time vaccine). If there are only two possible exposures (yes/no), then this question should be given an "NA," and it should not count negatively towards the quality rating.

Question 9. Exposure measures and assessment

Were the exposure measures defined in detail? Were the tools or methods used to measure exposure accurate and reliable–for example, have they been validated or are they objective? This issue is important as it influences confidence in the reported exposures. When exposures are measured with less accuracy or validity, it is

harder to see an association between exposure and outcome even if one exists. Also as important is whether the exposures were assessed in the same manner within groups and between groups; if not, bias may result.

For example, retrospective self-report of dietary salt intake is not as valid and reliable as prospectively using a standardized dietary log plus testing participants' urine for sodium content. Another example is measurement of BP, where there may be quite a difference between usual care, where clinicians measure BP however it is done in their practice setting (which can vary considerably), and use of trained BP assessors using standardized equipment (e.g., the same BP device which has been tested and calibrated) and a standardized protocol (e.g., patient is seated for 5 minutes with feet flat on the floor, BP is taken twice in each arm, and all four measurements are averaged). In each of these cases, the former would get a "no" and the latter a "yes."

Here is a final example that illustrates the point about why it is important to assess exposures consistently across all groups: If people with higher BP (exposed cohort) are seen by their providers more frequently than those without elevated BP (nonexposed group), it also increases the chances of detecting and documenting changes in health outcomes, including CVD-related events. Therefore, it may lead to the conclusion that higher BP leads to more CVD events. This may be true, but it could also be due to the fact that the subjects with higher BP were seen more often; thus, more CVD-related events were detected and documented simply because they had more encounters with the health care system. Thus, it could bias the results and lead to an erroneous conclusion.

Question 10. Repeated exposure assessment

Was the exposure for each person measured more than once during the course of the study period? Multiple measurements with the same result increase our confidence that the exposure status was correctly classified. Also, multiple measurements enable investigators to look at changes in exposure over time, for example, people who ate high dietary sodium throughout the followup period, compared to those who started out high then reduced their intake, compared to those who ate low sodium throughout. Once again, this may not be applicable in all cases. In many older studies, exposure was measured only at baseline. However, multiple exposure measurements do result in a stronger study design.

Question 11. Outcome measures

Were the outcomes defined in detail? Were the tools or methods for measuring outcomes accurate and reliable–for example, have they been validated or are they objective? This issue is important because it influences confidence in the validity of study results. Also important is whether the outcomes were assessed in the same manner within groups and between groups.

An example of an outcome measure that is objective, accurate, and reliable is death–the outcome measured with more accuracy than any other. But even with a measure as objective as death, there can be differences in the accuracy and reliability of how death was assessed by the investigators. Did they base it on an autopsy report, death certificate, death registry, or report from a family member? Another example is a study of whether dietary fat intake is related to blood cholesterol level (cholesterol level being the outcome), and the cholesterol level is measured from fasting blood samples that are all sent to the same laboratory. These examples would get a "yes." An example of a "no" would be self-report by subjects that they had a heart attack, or self-report of how much they weigh (if body weight is the outcome of interest).

Similar to the example in Question 9, results may be biased if one group (e.g., people with high BP) is seen more frequently than another group (people with normal BP) because more frequent encounters with the health care system increases the chances of outcomes being detected and documented.

Question 12. Blinding of outcome assessors

Blinding means that outcome assessors did not know whether the participant was exposed or unexposed. It is also sometimes called "masking." The objective is to look for evidence in the article that the person(s) assessing the outcome(s) for the study (for example, examining medical records to determine the outcomes that occurred in the exposed and comparison groups) is masked to the exposure status of the participant. Sometimes the person measuring the exposure is the same person conducting the outcome assessment. In this case, the outcome assessor would most likely not be blinded to exposure status because they also took measurements of exposures. If so, make a note of that in the comments section.

As you assess this criterion, think about whether it is likely that the person(s) doing the outcome assessment would know (or be able to figure out) the exposure status of the study participants. If the answer is no, then blinding is adequate. An example of adequate blinding of the outcome assessors is to create a separate committee, whose members were not involved in the care of the patient and had no information about the study participants' exposure status. The committee would then be provided with copies of participants' medical records, which had been stripped of any potential exposure information or personally identifiable information. The committee would then review the records for prespecified outcomes according to the study protocol. If blinding was not possible, which is sometimes the case, mark "NA" and explain the potential for bias.

Question 13. Followup rate

Higher overall followup rates are always better than lower followup rates, even though higher rates are expected in shorter studies, whereas lower overall followup rates are often seen in studies of longer duration. Usually, an acceptable overall followup rate is considered 80 percent or more of participants whose exposures were measured at baseline. However, this is just a general guideline. For example, a 6-month cohort study examining the relationship between dietary sodium intake and BP level may have over 90 percent followup, but a 20-year cohort study examining effects of sodium intake on stroke may have only a 65 percent followup rate.

Question 14. Statistical analyses

Were key potential confounding variables measured and adjusted for, such as by statistical adjustment for baseline differences? Logistic regression or other regression methods are often used to account for the influence of variables not of interest.

This is a key issue in cohort studies, because statistical analyses need to control for potential confounders, in contrast to an RCT, where the randomization process controls for potential confounders. All key factors that may be associated both with the exposure of interest and the outcome–that are not of interest to the research question–should be controlled for in the analyses.

For example, in a study of the relationship between cardiorespiratory fitness and CVD events (heart attacks and strokes), the study should control for age, BP, blood cholesterol, and body weight, because all of these factors are associated both with low fitness and with CVD events. Well-done cohort studies control for multiple potential confounders.

Some general guidance for determining the overall quality rating of observational cohort and cross-sectional studies

The questions on the form are designed to help you focus on the key concepts for evaluating the internal validity of a study. They are not intended to create a list that you simply tally up to arrive at a summary judgment of quality.

Internal validity for cohort studies is the extent to which the results reported in the study can truly be attributed to the exposure being evaluated and not to flaws in the design or conduct of the study–in other words, the ability of the study to draw associative conclusions about the effects of the exposures being studied on outcomes. Any such flaws can increase the risk of bias.

Critical appraisal involves considering the risk of potential for selection bias, information bias, measurement bias, or confounding (the mixture of exposures that one cannot tease out from each other). Examples of confounding include co-interventions, differences at baseline in patient characteristics, and other issues throughout the questions above. High risk of bias translates to a rating of poor quality. Low risk of bias translates to a rating of good quality. (Thus, the greater the risk of bias, the lower the quality rating of the study.)

In addition, the more attention in the study design to issues that can help determine whether there is a causal relationship between the exposure and outcome, the higher quality the study. These include exposures occurring prior to outcomes, evaluation of a dose-response gradient, accuracy of measurement of both exposure and outcome, sufficient timeframe to see an effect, and appropriate control for confounding–all concepts reflected in the tool.

Generally, when you evaluate a study, you will not see a "fatal flaw," but you will find some risk of bias. By focusing on the concepts underlying the questions in the quality assessment tool, you should ask yourself about the potential for bias in the study you are critically appraising. For any box where you check "no" you should ask, "What is the potential risk of bias resulting from this flaw in study design or execution?" That is, does this factor cause you to doubt the results that are reported in the study or doubt the ability of the study to accurately assess an association between exposure and outcome?

The best approach is to think about the questions in the tool and how each one tells you something about the potential for bias in a study. The more you familiarize yourself with the key concepts, the more comfortable you will be with critical appraisal. Examples of studies rated good, fair, and poor are useful, but each study must be assessed on its own based on the details that are reported and consideration of the concepts for minimizing bias.

Last Updated March 2014

Appendix 3. Study quality ratings using the Quality Appraisal Tool

	STUDIES														
QUESTION NUMBER	Bremner 1995	Stein 1999	Navalta 2006	Currie 2010	Gould 2012	Lovallo 2013	Niukulina 2013	Viola 2013	Rivera-Velez 2014	Dunn 2016	Geoffroy 2016	Daly 2017	Lu 2017	Saleh 2017	Danese 2017
1	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
2	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
3	YES	C/D	YES	YES	C/D	C/D	YES	N/R	N/R	YES	YES	N/R	C/D	N/R	YES
4	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
5	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO	NO
6	YES	YES	YES	YES	C/D	C/D	YES	YES	YES	YES	YES	YES	YES	YES	YES
7	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
8	YES	NO	YES	YES	YES	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES
9	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
10	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
11	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES	YES
12	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
13	N/A	N/A	N/A	NO	N/A	N/A	YES	N/A	N/A	YES	YES	N/A	N/A	N/R	YES
14	NO	NO	NO	YES	NO	YES	YES	NO	NO	YES	YES	YES	NO	YES	YES
QUALITY RATING	GOOD	GOOD	GOOD	GOOD	GOOD	GOOD	GOOD	GOOD	GOOD	GOOD	GOOD	GOOD	GOOD	GOOD	GOOD

C/D - Cannot Determine; N/R – Not Reported; N/A – Not Applicable.

Appendix 4. Access to data from BeST^2 Coordinator

DATA ACCESS/REQUEST FORM

NAME: MARIAM TORKAMANI

UNIVERSITY/ORGANISATION: UNIVERSITY OF GLASGOW

SUPERVISOR(S): HELEN MINNIS & HAMISH MCLEOD

PROJECT TITLE: Longitudinal study of cognitive and mental health outcomes in maltreated children entering care.

PROJECT SUMMARY (INCLUDING STUDY DESIGN):

Children entering care as a result of parental maltreatment often experience problems with cognition and mental health. Although research has shown that following entry to care, maltreated children can show improvements in their mental health and cognitive functioning, very little is known about the stability of their cognitive 'recovery', and the relationship between their mental health at entry to care and cognitive functioning at a later time.

The proposed study will be a longitudinal cohort study looking at cognition and mental health of maltreated children within 10 weeks of entering care, and at 15 and 30 months following entry to care. It will explore the stability of cognitive functioning over time, and investigate the relationship between mental health at entry to care and cognitive functioning after 30 months.

NUMBER OF PARTICIPANTS:

A minimum of approximately thirty seven to forty participants.

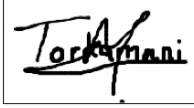
AGE OF PARTICIPANTS:

Between two to seven years old.

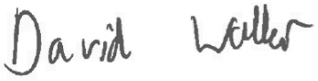
STUDY DATA REQUESTED (PLEASE TICK ALL THAT APPLY):

TIME ONE (CARE ENTRY)	TIME TWO (1 YEAR FOLLOW UP)	TIME THREE (2.5 YEAR FOLLOW UP)
CONSENT ☐	CONSENT ☐	CONSENT ☐
RANDOMISATION ☐	RANDOMISATION ☐	RANDOMISATION ☐
SDQ **X**	SDQ **X**	SDQ **X**
PIRGAS ☐	PIRGAS ☐	PIRGAS ☐
ITSEA ☐	ITSEA ☐	ITSEA ☐
DAI ☐	DAI ☐	DAI ☐
DAWBA **X**	DAWBA **X**	DAWBA **X**
SERVICE USE ☐	SERVICE USE ☐	SERVICE USE ☐

TIMB ☐ RAD QUECKLIST ☐ IRAD ☐ **WPPSI/WISC X** **BAYLEY X** **PEDS-QL X** PRQ ☐ DATA LINKAGE ☐ VIDEO DATA ☐ AUDIO DATA ☐ QUALITATIVE ☐	TIMB ☐ RAD QUECKLIST ☐ IRAD ☐ **WPPSI/WISC ☐** **BAYLEY ☐** **PEDS-QL ☐** PRQ ☐ DATA LINKAGE ☐ VIDEO DATA ☐ AUDIO DATA ☐ QUALITATIVE ☐	TIMB ☐ RAD QUECKLIST ☐ IRAD ☐ **WPPSI/WISC ☐** **BAYLEY ☐** **PEDS-QL ☐** PRQ ☐ DATA LINKAGE ☐ VIDEO DATA ☐ AUDIO DATA ☐ RAPT ☐ ACE ☐ MCS ☐ QUALITATIVE ☐
ARE YOU REQUESTING TO COLLECT ADDITIONAL MEASURES?	YES ☐ NO **X**	
IF YES, PLEASE GIVE FURTHER DETAILS **N/A**		
DATA ANALYSIS PLAN: Multilevel modelling analyses will be used to investigate the stability of cognitive scores between baseline, 15 and 30 months following entry to care. A linear multiple regression analysis will be used to investigate the relationship between mental health at entry to care and cognition after 30 months.		
TIMELINE OF PROJECT (INCLUDE START/END DATE, DATA COLLECTION/ANALYSIS PERIOD, ANY ARRANGED DEADLINES): Winter 2017 — Data collection/extraction Spring 2018 — Data analysis and write up July 2018 — Thesis submission September 2018 — Viva		
ETHICS:		

DO YOU NEED ADIDTIONAL ETHICS FOR YOUR PROJECT (E.G. INDIVIDUAL UNIVERSITY ETHICS)?	YES ☐ NO **X**
IF YES, HAVE ETHICS BEEN GRANTED?	YES ☐ NO ☐
PUBLICATIONS:	
WILL YOUR PROJECT BE PRESENTED AT ANY CONFERENCES?	YES ☐ NO ☐
IF YES, WHERE?	
WILL THE RESULTS BE SENT FOR PUBLICATION?	YES ☐ NO ☐
IF YES, WHICH JOURNAL?	
ADDITIONAL COMMENTS: **It is possible that the project results may be disseminated through presentation and/or publication. This is not yet planned and therefore details of the specific conference/journal not known.**	
APPICANTS SIGNATURE: 	**DATE:** **13/10/2017**

OFFICIAL USE ONLY:

APPROVAL FOR DATA ACCESS?	**GRANTED** X **DENIED** ☐
COMMENTS	
APPROVERS SIGNATURE: 	**DATE:** **13/10/2017**

Appendix 5. Access to data for research from NHS GG&C R&D

Coordinator/Administrator: JMcGarry/ RSyed
Telephone Number: 0141 232 1817
E-Mail: ray.syed@ggc.scot.nhs.uk
Website: www.nhsggc.org.uk/r&d

Research & Development
West Glasgow ACH
Dalnair Street
Glasgow G3 8SW

18 June 2018

Mariam Torkamani

Level 4,
Academic CAMHS,
Yorkhill Hospital,
Dalnair Street,
Glasgow
G3 8SW

Dear Ms Mariam Torkamani,

Letter of Access for Research

This letter confirms your right of access to conduct research through **NHS Greater Glasgow and Clyde** for the purpose and on the terms and conditions set out below. This right of access commences **18/06/2018** and ends on **01/02/2021** unless terminated earlier in accordance with the clauses below.

You have a right of access to conduct such research as confirmed in writing in the letter of permission for research from this NHS organisation. Please note that you cannot start the research until the Principal Investigator for the research project has received a letter from us giving permission to conduct the project.

The information supplied about your role in research at **NHS Greater Glasgow and Clyde** has been reviewed and you do not require an honorary research contract with this NHS organisation. We are satisfied that such pre-engagement checks as we consider necessary have been carried out.

You are considered to be a legal visitor to **NHS Greater Glasgow and Clyde** premises. You are not entitled to any form of payment or access to other benefits provided by this NHS organisation to employees and this letter does not give rise to any other relationship between you and this NHS organisation, in particular that of an employee.

While undertaking research through **NHS Greater Glasgow and Clyde**, you will remain accountable to your employer **The University of Glasgow** but you are required to follow the reasonable instructions of **Professor Helen Minnis** in this NHS organisation or those given on her behalf in relation to the terms of this right of access.

Where any third party claim is made, whether or not legal proceedings are issued, arising out of or in connection with your right of access, you are required to co-operate fully with any investigation by this NHS organisation in connection with any such claim and to give all such assistance as may reasonably be required regarding the conduct of any legal proceedings.

You must act in accordance with **NHS Greater Glasgow and Clyde** policies and procedures, which are available to you upon request, and the Research Governance Framework.

You are required to co-operate with **NHS Greater Glasgow and Clyde** in discharging its duties under the Health and Safety at Work etc Act 1974 and other health and safety legislation and to take reasonable care

for the health and safety of yourself and others while on **NHS Greater Glasgow and Clyde** premises. You must observe the same standards of care and propriety in dealing with patients, staff, visitors, equipment and premises as is expected of any other contract holder and you must act appropriately, responsibly and professionally at all times.

If you have a physical or mental health condition or disability which may affect your research role and which might require special adjustments to your role, if you have not already done so, you must notify your employer and the health board's HR department prior to commencing your research role at the Health board.

You are required to ensure that all information regarding patients or staff remains secure and *strictly confidential* at all times. You must ensure that you understand and comply with the requirements of the NHS Confidentiality Code of Practice (http://www.dh.gov.uk/assetRoot/04/06/92/54/04069254.pdf) and the Data Protection Act 1998. Furthermore you should be aware that under the Act, unauthorised disclosure of information is an offence and such disclosures may lead to prosecution.

You should ensure that, where you are issued with an identity or security card, a bleep number, email or library account, keys or protective clothing, these are returned upon termination of this arrangement. Please also ensure that while on the premises you wear your ID badge at all times, or are able to prove your identity if challenged. Please note that this NHS organisation accepts no responsibility for damage to or loss of personal property.

We may terminate your right to attend at any time either by giving seven days' written notice to you or immediately without any notice if you are in breach of any of the terms or conditions described in this letter or if you commit any act that we reasonably consider to amount to serious misconduct or to be disruptive and/or prejudicial to the interests and/or business of this NHS organisation or if you are convicted of any criminal offence. You must not undertake regulated activity if you are barred from such work. If you are barred from working with adults or children this letter of access is immediately terminated. Your employer will immediately withdraw you from undertaking this or any other regulated activity and you MUST stop undertaking any regulated activity immediately.

Your substantive employer is responsible for your conduct during this research project and may in the circumstances described above instigate disciplinary action against you.

NHS Greater Glasgow and Clyde will not indemnify you against any liability incurred as a result of any breach of confidentiality or breach of the Data Protection Act 1998. Any breach of the Data Protection Act 1998 may result in legal action against you and/or your substantive employer.

If your current role or involvement in research changes, or any of the information provided in your Research Passport changes, you must inform your employer through their normal procedures. You must also inform your nominated manager in this NHS organisation.

Yours sincerely

Joanne McGarry
Research Co-ordinator

Appendix 6. Major Research Project Proposal

Longitudinal study of cognitive and mental health outcomes in maltreated children entering care

ABSTRACT

Background: Children entering care as a result of parental maltreatment often experience problems with cognition and mental health. Although research has shown that following entry to care, maltreated children can show improvements in their mental health and cognitive functioning, very little is known about the stability of their cognitive 'recovery', and the relationship between their mental health at entry to care and cognitive functioning at a later time.

Aims: This study will explore the stability of cognitive functioning over time, and investigate the relationship between mental health at entry to care and cognitive functioning after 30 months.

Methods: The sample will consist of maltreated children, recruited for the on going Best Services Trial. Assessments of mental health and cognition were administered on three occasions: following entry to care, and subsequently repeated after 15 and then 30 months.

Applications: The results of this study will improve the understanding of cognitive outcomes in this population longitudinally.

INTRODUCTION

Childhood maltreatment can be defined as exposure to neglect, emotional, physical, and/or sexual abuse (Barnett, Manly, & Cicchetti, 1993). Maltreatment in children is associated with significant problems later in life. Outcome research on those surviving childhood adversity indicate higher prevalence of mental health problems and impaired cognitive profiles (Norman et al, 2012; Teicher & Samson, 2013; Gould et al, 2012; Felitti et al, 1998; Teicher et al, 2016).

Early adversity has been related to neural alterations reflecting changes in brain and stress response systems. One hypothesis explaining this association is that repeated exposure to maltreatment stimulates the developing limbic system responsible for managing responses to stress (van der Kolk & Greenberg, 1987). Subsequently, brain regions with high levels of stress hormone receptor density become more vulnerable to stress induced alterations and thus result in psychopathology (Teicher et al, 2003). The theory of evolution offers an alternative perspective. It suggests that modification of the brain as a result of early exposure to maltreatment can be potentially adaptive in facilitating survival. Accordingly, whilst the altered stress tolerance capacity and the increased sensitivity to hyper-arousal responses initially help the child cope with unpredictable and difficult environments, it can later increase their vulnerability to mental health problems (Teicher et al, 2016).

Findings from the Adverse Childhood Experiences study (ACE) indicated that multiple childhood adversity strongly predicts a range of adult health outcomes (Dong et al., 2004; Edwards et al., 2003; Felitti et al., 1998; McLaughlin, 2016).

Studies exploring factors related to the emotional wellbeing of maltreated children suggest a possible link with cognitive deficits (McLaughlin, 2016). The adverse impact of negative emotional experiences on cognitive processes can explain this, as cognition denotes high levels of information processing, which can be compromised in individuals experiencing emotional difficulties (Triveri, 2006). In a review of child maltreatment studies, Veltman & Browne (2001) reported that 75% of 65 studies showed cognitive and/or intellectual delay in the maltreated population. Others have also shown that maltreated children show emotion regulation and cognitive problems (Pechtel & Pizzagalli, 2012).

Although the incidence of child maltreatment is not known, looked after and accommodated children experience higher exposure to this type of harm. There are over 93,000 children in care across the UK, over 60% of whom have been placed in care due to maltreatment (National Society for the Prevention of Cruelty to Children, 2015). In an attempt to understand the impact of childhood maltreatment and to improve outcomes, there has been growing interest in the development of maltreated children in care.

Research suggests that although maltreated children show poorer outcomes when entering care, they can subsequently developmentally 'catch-up' to their peers (Rutter, 1998; Nelson et al., 2007; Ames et al., 1997; Smyke et al, 2009; O'Connor et al., 2000). Nelson and colleagues (2007) demonstrated cognitive recovery in children exposed to maltreatment, with the cognitive 'gains' coinciding with entering care. Others have also shown improvements in both mental health and cognitive outcomes (Fox et al., 2011; Zeanah et al., 2001).

Despite these developments in understanding the impact of childhood maltreatment on mental health and cognition, little is known about the stability of cognition, and the relationship between cognitive and emotional outcomes. Since maltreated children entering care can experience a significant adjustment process, their mental health at entry is also likely to impact their cognitive functioning.

The proposed study provides a unique opportunity to bridge this gap in understanding by using longitudinal data. This study will utilize data collected for the target population from the Best Services Trial (BeST$^?$), an ongoing randomised control trial exploring a mental health intervention for infants compared to an enhanced treatment as usual program. Children in the trial complete a thorough assessment at three intervals over 30 months covering various aspects of their neurodevelopment.

AIMS AND HYPOTHESIS

Aims

1) Investigate the stability of cognitive functioning in maltreated pre-school children over 30 months after entering foster care
2) Investigate the relationship between mental health outcomes at the time of entering care and cognitive functioning 30 months after entering foster care

Hypothesis

1) There will be an improvement in cognitive functioning at 30 months following entry to care
2) There will be a positive relationship between mental health outcomes at baseline and cognitive functioning at 30 months following entry to care

PLAN OF INVESTIGATION

Participants

The sample will consist of participants taking part in BeST$^?$. The age range for the participants will be between 6 months and 5 years. All participants in the trial, irrespective of their group allocation, will be included in this study.

Inclusion and exclusion criteria

Participants who have completed assessments at time 1 (within 10 weeks from entry to care); time 2 (after 15 months) and time 3 (after 30 months) will be included. They will have met the following inclusion criteria:

- Entering care at birth or during the first five years of life
- Entering care on the grounds of direct or sibling maltreatment only
- Parents contactable and available to take part in intervention

Recruitment procedure

Recruitment for BeST? started in December 2011 and is ongoing. The BeST? Trial Study Recruitment Co-ordinator, a social worker embedded within the family placement service in Glasgow, identified all children entering foster care due to child protection concerns. The children's parents were provided information about BeST? and those expressing an interest were subsequently approached.

Measures

The primary outcome measures will include assessment of mental health and cognitive functioning.

Measures of mental health:

Strengths and Difficulties Questionnaire (SDQ) (Goodman, 1997): A widely used screening measure for emotional and behavioural problems in children and adolescents. It has five subscales assessing emotional symptoms; conduct problems; hyperactivity/inattention; peer relationship problems and pro-social behaviour. The SDQ has been validated for use with a wide age range by various studies (Goodman, 2001).

Development and Wellbeing Assessment (DAWBA) (Goodman et al., 2000): A measure of mental health in children and adolescents. It collects information from interviews, questionnaires and ratings through parents, the young person, and their teachers. It generates six possible diagnoses with an associated probability score for each. The scale has strong evidence for validity (Getward & Meltzer, 2000; Meltzer et al, 2000).

Measures of cognitive functioning:

To measure cognition, age appropriate and developmentally relevant assessment tools are used. Therefore, cognitive functioning at the three time points may be one or a combination of the following tools, depending on the participant's chronological age at assessment.

Bayley Scales of Infant and Toddler Development (BSID-III) (Bayley, 2006): A comprehensive assessment tool for children measuring five key developmental domains: cognition, language, social-emotional, motor and adaptive behaviour. It

is recommended for use with children between 1 to 42 months old. All children under the age of 30 months were assessed using the BSID-III.

Wechsler Preschool and Primary Scale of Intelligence (WPPSI) (Wechsler, 1967): A commonly used and validated measure of cognitive functioning of children (Silverstein, 1970; Rust, 2004). It provides a subtest and composite scores indicating intellectual functioning in verbal and performance domains, and general intellectual ability. It is recommended for use with children between 30 to 91 months old. All children above the age of 30 months were assessed using the WPPSI.

Design

This will be a longitudinal cohort study looking at cognition and mental health of maltreated children within 10 weeks of entering care, and at 15 and 30 months following entry to care.

Research procedures

Due to the longitudinal nature of this study, existing data will be used and the trainee will not be involved in data collection. Their role will be to evaluate, analyse and interpret data outcomes. Relevant data collected as part of BeST[?] will be extracted from a central database, including outcomes from mental health (SDQ, DAWBA), and cognitive measures (BSID-III, WPPSI) at all three time points. Appropriate statistical analysis will be conducted to answer the research questions.

Data Analysis

A statistician at the Robertson Centre was consulted in planning the appropriate statistical techniques for the planned analyses.

Stability of cognitive functioning

Multilevel modelling analyses will be used to investigate the stability of cognitive scores between baseline, 15 and 30 months following entry to care. It is expected that cognitive scores in the same individual may be highly associated at the different time points. This statistical method allows for this association to be taken into account. Furthermore, guided by existing literature, a number of correlations will be carried out at baseline to identify any other factors that may be associated with cognitive outcomes, such as age of the child. These will be used as covariates in the analysis.

Relationship between mental health and cognition

A linear multiple regression analysis will be used to investigate the relationship between mental health at entry to care and cognition after 30 months. The analyses will take into account potential confounders such as age and gender. The predictors of variance in the regression model will be theoretically selected.

For the analysis where different measures have been used at different time points (such as the BSID-III & WPPSI), to make the results comparable, the age corrected scales for the raw scores will be used to generate the percentiles. The percentiles, as relative ranks based on normative data, will be the outcome score.

The above primary planned analyses relate to the main aims of the study. Additional exploratory analysis may be considered to look at the impact of age at the time of placement. The outcomes at 15 months (time 2) may also be explored to look at the trajectory of cognitive stability.

The Statistical Package for the Social Sciences (SPSS) version 23.0 will be used for data analysis.

Justification of sample size

The statistical programmes The Free Statistics Calculators Index (Soper, 2017) and G*Power (Faul, Erdfelder, Lang and Buchner, 2007) were used to determine the required sample size for the multilevel modelling and linear multiple regression analyses respectively. The calculations were made using a large effect size (0.35) (Cohen, 1988), and by setting the power at 0.8 and alpha at 0.05.

The power analysis calculations demonstrated that a sample size of 37 would be adequate for exploring the stability of cognition over time, and a sample size of 31 for investigating the relationship between mental health and cognitive outcomes.

In May 2017, 31 participants in the BeST$^{?}$ had completed assessment at all three time points. Due to the time bound nature of the assessment points, this number is expected to increase by the time of analyzing data for this study. Eighteen more participants are due to complete their final assessment at time 3 by February 2017, when data for this study will be analyzed.

The feasibility study for the BeST$^{?}$ Trial (Pritchett et al, 2013) predicted a 25% attrition rate between time 1 and time 3. Based on this, at least 13 more participants are expected to have a complete dataset at all three time points by then. As a result, the projected number of participants available for this study is 44 (which exceeds the sample needed).

Settings and Equipment

There are no equipment or specific setting requirements for the completion of the proposed study.

HEALTH AND SAFETY ISSUES

There are no researcher or participant safety issues identified at this stage.

ETHICAL ISSUES

The West of Scotland Ethics Committee 5 has granted ethics approval for the existing data collected as part of BeST[?]. As such this study will not require formal ethics approval. An amendment form will be submitted to inform and seek consent from the ethics committee of the researchers pending involvement.

FINANCIAL ISSUES

There are no funding or financial requirements envisaged for the completion of this research.

TIMETABLE

The preliminary timeline is expected to be as follows:

September 2016	Outline submission - submitted
December 2016	Proposal draft - submitted
April 2017	Proposal submission
May 2017	Final approval & relevant ethics applications
Autumn 2017	Relevant literature review
Winter 2017	Data collection/extraction
Spring 2018	Data analysis and write up
July 2018	Thesis submission
September 2018	Viva

PRACTICAL APPLICATIONS

The proposed study will provide a better understanding of the cognitive profile of maltreated children in the first few years of life following entry to care, and the exploration of how mental health outcomes can predict cognitive development.

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