Autobiographical and hippocampus-dependent spatial memory in depression

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Thesis declaration form

I confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

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Overview

Depression is associated with deficits in the recollection of specific autobiographical memories, a phenomenon referred to as overgeneral memory. Neither the modifiability nor the neural correlates of overgeneral memory are currently well understood. The aim of this thesis was to increase the understanding of autobiographical memory specificity and overgeneral memory in depression.

Part one of the thesis is a literature review investigating whether interventions for treating and preventing depression are effective in improving autobiographical memory specificity. Nineteen studies of varying methodological strength were identified and included in the review. There is evidence that memory specificity improves over the course of treatment for depression, but further research is required to establish the causal effects of different interventions and the effectiveness of prevention strategies.

Part two of the thesis presents an empirical study aimed at establishing the association between overgeneral memory and allocentric spatial memory as a measure of hippocampal function in depression. Depressed and non-depressed adults completed measures of autobiographical memory and allocentric spatial memory. The depression group showed impairment in autobiographical memory, but not in allocentric spatial memory, and there was no association between performance on the two memory tasks. The data was collected in the context of a joint project (Williams, 2017).

Part three of the thesis is a critical appraisal of the research. It offers reflections on study design and recruitment, benefits of a joint project, exclusion criteria and

generalizability, challenges in measuring autobiographical memory, and the role of a clinical researcher in the National Health Service.

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Part 1: Literature Review

Do interventions for treating and preventing depression improve autobiographical memory specificity?

Abstract

Aims: Depression is associated with deficits in autobiographical memory specificity (AMS). As these deficits often persist in recovery, the modifiability of AMS has been debated. The aim of this review was to establish the current evidence-base for clinical interventions in improving AMS in the treatment and prevention of depression.

Method: A systematic search of the databases PsychINFO, Medline and Embase was conducted to identify publications relevant to the research question. Nineteen controlled clinical trials and cohort studies were included in the review.

Results: Of the nineteen studies meeting inclusion criteria, fifteen reported an improvement in AMS following the intervention. The evidence for an increase in AMS was stronger for treatment than prevention studies. The evidence for the relationship between change in AMS and depressive symptoms was mixed.

Conclusions: There is evidence that AMS improves over the course of psychological treatment. The evidence from prevention studies is currently weak. Due to a lack of high-quality trials, further research is needed to establish the causal effects of interventions, the relative benefits of different treatments, and the relationship between change in AMS, depressive symptoms and other cognitive processes.

1. Introduction

1.1. Autobiographical memory retrieval

Autobiographical memory (AM) retrieval allows humans to mentally travel backwards in time and access personally experienced events from the past (Conway & Pleydell-Pearce, 2000; Tulving, 2002). AM retrieval consists of sensory, affective and cognitive material, and can vary in the level of specificity and detail accessed (Piolino, Desgranges & Eustache, 2009; Talarowska, Berk, Maes & Galecki, 2016). The Self Memory System (SMS) model of AM proposes a description of the specificity of memories reached through a hierarchical model with three interacting levels (Conway & Pleydell-Pearce, 2000). The most basic level is lifetime episodes (*Being at university*), the second level is repeated categories of events (*Parties at university*) and the third, and highest level, is specific memories (*Losing my bag at Jane's party*). When not disrupted, the SMS matches the level of specificity reached with the purpose of the memory search based on current goals and needs.

The functions of specific AM retrieval include self-continuity, social bonding, problem-solving and guiding behaviours (Bluck & Alea, 2011; Conway & Pleydell-Pearce, 2000; Talarowska et al., 2016). A number of clinical presentations are associated with disruptions in specific AM retrieval, including emotional disorders such as depression and post-traumatic stress disorder (PTSD) (Liu, Li, Xiao, Yang & Jiang, 2013; Williams et al., 2007). Improved understanding of AM retrieval in depression may provide insight for treatment and prevention of depressive disorders (Nader, Hardt & Lanius, 2013).

1.2.   Depression and autobiographical memory

Depression affects over 300 million people world-wide, and is associated with vast individual and societal suffering and cost (World Health Organisation, 2017). The emotional features of the disorder include depressed mood or loss of interest and pleasure, but depression is also associated with cognitive changes in both the content and process of AM retrieval (American Psychiatric Association, 2013; Dalgleish & Werner-Seidler, 2014; Köhler et al., 2015). A well-replicated link between depression and AM is the phenomenon of overgeneral memory (OGM), or reduced AM specificity (AMS) (Liu et al., 2013; Ono, Devilly & Shum, 2016; van Vreeswijk & de Wilde, 2004; Williams et al., 2007). OGM refers to the tendency for individuals with depression to retrieve less memories of specific events, and instead more general memories of categories of events, compared to non-depressed controls (Williams & Broadbent, 1986). This suggests that depression is associated with truncated memory retrieval before the highest, specific, level of the SMS is reached (Eade et al., 2006; Haque, Juliana, Khan & Hasking, 2014).

OGM has been replicated in a large number of studies across different depressive disorders (Liu et al., 2013; Ono et al., 2016; van Vreeswijk & de Wilde, 2004; Williams et al., 2007). The majority of studies have used the Autobiographical Memory Test (AMT), where participants are presented with a number of cue words, and for each word asked to recall a specific memory from their past within a given time frame (Williams & Broadbent, 1986). The number and valance of cue words, and the administration and time-limits, have varied between studies (Liu et al., 2013).

Retrieved memories are categorised as *specific* (events that lasted less than 24 hours), *categorical* (memories referring to a category of events), *extended* (events lasting longer than 24 hours), or *omissions* (no retrieval). Despite a small number of non-replications, the overall mean effect size of the relationship between depression and OGM is large and found across cue words of different valance (Liu et al., 2013; Williams et al., 2007). Similar findings have been replicated with other measures of AMS (Piolino et al., 2009; Sumner, Mineka & McAdams, 2013; Raes, Hermans, Williams & Eelen, 2007). OGM has also been linked with trauma and PTSD, but does not appear to be a transdiagnostic phenomenon and is generally not found in anxiety disorders (Ono et al., 2016; Williams et al., 2007).

Most theoretical models of OGM in depression have focused on the cognitive processes that may truncate AM retrieval. Williams and colleagues (2007) developed the CaR-FA-X model, which proposes that OGM is the result of memory retrieval being prematurely terminated due to a combination of capture and rumination, functional avoidance and deficits in executive function. This model has received support from a number of studies showing an association between OGM and these cognitive functions, although with variations in the strength of associations (Stewart, Hunter & Rhodes, 2017; Sumner, 2012; Sumner et al., 2014a; Williams et al., 2007).

1.3. Consequences of OGM

Whilst the association between depression and OGM is well established, the causal relationship lacks clarity. OGM does not appear to be just a symptom of depression, and has been linked with a number of adverse consequences and a worse prognosis of

the disorder (Kleim & Ehlers, 2008; Peeters, Wessel, Merckelbach & Boon-Vermeeren, 2002; Williams et al., 2007). OGM predicts future onset and symptoms of depression, and has been found both in individuals in remission and at high risk of depression (Liu et al., 2016; Rawal & Rice, 2012; Sumner et al., 2011; Sumner, Griffith & Mineka, 2010; Van Daele, Griffith, Van der Bergh & Hermans, 2014; Williams et al., 2007; Young, Bellgowan, Bodurka & Drevets, 2013). Talarowska and colleagues (2016) suggest that OGM is both a cause for, and a consequence of, depression, which could implicate OGM as a target in the treatment and prevention of depression.

OGM has been linked with deficits in problem solving, goal setting, and imagining the future (Arie, Apter, Orbach, Yefet & Zalzman, 2008; Beaman, Pushkar, Etezadi, Bye & Conway, 2007; Belcher & Kangas, 2014; Polock & Williams, 2001; Raes et al., 2005; Sarkohi, Bjärehed & Anderson, 2011; Williams et al., 2007). Reduced AMS may act as a risk and maintaining factor for depression due to the inability to rely on past experiences for problem solving (Foland-Ross & Gotlib, 2012). Repeated recall of general memories may also increase rumination and contribute to feelings of hopelessness (Hitchcock, Werner-Seidler, Blackwell & Dalgleish, 2017; Sumner et al., 2010).

OGM may impact the success of treatment for depression (Etkin, 2016). High levels of OGM have been linked with lower recovery rates, as well as reduced benefit from psychoeducation (Brittlebank et al., 1993; Van Daele, Van den Bergh, Van Audenhove, Raes & Hermans, 2013). The impact of OGM on goal setting and retention of therapeutic strategies might also influence therapeutic engagement and

outcomes (Harvey et al., 2016; Talarowska et al., 2016). Measuring OGM may provide information on whether interventions for depression are likely to be effective, and could contribute to guiding clinical interventions (Van Daele et al., 2013).

1.4. Is it possible to modify OGM?

An implication of the CaR-FA-X model is that OGM is modifiable through targeting rumination, avoidance or executive function. However, evidence for a lack of decrease in OGM following remission, has led to suggestions of OGM being a trait or vulnerability marker rather than a state feature of depression (Ahern & Semkovska, 2017; Brittlebank et al., 1993; Haddad, Harmer & Williams, 2014). Studies measuring OGM at different points in time suggest that OGM is moderately stable over time in both clinical and community samples (Hermans et al., 2008; Peeters et al., 2002; Sumner et al., 2014b).

A number of studies suggest that OGM can be manipulated in experimental settings. Brief distraction procedures aimed at reducing analytic thinking have been associated with a decrease in OGM in depressed and non-clinical populations (Raes, Watkins, Williams & Hermans, 2008; Watkins & Teasdale, 2001; 2004; Watkins, Teasdale & Williams, 2000). OGM can also be increased by inducing ruminative thinking (Crane, Barnhofer, Visser, Nightingale & Williams, 2007; Watkins, Ramponi & Barnard, 2006). Administration of hydrocortisone, which is naturally present in individuals under psychological stress, has been shown to increase OGM in non-depressed individuals (Schlosser et al., 2010; Young, Drevets, Schulkin & Erickson, 2011).

As OGM can be manipulated in the short term, it is possible that clinical interventions may also lead to changes in OGM. A number of therapeutic approaches directly target cognitive processes associated with OGM such as ruminative thinking and avoidance, including cognitive behavioural therapy (CBT) and third-wave therapies such as mindfulness-based cognitive therapy (MBCT) (Butler, Chapman, Forman & Beck, 2006). Changes in OGM might also be found as a result of changes in mood, but little is known about the impact of clinical interventions on OGM and AMS. It is possible that disturbances in AM are best targeted directly through memory training (Dalgleish & Werner-Seidler, 2014; Young et al., 2012). There is emerging evidence that targeting aspects of AM, including specificity, may have beneficial effects on depressive symptoms (Hitchcock et al., 2017). Evidence from PTSD trials suggest reductions in OGM following both general interventions and interventions targeting memory specificity (Akbarian et al., 2015; Moradi et al., 2014; Sutherland & Bryant, 2007).

The importance of understanding the modifiability of OGM and AMS is highlighted by the current challenges in treating and preventing depression (Sumner et al., 2010). Despite the availability of a range of effective interventions, current treatments for depression are effective for less than 50% of individuals, and for those who recover relapse rates are high (De Maat, Dekker, Schoevers & De Jonge, 2006; Hollon, Thase & Markowitz, 2002). Effectiveness of prevention strategies for depression is less well-established, but there is evidence that psychological interventions may prevent recurrent episodes or onset in individuals identified as being at high risk of developing depression (Biesheuvel-Leliefeld et al., 2015; Calear & Christensen, 2010; Horowitz & Garber, 2006; Spence & Shortt, 2007).

1.5. Rationale of the review

OGM is a well-replicated feature of depression, with potentially important implications for the development, course and reoccurrence of the disorder. Whilst early studies viewed OGM as a trait vulnerability marker for depression, there is evidence that OGM is amenable to change. OGM may be altered by established psychological approaches, particularly those targeting rumination and thinking style, or by targeted memory training. Given that OGM often persists following symptom reduction, it is not clear how effective current treatment and prevention strategies are in modifying OGM. To date, no review known to the author has investigated the effectiveness of treatment and preventative interventions for depression in producing changes in OGM/AMS.

1.6. Aim of the review

The aim of this review was to establish whether clinical interventions for treating and preventing depression are effective in reducing OGM and improving AMS. The relationship between change in AMS and change in depressive symptoms was also considered and discussed. Due to a lack of high quality randomised controlled trials, along with the heterogeneity of studies, meta-analysis was not performed.

2. Method

2.1. Inclusion and exclusion criteria

Publications: Publications in peer-reviewed journals and available in English were included in the review.

Studies: Intervention studies with a longitudinal design and outcome measures from at least two separate points in time were included in the review.

Participants: Studies were included regardless of the depression status of participants (including depressed, formerly depressed and non-depressed). Studies were excluded if the participants had another primary psychiatric or neurological diagnosis.

Interventions: All interventions aimed at treating or preventing depression were included, except electro-convulsive therapy (ECT) due to its potential negative impact on AM (Fraser, O'Carroll & Ebmeier, 2008). Studies in laboratory settings (such as single mood induction or a single dose of a substance) were excluded.

Outcome measures: Studies were included if they provided a measure of AMS and a measure of depressive symptoms.

2.2. Search strategy

A systematic search to identify relevant publications was conducted using the databases PsychINFO, Medline and Embase. All database searches were limited to publications between 1986, when the initial paper on OGM was published (Williams & Broadbent, 1986), and 1st December 2016. Searches were also limited to publications in English and publications on humans.

The search strategy consisted of the terms "overgeneral memory" OR "autobiographical memory" OR "memory specificity" cross-referenced with "depress*". The medical subject headings (MeSH) "autobiographical memory" and "depression" were applied where these terms were available. The search terms are presented in Table 1.

Table 1

Search terms and number of results for each database

	PsychINFO	Medline	Embase
Autobiographical memory: Free text	"autobiographical memory" *OR* "overgeneral memory" *OR* "memory specificity"		
Autobiographical memory: MeSH terms	Autobiographical memory		Not available
Depression: Free text	"depress*" (truncated to allow for multiple endings of the term)		
Depression: MeSH terms	Depression (emotion)	Depression	
Limits	Human, English language, 1986-1 December 2016		
Number of results	852	529	649
Total number of results after removing duplicates	1189		

The reference lists of all included papers were hand-searched to identify possible publications missed by the database searches. The "cited by" function in Ovid was also used to identify papers that had cited the original paper on OGM (Williams &

Broadbent, 1986) or one of the most widely cited reviews of OGM (Williams et al., 2007).

2.3.   Outcome of systematic search

The database searches were screened by one researcher. The referencing manager programme Mendeley was used to organise the results and remove duplicates. The database searches identified 1189 publications. The stages of the search and screening process are presented in *Figure 1*.
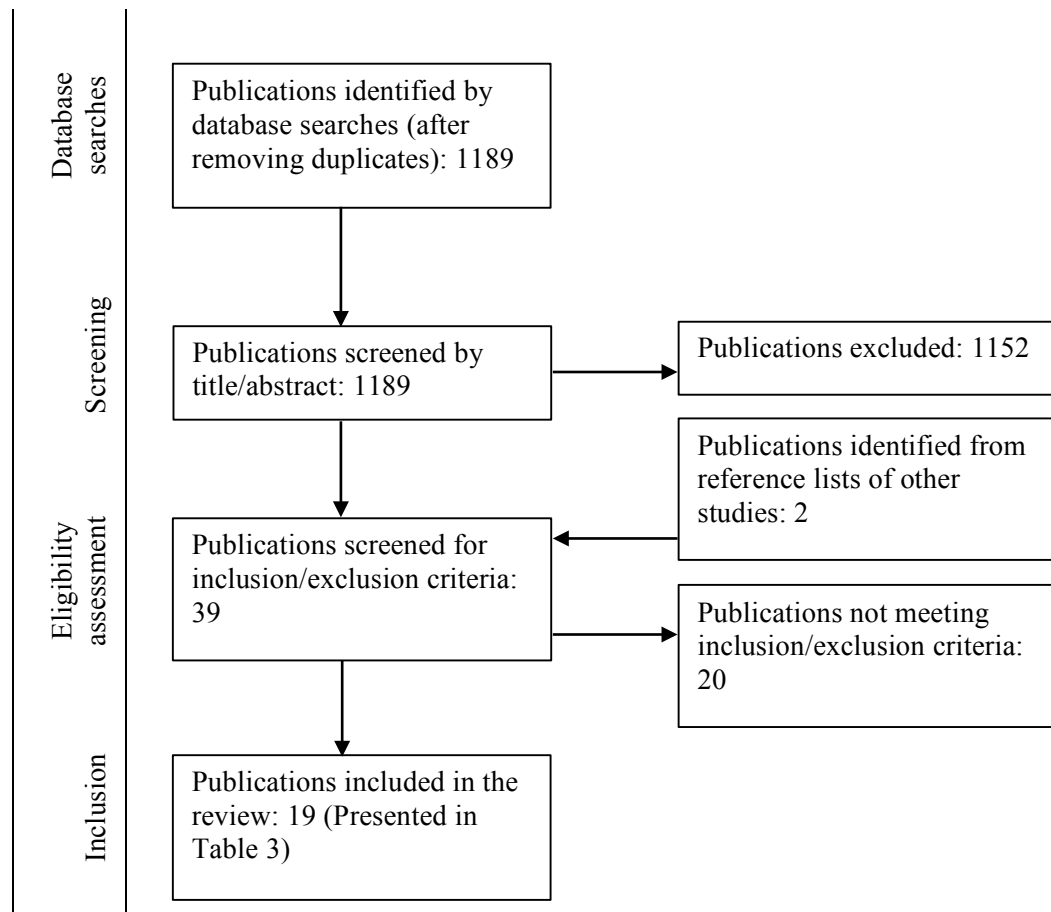
Figure 1. Flow chart of search results and screening process

In the initial selection process, publications were excluded on the basis of the title or abstract. Thirty-nine publications were screened in more depth and excluded if they did not meet the inclusion criteria (for example, not a clinical intervention, not measuring AMS, population with a different psychiatric diagnosis). One study, investigating the effect of MBCT on specificity of life goals, was excluded as it, despite measuring AMS at two points in time, only reported its correlational relationship with specificity of life-goals and not the outcomes of AMS (Crane, Winder, Hargus, Amarasinghe & Barnhofer, 2012). Nineteen studies met the inclusion criteria and were included in the review.

2.4. Data extraction

One researcher extracted the relevant study, population and intervention characteristics. A data extraction template was developed for the purpose of this review and included:

- Publication details

- Study location

- Study design

- Participant demographics

- Depression status

- Details of intervention

- Details of control condition (where applicable)

- Outcome measures

- Data analysis

- Outcomes

2.5. Quality assessment

One researcher rated the methodological quality of the included studies using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for Quantitative Studies (available at http://www.ephpp.ca/tools.html) (Thomas, Ciliska, Dobbins & Micucci, 2004). The EPHPP Quality Assessment Tool for Quantitative studies was developed to help researchers establish the quality of public health interventions when conducting systematic reviews, and has excellent inter-rater agreement (Armijo-Olivo, Stiles, Hagen, Biondo & Cummings, 2012). It was chosen for this review as it can be used across different study designs, and produces overall study ratings of *weak*, *moderate* or *strong,* which are easily accessible to the reader. Due to lack of high-quality trials regarding the current research question, no studies were excluded on the basis of the quality ratings. Quality was instead considered in the interpretation of the results.

The EPHPP Quality Assessment Tool for Quantitative Studies rates study quality across six domains including selection bias, study design, confounders, blinding, data collection methods, and withdrawal and drop-out rates. Each domain is given a rating of weak, moderate or strong based on a number of criteria. The component ratings are then used to give the study an overall quality rating of weak (two or more weak ratings), moderate (less than four strong ratings, not more than one weak rating) or strong (at least four strong ratings, no weak ratings). The tool also includes questions on intervention integrity and analysis, which are not used in the overall rating of study quality.

3. Results

3.1. Study design and quality assessment

3.1.1. Study design

The study designs for the nineteen studies included in the review were categorised using the EPHPP Quality Assessment Tool for Quantitative Studies (Thomas et al., 2004). Due to an absence of descriptions of the randomisation process in controlled studies, none of the studies qualified as a Randomised Controlled Trial (RCT). The study designs included controlled clinical trials (CCTs) (n=12), controlled cohort analytic trials (n=3) and uncontrolled cohort trials (n=4). The majority of control conditions consisted of no intervention or treatment as usual (TAU).

All studies included measures from before and after the interventions. The times between the assessments varied depending on the length of the intervention, which ranged from one (Mogoaşe, Brăilean & David, 2013) to twenty weeks (Boritz, Angus, Monette & Hollis-Walker, 2008). Five studies included additional follow-up assessment of AMS and depression, and two of depression only.

3.1.2. Quality assessment

The component and overall quality ratings of the included studies are presented in Table 2. Of the nineteen studies, five studies were given an overall rating of strong, eleven studies of moderate and three studies of weak.

Table 2

Quality assessment of included studies using the EPHPP Quality Assessment Tool for Quantitative Studies

Study	Selection Bias	Design	Confounders	Blinding	Data Collection Methods	Withdrawals & drop-outs	Overall rating
Williams et al. (2000)	Moderate	Strong	Strong	Moderate	Strong	Strong	Strong
Serrano et al. (2004)	Moderate	Strong	Strong	Moderate	Strong	Strong	Strong
McBride et al. (2007)	Moderate	Strong	Strong	Moderate	Strong	Strong	Moderate
Boritz et al. (2008)	Weak	Moderate	Weak	Moderate	Weak	Weak	Weak
Gonçalves et a. (2009)	Moderate	Strong	Strong	Moderate	Strong	Strong	Moderate
Heeren et al. (2009)	Weak	Moderate	Strong	Moderate	Strong	Strong	Moderate
Raes et al. (2009)	Weak	Moderate	N/A	Weak	Moderate	Moderate	Weak
Hargus et al. (2010)	Weak	Strong	Strong	Moderate	Strong	Strong	Moderate
Maestas & Rude (2012)	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
Serrano Selva et al. (2012)	Strong	Strong	Weak	Moderate	Strong	Strong	Moderate
Jermann et al. (2013)	Weak	Strong	Weak	Moderate	Strong	Strong	Weak
Mogoaşe et al. (2013)	Weak	Strong	Strong	Moderate	Strong	Strong	Moderate
Neshat-Doost et al. (2013)	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
Ramírez et al. (2014)	Weak	Strong	Strong	Moderate	Strong	Strong	Moderate
Latorre et al. (2015)	Moderate	Strong	Strong	Moderate	Strong	Strong	Strong
Rice et al. (2015)	Strong	Moderate	Strong	Moderate	Moderate	Strong	Moderate
Hitchcock et al. (2016)	Weak	Moderate	N/A	Moderate	Strong	Strong	Moderate
Sabatelli (2016)	Weak	Moderate	N/A	Moderate	Strong	Strong	Moderate
Eigenhuis et al. (2017)	Moderate	Moderate	N/A	Moderate	Strong	Strong	Moderate

N/A — (black)
Weak — (red)
Moderate — (yellow)
Strong — (green)

The CCTs were rated as strong for study design, and the cohort studies as moderate. Four studies were rated as strong on selection bias, and the rest as moderate or weak due to potential of bias in the recruitment process or lack of reporting. Where a control group was used, most studies were rated as strong on confounders. Three studies received a rating of weak due to group differences not being described or controlled for in the analysis. Double-blinding was not clearly described in any of the studies. The majority of studies were single-blind with the assessor being unaware of the condition of participants, and studied were rated as moderate or weak on blinding. Despite the AMT not being a standardised measure, its validity and reliability have been demonstrated (Griffith et al., 2012; Williams et al., 2007). For the purpose of this review, studies using the AMT and an established measure of depression symptoms

were given a rating of strong for data collection methods. Other measures of AMS were rated as moderate or weak. Ten studies were rated as strong on withdrawals and drop-outs, the rest receiving a rating of moderate or weak based on the reported drop-out rates or a lack of description. The overall quality ratings in the EPHPP assessment tool do not include data analysis, and it is worth noting that a weakness of the studies overall was a lack of intention to treat analysis.

3.2. Study characteristics

Key information about each of the included studies is presented in Table 3. The nineteen studies included in the review were published between 2000 and 2017.

3.2.1. Demographic characteristics

The sample sizes of studies ranged from 10 to 227, with a total number of participants across studies of 1051. Two studies were aimed at adolescents (Neshat-Doost et al., 2013; Rice et al., 2015), and two studies at undergraduate university students (Maestas & Rude, 2012; Mogoaşe et al., 2013). Five studies recruited older adults, with the mean age ranging from 65.35 to 80.7 (Gonçalves, Albuquerque & Paúl, 2009; Latorre et al., 2015; Ramírez, Ortega, Chamorro & Colmenero, 2014; Serrano, Latorre, Gatz & Montanes, 2004; Serrano Selva et al., 2012). The remaining ten studies were targeted at adults, with the mean ages ranging from 39.64 to 54.28.

Table 3

Description of study characteristics and findings

Study	Study design	Participants and setting	Depression status/history	Gender	Age	Intervention	Control condition	Measures	Statistical design	Main findings
Williams et al. (2000)	Controlled clinical trial	N=45 Adults Recruited from Community Mental Health Services United Kingdom	Remission from depression. At least 2 previous episodes, most recent within 2 years	33 female 12 male	M=44.0 SD=9.5	MBCT	TAU	AMT HRS-D	ANCOVA	◆ ○
Serrano et al. (2004)	Controlled clinical trial	N=43 Older adults Recruited through social services Spain	Symptoms of depression	33 female 10 male	M=77.19 SD=7.68	LRT	No intervention	AMT CES-D	ANOVA	◆ ○
McBride et al. (2007)	Controlled clinical trial (two treatment groups)	N=42 Adults Canada	Diagnosis of depression	29 female 13 male	M=40.71 SD=10.79	CBT Pharmacotherapy		AMT BDI-II	ANOVA	◆ ○
Boritz et al. (2008)	Cohort (analytic)	N=34 Adults Canada	Diagnosis of depression	25 female 9 male	M=39.64 SD=11.97	EFT PCT		Analysis of therapy transcripts SCID, BDI	Hierarchical linear modelling analysis	◆

Study	Study design	Participants and setting	Depression status/history	Gender	Age	Intervention	Control condition	Measures	Statistical design	Main findings
Gonçalves et al. (2009)	Controlled clinical trial	N=22 Attendees of social day-care centre Portugal	Symptoms of depression	All female	M=80.7 SD=4.5	LRT	No intervention	AMT GDS	T-tests	◆ (green) ○ (green)
Heeren et al. (2009)	Cohort (analytic)	N=36 Adults Belgium	No depression	30 female 6 male	M=54.28 SD=13.62	MBCT	No intervention	AMT BDI-II	ANOVA	◆ (green) ○ (red)
Raes et al. (2009)	Cohort (one group pre+post)	N=10 Psychiatric inpatients Belgium	Symptoms of depression	All female	M=47.40 SD=7.56	MeST		AMT, SCEPT MDQ, BDI-II	ANOVA	◆ (orange) ○ (orange)
Hargus et al. (2010)	Controlled clinical trial	N=27 Adults United Kingdom	Depression and past suicidal crisis At least 3 previous episodes of depression	18 female 9 male	M=41.89 SD=10.47	MBCT	TAU	ReSSI SCID, BDI-II	ANOVA	◆ (green) ○ (green)
Maestas & Rude (2012)	Controlled clinical trial	N=207 College students United States	No depression	70% female 30% male	M=20.9 SD=1.77	Specific expressive writing Traditional expressive writing	Control writing	AMT BDI	ANCOVA ANOVA	◆ (red) ○ (red) FU (6 months): ◆ (green) ○ (red)

Study	Study design	Participants and setting	Depression status/history	Gender	Age	Intervention	Control condition	Measures	Statistical design	Main findings
Serrano Selva et al. (2012)	Controlled clinical trial	N=37 Older adults Spain	Symptoms of depression	31 female 6 male	M=73.9	LRT	Supportive therapy	AMT MINI	PROC MIXED	◆ ◯ FU (6 weeks and 6 months): ◆ ◯
Jermann et al. (2013)	Controlled clinical trial	N=36 Adults Switzerland	Remission from depression At least 3 previous episodes	25 female 11 male	M=46.8 SD=10.5	MBCT	TAU	AMT MADRS, BDI-II	ANOVA	◆ ◯ FU (9 months): ◆ ◯
Neshat-Doost et al. (2013)	Controlled clinical trial	N=23 Bereaved refugee adolescents from Afghanistan (recruited through school) Iran	Symptoms of depression	11 female 12 male	M=14.88 SD=1.89	MeST	No contact	AMT MFQ	ANOVA Hierarchical regression	◆(green) ◯ FU (3 months): ◯(green)
Mogoaşe et al. (2013)	Controlled clinical trial	N=42 Undergraduate students Romania	Dysphoria	40 female 2 male	M=22.87 SD=4.27	Concreteness training	WL	AMT BDI-II	ANOVA	◆ ◯

Study	Study design	Participants and setting	Depression status/history	Gender	Age	Intervention	Control condition	Measures	Statistical design	Main findings
Ramírez et al. (2014)	Controlled clinical trial	N=46 Older adults attending Citizens' Day Centre Spain	No depression	29 female 17 male	M=71.18 SD=7.06	LRT/positive psychology group	Positive psychology group	AMT BDI	ANOVA	◆ ◯ FU (3 and 9 months): ◆ ◯
Latorre et al. (2015)	Controlled clinical trial	N=55 Older adults Recruited though adult education courses Spain	No depression	18 female 37 male	M=65.35 SD=8.45	LRT	Media workshop	AMT CES-D	ANOVA ANCOVA	◆ ◯
Rice et al. (2015)	Cohort (analytic)	N=227 Students recruited in schools United Kingdom	No depression	124 female 122 male	13-14	TRY CBT MBCT	No intervention	SCEPT MFQ	Linear random effects regression models	◆ ◯
Hitchcock et al. (2016)	Cohort (one group pre+post)	N=38 Adults United Kingdom	Remission from depression	30 female 8 male	M=44.32, SD=14.50	MemFlex		AMT , BDI-II	Repeated measures MANOVA	◆ ◯

Study	Study design	Participants and setting	Depression status/history	Gender	Age	Intervention	Control condition	Measures	Statistical design	Main findings
Sabatelli (2016)	Cohort (one group pre+post)	N=55 Adults United Kingdom	Depression and AMT score of less than 0.70	50% female 50% male	M=37.90 SD=8.79	MeST		●AMT BDI-II	ANOVA	◆ ○ FU (3 months): ◆ ○
Eigenhuis et al. (2017)	Cohort (one group pre+post)	N=26 Outpatients Netherlands	Depression	57.7% female 42.3% male	M=41.7 SD=9.8	MeST		AMT BDI-II, MADRS	T-tests	◆ ○ FU (3 and 9 months): ○

M: Mean, SD: Standard deviation, FU: Follow-up. **Interventions**: CBT: Cognitive behavioural therapy; EFT/PCT: Emotion focused therapy/person centred therapy; LRT: Life review therapy; MBCT: Mindfulness-based cognitive therapy; MeST: Memory specificity training; MemFlex: Memory flexibility training; TAU: Treatment as usual; TRY: Thinking about reward for young people; WL: Wait-list **Autobiographical memory measures**: AMT: Autobiographical Memory Test; SCEPT: Sentence completion for events from the past test; ReSSI: Relapse Specificty Signature Interview **Depression measures**: BDI: Beck Depression Inventory; CES-D: Centre of Epidemiological Studies – Depression; GDS: Geriatric Depression Scale; HRD-S: Hamilton Rating Scale for Depression; MADRS: Montgomery-Asberg Depression Scale; MFQ: Mood and Feelings Questionnaire; MINI: Mini International Neuropsychiatric Interview; MDQ: Major depression questionnaire; SCID: Structured Clinical Interview for DSM disorders

◆ Statistically significant change in AMS compared to control group ◆ Statistically significant change in AMS (no control group) ◆ No statistically significant change in AMS

○ Statistically significant change in depression symptoms compared to control group ○ Statistically significant change in depression symptoms (no control group)

○ No statistically significant change in depression symptoms ●Different sets of AMT cue word used at different time-points

Two studies only included women (Gonçalves et al., 2009; Raes, Williams & Hermans, 2009), and across studies 66% of the participants were female. The majority of studies were conducted in Europe, and participants were predominantly White Europeans.

3.2.2. *Depression status*

Ten studies were treatment studies targeting individuals with a current diagnosis or symptoms of depression, and nine studies were prevention studies for individuals without current symptoms of depression. Of the prevention studies, four targeted individuals in remission or with sub-clinical symptoms, whereas five targeted individuals without an identified risk for depression.

3.2.3. *Overview of measures used*

The Autobiographical Memory Test (AMT)

Sixteen of the studies used the Autobiographical Memory Test (AMT) originally developed by Williams and Broadbent (1986). The operational definition of change in AMS in this review refers to the number of memories categorised as specific.

The AMT is described in the Introduction of this review. Administration of the AMT included verbal, written and computerised versions of the task and was delivered in a number of different languages. The number of cue words used ranged from ten to eighteen. Where a novel set of cue words was used, studies reported the selection

method for these. Seven studies used only positive and negative cues, whilst the rest also included neutral words. The retrieval time-limit ranged from 30 seconds to unlimited time. Six studies specified having used different sets of cue words at different measurement times (Heeren, Van Broeck & Philippot, 2009; Hitchcock et al., 2016; Jermann et al., 2013 Maestas & Rude, 2012; Sabatelli, 2016; Williams, Teasdale, Segal & Soulsby, 2000). The rest of the studies either used the same set of cue words, or did not include details of the word lists used.

Alternative measures of AMS

Four studies used alternative measures of AMS. One study analysed transcripts of six therapy sessions, with narrative sequences identified and categorised as specific, generic or extended events (Boritz et al., 2008). A second study used a semi-structured interview regarding warning signs for a past suicidal crisis (Relapse Signature of Suicidality Interview; ReSSI) (Hargus, Crane, Barnhofer & Williams, 2010). Participants' symptom descriptions were classified as specific, extended or categorical using the AMT criteria. One study used the Sentence Completion for Events from the Past Test (SCEPT; Raes et al., 2007) (Rice et al., 2015). Participants were provided with eleven sentence stems to complete, all developed to probe a memory from the past (e.g. *I will never forget…*) and responses were classified using AMT criteria. The SCEPT was also used by Raes and colleagues (2009) in addition to the AMT.

Depression symptoms

A number of validated self-report measures of depressive symptoms were used and are presented in Table 3. As only two studies reported change in diagnostic criteria, but all studies reported change in self-report depression symptoms, the self-report scores were used to assess change in symptoms in this review.

3.3. Interventions targeting AMS: Description of interventions and outcomes

Descriptions of interventions and outcomes are organised based on whether they were general depression interventions or interventions designed to target AMS, and whether they were aimed at treatment or prevention of depression.

Eleven studies investigated the effectiveness of interventions designed to target AMS, including seven treatment studies and four prevention studies. The outcomes of these studies are presented in Table 4.

3.3.1. Interventions targeting AMS: Treatment studies

Three CCTs explored the effect of Life Review Therapy (LRT) for older adults with depression (Gonçalves et al., 2009; Serrano et al., 2004; Serrano Selva et al., 2012). The LRT protocol used in the studies was developed by Serrano and colleagues (2004) to improve retrieval of positive specific memories. All three studies used a similar structure of four to six weekly individual sessions, with each session focusing on autobiographical retrieval practice for a particular life period.

Table 4

Outcomes of interventions targeting AMS

Study	Intervention (T/P)	Assessment times	Change in AMS	Change in depression symptoms	Association between change in AMS and depression	Mediation of AMS on depression symptoms	Relationship between AMS change and other cognitive outcomes
Serrano et al. (2004)	LRT (T)	Pre + post	◆ (green)	◆ (green)	◆ (green)	◆ (red)	
Gonçalves et al. (2009)	LRT (T)	Pre + post	◆ (green)	◆ (green)	-	-	
Raes et al. (2009)	MeST (T)	Pre + post	◆ (yellow)	◆ (yellow)	-	-	Changes in AMS correlated with changes in rumination, experiential avoidance and problem-solving.
Ramírez et al. (2009)	LRT (P)	Pre + post 4 month FU	◆ (green) ◆ (red)	◆ (green) ◆ (red)	-	-	
Maestas & Rude (2012)	Creative writing (P)	Pre 1 month FU 6 month FU	◆ (red) ◆ (green)	◆ (red) ◆ (red)	◆ (red)	-	Avoidance mediated change in AMS. Rumination did not mediate change in AMS.
Serrano Selva et al. (2012)	LRT (T)	Pre+post 6 week FU 6 month FU	◆ (red)	◆ (red)	◆ (green)	-	
Neshat-Doost et al. (2013)	MeST (T)	Pre + post 2 month FU	◆ (green)	◆ (red) ◆ (green)	◆ (green)	◆ (green)	
Latorre et al. (2015)	LRT (P)	Pre + post	◆ (green)	◆ (green)	◆ (red)		
Hitchcock et al. (2016)	MemFlex (P)		◆ (yellow)	◆ (red)	-	-	

Study	Intervention (T/P)	Assessment times	Change in AMS	Change in depression symptoms	Association between change in AMS and depression	Mediation of AMS on depression symptoms	Relationship between AMS change and other cognitive outcomes
Sabatelli et al. (2016)	MeST (T)	Pre + post	♦	♦	-	-	
		3 month FU	♦	♦			
Eigenhuis et al. (2017)	MeST (T)	Pre + post	♦	♦	-	-	
		3 month FU		♦			

T: Treatment, P: Prevention, FU: Follow-up, LRT: Life review therapy, MeST: Memory specificity training, MemFlex: Memory flexibility programme ♦: Statistically significant change/association, ♦: Statistically significant change but no control group, ♦: No statistically significant change/association -: No statistical analysis reported

The two initial studies found an increase in AMS and a decrease in depressive symptoms following LRT compared to TAU (Gonçalves et al., 2009; Serrano et al., 2004). Serrano and colleagues also reported a trend in change in AMS predicting post-intervention depression scores, but no evidence for AMS as a mediator for the change.

The first LRT study had a strong quality rating (Serrano et al., 2004) whilst the second study was given a moderate rating due to a lack of description of selection procedures and blinding (Gonçalves et al., 2009). The third LRT study included a placebo control group receiving supportive therapy, and additional follow-up assessments (Serrano Selva et al., 2012). AMS increased and depression scores decreased in both conditions, but there were no differences in these changes between the groups. Using only data of individuals who completed the measures at six-month follow-up, there was some support for AMS scores increasing over time in the intervention group, and evidence of improvement in AMS being associated with change in depression scores. Due to high drop-out rates before follow-up, these analyses can only be considered to be of moderate quality.

Four treatment studies used the Memory Specificity Training (MeST) programme (Eigenhuis, Seldenrijk, van Schaik, Raes & van Oppen, 2017; Neshat-Doost et al., 2013; Raes et al., 2009; Sabatelli, 2016). MeST was developed by Raes and colleagues (2009) to improve AMS through memory practice of both positive and negative memories. MeST is delivered in a group format over four to five sessions, and includes psychoeducation and training in recalling specific events.

MeST has been evaluated in three uncontrolled trials and one CCT. The initial uncontrolled pilot study of psychiatric inpatients suggested an increase in AMS measured by both the AMT and the SCEPT (Raes et al., 2009). Depression symptoms also decreased, and analysis showed that change in AMS correlated with changes in rumination, experiential avoidance and problem-solving. However, this could have been due to an overall decrease in depression symptoms, and the study rating was weak due to potential of selection bias, a small sample size, lack of blinding, high drop-out rates, and the possibility that other psychiatric treatments may have influenced the outcomes. Two further uncontrolled trials investigated the effect of MeST in depressed outpatients, one as a stand-alone treatment (Eigenhuis et al., 2017) and one in conjunction with CBT techniques (Sabatelli, 2016). In both studies, the intervention led to an increase in AMS and a reduction in depressive symptoms which persisted at three-month follow-up. The quality ratings for these studies were moderate, and in both studies other interventions received simultaneously may have impacted the results, which limits the conclusions that can be drawn about the effectiveness of MeST. The study by Sabatelli (2016) was the only study with OGM as an inclusion criteria, with all participants initially scoring less than 70% for memory specificity on the AMT.

The CCT of MeST recruited depressed adolescent refugees from Afghanistan, some of whom also had symptoms of PTSD (Neshat-Doost et al., 2013). Compared to the control condition that received no intervention, participants showed an increase in AMS. A difference in depression symptoms was not present following the intervention, but found at two-month follow-up. Analysis suggested that change in AMS independently predicted follow-up depression, and that the change in AMS

mediated the relationship between group allocation and follow-up depression. This study received an overall rating of strong, and is the only study on MeST that included a control condition. However, due to the limited sample size, and the lack of an active control condition, generalisations should be made with caution.

3.3.2. Interventions targeting AMS: Prevention studies

One prevention study targeted individuals in remission from depression (Hitchcock et al., 2016). In this uncontrolled trial, participants took part in the Memory Flexibility (MemFlex) programme, which consisted of an orientation session, followed by six work-book based sessions that participants completed at home over one month. The workbook included training exercises to develop the ability to balance and alternate between different types of thoughts and to elaborate details of memories. Participants showed an improvement in AMS, and no change in depressive symptoms. However, the study did not include a control group which, in addition to lack of clarity about potential selection bias and lack of blinding, meant that the study quality was rated as weak.

The final three prevention studies recruited participants without an identified risk of depression. Two CCTs investigated the effect of Serrano and colleagues' (2004) LRT protocol for older adults without depressive symptoms compared to an active control condition (Latorre et al., 2015; Ramírez et al., 2014). Ramírez and colleagues (2014) randomised participants to take part in either nine weeks of a LRT/positive psychology group, or a positive psychology group. The results suggested an increase in AMS and a decrease in depressive symptoms in the intervention group compared to the control

conditions. However, these effects were no longer present at four-month follow-up, and due to a high risk for selection bias the study had a moderate quality rating. In the study by Latorre and colleagues (2015), which had an overall quality rating of strong, participants were allocated to either six sessions of individual LRT or to a six-week media workshop. The results showed an increase in AMS and a decrease in depressive symptoms in the intervention group compared to the control condition. The change in AMS scores was not related to change in depression scores.

The final prevention study recruited undergraduate students who were allocated to either a traditional expressive writing condition, a specific expressive writing condition or a control writing condition (Maestas & Rude, 2012). All groups engaged in a writing task for twenty minutes over three consecutive days. One month after the intervention there was no difference between the groups, but at six-month follow-up both the traditional and specific writing had led to an increase in AMS compared to the control condition. There was no difference in depressive symptoms between groups. The study also included measures of rumination and avoidance, and analysis suggested that whilst rumination at post-intervention did not mediate follow-up AMS, avoidance partially did. The authors suggested that the delay in change in AMS was due to initial change in avoidance following the intervention. The study quality was rated as strong, and the sample size in this study was large.

3.3.3. Interventions targeting AMS: Summary of outcomes

All eleven studies targeting memory specificity showed evidence of improvement in AMS. In one of these studies, the improvement was equivalent in the intervention and

control condition. The results, however, should be interpreted cautiously as four of the studies showing an increase in AMS were uncontrolled trials, and only three of the controlled trials received a strong quality rating. In the treatment studies, there was evidence of a decrease in depressive symptoms following the interventions. Results regarding the association between change in AMS and in depression symptoms were inconsistent. As only two studies included analysis of other cognitive functions, there is no consistent evidence for the relationship between change in AMS and other cognitive processes.

3.4. General depression interventions: Description of interventions and outcomes

Eight studies investigated the effectiveness of general depression interventions, including three treatment studies and five prevention studies. The results of these studies are presented in Table 5.

3.4.1. General interventions: Treatment studies

One study randomised adults with depression to sixteen weeks of individual CBT or pharmacological treatment (McBride, Segal, Kennedy & Gemar, 2007). The results showed that both interventions led to an increase in AMS, and a decrease in depressive symptoms. There were no differences between the two treatment groups, and the study had an overall rating of moderate due to lack of reporting across a number of domains. It is worth noting that in most other treatment studies the TAU condition included use of pharmacological treatment for depression.

Table 5

Outcomes of general interventions

Study	Intervention (T/P)	Assessment times	Change in AMS	Change in depression symptoms	Association between change in AMS and depression symptoms	Mediation of AMS on depression symptoms	Relationship between AMS and other cognitive outcomes
Williams et al. (2000)	MBCT (P)	Pre + FU (mean: 4 months)	◆ (green)	◆ (red)			
McBride et al. (2007)	CBT/ Psychopharmacology (T)	Pre + post	◆ (yellow)	◆ (yellow)			
Boritz et al. (2008)	EFT/PCT (T)	Early, mid and late therapy	◆ (yellow)	−	◆ (red)		
Heeren et al. (2009)	MBCT (P)	Pre + post	◆ (green)	−	◆ (red)		Cognitive inhibition did not mediate change in AMS. Cognitive flexibility partially mediated change in AMS.
Hargus et al. (2010)	MBCT (T)	Pre + post	◆ (green)	◆ (green)	◆ (red)		
Jermann et al. (2013)	MBCT (P)	Pre+post 9 month FU	◆ (red) ◆ (red)	◆ (red) ◆ (red)			
Mogoaşe et al. (2013)	Concreteness training (P)	Pre + post	◆ (red)	◆ (red)			

Study	Intervention (T/P)	Assessment times	Change in AMS	Change in depression symptoms	Association between change in AMS and depression symptoms	Mediation of AMS on depression symptoms	Relationship between AMS and other cognitive outcomes
Rice et al. (2015)	MBCT/CBT/TRY	Pre + post	♦	♦			

T: Treatment, P: Prevention, FU: Follow-up; MBCT: Mindfulness-based cognitive therapy, CBT: Cognitive behavioural therapy, EFT: Emotion-focused therapy, PCT: Person-centred therapy, TRY: Thinking about reward for young people ♦: Statistically significant change/association, ♦: Statistically significant change but no control group, ♦: No statistically significant change/association -: No statistical analysis reported

Hargus and colleagues (2010) randomised adults with depression, at least three previous depressive episodes, and a history of a suicidal crisis, to an eight week MBCT programme (Segal et al., 2002) or TAU. AMS was measured through coding transcripts from a semi-structured interview for events associated with the lead-up to the crisis (Relapse Signature of Suicidality Interview; ReSSI).

In the control group, the specificity of answers on the ReSSI decreased. In the intervention group, however, there was no decrease, suggesting a benefit of the intervention. The authors proposed that the sustained ability to recall the context around the past suicidal crisis may contribute to earlier recognition of warning signs in the future. There was also a decrease in depressive symptoms in the intervention group compared to the control group. There was a correlational relationship between change in depressive symptoms and change in relapse signature specificity across the two conditions, but this association was not present in the intervention group alone. Due to a potential of selection bias, lack of blinding and the use of a new measure of AMS, the study quality rating was moderate.

Boritz and colleagues (2008) investigated how the disclosure of specific events changes over the course of Emotion Focused Therapy and Person Centred Therapy. Both groups received therapy once a week for 15-20 weeks. For each participant, the content of six therapy sessions from different stages of therapy were transcribed and rated on specificity. The analysis showed an increase in disclosures of specific memories over the course of therapy in both groups. There was no difference in disclosure of specific memories between individuals who did and did not recover from depression. Due to the measurement methodology, it is not possible to establish

whether the changes reflect change in AMS ability, or the development of the therapeutic process, and due to a lack of reporting across a number of study features the overall quality rating of this study was weak.

3.4.2. *General interventions: Prevention studies*

Two studies investigated the effect of MBCT in individuals in remission from recurrent depression (Jermann et al., 2013; Williams et al., 2000). Both studies used a standard MBCT protocol of eight weekly sessions (Segal, Williams & Teasdale, 2002).

Williams and colleagues' (2000) study was rated as strong, and found an increase in memory specificity. This was not replicated by Jermann and colleagues (2013), whose study was rated as weak due to high attrition rates and lack of clarity around confounding factors. Neither study found a change in depression scores. A third study, using a similar MBCT protocol, recruited adults without an identified risk of depression, and compared them to matched controls (Heeren et al., 2009). The results suggested an increase in AMS following the intervention compared to the control group. No difference in depressive symptoms was found. Due to a lack of randomisation, and lack of reporting on selection bias and blinding, the overall quality of this study was moderate.

Mogoaşe and colleagues (2013) investigated the effectiveness of a seven-day online concreteness training programme for undergraduate students with symptoms of dysphoria. Participants completed daily exercises aimed to facilitate and develop concrete thinking using hypothetical scenarios. The study, which had a quality rating

of moderate, did not find a benefit of the intervention on AMS or symptoms of depression.

The largest study in the review was a controlled cohort study investigating the effects of depression prevention intervention in schools (Rice et al., 2015). Three eight-week prevention programmes, including CBT, MBCT and a reward processing intervention, were compared to a control condition receiving no intervention. None of the conditions showed a benefit on AMS or on depressive symptoms compared to the control group. Due to the study design, lack of reporting on blinding, and the use of SCEPT, the overall study rating was moderate.

3.4.3.   General interventions: Summary of outcomes

Of the eight studies investigating the effect of general depression interventions, five showed a benefit on AMS and three did not. All treatment studies showed an increase in AMS, but due to the quality of the studies and and variability in interventions and methodologies for assessing AMS, few conclusions can be drawn. There was mixed evidence for MBCT improving AMS in prevention studies. The general interventions provided no evidence for a relationship between change in AMS and change in depression symptoms, and only one study examined the association between AMS and change in other cognitive factors.

4. Discussion

The aim of this review was to establish the current evidence-base for clinical interventions in improving AMS in the treatment and prevention of depression. The evidence from the studies is summarised and discussed, followed by methodological considerations, implications of the findings, and a summary of the limitations of this review.

4.1. Summary of findings

4.1.1. Do interventions for depression improve AMS?

Of the nineteen studies included in the review, fifteen reported an increase in AMS following the intervention, one study equivalent improvements in the intervention and control condition, and three studies no change in AMS. All treatment studies were associated with changes in AMS, with the three studies reporting no change all being prevention studies. Despite these promising results, study design and quality pose limitations to the causal attributions of the interventions. Of the nineteen studies, seven were uncontrolled trials, and only five of the controlled trials had an overall quality rating of strong. Whilst the effectiveness of interventions needs to be further considered, the results strongly support that OGM in depression should be viewed as a modifiable rather than stable trait (Brittlebank et al., 1993). This is consistent with the predictions of the CaR-FA-X model, which suggests that change in cognitive processes can be associated with change in AMS (Williams et al., 2007), and with

emerging evidence of AMS being modifiable in other psychiatric conditions (Moradi et al., 2014; Ricarte, Hernández-Viadel, Latorre, Ros & Serrano, 2014).

For treatment studies, a larger number of higher quality trials were available for interventions targeting AMS than for general depression interventions. The strongest evidence came from the controlled trials of LRT in older adults, with LRT leading to an increase in AMS in four trials, and the final trial finding equivalent benefits of LRT and supportive therapy. There was preliminary evidence for MeST improving AMS in four studies, but only one of these was a controlled clinical trial, and a significant weakness in the uncontrolled studies was the possibility of other treatment strategies influencing the outcomes. The encouraging results from the uncontrolled studies targeting memory need to be interpreted cautiously as improvements in AMS could arise both from a placebo effect or due to the natural progression of depression which often includes symptom reduction even in the absence of treatment (Keller et al., 1992). The evidence of long-term benefits of targeted AMS interventions is currently limited.

Due to study characteristics it would be premature to interpret the overall results as a relative superiority of the treatments targeting memory. For general depression interventions, there was some evidence for effectiveness of MBCT, CBT and anti-depressant medication on AMS, with CBT and anti-depressant use showing equivalent outcomes. It should be noted that only one of the other treatment studies excluded participants based on anti-depressant use (Gonçalves et al., 2009), which may have influenced the results in both the treatment and control groups through independent effects of medication on mood and cognition. Despite some evidence for LRT having

superiority over active control conditions, the equivalent outcomes of LRT and supportive therapy suggests that different types of psychological support, whether targeting AMS or not, may lead to similar outcomes (Serrano Selva et al., 2012).

The studies included proposed a number of different pathways to the improvements in AMS, including direct effects on memory retrieval, changes in mood, or changes in cognitive processes targeted by interventions, such as rumination, flexibility and awareness (Maestas & Rude, 2012; Neshat-Doost et al., 2014; Williams et al., 2000). There is currently insufficient evidence for treatments targeting any particular factors, and further research is needed to distinguish between the effectiveness of different interventions and the active ingredients associated with change. In addition, interventions with different aims are likely to target a number of shared features, such as emotional regulation and memory processing (Lane, Ryan, Nadel & Greenberg, 2015; Moyal, Cohen, Henik & Anhold, 2015). In light of the CaR-FA-X model and the bidirectional relationship between OGM and depressive symptoms, it is likely that change in AMS can be driven by several factors (Talarowska et al., 2016; Williams et al., 2007). The "dodo bird verdict" of psychological treatments, suggesting an equivalence of benefits and outcomes for mood across a number of different psychological interventions due to shared therapeutic features, may be applicable to the improvements in AMS as well as in depressive symptoms more generally (Hollon et al., 2002, Luborsky, 1995). Individual factors, such as the chronicity of depression symptoms, are likely to contribute to the effectiveness of interventions in improving AMS, but the studies included in the review did not allow for analysis or conclusions about this (Nandrino, Pezard, Posté, Réveillère & Beaune, 2002). Promisingly, there

was some evidence of improvement in OGM in chronic and recurrent depression (Hargus et al., 2010; Williams et al., 2000).

The results from the prevention studies provided mixed and limited evidence of effectiveness. Whilst LRT produces benefits in AMS in non-depressed older adults, the other interventions targeting AMS lacked replication. One large study provided evidence that creative writing could lead to changes in AMS, but these results were only present at six-month follow-up (Maestas & Rude, 2012). The evidence for MBCT was mixed, with two studies suggesting a benefit whilst two studies did not replicate these findings, and concreteness training had no impact on AMS. The largest study in the review investigated the effect of CBT, MBCT and a reward processing programme for adolescents, with none of these showing a benefit on AMS compared to the control group (Rice et al., 2015). This lack of change in AMS in prevention studies may, however, be due to participants already having high levels of AMS. Previous reviews on prevention strategies for depression have similarly produced mixed results, and the use of immediate cognitive and symptom reduction measures in prevention studies can be problematic given the absence of dysfunction (Merry et al., 2009). The AMT may also have lower sensitivity for measuring AMS in non-clinical samples compared to individuals with depression (Griffith et al., 2009; Raes et al., 2007).

4.1.2. *What are the links between improvement in AMS and depression symptoms?*

Overall, depression symptoms decreased in the treatment studies. As these included several uncontrolled trials, however, this result may partly be attributed to the natural progression of depression rather than the effectiveness of interventions (Keller et al.,

1992). For the studies that reported statistical analysis of the association between change in AMS and change in depressive symptoms, the evidence was mixed. The conceptualization of OGM as both a risk factor and a consequence of depression suggests that the relationship between the variables may be complex and influenced by other factors, and a fuller understanding of the relationship may require subgroup analysis, inclusion of further cognitive measures, and larger sample sizes (Talarowska et al., 2016). The causal association between AMS and depression can also be interpreted in several ways. In some of the included studies, the authors argued that a lack of relationship between the two supports the effectiveness of interventions targeting memory, as the AMS improvement is not attributable to changes in mood (Williams et al., 2000). Others have interpreted an association as evidence of a causal relationship between AMS on depressive symptoms (Neshat-Doost et al., 2013). Overall, analyses of OGM controlled for changes in mood, suggesting that the changes in AMS were at least partially independent. In the small number of studies where mediation analyses were performed, the evidence of whether change in AMS mediates change in depression symptoms was conflicting.

In the prevention studies, only two studies reported a change in depressive symptoms. Measuring symptom reduction in prevention studies and populations with sub-clinical levels of depression may not, however, provide a measure of clinically meaningful change due to low baseline scores (Merry et al., 2009).

Across the prevention and treatment studies, only three trials reported statistical analysis of the relationship between change in AMS and other cognitive processes (Heeren et al., 2009; Maestas & Rude, 2012; Raes et al., 2009). Whilst these studies

reported correlations and partial mediation effects of measures of cognitive flexibility, avoidance, rumination and problem-solving, the limited amount of analyses and lack of replications does not allow for any conclusions to be drawn concerning the relationship between AMS and other cognitive processing. Distinction between these factors is likely to be complex due to their close relationship, and the likelihood of bidirectional and confounding associations, with OGM (Liu et al., 2017; Raes et al., 2005; Raes et al., 2006).

4.2. Methodological limitations of the included studies

The studies in this review included a number of methodological limitations. Firstly, none of the trials met the EPHPP criteria for RCTs (Thomas et al., 2004), which would provide the strongest evidence for effectiveness. Study methodologies of the CCTs could have been improved through reporting of randomisation procedures, double-blinding and intention to treat analysis. Only five studies had an overall quality rating of strong. This, along with inclusion of uncontrolled trials, poses challenges to the attribution of change to the effectiveness of the interventions.

Secondly, a number of limitations arise from the use of the AMT. The AMT is not a standardised scale, and different versions of this measure was used across studies. Whilst the relationship between OGM and depression is established across different versions of the AMT, it is possible that the variations in the demands of the tasks are associated with different outcomes (Liu et al., 2013). As a consequence of the variability between AMT versions, as well as interventions and populations, of studies, drawing conclusions about the possible relationship between features of the AMT and

outcomes was not possible. As this review addressed change within studies rather than the strength of the association, this is unlikely to have had a big impact on the results. A greater issue, however, is the potential influence of learning effects as a result of repeated administrating of the AMT, especially when the same cue words are used at different time points (Sumner et al., 2010). Only six studies in the review reported the use of different cue word at the different measurement times, but the pattern of results in these studies did not differ from the other trials.

Thirdly, only one study included OGM in the inclusion criteria (Sabatelli, 2016). Interventions for individuals with high initial levels of AMS are unlikely to lead to statistically significant changes due to the limited scope for improvement.

Fourthly, the included studies reported change in terms of statistical significance, which does not necessarily translate into clinical significance or benefit (Jacobson & Truax, 1991). Based on the studies included, it is possible to conclude that there was some improvement on performance on the AMT and other measures, but not whether this improvement had a further beneficial impact for individuals. Measurement methods of AMS that are more closely linked to an individual, such as diaries, self-defining memory narratives, or the ReSSI used by Hargus and colleagues (2010), may provide more individually relevant information than the AMT (Sumner et al., 2013). The majority of studies also only reported change on depression measures in terms of statistical, but not clinical, significance.

Finally, the generalisability of studies should be considered. For example, whilst evidence suggests that LRT increases AMS in older adults, it is unclear whether this

intervention would be effective in younger populations. The evidence in children and adolescents was limited, and the majority of participants were White European. The information in the studies did not allow for analysis or conclusions about sub-groups, including the effect of chronicity of depression on change in AMS. The quality of studies, along with heterogeneity between studies, meant that meta-analysis of results across studies was not possible.

4.3. Implications and future directions

Despite the evidence that interventions, particularly for treating depression, can improve AMS, it was not possible to establish the relationship between these improvements and changes in depression symptoms. It was also not possible to establish whether any of the interventions were superior compared to others, or whether interventions targeting AMS were more effective in reducing OGM than general interventions. Further research is needed to build on the results from the uncontrolled trials. Encouragingly, two randomised trials for MeST and MemFlex, comparing the interventions to psychoeducation and support, are currently being conducted (Dalgleish et al., 2014; Hitchcock et al., 2015). For interventions targeting AMS, more research is needed to establish whether these interventions should be used as stand-alone therapies or in conjunction with existing treatments such as CBT. Given the mixed evidence from prevention studies, interventions should initially target people with current depressive symptoms. As the rationale for targeting AMS is to improve depression outcomes, there is a need for future research to address the links between change in AMS and changes in depression symptoms and outcomes. Future research should also target the relationship between change in AMS and rumination,

problem-solving and avoidance (Williams et al., 2007). If OGM is conceptualised as a risk factor for depression, measures of relapse or future depressive episodes may be more useful than symptom measures, in particular in prevention studies.

Depression is a heterogeneous disorder in terms of both symptomology and cognitive profile. One of the challenges in treating and preventing depression is that no single treatment methods works for all, and little is currently known about factors that predicts treatment success. Interventions are often generic across individuals, although there may be an increased benefit of interventions that are individually tailored to the specific symptoms present, including problems with memory (Brewin et al., 2009). It may be, that some individuals would particularly benefit from interventions designed to improve AMS, whilst others may not.

4.4.   Limitations of this review

A number of limitations of this review should be acknowledged. Firstly, all steps of the systematic review was conducted by a single researcher, which introduces the risk of bias and inaccurate accounts. Secondly, despite a thorough search methodology, it is possible that some publications that would have provided important information were not identified. Thirdly, due to the heterogeneity and mixed results of the studies, it was not possible to draw conclusions about sub-groups of participants and interventions, or to further discuss the implications of the different measures of AMS that were used.

4.5.   Concluding summary

There is promising evidence that clinical interventions for treating depression are followed by increases in AMS, but there is no clear evidence for superiority of any particular intervention, or for the association with change in depressive symptoms. The evidence for preventative strategies improving AMS is limited. Further research is needed to establish the effectiveness of interventions in improving AMS and their clinical benefits.

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Part 2: Empirical Paper

Autobiographical and hippocampus-dependent spatial memory in depression

Abstract

Aims: Depression is associated with deficits in autobiographical memory (AM) specificity. As the hippocampus underlies AM recall, and is associated with atrophy in depression, it provides an area of interest for understanding the neural correlates of memory deficits in depression. The aim of this study was to investigate the association between AM and allocentric spatial memory as a measure of hippocampal function in depression.

Method: 34 adults with chronic or recurrent symptoms of depression, and 35 adults without depression, completed the Autobiographical Memory Test (AMT) and the Four Mountains Test (4MT) as a measure of allocentric spatial memory, along with a number of clinical symptom measures.

Results: There was no association between performance on the AMT and the 4MT. The depression group had lower scores on the AMT than the comparison group, but there was no difference between 4MT scores. Performance on the memory tasks was not associated with chronicity or severity of depressive symptoms.

Conclusions: Findings of AM deficits in depression were replicated. No deficits in hippocampus-dependent spatial memory, or evidence of an association between AM performance and hippocampal function measured by spatial memory, were found. Further research is needed to understand the neurological correlates of AM deficits in depression.

1. Introduction

1.1. Depression, memory and the hippocampus

Depression is a common mental health problem, with estimates suggesting a global prevalence of 4.4% (World Health Organisation, 2017). Whilst a range of evidence-based interventions are available, current treatments do not benefit everybody, and relapse rates are high (Burcusa & Iacono, 2007; Cuijpers et al., 2014; De Maat, Dekker, Schoevers & De Jonghe, 2006; Malhi et al., 2015). The suffering and costs associated with depression, along with the limitations of existing treatments, highlights the importance of increasing the understanding of the aetiology and features of depression.

Diagnostic criteria for depression are based on the emotional features of the disorder, with the core symptoms including depressed mood and loss of interest and pleasure (American Psychiatric Association, 2013). In addition, depression is associated with a range of cognitive and executive symptoms, including effects on memory, which contribute to the disability burden (Dalgleish & Werner-Seidler, 2014; Darcet, Gardier, Gaillard, David & Guilloux, 2016; Gonda et al., 2015; Köhler et al., 2015; Rock, Roiser, Riedel & Blackwell, 2014; Snyder, 2013). There has been increased interest in linking the deficits in memory with the neurological features of depression, and improved understanding of the interaction between cognitive and biological factors may contribute to the improvement of treatment strategies (Rock et al., 2014).

Neuroimaging studies have demonstrated differences between healthy controls and individuals with depression in a range of cortical regions, including areas associated with emotional regulation and reward seeking (Kupfer, Frank & Phillips, 2012; Liu et al., 2017). One of the most widely studied brain regions in depression is the hippocampus (Liu et al., 2017). As the notable functions of the hippocampus include episodic and spatial memory, it provides an area of interest for understanding memory deficits in depression (Campbell & MacQueen, 2004; Eichenbaum & Cohen, 2014; Schiller et al., 2015). Bilateral structural and functional differences, including reductions in volume, have consistently been found in the hippocampus and surrounding structures in depression, particularly when symptoms are chronic and recurrent (Campbell & MacQueen, 2004; Chan et al., 2016; Finkelmeyer et al., 2016; Kaymak et al., 2010; McKinnon, Yucel, Nazarov & MacQueen, 2009; Schmaal et al., 2016). Changes in the hippocampal structure are also found in individuals with post-traumatic stress disorder (PTSD) (Smith, 2005). Exposure to periods of stress is associated with neurotoxic levels of cortisol and dysregulation of the hypothalamic pituitary adrenal (HPA) axis, leading to alterations in hippocampal development and function, and offering an explanation for the hippocampal deficits in emotional disorders (Frodl & O'Keane, 2013; Heim, Newport, Mletzko, Miller & Nemeroff, 2008; McEwen, 2005; Stein, Koverola, Hanna, Torchia & McClarty, 1997; Talarowska, Berk, Maes & Galecki, 2016; Wilkinson & Goodyer, 2011).

Despite compelling evidence linking depression with hippocampal alterations, the associated behavioural changes are not well understood (Fairhall, Sharma, Magnusson & Murphy, 2010). This study investigated the well-established impairments in

autobiographical memory in depression with the potential association with allocentric spatial memory as an indicator of hippocampal functioning.

1.2.   Overgeneral autobiographical memory in depression

A robust evidence base suggests that impairment in autobiographical memory (AM) recall is a feature of depression (Liu, Li, Xiao, Yang & Jiang, 2013; Ono, Devilly & Shum, 2016; Williams et al., 2007). AM is the memory function that allows humans to recall past experiences and relive past events in the present (Tulving, 2002). It is part of the human declarative memory system, but distinct from semantic memory as it relies on access to specific contexts and spatio-temporal information about events (Moscovitch, Cabeza, Wincour & Nadel, 2016). Access to AM provides a basis for social interaction, problem solving, decision making, and sense of identity, and accordingly deficits can lead to profound impacts on functioning and well-being (Talarowska et al., 2016; Tulving, 2002).

The impairment of AM in depression, also referred to as overgeneral memory (OGM), was first described by Williams and Broadbent (1986) who compared the ability to retrieve specific autobiographical memories (defined as personally experienced events that lasted less than a day) between suicide attempters and controls using the Autobiographical Memory Test (AMT). In the AMT, participants are presented with cue words (e.g. *happy*), and asked to recall a memory of a specific event that the word reminds them of (e.g. *the day my daughter was born*). Suicidal patients were less likely to recall specific events and more likely to recall categorical events and longer time-periods of their life (e.g. *when my daughter was a baby*). Overgenerality appears to be

specific to AM, with deficits in specificity not being found in semantic memory tasks, and OGM being present when other aspects of cognition are controlled for (Söderlund et al., 2014; Williams & Broadbent, 1986; Williams et al., 2007).

Subsequently, a large number of studies across different settings have replicated OGM as a feature of depressive disorders (Liu et al., 2013; Sumner, 2012; Williams et al., 2007). OGM is also associated with remitted and sub-clinical depression, and is predictive of future episodes and relapse (Sumner, Griffith & Mineka, 2010). OGM may contribute to the maintenance of depression by interfering with problem-solving and enhancing rumination (Sumner et al., 2010). However, there is seemingly no correlation between symptom severity and OGM, and the links with length of illness are unclear (Gibbs & Rude, 2004; King et al., 2010; Wessel, Meeren, Peeters, Arntz & Merckelbach, 2001; Williams et al., 2007).

Explanatory models of OGM have focused on the cognitive processes that can interfere with AM retrieval. Early models proposed that OGM, which is also found in PTSD, could be explained by a single main factor such as trauma and subsequent avoidance of specific memories (Moore & Zoellner, 2007; Valentino, 2011). More recent models recognise a number of factors that contribute to OGM, including rumination and deficits in executive function (Sumner, 2012; Williams et al. 2007). The neural underpinnings and correlates of AM may offer a novel avenue for understanding OGM (Piolino, Desgranges & Eustache, 2009; Valentino, 2011). The hippocampus, being one of the key brain structures involved in AM, and associated with depression and trauma, offers an area of interest when considering the neurology of AM deficits in depression (Campbell & MacQueen, 2004; Conway, 2005; Talarowska et al., 2016).

1.3. Autobiographical memory and the hippocampus

Early evidence for hippocampal involvement in AM was demonstrated by lesion studies where hippocampal damage was associated with the loss of AM, whilst other forms of declarative memory remained intact (Bird & Burgess, 2008; Eichenbaum, 2004; Eichenbaum & Cohen, 2014; Eichenbaum, Sauvage, Fortin, Komorowski & Lipton, 2012). Extensive neuroimaging data has since further supported the hippocampal role in AM (Greenberg & Rubin, 2003; Martinelli, Sperduti & Piolino, 2013; Moscovitch et al., 2005; Piolino et al., 2009; Svoboda, McKinnon & Levine, 2006). The hippocampus appears to have a selective role in AM compared to other forms of declarative memory, such as semantic information, possibly through providing and incorporating a range of contextual information (Eichenbaum et al., 2012; Holland, Addis & Kensinger, 2011; Martinelli et al., 2013; Moscovitch et al., 2005). Whilst early models of AM suggested that hippocampal involvement decreased with the time passed since formation of a memory, current evidence suggests continuous hippocampal involvement regardless of memory age (Cabeza & St Jaques, 2007; Moscovitch et al., 2005; Piolino et al., 2009). The hippocampus is not a uniform structure, and evidence suggests that different subfields may be associated with different aspects of AM, such as encoding, consolidation, and clarity of memories (Chadwick, Bonnici & Maguire, 2014; Mueller, Chao, Berman & Weiner, 2011). The Cornu Ammonis region 3 (CA3) of the hippocampus appears to be particularly important for AM, and there is also evidence of the left hippocampus playing a larger role in AM than the right hippocampus (Chadwick et al., 2014; Martinelli et al., 2013).

A smaller number of studies have investigated the link between OGM, depression and the hippocampus. Associations have been found between lower grey matter volume in the hippocampus and OGM (Young, Bellgowan, Bodurka & Drevets, 2015a). Differences in blood-oxygen-level dependent (BOLD) responses in functional magnetic resonance imaging (fMRI) between depressed individuals and controls performing AM tasks have also been identified in regions including the prefrontal cortex, the amygdala, occipital regions and the hippocampus (Whalley, Rugg & Brewin, 2012; Young et al., 2012; 2016; Young, Bellgowan, Bodurka & Drevets, 2013). One study found decreased hippocampal activation during AM retrieval in depressed individuals, but the difference between groups was not evident when specific memories were retrieved (Young et al., 2012). Two studies have found increased BOLD activity in the left hippocampus in individuals with depression or high risk for depression during recall of specific memories (Young, Bellgowan, Bodurka & Drevets, 2014; Young et al., 2016). The authors interpreted this as reflecting increased hippocampal activity to compensate for atrophy in this region. Other studies have reported no significant differences in hippocampal activation between depressed and non-depressed individuals during AM tasks (Hach, Tippett & Addis, 2014; Young et al., 2013; Young, Bellgowan, Bodurka & Drevets, 2015b).

1.4. Hippocampus-dependent spatial memory

Another key function of the hippocampus is its involvement in spatial navigation and memory (Bird & Burgess, 2008). Spatial memory depends on multiple parallel memory systems, including allocentric (view-point independent) and egocentric (observer/view-point dependent) spatial memory (Burgess, 2008). Allocentric spatial

memory (ASM) stores representations that are not bound to a specific view-point or perspective, and hence underlies recognition of locations from new perspectives, recollection of environmental topography, and flexible navigation (Hartley et al., 2007).

The hippocampus is involved in long-term egocentric spatial memory, but short-term egocentric spatial memory largely depends on different cortical regions (Moscovitch et al., 2005; Weniger, Ruhleder, Wolf, Lange & Irle, 2009). For ASM, however, the hippocampus is the crucial cortical structure for both long-term and short-term recollections (Burgess, Maguire & O'Keefe, 2002; Byrne, Becker & Burgess, 2007; Holdstock et al., 2000; King, Burgess, Hartley, Vargha-Khadem & O'Keefe, 2002; Yee, Hannula, Tranel & Cohen, 2014). Early literature on spatial memory and the hippocampus came from animal studies, including the identification of the hippocampus creating a cognitive map of the environment through the firing of "place cells" that respond to different features of the external surroundings (O'Keefe & Nadel, 1978). Place cells, that have subsequently also been identified in humans, respond to topographic features of the environment regardless of egocentric properties (Doeller, Barry & Burgess, 2012; Ekström et al, 2003). Functional imaging has further shown that the hippocampus is a key structure in ASM in humans, and distinguished its neural underpinnings from those of semantic memory and general cognitive functioning (Ekström et al., 2003; Hartley & Harlow, 2012; Hartley, Lever, Burgess & O'Keefe, 2014; Hartley, Maguire, Spiers & Burgess, 2003; Spiers, Maguire & Burgess, 2001).

Due to its specialised role in ASM, a number of virtual reality and topographical spatial memory tasks have been developed to reflect hippocampal functioning (Burgess et al., 2002; Hartley et al., 2007; King et al., 2002). Hartley and colleagues developed the computer-based Four Mountains Test (4MT), where spatial memory is measured using a virtual landscape that is manipulated to vary on features dependent on allocentric and non-spatial memory. Their findings suggest that individuals with hippocampal damage show specific impairments in the allocentric condition, along with unaffected memory performance in the non-spatial condition. The 4MT has also been used with individuals with mild cognitive impairment and Alzheimer's Disease, in which hippocampal atrophy is an early factor, and has shown sensitivity in identifying, predicting and distinguishing Alzheimer's disease from other dementias (Bird, Chan, Hartley, Pijnenburg, Rossor & Burgess, 2010; Chan et al., 2016; Guderian et al., 2015; Moodley et al., 2015; Pengas et al., 2012; Wood, Moodley, Lever, Minati & Chan, 2016). In healthy adults, performance on the test is associated with hippocampal volume (Hartley & Harlow, 2012). Together, these findings suggest that performance on the 4MT can offer an indication of hippocampal function.

Compared to the literature on OGM, less is known about the relationship between depression and spatial memory. Emerging evidence from studies using virtual reality tasks suggests that ASM may be impaired in depression, but this has not been consistently found across tasks (Cornwell et al., 2010; Gould et al., 2007; Wong, 2015). A study comparing individuals with PTSD with trauma-exposed controls, showed that PTSD was associated with a selective impairment in ASM, whilst egocentric and non-spatial memory was intact (Smith, Burgess, Brewin & King, 2015). Animal studies suggest that repeated exposure to stress causes impairment on spatial

memory tests, which is possibly linked with the effect of cortisol and the HPA-axis on the hippocampus (Conrad, 2010; Darcet et al., 2016). Depression, or negative life events, may similarly interfere with human spatial memory through the effect of stress responses on the hippocampus.

Whilst there is some evidence for functional specialisation of the hippocampus, such as the left hippocampus showing specialisation in AM and the right hippocampus in ASM, and the anterior hippocampus showing relatively higher involvement in the construction of conceptual representation whilst the posterior hippocampus is responsible for perceptual representations, there appears to be significant overlap between the neural underpinnings of the two types of memory (Burgess et al., 2002; Martinelli et al., 2013; Piolino et al., 2004; Sheldon & Levine, 2016). A number of theories have been proposed to explain the relationship and shared neural structures of AM and ASM, including AM depending on allocentric processing for the contextualising of and distinguishing between spatial and temporal information (Bird & Burgess, 2008; Burgess et al., 2002). Others suggest that the link between episodic and spatial memory in the hippocampus is best explained through conceptualising the function of the hippocampus as a cognitive map that can organise and bind information across a number of domains (Eichenbaum, 2015; Olsen, Moses, Riggs & Ryan, 2012; Schiller et al., 2015). Despite the shared dependence on the hippocampus, there is a lack of behavioural research linking AM and ASM (Moscovitch et al., 2005). Based on current evidence, however, it is plausible that impaired hippocampal function and ASM could contribute to impairments in accessing specific memories in depression.

1.5. Rationale and aim of the study

Improved understanding of the behavioural and neuropsychological correlates and processes involved in depression can contribute to the development of more effective treatments. The aim of this study was to unite some of the separate strands of research on correlates of depression to increase the understanding of AM deficits and the role of the hippocampus in depression. There is robust evidence for deficits in AM in depression and for the hippocampal involvement in AM and ASM. Whilst the effects of depression on ASM are less well understood, it is possible that impairments are present. To date, no studies known to the author have investigated the relationship between AM and ASM deficits in depression. This study aims to investigate the link between AM specificity and ASM as an index of hippocampus function in individuals with and without depression.

1.6. Hypotheses

Primary hypothesis: There will be an association between AM specificity and hippocampus-dependent ASM in depressed and non-depressed adults.

Hypothesis two: The depression group will show impairment in AM specificity compared to the non-depressed comparison group.

Hypothesis three: The depression group will show impairment in ASM compared to the non-depressed comparison group.

Hypothesis four: Earlier onset and chronicity of depression will be associated with increased impairments in AM and ASM.

2. Method

2.1. Joint project arrangement

The data for this study was collected as part of a joint project with a fellow trainee clinical psychologist (Williams, 2017). The research questions for the two projects were based on separate measures of memory. As the measures used for the other project were unlikely have an impact on the results, and were not used for analysis, only measures relevant to this project will be described. Further details about the joint project arrangement are presented in Appendix A and B.

2.2. Design

The study had a cross-sectional correlational design, with the primary hypothesis investigating the association between AM specificity and performance on a hippocampus-dependent ASM task across depressed and non-depressed adults.

2.3. Setting

Individuals with depression were recruited from current service users of Improving Access to Psychological Therapies (IAPT) services within a National Health Service (NHS) mental health trust. Participants without depression were recruited through two

online research participation websites (uclpsychology.sona-systems.com and callforparticipants.com).

2.4. Ethical approval and reimbursement

Ethical approval for this study was provided by the National Research Ethics Service Committee East Midlands – Nottingham 2 (Reference: 14/EM/0222) and by the University College London Clinical, Education and Health Psychology (CEHP) Programme Ethical Approval (Reference: SHaPS-2014-JK-009) (Appendix C and D).

All participants received a copy of the participant information sheet by email prior to their participation. Before testing, the researchers ensured that the participants had understood this information, and participants signed a consent form (Appendix E and F).

Participants received £12.50 in reimbursement for study participation. In the comparison group, five participants received course credit instead of the cash payment.

2.5. Participants

2.5.1. Sample size

The sample size calculation for the study was conducted using G*Power (version 3.1) (Faul, Erdfelder, Buchner & Lang, 2009). As no previous literature on AM and hippocampus dependent ASM was available, estimation of the effect size relied on

related literature. Williams and colleagues (2007) examined 28 studies looking at depressive disorders and OGM, and found the mean effect size to be large (d=0.94). Wong (2015) found a large effect size in ASM performance between individuals with and without depression (d=0.83), but this effect was not found across different tests of allocentric memory. A study investigating ASM in individuals with and without PTSD found a medium effect size between memory impairment and diagnosis (η_p^2=0.10) (Smith et al., 2015). Based on these results, the effect size estimate was set at medium to maximize the chances of identifying an existing effect within the practical scope of this project.

The calculation for linear multiple regression with one dependent (AM specificity) and two independent variables (depression status and ASM performance), alpha level of 0.05 and power of 0.80 indicated a sample size of 68 to detect a medium effect size (f^2=0.15). Due to the joint project's sample size calculation relying on comparison between the depression and the comparison group, this sample was split into two groups. The target sample was reached, with 34 participants in the depression group and 35 participants in the comparison group.

2.5.2. Inclusion and exclusion criteria

Right-handed, English-speaking adults aged between 18 and 65 were eligible to take part in the study. The exclusion criteria included features that may influence memory performance independently from depression. A subset of the screening questions from the Structured Clinical Interview for DSM Axis I Disorders (SCID-I; First, Spitzer, Gibbon & Williams, 1996) were used to screen for exclusion criteria of current

psychiatric disorders other than depression. Self-report questions were used to screen for depression history, past diagnosis of PTSD or psychosis, history of a head injury, current use of tranquilisers, current substance misuse, a diagnosed learning disability, or visual impairment that would interfere with ability to use a computer.

For the clinical group, inclusion criteria further included a current score of ten or above (indicating at least moderate symptoms of depression over the last two weeks) on the Patient Health Questionnaire (PHQ-9; Kroenke, Spitzer & Williams, 2001). The PHQ-9 question about suicidality was not used during the screening process, and the inclusion score was calculated on the basis of eight rather than the standard nine questions. Based on evidence of hippocampal changes in depression being associated with chronicity and severity of symptoms, further inclusion criteria included a history of long-term or recurrent depression (first episode more than 2.5 years ago; or current episode lasting over 2.5 years) (Schmaal et al., 2016). Given the high co-morbidity between depression and anxiety, participants in the depression group were not excluded based on symptoms of generalized anxiety or panic disorder (Spitzer, Kroenke, Williams & Lowe, 2006).

For the comparison group, inclusion criteria included a score of five or less on the PHQ-9 and the Generalised Anxiety Disorder Scale (GAD-7; Spitzer et al., 2006), and no more than one historic episode of depression.

2.5.3. Recruitment

The depression group was recruited through the IAPT services in a NHS mental health trust. Participants were recruited for the study through two different routes:

1) Participants were given information about the study by their therapist. If a service-user was interested in taking part and consented to being contacted by the researchers, the therapist gave their contact details to the researchers.

2) The IAPT services keep a record of current service-users who have consented to being contacted about research participation. This record also includes some clinical information, such as PHQ-9 scores. Service-users who had consented to being contacted and whose last recorded PHQ-9 score was ten or above were emailed information about the study. If no response was received for at least a week, follow-up phone calls were attempted to enquire about interest in the study.

Participants for the comparison group were recruited through adverts on two research participation websites.

For all participants who expressed an interest in taking part in the study, a screening phone call was arranged to assess eligibility. For participants who were eligible, a testing slot was arranged at one of the clinical sites of the IAPT services (depression group) or at University College London (comparison group).

The recruitment sources and number of participants at each stage are presented in Table 1.

Table 1

Number of participants at each stage of recruitment

	Depression group	Comparison group
Recruitment source	Current service-users of Improving Access to Psychological Therapies Service	General public
Recruitment method	Emails/phone calls to individuals having consented to contact about research participation	Research recruitment websites available to the general public (uclpsychology.sona-systems.com and callforparticipants.com)
Number contacted (N)	282	–
Number screened (N)	60	39
Screened but not eligible (N)	21	2
Completed testing (N)	36	35
Included in analysis (N)	34	35
Total Sample (N)	**69**	

2.6. Measurement tools and data collection

2.6.1. Measurement tools

Demographic information was collected through a self-report questionnaire, which included questions on age, gender, ethnicity, educational history, occupation, household income and first language (English or not).

The Beck Depression Inventory II (BDI-II; Beck, Steer & Brown, 1996) (clinical group only) was used to assess current depression symptoms for the clinical group. The BDI-II was developed as a screening tool to assess symptoms of depression based

on the criteria for depressive disorders in the Diagnostic and Statistical Manual IV (American Psychiatric Association, 2000), and is a widely used tool in clinical research. The BDI-II is a 21-item self-report questionnaire, assessing symptoms of depression during the past two weeks. Each item has four response options, ranging from not present (0) to severe (3). Respondents receive an overall score between 0 and 63. Review of the BDI-II has shown good validity, sensitivity and specificity for detection of depression compared to diagnostic criteria, an internal consistency of around $\alpha=0.9$ and test-retest reliability of $r=0.73-0.96$ (Wang & Gorenstein, 2013).

The Generalised Anxiety Disorder Scale 7 (GAD-7; Spitzer et al., 2006) (clinical group only) was used to assess current anxiety symptoms in the clinical group. The GAD-7 is a seven-item self-report measure for symptoms of generalized anxiety disorder over the past two weeks. For each item, respondents are asked to rate the frequency of symptoms using four response options ranging from not at all (0) to nearly every day (3). Respondents receive an overall score between 0 and 21. In psychiatric populations, the GAD-7 has shown good internal consistency and good validity when compared to other measures of worry, anxiety and stress (Kertz, Bigda-Peyton & Bjorgvinsson, 2013; Spitzer et al., 2006).

Depression history (clinical group only) was assessed through a structured interview, including the date of the start of the initial and current episodes, number of past episodes, and details of treatment history. If participants were unsure about an answer, they were asked to provide an estimate.

The Autobiographical Memory Test (AMT; Williams & Broadbent, 1986) was used to assess autobiographical memory specificity. The cue words from the original AMT were used, and included five positive (*happy, safe, interested, successful, surprised*) and five negative *(sorry, angry, clumsy, hurt, lonely*) words. Participants were told to think of and describe a specific memory for each cue word. It was explained that a specific memory refers to an event that they have experienced, that occurred at a particular time and place, and lasted less than 24 hours. Participants were told that the memory could have occurred recently or a long time ago, that it could be an important or trivial event, and to think of a different memory for each cue word. Before starting the task participants were given an example of a specific (*Jane's party last Friday*) and a non-specific memory (*I enjoyed going to parties*), and completed two practice trials (*relieved, tired*) verbally without a time limitation to ensure they had understood the instructions. The cue words were presented verbally and in written form in a booklet with one cue word per page. Participants had to provide a verbal response within 30 seconds, which they then wrote down in the booklet provided. If their verbal response within 30 seconds was not specific, they were prompted one time (*Can you think of a specific event?*). If participants could not think of a memory within 30 seconds, they were asked to move on to the next cue word.

Participant responses were coded by a trainee clinical psychologist who was blind to the clinical status of participants and to the hypotheses of the study. Memories were coded as *specific* (events that happened once and took place over a day or less), *categorical* (recurrent events), *extended* (events that lasted longer than a day), *omissions* (no memory recalled within time limit), or as *non-memories* (e.g. statements about current feelings). The primary researcher additionally coded the results of 20

participants (200 items), to calculate the inter-rater reliability, which was 90% (κ=.81). This is similar to previous studies, and suggests good inter-rater reliability (Griffith et al., 2012). The total number of specific memories were calculated for each participant with the maximum possible score being ten. Whilst the AMT is the standard tool for assessing AM specificity, it is a testing paradigm rather than a standardized measure, (Liu et al., 2013). It has, however, proved to be feasible and reliable across a large range of settings, and has demonstrated validity through its relationship with other features of depression (Griffith et al., 2009; 2012; Williams et al, 2007).

The Four Mountains Test (4MT, Hartley et al., 2007) was used to measure hippocampus-dependent allocentric topographical memory. The study used the revised version of the original task that includes 30 topographical memory items, without any trials that can be solved using non-spatial memory (Hartley & Harlow, 2012). The 4MT was presented to participants using Microsoft Office PowerPoint software on a 15-inch laptop.

The 4MT measures participants' ability to recognize topographical scenes of landscapes from different viewpoints (Figure 1). Participants are presented with the target landscape, including four mountains of differing sizes, shapes and topographical relations, for ten seconds. They are then asked to identify the target landscape from a new viewpoint from four choices that are presented simultaneously for 20 seconds. Non-spatial aspects of the scenes (e.g. colour, shadows, light) are manipulated, so that memory relies only on topographical aspects of the landscape.

Before starting the task, participants were given verbal instructions, and completed four practice trials for which they received performance feedback. Participants recorded their answers for each item on a record sheet. The total score for the 4MT was calculated based on the number of correct responses (maximum score: 30), with a chance score of 7.5 (Hartley & Harlow, 2012).

As the 4MT has been used in experimental studies across different populations, its formal psychometric properties are not yet established. However, it has been used as a feasible measurement tool across populations with neurological injury, cognitive impairment, depression and healthy controls, and has demonstrated sensitivity to hippocampal impairment and function across populations with brain injury and cognitive impairment (Bird et al., 2010; Chan et al., 2016; Guderian et al., 2015; Moodley et al., 2015; Pengas et al., 2012; Wood et al., 2016).
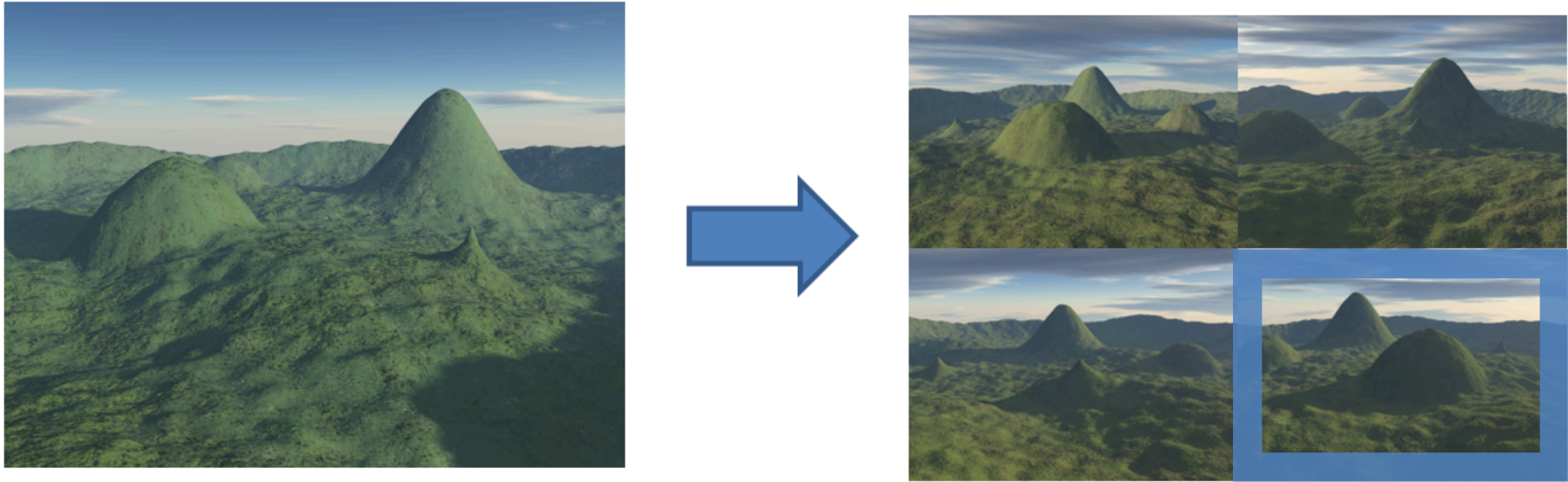
Figure 1.   Example of trial and correct response from the 4MT

2.6.2. Procedure

Participants attended the testing session at either one of the IAPT clinics (depression group) or at University College London (comparison group). The researchers went through the participant information form (which had been provided to participants by email prior to the session), and the participants signed the consent form. Participants then filled in the questionnaires, after which the clinical group completed the depression history interview. Participants then completed the AMT, followed by the 4MT. A third memory task that was not used in the analysis of this study was then completed. The total testing time was approximately 75 minutes. At the end of the testing session, participants were given the opportunity for a debrief.

2.7. Data analysis

The data analysis was performed using the Statistical Package for Social Sciences (SPSS) version 22. The distributions of all variables were explored to ensure normality assumptions were met, and potential differences on demographic variables between the groups were explored. The primary hypothesis was tested using multiple linear regression. Differences in memory performance between groups were explored using t-tests. For the clinical group, the relationship between memory performance and clinical variables were explored using correlational analysis.

3. Results

3.1. Data preparation

3.1.1. Missing data

One participant was excluded from analysis due to not completing the 4MT (reported finding this task too difficult). There was no further missing data for the AMT and the 4MT. The number of past episodes of depression was missing for five participants. They were excluded from the correlational analysis on number of past depressive episodes.

3.1.2. Outliers

The presence of potential outliers was examined through inspection of histograms, box plots and z-scores using a threshold of z<3. No outliers were identified for the AMT and 4MT scores. One outlier was identified for number of past depressive episodes, and was excluded in the correlational analysis of that variable.

3.1.3. Normality checks

The distributions of scores of the variables included in the statistical analysis were examined through calculating z-scores for kurtosis and skewness, and the Kolmogorov-Smirnov statistic. The scores on the AMT and the 4MT met the assumptions for parametric testing. The clinical variables (BDI-II scores, GAD-7 scores, time since onset, number of past episodes and time since first episode) were

not normally distributed, and statistical methods not assuming normality were used for analysis of these.

3.2. Descriptive statistics

3.2.1. Demographics

36 participants in the depression group and 35 participants in the comparison group completed testing. In the depression group, one participant was left-handed (part of exclusion criteria) and another participant did not complete the 4MT. These participants were excluded from the analysis, leaving 34 participants in the depression group and a total sample of 69 participants.

Demographic data for participants are presented in Table 2. The age range across the two groups was 18 to 62 with a mean age of 32.96 (SD=12.10). The sample was 56.5% female, and 71% had English as their first language. Overall, the sample was highly educated, with 72% of participants having a university degree. As these variables could have had an impact on memory performance, potential differences between the groups were explored. There were no statistically significant difference between the depression and the comparison group for age (t(67)=-.904, p=.369), gender (X^2(1)=1.16, p=.281), English as first language (X^2(2)=2.30, p=.130) or educational background (X^2(5)=3.102, p=.684).

Table 2

Participant demographics

	Clinical group (N=34)	Comparison group (N=35)	Total (N=69)
Age *M(SD)*	34.29 (12.81)	31.66 (11.40)	32.96 (12.10)
Gender *N(%)*			
Female	17 (50)	22 (62.9)	39 (56.5)
Male	17 (50)	13 (37.1)	30 (43.5)
English as first language *N(%)*			
First language	27 (79.4)	22 (62.9)	49 (71)
Not first language	7 (20.6)	13 (37.1)	20 (29)
Ethnicity *N(%)*			
White British	18 (52.9)	6 (17.1)	24 (34.8)
White Other	8 (23.5)	8 (22.9)	16 (23.2)
Mixed	2 (5.9)	3 (8.6)	5 (7.2)
Asian	6 (17.6)	12 (34.3)	18 (26)
Black		5 (14.3)	5 (7.2)
Other		1 (2.9)	1 (2.9)
Education *N(%)*			
Secondary or less	3 (8.8)	2 (5.7)	5 (7.2)
Post-secondary	5 (14.7)	5 (14.3)	10 (14.5)
Vocational	2 (5.9)	2 (5.7)	4 (5.8)
Undergraduate	13 (28.2)	11 (31.4)	24 (34.8)
Postgraduate	11 (32.4)	15 (42.9)	26 (37.7)
Income *N(%)*			
Less than £15.000	10 (29.4)	9 (25.7)	19 (26.8)
£15.000-£25.000	4 (11.8)	7 (20)	11 (15.5)
£26.000-£35.000	4 (11.8)	8 (22.9)	13 (18.3)
£35.000-£50.000	6 (17.6)	9 (25.7)	16 (22.5)
£50.000-£70.000	3 (8.8)		2 (4.2)
£70.000 or more	5 (14.7)	2 (5.7)	7 (9.9)

3.2.2. Clinical symptoms and depression history

The clinical data and depression history of participants in the depression group are presented in Table 3.

The BDI-II scores ranged from 11 to 48, with the mean being 29.00 (SD=8.05). Using the standard categories for the BDI-II, 5.9% of scores were in the category for mild

depression, 44.1% for moderate depression and 50% for severe depression (Beck et al., 1996). The mean number of previous episodes was 2.97 (SD=1.43). The mean length of the current episode was 25.12 months (SD=37.56), and the mean number of months since initial onset was 204 (SD=147.43), or around 17 years. Fifty-three percent of participants were currently taking anti-depressant medication, and 70% reported having a first-degree relative who had also suffered from depression.

Table 3

Depression characteristics in depression group

BDI-II score M(SD)	29 (8.05)
BDI-II category N(%)	
Mild depression	2 (5.9)
Moderate depression	15 (44.1)
Severe depression	17 (50.0)
GAD-7 score M(SD)	11.24 (3.49)
GAD-7 category N(%)	
Minimal	1 (2.9)
Mild	11 (32.4)
Moderate	17 (50.0)
Severe	5 (14.7)
Length of episode (months) M(SD)	25.12 (37.56)
Number of past episodes M(SD)*	2.97 (1.43)
Time since first episode (months) M(SD)	204.35 (147.43)
Anti-depressant medication N(%)	18 (53)
Family history N(%)	23 (70)

*Data missing for five participants

The GAD-7 scores ranged from 4 to 21, with the mean being 11.24 (SD=3.49). Only one participant showed minimal symptoms of anxiety, whilst 32.4% fell in the category for mild symptoms, 50% for moderate symptoms and 14.7% for severe symptoms (Spitzer et al., 2006).

3.2.3.   Memory performance

The scores for the AMT and 4MT are presented *Table 4*. The mean number of specific memories on the AMT was 6.85 (SD=1.88) in the depression group and 8.29 (SD=1.53) in the comparison group. The mean score on the 4MT was 21.18 (SD=3.82) in the depression group and 20.26 (SD=4.13) in the comparison group. None of the participants scored below chance level on the 4MT.

Table 4

Mean scores and significance testing for the Autobiographical Memory Test (AMT) and the Four Mountains Test (4MT)

	Depression group (N=34)	Comparison group (N=35)	t	p value
AMT M(SD)				
Specific memories	6.85 (1.88)	8.29 (1.53)	3.48	.01
Positive specific memories	3.62 (1.26)	4.42 (0.78)	3.24	.002
Negative specific memories	3.23 (1.04)	3.86 (1.06)	2.45	.017
4MT M(SD)	21.18 (3.82)	20.26 (4.13)	-.960	.340

3.2.4. Relationships between demographic variables and memory performance

As age and educational attainment may be associated with memory performance, their relationship with AMT and 4MT scores were explored. Comparing performance between participants with and without university level education, the university educated group showed higher scores on the AMT (M=7.9, SD=1.80) than the non-university educated group (M=6.74, SD=1.69) ($t(67)$=-2.425, p=.018, 95% CI -2.12- -0.21, d=.66) There was no statistically significant difference between the groups on the 4MT scores ($t(67)$=.614, p=.614, 95% CI -1.60-2.70). There was no correlation between age and AMT scores, ($r(67)$=-.66, p=.593) or age and 4MT scores, ($r(67)$=-.128, p=.293).

3.3.   Hypothesis testing

3.3.1. Primary hypothesis: Association between AMT scores and 4MT scores

The primary hypothesis concerned the association between scores on the AMT and the 4MT across both groups. Multiple regression analysis was conducted to establish whether depression status and 4MT scores predicted AMT scores. An interaction term between depression status and 4MT scores was included in the regression to investigate the potential of a moderation effect. The overall regression showed a significant effect in predicting AMT scores ($F(3,68)=4.96$, $p=.004$, $R^2=.19$). However, the analysis showed that whilst depression status predicted AMT scores (β=-1.266, $t(68)$=-2.09, p=.041), scores on the 4MT did not (β=-.398, $t(68)$=-1.145, p=.256). The interaction term was not statistically significant (β=1.049, $t(68)$=1.453, p=.151), suggesting that the relationship between 4MT scores and AMT scores did not differ between the groups. There was no evidence of an association between 4MT and AMT scores, and the primary hypothesis was therefore not supported.

3.3.2. Hypothesis two: Difference in AMT scores between groups

The second hypothesis aimed to replicate the findings of lower scores on the AMT in the depression group compared to the comparison group. The AMT scores and t-test results are presented in Table 4. There was evidence for a statistically significant difference between the clinical and the comparison group on scores on the AMT across both negative and positive cue words, with the depression group having lower scores on the AMT than the comparison group ($t(67)$=3.48, p=.01, 95% CI 0.61-2.25,

d=0.84). As the number of specific memories was lower in the clinical group compared to the comparison group, the second hypothesis was supported (Figure 2).
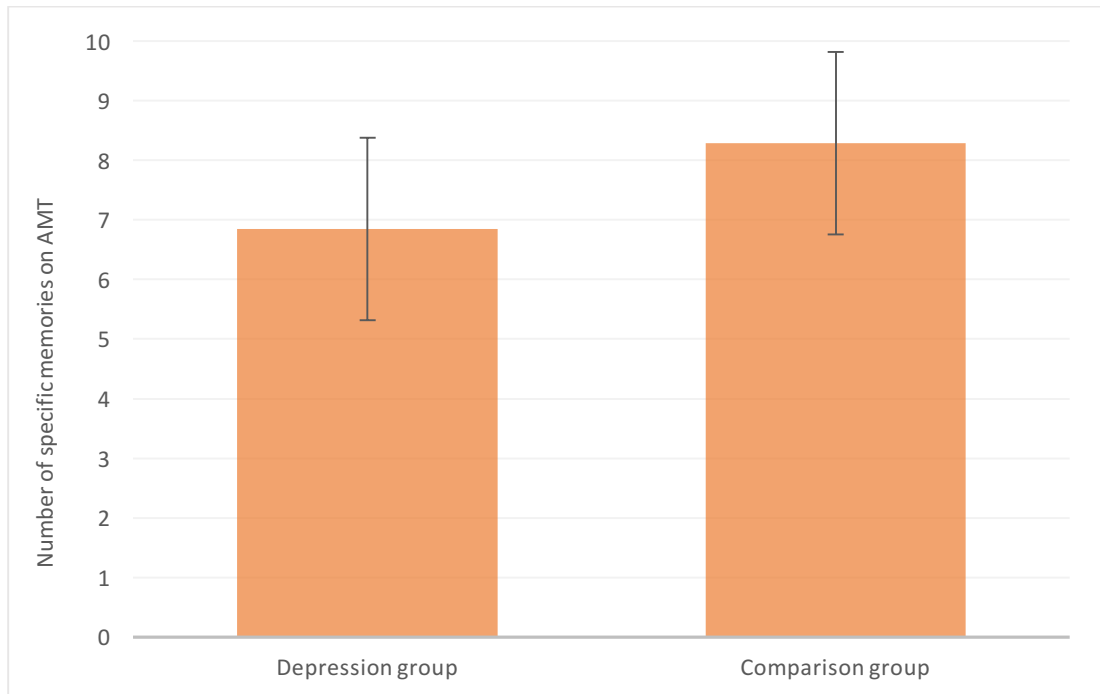
Figure 2. Mean number of specific memories and standard deviations on the AMT in the depression and the comparison group

To investigate influence of cue word valance on specificity, a mixed ANOVA was conducted with depression status as the between-subjects factor and valance as the within-subjects factor (Figure 3). The results showed an overall valance effect, with the mean number of positive specific memories being higher than the mean number of negative specific memories for both groups ($F(1, 67)=10.66$, $p=.002$), and an effect of group, confirming the higher number of specific memories in the depression group than the comparison group ($F(1,67)=12.13$, $p=.01$). The interaction between valance and group was not significant ($F(1,67)=.419$, $p=.520$), suggesting a similar valance effect in both groups.
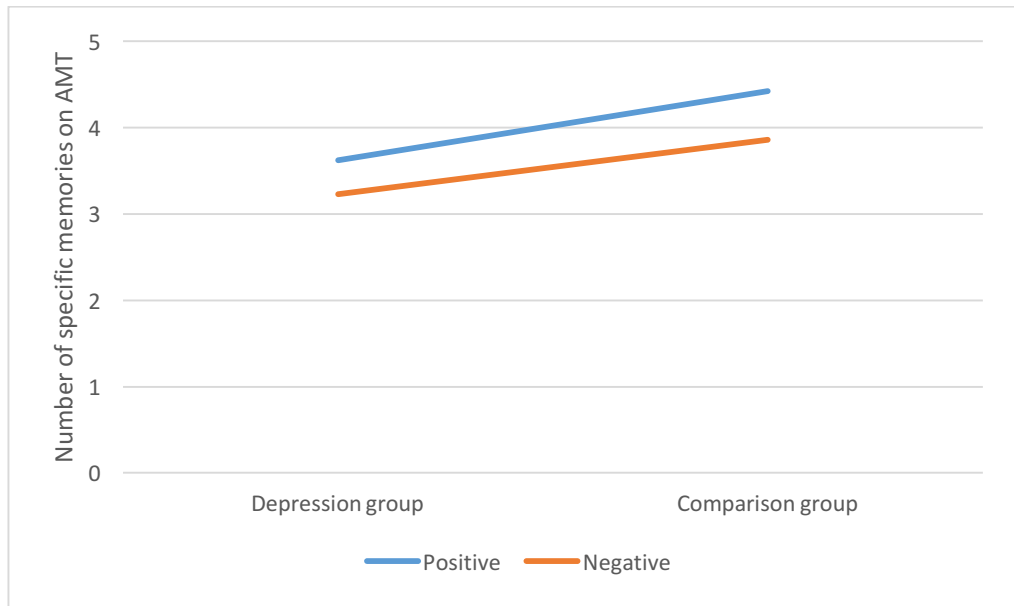
Figure 3. Valance effects on number of specific memories in the depression and the comparison group

3.3.3. *Hypothesis three: Difference in 4MT scores between groups*

The third hypothesis was that the depression group would have lower scores on the 4MT than the comparison group. The 4MT scores and t-test results are presented in Table 4. There was no evidence for a difference in scores between the depression and the comparison group and the third hypothesis was not supported (Figure 4).
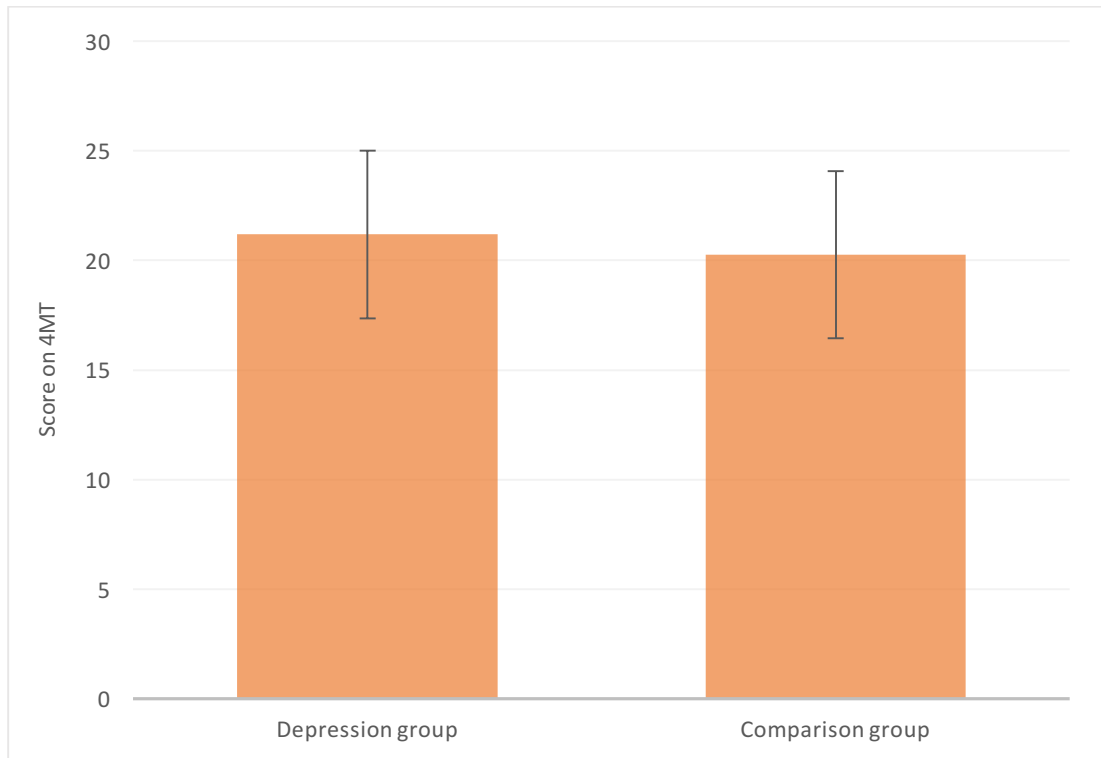
Figure 4. Mean scores and standard deviations on the 4MT in the depression and the comparison group

3.3.4. Hypothesis four: Chronicity of depression and memory scores

The fourth hypothesis was that earlier onset and longer duration of depression would be associated with lower memory scores on both the AMT and the 4MT. For the depression group, correlations were conducted using Spearman's Correlation Coefficient between both AMT and 4MT scores and a number of clinical characteristics, including the length of current episode, number of past episodes, time since initial episode onset and BDI-II and GAD-7 scores. The results are presented in Table 5. There were no significant correlations found between either AMT or 4MT scores and any of the clinical variables, and the hypothesized association between chronicity of depression and autobiographical and spatial memory was not supported.

Table 5

Spearman's Correlations between memory scores and depression variables (N=34)

	AMT		4MT	
	ρ	*p* value	ρ	*p* value
Length of current episode	.012	.946	.180	.308
Number of previous episodes*	-.045	.821	-.033	.869
Time since initial onset	-.022	.900	-.326	.060
BDI-II score	-.224	.203	-.308	.076
GAD-7 score	0.16	.927	-.298	.087

*Data missing for five participants

In addition to testing the hypotheses about depression severity and performance on the memory tasks, t-tests were conducted to assess whether there were any differences in performance between participants taking anti-depressant medication and those who were not. No differences between the groups were found for the AMT (t(32)=.297, p=.768). For the 4MT, individuals taking anti-depressants had lower scores than those who did not take medication. However, when taking the Bonferroni correction for multiple testing into account, the results could not be considered statistically significant (t(32)=-2.096, p=.044, 95% CI -5.16- -.073).

4. Discussion

4.1. Summary of findings

The aim of this study was to investigate the relationship between AM specificity and performance on a hippocampal-dependent ASM test in adults with and without depression. The primary hypothesis, that there would be an association between AM specificity and ASM performance, was not supported. The depression group recalled

fewer specific memories on the AMT than the comparison group, but there were no differences in ASM performance on the 4MT between the groups. There was no association between severity or chronicity of depressive symptoms and memory performance.

4.2. Is the memory deficit in depression specific to AM?

This study replicated the findings of OGM in depression, with the identified effect size corresponding to past research (Liu et al., 2013; Ono et al., 2016). The results suggest that depression is associated with a specific memory deficit in AM that is not present in ASM. As both AM and ASM are dependent on the hippocampus, these results could further indicate that the observed deficits in AM do not reflect general hippocampal dysfunction (Eichenbaum & Cohen, 2014). Whilst this study failed to replicate past findings of impaired ASM in depression, it supports previous evidence that OGM cannot be explained by a general memory deficit in depressive disorders (Cornwell et al., 2010; Gould et al., 2007; Williams et al., 2007; Wong, 2015). Whilst some associations have been found between OGM and other forms of episodic memory, such as recognition, other studies have failed to find associations (Raes et al., 2006; Williams et al., 2007). Semantic memory is intact in depression, which has led to proposals that memory impairment is only present when recollection relies on the access to contextual details (Söderlund et al., 2014). However, given the lack of evidence of an impairment in ASM in this study, another possibility is that an impairment is present in memory tasks that involve emotional processing (Foland-Ross & Gotlib, 2012). Recollection of AM can, depending on content, arguably be a painful process, and some definitions of AM have highlighted its contribution to

emotional regulation (Conway & Pleydell-Pearce, 2000; Köhler et al., 2015). A distinction can be made between "hot" and "cold" cognitive processes, with performance on "hot" tasks including emotional stimuli or processing (such as the AMT) possibly having a stronger relationship with depression compared to "cold" tasks that are less likely to trigger affective responses (such as the 4MT) (Gonda et al., 2015; Miskowiak & Carvalho, 2014). Both the AMT and the 4MT are likely to rely on hippocampal function, but only the AMT involves self-relevant emotional processing.

Conway and Pleydell-Pearce's (2000) Self Memory System (SMS) model of AM offers an account of how emotional regulation can halt the retrieval of specific memories. The SMS suggests that deliberate AM retrieval occurs through the hierarchical activation of three different levels of AM, including lifetime episodes, categories of events, and event-specific knowledge. Conway and Pleydell-Pearce propose that the SMS can truncate searches to avoid retrieval of emotional event-specific knowledge. OGM may represent a strategy for avoiding emotional content and regulate emotions in depression (Conway, Singer & Tagini, 2004; Raes, Hermans, Williams & Eelen, 2006). Williams and colleagues (2007) added to this hypothesis, suggesting that emotional and self-relevant retrieval cues may trigger rumination processes in depression, which can also contribute to the premature termination of AM retrieval. General executive function, which may be linked with the ability of the SMS to modulate memory retrieval, has also been linked with deficits in OGM (Dalgleish et al., 2007; Raes et al., 2006). The wealth of information needed for successful recollection of specific AMs, including self-reflection, emotion and imagery, may distinguish between AM and ASM performance in this study, and may implicate

distinct neural correlates independent of hippocampal function (Piolino et al., 2009; Svoboda et al., 2006). The emotional regulation hypothesis can provide an explanation as to why negative cue words were associated with a lower number of specific memories across both groups. The impairment in accessing specific AM in depression across both positive and negative words corresponds to the current literature and may reflect a global and indiscriminate avoidance function in depression (King et al., 2010; Liu et al., 2013).

4.3.   Is OGM in depression associated with hippocampal function?

The overlap of the neural structures involved in AM and depression has led to a compelling argument that OGM may be associated with hippocampal deficits. This study, however, found no association between OGM and performance on the 4MT, which has been shown to be sensitive to hippocampal impairment. Considering these findings, along with past neuroimaging studies yielding conflicting evidence for the association between OGM and differential hippocampal activation in depression, current support for a relationship between OGM and hippocampal dysfunction is modest (Hach et al., 2014; Young et al., 2012; 2013; 2014; 2015b; 2016). Whilst the hippocampus is a key structure in AM, other processes and structures may underlie OGM. If a key driver for OGM is affective, self-reflective and executive functions, its neural basis may include regions such as the prefrontal cortex and the amygdala (Levin, Heller, Mohanty, Herrington & Miller, 2007; Martinelli et al., 2013; Talarowska et al., 2016). King and colleagues (2010) suggest that whilst the hippocampus binds information into memories, the activation of the correct retrieval processes rely on the prefrontal cortex, which could suggest that OGM arises through

other cortical regions inhibiting hippocampal function during AM retrieval. Whilst this study has focused on hippocampal function and OGM, a full account of AM dysfunction can only be provided by considering the interactivity and connectivity between a large range of cortical regions (Piolino et al., 2009; Sheldon & Levine, 2016; Svoboda et al., 2006).

Although the results of this study can be interpreted as OGM occurring in the absence of hippocampal neurogenesis, a number of other explanations should also be considered. Firstly, OGM may be linked with changes in hippocampal function that are not reflected in performance on the 4MT. The 4MT, along with other ASM tasks, have primarily been used in populations with well-established cognitive impairments (such as hippocampal damage and dementia), and may not be sensitive to the changes in cognition found in depression (Bird et al., 2010; Chan et al., 2016; Guderian et al., 2015; Hartley et al., 2007; Moodley et al., 2015; Pengas et al., 2012; Wood et al., 2016). One past study of depression found an association between depression and ASM measured by the Town Square Task (King et al., 2002), but not measured by the 4MT (Wong et al., 2015). This study's joint project, however, also failed to find an impact of depression on ASM using the Town Square Task, suggesting a lack of ASM deficits in the depression group across two hippocampal-dependent tasks (Williams, 2017). Further, differences in neural activation may not always translate into behavioural differences between groups. For example, an fMRI study of associative memory and hippocampal activity in depression found that depression was associated with hippocampal dysregulation without observed differences in memory performance (Fairhall et al., 2010). The authors suggested that the hippocampal dysfunction may be presymptomatic, or counteracted by compensatory mechanisms. Two studies have

found increased activation in the hippocampus when specific memories were retrieved in depressed individuals compared to controls, and suggested that the increased activation may provide evidence for compensation of hippocampal atrophy (Young et al., 2014; 2016). Secondly, whilst neuroimaging studies have identified structural and functional hippocampal changes across the hemispheres, depression may be associated with dysfunction in sub-regions of the hippocampus that specialise in different memory functions (Burgess et al., 2002; McKinnon et al., 2009). Although there is significant overlap between the neural structures underlying AM and spatial memory, there is some support for specialisation across the longitudinal axis of the hippocampus, and between the left and the right hippocampus (Burgess et al., 2002; Fanselow & Dong, 2010; Iglói, Doeller, Berthoz, Rondi-Reig & Burgess, 2010; Sheldon & Levine, 2016). Sheldon and Levine (2016) suggest that the relative involvement of the anterior and posterior hippocampus depends on task demands, with the anterior hippocampus being preferentially involved in conceptual representations and the posterior hippocampus in perceptual representations. In line with this, they also suggest that the anterior hippocampus shows more involvement in open-ended memory retrieval tasks, whilst more well-defined memory tasks can rely on the posterior hippocampus. The specific deficit in AM compared to ASM in this study could hence reflect different task-demands between the AMT and the 4MT relying on different sub-regions of the hippocampus. Finally, trauma and PTSD have also been linked with changes in the hippocampus and with impaired ASM (Smith et al., 2015; Talarowska et al., 2016). As these were exclusion criteria of the study, participants may not have been representative of the adverse life events and stress often associated with depressive symptomology (Hammen, 2005).

4.4.   The links between depression severity, chronicity and memory

This study found no associations between symptoms or chronicity of depression and OGM. Whilst there is some evidence for a link between number of depressive episodes and OGM, this corresponds with the general findings that OGM and other cognitive symptoms do not correlate with depression severity (Kuyken & Brewin, 1995; Liu et al., 2013; Reppermund, Ising, Lucae & Zihl, 2009; Williams et al., 2007). The cognitive features of depression may represent a categorical difference in processing and thinking styles, and a trait marker of depression rather than a mood-dependent state marker (King et al., 2010). However, the results of this study are only representative of individuals with depression onset at least 2.5 years prior to testing, and currently experiencing at least moderate symptoms of depression. Within the depression group, there was a trend towards time since initial onset, BDI-II scores, GAD-7 and medication use being associated with lower scores on the 4MT. If cognitive changes were associated with dysregulation of the HPA-axis and the impact on the hippocampus, a dose-response relationship between chronicity and memory deficits on the 4MT could be predicted. Given that this was a trend rather than an association of statistical significance, and that no differences were found in performance on the 4MT between the depression and comparison groups, it is not possible to draw any conclusions based on this data.

4.5.   Clinical and theoretical implications

Understanding OGM and other memory deficits in depression is important due to their potential consequences on functioning, well-being and the course of the disorder

(Sumner et al., 2010; Williams et al., 2007). High levels of OGM may also interfere with the engagement in and the success of treatment (Etkin, 2016; Köhler et al., 2015; Talarowska et al., 2016). Current pharmacological and psychological treatment strategies for depression mainly target the emotional features of the disorder, whilst the cognitive features are often not recognised or addressed (Darcet et al., 2016, Gonda et al., 2015; Hammi et al., 2014). As this study replicated the finding of OGM in depression being present within a population of service-users of the NHS IAPT services, it could provide support for improved recognition and treatment of memory deficits in chronic depression.

The lack of an association between OGM and ASM in this study provided no evidence for integrated theories of hippocampal involvement in AM and ASM. Given the vast evidence-base for the hippocampal involvement in both, however, this absence of evidence should not be interpreted as evidence of an absence in the association between the neural underpinnings of the two types of memory (Eichenbaum & Cohen, 2014). It should also be noted that the power calculation and sample size of this study only allowed for detection of a moderate effect size with 80% power.

4.6. Limitations

A number of limitations of this study should be considered when interpreting the results.

Firstly, whilst no differences were identified in terms of demographic variables, it is possible that the motivations for research participation differed between the groups

which could have led to differences in the two samples. Secondly, the representativeness of both groups should be considered. The results in the depression group should only be regarded as representative of individuals with at least moderate symptoms of depression, a history of depression of more than 2.5 years. In addition, a third of the participants screened for the depression group were excluded from participation, mainly due to potential co-morbidities. Despite the symptom severity and chronicity, the majority of participants in the depression group were highly functioning in regards to employment status and income, which is not representative of all individuals with depression. A number of participants in the depression group also reported an interest in the study due to subjective memory problems, which may have led to selection bias in the recruitment.

Thirdly, the validity and reliability of the measurement tools in this study should be considered. Whilst the AMT is considered the gold standard method of measuring OGM, it is a testing paradigm rather than a standardised measurement tool (Liu et al., 2013). The AMT is considered to have adequate psychometric properties, but studies have used a range of different variations, and it is possible that features of the administration such as cue words used, time limit and task instructions can influence participant performance (Griffith et al., 2012; Yanes, Roberts & Carlos, 2008). The study did also not measure remoteness or qualitative aspects of memory retrieval, such as subjective vividness, detail, emotional arousal or perceptual features, which may be associated with distinct neural regions (Addis, Moscovitch, Crawley & McAndrews, 2004; Falco, Peynircioglu & Hohman, 2015; St-Laurent, Moscovitch & McAndrews, 2016; Piolino et al., 2009). The 4MT has similarly not had its psychometric properties formally evaluated, and it is possible that the 4MT is not sensitive enough to identify

hippocampal deficits in depression. This study used the version of the 4MT that only includes allocentric memory trials (Hartley & Harlow, 2012), and the use of the original tasks which calculates a score between non-spatial and ASM as an index of hippocampal function could have potentially provided a more sensitive measure, especially given previous null findings in depression using the 4MT (Hartley et al., 2007; Wong et al., 2015). The 4MT was also used as a measure of overall hippocampal function, rather than considering the potential functional specialisation of regions of the hippocampus. Depression history was measured using self-report questions, and a number of participants found it difficult to provide accurate answers, which may have impacted the reliability of the data. Measures of current state, such as tiredness, or task effort, were not included. A challenge in depression research is the heterogeneity of presentations, and further exploration of other cognitive symptoms could have provided useful information about current symptomology. This, however, was not possible within the scope of this project.

Lastly, the cross-sectional design of this study meant that it could not address the lack of knowledge about the causal relationships or aetiology between the measured variables (Darcet et al., 2016; Gonda et al., 2015).

4.7. Conclusions and future directions

This study replicated the presence of AM deficits in depression. There was no support for deficits in hippocampus-dependent ASM, or evidence for an association between OGM and ASM. Whilst this can be interpreted as a lack of support for hippocampal deficits underlying OGM in depression, this conclusion may be premature due to the

potential lack of sensitivity to detect hippocampal function in depression in the measure used. It does, however, highlight the need for further investigation to understand both the affective, cognitive and neural correlates of OGM. Whilst both neuroimaging and behavioural measures of hippocampal function have their limitations, they can be used to complement each other in future research (Fairhall et al., 2010; Svoboda et al., 2006). There are strong reasons to believe that the cognitive features of depression have structural and functional neural correlates, and much potential for research in this area. As these are currently not well understood, there is great potential for further research in this area.

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Part 3: Critical Appraisal

1. Introduction

The aim of the critical appraisal was to undertake and provide reflections on the process of conducting this research project. From the initial thoughts and ideas to the write-up phase, this process has spanned over two years, offering vast opportunities for learning and reflection. In this section, I will focus on the topics that have been most thought-provoking or that have had the most tangible impact on my professional development during the course of the project. I will discuss the benefits of conducting a joint project, challenges with the exclusion criteria and generalisability, limitations of the Autobiographical Memory Test (AMT), and also reflect on the implications of taking on a clinical research role within the National Health Service (NHS). More general considerations, relating to study design and recruitment of participants, will be considered under several of these headings.

2. Benefits of a joint project

As a third year trainee clinical psychologist, you are frequently asked by trainees in earlier stages of the course what to think about when selecting a major research project. My response to such questions has invariably been "Have you considered a joint project?".

My choice of project at the time, however, was not based on the fact that it was a joint project arrangement. Rather, what triggered my interest was my experience of working with depression and the appreciation of the vast heterogeneity within this diagnostic category. It is often cited that the current diagnostic criteria for depression allow for two individuals with no overlapping symptoms to receive the same diagnosis (APA,

2013). Limitations and variability in treatment responses reflect the need for increased understanding of the affective, cognitive, biological and social factors involved in depression. It was my hope that I with this project would be able to make my own contribution to the knowledge base by shedding some additional light on the memory features associated with the disorder. My specific interest in autobiographical memory (AM) originated from my undergraduate thesis on memory and eating pathology. The fact that I ended up having a research partner, was a lucky coincidence based on shared interests.

Whilst I was very open to the idea of a joint project from the outset, I did not appreciate all the benefits until much later in the process. In practical terms, recruitment and data collection was very time-consuming, and a sample of 69 participants could only be achieved through a joint project. The consensual decision-making and problem-solving, and the opportunity to fine-tune various aspects of the research through an on-going dialogue with my project partner (in addition to my supervisor), definitely benefitted the final research design.

Another big advantage of being part of a joint project was the mutual support and the informal peer-supervision we could provide to each other on a continuous basis. It is not without reason that the major research project component of the Doctorate in Clinical Psychology is seen as a strenuous task, and the pressures of post-graduate studies are reflected in high stress-levels in this population (Hyun, Quinn, Madon & Lustig, 2006). The joint project arrangement helped me manage both the daily stress and the occasional feelings of despondency. It is, of course, textbook knowledge that social support is a powerful buffer between stress and distress (Cohen & Wills, 1985).

Indeed, studies have demonstrated the benefits of social support, and emotional focus and venting as a coping strategy, specifically in psychology graduate students (Myers et al., 2012; Nelson, Dell'Oliver, Koch & Buckler, 2001). Having a project partner also opened a path for discussing small dilemmas and interactions with research participants, which would not have been appropriate to do with individuals outside the project, and equally would not always have met my personal threshold for contacting my project supervisor. At times where there were challenges, for instance with slow recruitment, sharing this helped me maintain an overall positive attitude.

Whilst the joint project was an overwhelmingly good experience, it does, of course, also involve a risk of interpersonal difficulties. After some reflection, I believe that the key to our successful cooperation was free and open communication and a practical approach to the tasks of the study. All tasks were not divided exactly equally at all times, but we worked in tandem towards the joint goal of finishing the project. The importance of good interpersonal relationships when conducting research was also highlighted by the invaluable support we received from staff working in the services where the depression group was recruited, not to mention the excellent support I received from my research supervisor throughout the process.

It is also worth mentioning that the joint project arrangement had an impact on the design of the study as it was based on a balance between the aims and the needs of two projects. In a single project it would have been possible to investigate the association between AM and spatial memory using two measures rather than one, but to keep a clear distinction between the projects we did not use the other project's spatial memory data for analysis. In addition, the testing time for the measures of both projects was

about 75 minutes, and limiting the time-demands on participants required careful planning and consideration of the tasks and measures to be included. The decision to use the standard ten cue word AMT with a 30 second time-limit, for instance, was largely based on the practical consideration that administration of other versions would have been more time-consuming. Balancing the needs of the two projects also meant that it was not possible to include other measures that might have provided interesting information, such as scales of rumination. In retrospect, due to the established association between OGM and general intellectual functioning and working memory, it would have been useful to include a measure to establish whether there were differences between the groups in these abilities (Heron et al., 2012; Raes et al., 2006; Wessel, Merckelbach & Dekkers, 2002).

3. Exclusion criteria and the effects on generalisability

This project has made me appreciate the challenges of determining and screening for inclusion and exclusion criteria in clinical research. The exclusion criteria of this study were based on factors that may have influenced memory performance independently of depression status. Due to practical limitations, some of the screening procedures for the exclusion criteria, however, somewhat lacked sensitivity and specificity. For example, the exclusion of participants for alcohol or substance abuse was based on a self-report question and not on a standardised scale. On the other hand, the use of psychiatric screening questions from the Structured Clinical Interview for DSM Axis I Disorders (SCID-I) (First, Spitzer, Gibbon & Williams, 1996) may have excluded participants with no actual psychopathology. It is also worth noting that the inclusion criteria for the depression group were based on the presence of symptoms of

depression rather than on a confirmed diagnosis. Additional exclusion criteria may also have been warranted. For example, one participant reported a medical condition influencing their memory and was therefore excluded, even though the set screening procedure did not specifically address this. In addition, whilst a third of the participants screened for the depression group did not meet the eligibility criteria for the study, this was only the case for two participants in the comparison group. Indeed, the presence of co-morbid psychiatric problems is likely to be much higher in the depression group, but it also seems unlikely that only two participants in the comparison group actually met the exclusion criteria. This could be interpreted as a failure of the screening procedure to capture the exclusion criteria, but perhaps also reflects different motivations for participation and eligibility between the two groups. Calling the non-depressed group a "comparison" rather than a "control" group was a conscious decision as I do not think the two groups were perfectly matched across all features and characteristics.

In addition, the impact of the inclusion and exclusion criteria on the external validity, or generalizability, of studies should be considered. This is relevant to the data collection in the empirical study, but also to the studies included in the literature review. Treatment studies for depression are often criticised for their narrow inclusion criteria and for excluding participants with co-morbid psychiatric symptoms (Stirman, DeRubeis, Crits-Cristoph & Brody, 2003). For example, the exclusion criteria used in most anti-depressant research implies that only around 15% of those seeking support for depression meet the eligibility criteria for participation in randomised controlled trials (Zimmerman, Mattia & Posternak, 2002). Similar problems with selection bias apply to cross-sectional research, including this study, where the exclusion of

participants with co-morbid symptomology potentially leads to less complex depression samples than those found in the actual population. In retrospect, excluding participants based on potential symptoms of obsessive-compulsive disorder (OCD) is unlikely to have been a useful criterion, in particular given that general symptoms of anxiety were not screened for. I would now reconsider this exclusion criterion. This could potentially have facilitated the recruitment of the depression group, which was very lengthy, partially due to strict eligibility criteria. In addition, not excluding participants based on trauma history or potential symptoms of post-traumatic stress disorder (PTSD), and instead including relevant symptom measures in the study, could have provided additional information about the links between depression, life events, memory and hippocampal function. Due to the exclusion criteria, the depression group in this study is likely to have experienced less trauma than would usually be expected in a depression sample. It is possible that whilst depression is independently associated with deficits in AM, deficits in spatial memory may be particularly associated with the emotional and neurological reactions to trauma-exposure (Smith, Burgess, Brewin & King 2015). Including trauma symptoms measures, however, was not pursued, partly due to practical limitations, and partly due to the additional ethical considerations required when asking more detailed questions about trauma and PTSD.

Whilst the question of generalizability of findings is of key importance, the ethical implications of excluding participants from research, and hence preventing them from contributing to the evidence-base of the symptoms they are experiencing, should also be considered. Whilst most excluded participants reported no questions or concerns about not meeting eligibility criteria for the study, two voiced frustration with not being able to take part due to psychiatric history or demographic features, both

reporting a feeling of being "dismissed" by clinical research. Whilst the theoretical reasons for excluding participants can be defended, I can also empathise with service-users feeling excluded from research they find relevant to themselves. There is perhaps an argument to be made about decision about research eligibility being too clinician-led, and that this study, like many others, would have benefitted from more service-user input across different stages of the research.

4. Validity and reliability of the Autobiographical Memory Test (AMT)

The AMT is the dominant measure for AM specificity and overgeneral memory (OGM) (Liu, Li, Xiao, Yang & Jiang, 2013; Williams et al., 2007). The reliance on the AMT as a measure of OGM in both the literature review and the empirical study of this paper, however, warrants some considerations of its weaknesses.

For the purpose of the literature review, the AMT was rated as a high-quality measurement tool in terms of validity and reliability. This decision was largely pragmatic, and based on the research question assuming that OGM is a measurable construct. However, this could be challenged both based on evidence that different modes of administration could affect the results, and on the validity of the AMT as a measurement tool (Liu et al., 2013).

Regarding the validity of the AMT, it should be considered what exactly the AMT measures. The underlying assumption in the OGM literature is that the AMT provides a measure of AM retrieval, and that this is of clinical relevance to the onset,

maintenance and course of depression (Conway & Pleydell-Pearce, 2000; Griffith et al., 2012; van Vreeswijk & de Wilde, 2004; Williams et al., 2007). Whilst current evidence suggests that the AMT measures an independent feature of depression, the links to other features and correlates of depression, such as rumination, executive function, avoidance and trauma, highlights the possibility that the outcomes of the AMT may represent a variety of both independent and interdependent processes (Griffith et al., 2012; Williams et al., 2007). It should also be made explicit what the AMT is *not* measuring. Studies have, for example, demonstrated a distinction between specificity and detail in autobiographical memories, as well as specific memories differing substantially on features such as the subjective experience of remembering (Kyung, Yanes-Lukin & Roberts, 2016; Piolino, Desgranges & Eustache, 2009). The validity of the AMT is also challenged by the over-reliance of a single measure of OGM (Williams et al., 2007; Sumner, Mineka & McAdams, 2013). The most widely used version of the AMT is the original version that initially identified and labelled the OGM phenomenon (Williams & Broadbent, 1986). There is a lack of studies investigating OGM using several different measures of AM within the same sample, which could strengthen the validity of the AMT as the gold standard measure for memory specificty (Sumner et al., 2013).

The stability of OGM, and whether the AMT measures a trait or a state feature of depression, has also been debated (van Vreeswijk & de Wilde, 2004). Studies examining AM at different points in time have suggested that OGM is a relatively stable trait when measured at monthly intervals, but the association is modest over time-periods of several years (Griffith et al., 2012; Sumner et al., 2014). This highlights the importance of controlled and randomised clinical trials as some variation

is to be expected in the absence of any intervention. The learning effect on performance on the AMT is currently unclear, and a problem in the literature review included several studies not reporting whether they used the same cue words during administration at different time-points.

Evidenced by the studies in the literature review, a number of different administration procedures and cue words have been used for the AMT. Across a number of versions, the investigation of the psychometric properties of the AMT suggested good internal consistency and that the AMT had a unifactorial structure, with emerging evidence for these properties applying across different languages and cultural backgrounds (Griffith et al., 2009; Heron et al., 2012; Takano, Mori, Nishiguchi, Moriya & Raes, 2017). Compared to more in-depth and resource-intensive ways of assessing autobiographical memory (such as semi-structured interviews), it offers a measure that is relatively easy to administer and provides data that can be reliably coded (Griffith et al., 2012; Heron et al., 2012).

Memory specificity may be associated with administration features of the AMT, including the number of cue words, time allowed for retrieval, the methods of recording responses, and whether prompting is used (Liu et al., 2013). It has also been proposed that OGM in depression may be a result of poor recollection of task instructions (Yanes, Roberts & Carlos, 2008). In non-clinical populations, however, detailed task-instructions may decrease the sensitivity of the AMT and produce ceiling effects in the data, and it has been proposed that an AMT with minimal instructions offers the most sensitive way of measuring OGM in non-clinical populations (Deeber, Hermans & Raes, 2009). In this study, the standard AMT procedure (which includes

detailed instructions, examples and prompting) was used (Williams & Broadbent, 1986). The use of more detailed instructions and prompting increases the risk of researcher bias, which is relevant to this study as the researchers were not blind to participant condition (van Vreeswijk & de Wilde, 2004). Liu and colleagues (2013) have suggested that the AMT is most sensitive when 15 cue words are used, and participants are given 60 seconds to retrieve a memory. Based on their meta-analysis, the use of 10 cue words in this study could have underestimated OGM, whilst the 30 second retrieval time may have overestimated it by not giving depressed participants enough time. Griffith and colleagues (2012) suggest that efforts should be made to establish a more standardised version of the AMT to facilitate comparison across studies. Notwithstanding, it is also possible that different populations and measurement purposes warrant different versions.

Lastly, the AMT is considered as a measure of memory retrieval, but memory encoding may also be impacted by depression and influence performance on the AMT (Harvey et al., 2016). Considering effects of depression on encoding was out of the scope of this thesis, but could also be associated with differences in neurological patterns or responses to interventions for depression (Harvey et al., 2016; van Eijndhoven et al., 2011).

5. Reflections on the different roles of a trainee clinical psychologist

When balancing the plural roles of a trainee clinical psychologist in the NHS, I have found the analogy of "wearing different hats" helpful (May, 1978; Leavitt, Reynolds,

Barnes, Schilpzand & Hannah, 2012; Resnikoff & Lapidus, 1990). This project was my first experience of wearing a "researcher hat" in the context of depression. Whilst many aspects of this role drew on my therapeutic skills, I am more experienced and comfortable as a therapist than as a researcher. My new professional role (or hat) did therefore not always feel entirely comfortable.

The nature of the depression questions used in this research often prompted participants to further elaborate on their depression history and their current context and difficulties. These interactions sometimes tempted me to replace my "researcher hat" with my "therapist hat", and to further engage in a therapeutic conversation. Arguably, however, this would not have been in conformity with my research role, and any attempt on my side to provide a therapeutic intervention would have been inappropriate as I lacked both the information needed for a formulation and the time and resources for an intervention. It was a good to know that all participants with depression were currently receiving psychological support. However, throughout the data collection, I became more confident as to which psychological support skills would fit under my "research hat", such as empathic listening, and sometimes reflecting back dilemmas or strengths present the participant narratives. This sometimes also included some basic psychoeducation about depression, such as normalising symptoms. I also believe that a number of participants found the topic of the study normalising of their cognitive symptoms, as several people mentioned that they considered memory and attention problems as part of their depression.

I wonder whether participants perhaps also found it difficult to clearly distinguish between their roles as patients or clients from that of research participants. Importantly,

all the data collection for the depression group took place at the local mental health services, which may have blurred this distinction. I did therefore find it important to listen and validate participant experiences, as a dismissive attitude could have impacted their relationship with the service or their inclination to seek help later (Reder & Fredman, 1996).

Whilst the aims of the researcher sessions were very different from therapeutic work with depressed individuals, this experience has made me understand which of my skills are perhaps best conceptualised under a general "clinical psychologist hat" rather than a "therapist hat", and also made me more comfortable applying these skills in a new and different setting.

6. Conclusions and final comments

Conducting this research project, which spanned over two years, offered me insight into some of the theoretical and practical challenges associated with clinical research and gave me a range of new skills. Particularly, it has helped me understand the complexity and the need to strive for balance between different priorities within a study. This knowledge and understanding will not only help me when conducting future research, but also when reading and interpreting published studies.

This project was based on literature about depression, memory and the human brain. Despite the vast amount of research and theories available across these topics, they all represent areas of human functioning where there are perhaps still more questions than answers. As science has increasingly managed to map out the complexities of the

human body and address physical disease, mental health problems such as depression have become the main contributors to disability in many parts of the world, which highlights the importance of taking our understanding of its features further to inform prevention and treatment strategies (World Health Organisation, 2017). I look forward to seeing how our knowledge and conceptualisation of depression will develop throughout my career as a clinical psychologist.

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Appendices

Appendix A: Details of stages of research conducted individually and jointly

	Individual	Joint	Comments
Literature Review	√		
Empirical paper			
Research question	√		
Research design	√	√	Initially individual, with collaboration on the final design and procedures
Ethical approval		√	Tasks conducted jointly or shared
Liaison with IAPT services		√	Tasks conducted jointly or shared
Participant recruitment		√	Tasks shared
Participant testing		√	Tasks shared
Data scoring and input		√	Tasks shared
Data analysis	√		
Write-up	√		
Critical appraisal	√		

Appendix B: Details of measures used in joint project

	Joint	Individual: Janice Williams' project	Individual: Line Sågfors' project
Beck Depression Inventory II (BDI-II) (Beck, Steer, Ball & Ranieri, 1996)	√		
Generalised Anxiety Disorder – 7 (GAD-7) (Spitzer, Kroenke, Williams Lowe, 2006)	√		
Bespoke clinical information questionnaire	√		
Demographic information	√		
Ten Item Personality Measure (TIPI) (Gosling, Rentfrow & Swann, 2003)		√	
Town Square Test (King, Burgess, Hartley, Vargha-Khadem & O'Keefe, 2002)		√	
Four Mountains Test (Hartley et al., 2007)			√
AMT (Williams & Broadbent, 1986)			√

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Appendix C: NHS Ethical Approval Letter

NHS
Health Research Authority

NRES Committee East Midlands - Nottingham 2
Royal Standard Place
Nottingham
NG1 6FS

Telephone: 0115 8839695

09 June 2014

█████████

Lecturer
UCL, 1-19 Torrington Place,
Research Department of Clinical,
Education and Health Psychology
London
WC1E 7HB

Dear █████████

Study title:	The Relationship Between Depressive Symptoms and Hippocampally-dependent Allocentric Memory
REC reference:	14/EM/0222
IRAS project ID:	148009

Thank you for your recent letter responding to the Proportionate Review Sub-Committee's request for changes to the documentation for the above study.

The revised documentation has been reviewed and approved by the sub-committee.

We plan to publish your research summary wording for the above study on the NRES website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the REC Manager, Ms Liza Selway, at NRESCommittee.EastMidlands-Nottingham2@nhs.net

Confirmation of ethical opinion

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

Conditions of the favourable opinion

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

study.

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers.   The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

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

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

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

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

Registration of Clinical Trials

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

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

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

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

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

Ethical review of research sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management

permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" above).

Approved documents

The documents reviewed and approved by the Committee are:

Document	Version	Date
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only)	UCL	24 February 2014
GP/consultant information sheets or letters	1	02 February 2014
Letters of invitation to participant	LDC Register version 2	09 April 2014
Letters of invitation to participant	GP version 2	09 April 2014
Letters of invitation to participant	UHL version 2	09 April 2014
Non-validated questionnaire [PHQ-9 Depression]	1	20 March 2014
Other [Inclusion and Exclusion Criteria List]	1	07 February 2014
Other [Pittsburgh Sleep Quality Index]		
Participant consent form	2	29 April 2014
Participant information sheet (PIS)	2	29 April 2014
REC Application Form	148009/607422/1/778	09 May 2014
Research protocol or project proposal	Online Rationale version 1	14 March 2014
Research protocol or project proposal	1	20 March 2014
Response to Request for Further Information	Email from Yen Peng Wong	22 May 2014
Summary CV for Chief Investigator (CI)	Yen Wong	
Summary CV for Chief Investigator (CI)	Dr John King	
Summary CV for Chief Investigator (CI)	Dr Neil Ralph	12 December 2013
Validated questionnaire [SCID Screening]	1	20 March 2014
Validated questionnaire [Insomnia Severity Index]		
Validated questionnaire [GAD-7]	1	20 March 2014

Statement of compliance

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

After ethical review

Reporting requirements

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

- Notifying substantial amendments
- Adding new sites and investigators

- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

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

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance

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

14/EM/0222	Please quote this number on all correspondence

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

Yours sincerely

pp

Chair

Email: NRESCommittee.EastMidlands-Nottingham2@nhs.net

Enclosures: *"After ethical review – guidance for researchers"*

Copy to: ▮▮▮▮▮▮▮▮▮▮▮, *Camden & Islington NHS Foundation Trust*

Appendix D: NHS Ethical Approval of Substantial Amendment

NHS
Health Research Authority

East Midlands - Nottingham 2 Research Ethics Committee

Royal Standard Place
Nottingham
NG1 6FS

22 March 2016

█████████████

R&D (1st Floor, Maple House), Rosenheim Wing, Ground Floor
25 Grafton Way, London
WC1E 6DB

Dear ███████

Study title:	**The Relationship Between Depressive Symptoms and Hippocampally-dependent Allocentric Memory**
REC reference:	**14/EM/0222**
Amendment number:	**third amendment**
Amendment date:	**13 February 2016**
IRAS project ID:	**148009**

The above amendment was reviewed at the meeting of the Sub-Committee held on 21 March 2016.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Notice of Substantial Amendment (non-CTIMP)	third amendment	13 February 2016
Other [Developing a word based version of the Town Square Task]	1.0	03 March 2016
Other [Autobiographical Memory Test]	1.0	03 March 2016
Participant consent form	5 - tracked	01 February 2016
Participant information sheet (PIS)	5 - tracked	01 February 2016
Research protocol or project proposal [study protocol (= Outline Rationale + Study Overview)]	5 - tracked	01 February 2016
Research protocol or project proposal	5 - tracked	01 February 2016
Summary CV for student [Line Sagfors]		
Summary CV for student [Janice Williams]		
Validated questionnaire [BDI - II]		

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

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

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

14/EM/0222:	Please quote this number on all correspondence

Yours sincerely

pp.

Chair

E-mail: NRESCommittee.EastMidlands-Nottingham2@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: ▉▉▉▉▉▉▉▉, *Camden & Islington NHS Foundation Trust*
▉▉▉▉▉▉▉ *UCL*

– X –

Appendix E: Participant information and consent form for depression group

RESEARCH DEPARTMENT OF CLINICAL, EDUCATIONAL AND HEALTH PSYCHOLOGY

Camden and Islington **NHS**
NHS Foundation Trust

UCL

Understanding the Effects of Depression on Memory

This study has been approved by the Research Ethics Committee for East Midlands – Nottingham 2 (Project ID Number): 14/EM/0222.

We would like to invite you to participate in this research project.

We would like to invite you to take part in our research study. You should participate only if you want to do so. Before you decide whether to take part, we would like you to understand why the study is carried out, what you would be asked to do, and how the study will be conducted. Please take some time to read this sheet thoroughly, and to discuss it with other people if you wish. One of our team will go through the information sheet with you and answer any questions you have. Please feel free to ask any further questions about the study, or if you find anything on this sheet unclear.

Why is this study being done?

Little is currently known about the impact of depression on the way memories are processed in the brain, but we know that memory can be affected. By investigating spatial memory (remembering where things are) - as well as autobiographical memory (remembering things we have experienced) - we hope to gain a better understanding of depression and to develop more effective screening tools to measure the impact of depression.

Why have you been invited to take part?

You have been invited to take part in this study because you have recently been referred to (or self-referred) for depression and assessed at one of the clinical services in collaboration with the research team. Alternatively, you may have completed an intake form indicating your consent to be contacted by a researcher affiliated with the Camden and Islington Psychological Therapies Service to contact you for research matters. There will be approximately 33 other participants recruited for this study.

Do I have to take part?

No. Your participation in the study is entirely voluntary. It is your choice whether or not you would like to participate. Deciding not to take part in the study will not affect the care you receive from services either now or in the future. If you do decide to participate, you will be given this information sheet to keep, and your therapist will ask you to sign a consent form stating that you wish to take part. You may either sign this consent form and return it immediately to your therapist or bring it back to the psychology department within 24 hours. Alternatively, you may post it back to the psychology department. We will provide you with a stamp and envelope for postage. If you do give consent to take part in the study, you are still free to leave the study at any point, without giving a reason. This

**RESEARCH DEPARTMENT OF CLINICAL,
EDUCATIONAL AND HEALTH PSYCHOLOGY**

will not affect the care you are currently receiving, or will receive in the future. If you leave, any information for the research that we have already collected from you will be destroyed.
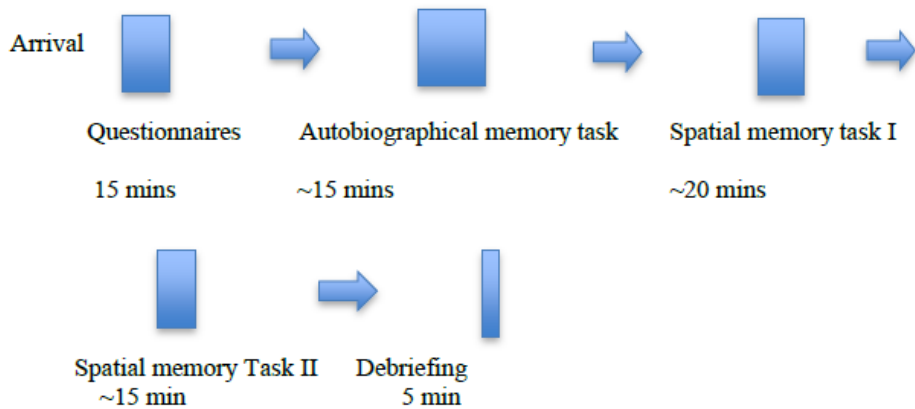
What will happen if I decide to take part?

Your psychological therapist at the clinical service will give you some details of the study during your first session. If you wish to take part in the study, your therapist will then ask you some questions to determine your eligibility to participate, as not everyone would be suitable. The participant information sheet will be handed to you. Your therapist will provide us with your contact details after you have provided consent to participate in the study. During a telephone call with one of our researchers, we will ask you some further questions to verify your eligibility. During this time, any other questions you may have about your participation will be addressed. If you decide to participate and are suitable, the researcher will arrange a convenient time to meet with you, preferably prior to your third therapy session with your therapist.

If you had previously indicated your consent on an intake form, the Camden and Islington Psychological Services will provide the researcher with your contact number. The researcher will contact you to find out if you are still interested to participate in the study. If so, the researcher will tell you about the current study and ask you some questions to verify your eligibility. A copy of the participant information sheet will be posted to you. The researcher will phone you in about a week to find out if you have received the participant information sheet. If you still express interest in the study, the researcher will arrange a convenient time to meet with you.

Study overview:

The session will take approximately 70 minutes as follows:

Arrival

Questionnaires

15 mins

Autobiographical memory task

~15 mins

Spatial memory task I

~20 mins

Spatial memory Task II
~15 min

Debriefing
5 min

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If you agree to participate in this study, you will be asked to come to a site most convenient for you, within the Camden and Islington NHS Foundation Trust. Upon your arrival, you will meet a member of the research team and you can ask any other questions you may have. Following this, you will be asked to complete questionnaires on depression and anxiety. The next task is an autobiographical memory test where the researcher will give you a number of cue words and ask you to recall events from the past that relate to these words. You will then perform a pen-and-paper task (Spatial memory task I), in which you will be asked to view some pictures of landscapes, then select the correct answer from a few options. Spatial memory task II is a computerized task. You will view some scenes, then answer some questions to see how well you remember what you saw. Most people find these tasks quite interesting to do. At the end of the session, the study researcher will conduct a debriefing and address any other questions or concerns you may have.

What are the possible disadvantages and risks for taking part?

We do not anticipate any potential disadvantages or risks in your participation. However, we will support you if you become upset or distressed during the study. You will be given time at the end of the study to be fully debriefed with a member of the research team. Your personal therapist will also be aware of your participation in the study and able to support you should you find discussing your experiences difficult.

What are the possible benefits of taking part?

You may find it interesting to complete these tasks and the information gathered during this study will also help to inform our understanding of depression, which will hopefully be a step towards helping the development of novel screening tools in the future.

Will I be paid for taking part in this study?

We will give you £12.50 when you have completed the tasks and questionnaires to compensate you for your time and any travel expenses you may have incurred.

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Who will know you are taking part in the study?

We will inform your personal therapist and your GP of your participation. Information collected during all stages of the study will be kept strictly confidential. All information will only be viewed by members of the research team at University College London. However, if through the course of the study it was found that you are at immediate risk of harm to yourself or others, this information will be shared with your therapist or GP and if necessary, emergency services.

Will my taking part in the study be kept confidential?

Your consent form will be kept in a separate location from all your other data, ensuring that this remains anonymous. All data will be stored in secure location whereby a participant ID will be assigned to your data, with no identifiable personal information. Any data with your identifying details removed and stored on computers will be password protected. Any published data will also be entirely anonymous, meaning that individuals cannot be identified.

The data from this study will be stored in accordance with the UCL and NHS Data Protection and Records Management policies. We will follow ethical and legal practice and all information about you will be handled in confidence.

All data will be collected and stored in accordance with the Data Protection Act 1998.

What will happen to the results of the research study?

The results will be written up in the form of reports to be submitted as a doctoral thesis project. As mentioned, you will not be identifiable from the results. On completion, you will be sent a summary of the study results if you request for it. You may contact one of the study researchers listed below via phone or email.

What if there is a problem?

Every care will be taken in the course of this study. If you wish to complain, or have any concerns about any aspect of the way you have been approached or treated by members of staff you may have experienced due to your participation in the research, National Health Service or UCL complaints mechanisms are available to you. Please ask the researcher if you would like more information on this. In the unlikely event that you are harmed by taking part in this study, compensation may be available.

If you suspect that the harm is the result of the Sponsor's (University College London) negligence, then you may be able to claim compensation. After discussing with the researcher, please make the claim in writing to Dr. Neil Ralph, who is the Chief Investigator for the research and is based at UCL. The Chief Investigator will then pass the claim to the Sponsor's Insurers, via the Sponsor's office. You may have to bear the costs of the legal action initially, and you should consult a lawyer about this.

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Who has reviewed the study?

All research in the NHS is looked at by independent group of people, called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the NRES Committee (East Midlands – Nottingham 2).

Contact Details

If you wish to contact the research team to discuss any of the information further or any concerns you have about the study, then please do so by getting in touch with the members of the research team listed below:

███████████████

Research Department of Clinical, Education and Health Psychology
Room 440, 4th Floor
1-19 Torrington Place, London, WC1E 7HB

███████████████████████████

███████████████

Research Department of Clinical, Education and Health Psychology
Room 442, 4th Floor
1-19 Torrington Place, London, WC1E 7HB

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███████████████████████████████████

Centre Number:

Study Number:

Patient Identification Number for this trial:

CONSENT FORM

Title of Project: **Understanding the Effects of Depression on Sleep and Memory**

Name of Researcher: ████████████████

Please initial all boxes

1. I confirm that I have read and understand the information sheet dated 1st February 2016 (version 5) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of my medical notes and data collected during the study, may be looked at by individuals from University College London, from regulatory authorities or from the NHS Trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐

4. I agree to my GP being informed of my participation in the study. ☐

5. I agree to take part in the above study. ☐

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_____   _____   _____
Name of Participant   Date   Signature

_____   _____   _____
Name of Person   Date   Signature
taking consent.

Please feel free to contact us if you have any further concerns.

███████████████
Research Department of Clinical, Education and Health Psychology
Room 440, 4th Floor
1-19 Torrington Place, London, WC1E 7HB
████████████████████████

██████████████
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Appendix F: Participant information and consent form for comparison group

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Camden and Islington **NHS**
NHS Foundation Trust

Understanding the Effects of Depression on Memory

This study has been approved by the University College London Ethics Committee (Project ID Number): SHaPS-2014-JK-009

Name, Address and Contact Details of Investigators:

Principal investigator:

███████████

Research Department of Clinical, Education and Health Psychology
University College London
1-19 Torrington Place, London, WC1E 7HB
United Kingdom

████████████████
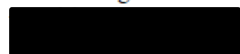
Researchers:

███████████████████████

Doctorate in Clinical Psychology
Research Department of Clinical, Education and Health Psychology
University College London

██████████████████

We would like to invite you to participate in this research project.

We would like to invite you to take part in our research study. You should participate only if you want to do so. Before you decide whether to take part, we would like you to understand why the study is carried out, what you would be asked to do, and how the study will be conducted. Please take some time to read this sheet thoroughly, and to discuss it with other people if you wish. One of our team will go through the information sheet with you and answer any questions you have. Please feel free to ask any further questions about the study, or if you find anything on this sheet unclear.

Why is this study being done?

Little is currently known about the impact of depression on the way memories are processed in the brain, but we know that memory can be affected. To understand the effects of depression on memory, we are investigating memory in both people with depression and people without depression. **In this study, we are investigating memory in people who are not currently suffering from depression.**

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By investigating spatial memory (remembering where things are) - as well as autobiographical memory (remembering things we have experienced) - we hope to gain a better understanding of depression and to develop more effective screening tools to measure the impact of depression.

Do I have to take part?

No. Your participation in the study is entirely voluntary. It is your choice whether or not you would like to participate. If you do give consent to take part in the study, you are still free to leave the study at any point, without giving a reason. If you leave, any information for the research that we have already collected from you will be destroyed.

What will happen if I decide to take part?

During a telephone call with one of our researchers, we will ask you some further questions to verify your eligibility. This will include questions about your mood and questions about whether you have had mental health problems in the past. During this time, any other questions you may have about your participation will be addressed. If you decide to participate and are suitable, the researcher will arrange a convenient time to meet with you at University College London.

If you decide to participate, you will when we meet complete a series of tasks and questions, some of them using a computer. We will ask you till fill in a short questionnaire about personality and ask you give some basic information about your age, sex, occupation and education. There will be three tasks investigating memory. One of the tasks is an autobiographical memory test where the researcher will give you a number of cue words and ask you to recall events from the past that relate to these words. You will then perform a pen-and-paper task in which you will be asked to view some pictures of landscapes, then select the correct answer from a few options. The third task is a computerized memory task where you will view some scenes, then answer some questions to see how well you remember what you saw. Most people find these tasks quite interesting to do. At the end of the session, the study researcher will conduct a debriefing and address any other questions or concerns you may have. Your participation should take approximately 60 minutes.

What are the possible disadvantages and risks for taking part?

We do not anticipate any potential disadvantages or risks in your participation. However, we will support you if you become upset or distressed during the study. You will be given time at the end of the study to be fully debriefed with a member of the research team.

What are the possible benefits of taking part?

You may find it interesting to complete these tasks and the information gathered during this study will also help to inform our understanding of depression, which will hopefully be a step towards helping the development of novel screening tools in the future.

Will I be paid for taking part in this study?

**RESEARCH DEPARTMENT OF CLINICAL,
EDUCATIONAL AND HEALTH PSYCHOLOGY**

We will give you £12.50 when you have completed the tasks and questionnaires to compensate you for your time and any travel expenses you may have incurred.

What will happen to the results of the research study?

The results will be written up in the form of reports to be submitted as a doctoral thesis project. As mentioned, you will not be identifiable from the results. On completion, you will be sent a summary of the study results if you request for it. You may contact one of the study researchers listed below via phone or email.

All data will be collected and stored in accordance with the Data Protection Act 1998. Only UCL researchers working with Dr. King will analyze these data.

If you wish to discuss participation either before or after taking part, you can contact us by email or phone using the contact details at the top of this document.

– XX –

**RESEARCH DEPARTMENT OF CLINICAL,
EDUCATIONAL AND HEALTH PSYCHOLOGY**

CONSENT FORM

Title of Project: **Understanding the Effects of Depression on Memory**

Name of Researchers: █████████████████

Please initial all boxes

1. I confirm that I have read and understand the information sheet for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. I have received the contact details for the investigators, who I can contact if I wish to discuss my participation.

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason.

3. I agree to take part in the above study.

| Name of Participant | Date | Signature |

| Name of Person taking consent. | Date | Signature |

Appendix G: Researcher script

1. Introduction

Here is a sheet that has some information about the study. Please read through it and ask me any questions you may have (or go through it with them).

You will get paid 12.5 when you have completed the tasks.

Opportunity to ask questions.

2. Questionnaires

Demographics (participant to fill in)

BDI (participant to fill in) CLINICAL GROUP ONLY

GAD-7 (participant to fill in) CLINICAL GROUP ONLY

Depression questions (interview) CLINICAL GROUP ONLY

Ten Item Personality Inventory (TIPI) (participant to fill in) CONTROL GROUP ONLY

3. AMT

In this task, we will ask you to remember events from the past and describe them in a sentence or two. We will then ask you to write this sentence down.

I am going to give you a number of different words. For each word, we want you to think of an event that happened to you which the word reminds you of. I will read you the word, and you will also see it in this booklet. The event could have happened recently or a long time ago. It might be an important event, or trivial event. Once you have thought of the event, we would like you to describe the event in a sentence or two.

*The memory you tell us should be a specific event – **an event that lasted less than a day, and occurred at a particular time and place**.*

It is important to try to tell us a different memory or event for each cue word. If you cannot think of a memory within a specified amount of time, we will move to the next cue word. I will write down your answers.

Let me give you an example: If the word was 'enjoy', "I always enjoyed a good party" would not be a specific memory because it does not mention a particular time, but saying "Jane's party last Friday" would be a specific memory.

Practice trials to confirm that the participant has understood the instructions (results not used in analysis):

Let's try a couple of practice words before we get started. Please first tell me the memory, and I will then ask you to write it down.

Please think of an event that this word reminds you of (provide word verbally and present cue card):

- *Relieved*

- *Tired*

That's exactly the sort of thing we are looking for – that is a specific memory because it refers to a particular event.

Give participant more than 30 seconds if needed.
If participant recalls a memory that is non-specific, prompt for a specific memory: *Can you think of a specific time – one particular episode?*

If participant is not able to think of a specific memory – provide example: *So an example of a specific memory here could be "When I passed my driving test" (relieved)/ "Yesterday when I got home from work (tired).*

Autobiographical memory test

Okay, let's get started with the task. If you cannot recall a memory within the specified amount of time, we will move to the next cue word. Please first tell me the memory and then write it down. Please don't turn to the next page in the booklet until I ask you to do so.

Time limit for retrieval – 30 seconds. Record time taken for retrieval.

Please think of an event that this word reminds you of (provide word verbally and present cue card)

If not specific: provide prompt - *Can you think of a specific time—one particular episode?*

- *Happy*

- *Sorry*

- *Safe*

- *Angry*

- *Interested*

- *Clumsy*

- *Successful*

- *Hurt (emotional)*

- *Surprised*

- *Lonely*

Thank you - that is the end of the task.

If long descriptions: *That is great – but you only have to give a very short description. One or two sentences is enough.*

4. Spatial memory task I – 4 mountains

(START AT SLIDE 1) We're going to do a test that requires you to look at pictures of landscapes with mountains in them (SHOW SLIDE 2) . Before we start the test we'll do some practice examples, so please don't mark your response sheets at this stage until I tell you the main test is beginning. When you first hear about it, the test might sound easy, but most people find it quite difficult, so it is important to listen carefully to the instructions"

(CHANGE TO SLIDE 3) First you will see a picture of one landscape with mountains. The next slide will show four similar pictures seen from different points of view and under different conditions, as if taken at different times of the year and times of the day." (SHOW SLIDES 3)

"One of the pictures in the second slide will show exactly the same place as the one in the first, although it will be shown from a different viewpoint. Your task is to identify which of the four pictures shows the same place as the first picture."

"The test is hard, because when you first see the mountains you cannot guess where you will next see them from, so it is important to focus on their layout which doesn't change.
The shadows and clouds and the patterns of colour on the ground don't help because they might change when you view the place from another direction at another time of day or year."

Let's see what the test will look like:

"Here you have a picture of a mountain landscape. (SHOW SLIDE 4)

Try to focus on the layout of the scene – so concentrate on the shape and arrangement of the mountains relative to each other.

[Wait for 10 seconds]

Now here are four pictures to choose from. Which one of these shows the same place as the one in the previous slide? Work out your answer but don't write anything down." (SHOW SLIDE 5)

[Wait a few seconds while participants think about it.]

[Show next slide.]

"if you thought it was this one [indicate yellow highlighted picture] you are right. In each of the other pictures the layout of the mountains is different. (SHOW SLIDE 6)

For example, in this picture [indicate picture with red arrows] these two hills are closer together than in the first picture, and there are other differences. (SHOW SLIDE 7)

We'll do a few more practice questions now. After each practice item, you will be shown the correct answer, and the original picture you looked at – take a moment to see whether you were right or wrong. If you were wrong try to figure out why the answer you chose did not match the correct one. In the main test, you will not find out about the right and wrong answers, so this is a good chance to make sure you have understood the instructions.

PRACTICE 1: SLIDES 8 – 9 – 10 - 11

PRACTICE 2: SLIDES 12 – 13- 14- 15

PRACTICE 3: SLIDES 15 – 16

There are 30 items in the test, and for each item you will have ten seconds to study the first picture and then 20 seconds to choose which of the four pictures on the next slide shows the same place. When you have decided which of the four pictures shows the same place – mark your response sheet. Each numbered item there is a grid of four boxes – tick the box corresponding to the picture you have chosen, so if the top-left picture shows the same place, you would mark the top left box for that question. If you are not sure, you should just make the best guess you can in the time available.

The main test begins in just a moment. Please get ready to start marking your response sheet.

5. **Spatial memory task II – Town Square**

See separate form

6. Word ratings

See separate form

7. Debriefing and payment (remember signing!)

That is the end of the tasks. Thank you so much for participating. Do you have any questions?

Appendix H: Acronyms and abbreviations

4MT	Four Mountains Test
AM	Autobiographical Memory
AMS	Autobiographical Memory Specificity
AMT	Autobiographical Memory Test
ASM	Allocentric Spatial Memory
BDI II	Beck Depression Inventory II
BOLD	Blood Oxygen Level Dependent
CA3	Cornu Ammonis region 3
CaR-FA-X	Capture and Rumination – Functional Avoidance – eXecutive function
CBT	Cognitive Behavioural Therapy
CCT	Controlled Clinical Trial
ECT	Electro-Convulsive Therapy
EPHPP	Effective Public Health Practice Project
fMRI	Functional Magnetic Resonance Imaging
GAD-7	Generalised Anxiety Disorder scale 7
HPA	Hypothalamic Pituitary Adrenal
IAPT	Improving Access to Psychological Therapies
LRT	Life Review Therapy
MBCT	Mindfulness-Based Cognitive Therapy
MemFlex	Memory Flexibility
MeSH	Medical Subject Heading
MeST	Memory Specificity Training
NHS	National Health Service
OCD	Obsessive-Compulsive Disorder
OGM	OverGeneral Memory
PHQ-9	Patient Health Questionnaire 9
PTSD	Post-Traumatic Stress Disorder
RCT	Randomised Controlled Trial
ReSSI	Relapse Signature of Suicidality Interview
SCEPT	Sentence Completion for Events from the Past Test
SCID-I	Structured Clinical Interview for DSM Axis I Disorders
SMS	Self Memory System
TAU	Treatment As Usual
UCL	University College London