

## **Allocentric spatial memory performance predicts intrusive memory severity in posttraumatic stress disorder**

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## Abstract

**Background:** Posttraumatic stress disorder (PTSD) is characterised by distressing trauma-related memories. According to the dual representation theory, intrusive memories arise from strengthened egocentric encoding and a poor contextual encoding, with spatial context requiring allocentric processing. Contextualization of mental imagery is proposed to be formed hierarchically through the ventral visual stream (VVS) to the hippocampal formation. Here, we tested this notion by investigating whether neuronal aberrations in structures of the VVS or in the hippocampus, as well as allocentric memory performance are associated with intrusive memory severity.

**Methods:** The sample comprised 33 women with PTSD due to childhood trauma. Allocentric memory performance was measured with the virtual Town Square Task and T1-weighted images acquired on a 3T Siemens Scanner. Intrusive memories were evoked by presenting an audio script describing parts of their trauma (script-driven imagery).

**Results:** Using **hierarchical** linear regression analysis, we found a significant association between lower intrusive memory severity and higher allocentric spatial memory, controlling for age, working memory, and general visuospatial ability. No significant association was found between cortical thickness of VVS structures, hippocampal volume and intrusive memory severity. Post hoc exploratory analyses revealed a negative correlation between years since index trauma and left hippocampal volume.

**Limitations:** Our results are based on correlational analyses, causality cannot be inferred.

**Conclusion:** This study supports the dual representation theory, which emphasizes the role of allocentric spatial memory for the contextualization of mental imagery in PTSD. Clinical implications are discussed.

**Keywords:** Trauma, PTSD, Allocentric processing, Hippocampus, MRI

## 1. Introduction

The understanding and treatment of trauma-related disorders is a crucial challenge in the field of global mental health to date. One potential sequela of trauma is posttraumatic stress disorder (PTSD) with a life time prevalence of 6.8% in the general population (Kessler et al., 2005), which can rise to 69%-92% in populations affected by war and torture (Kolassa, Kolassa, Ertl, Papassotiropoulos, & De Quervain, 2010; Moisander & Edston, 2003). A core symptom of PTSD consists of recurrent involuntary memories of the traumatic event. Intrusive memories are thought to be triggered by internal or external cues and often get actively avoided due to their distressing mnemonic content (American Psychiatric Association, 2013).

For visual intrusions, the dual representation model proposed by Brewin and co-workers (Brewin, Dalgleish, & Joseph, 1996; Brewin, Gregory, Lipton, & Burgess, 2010; following Nadel & Jacobs, 1998) assumes two connected types of memory to be involved in storing and retrieving intrusive images: (1) Contextualized representations, which are responsible for storing **highly-processed information about scenes within a** spatiotemporal context and (2) sensory-bound representations, **which capture lower-level perceptual information that is closer to the sensory input, along with emotion and body state information**. The contextual representation is thought to rely on the hippocampal formation, located in the medial temporal lobe, and is assumed to be coded within the ventral visual stream (VVS), allowing integration with other autobiographical memories (cf. Brewin, 2015). Sensory-bound representations are hypothesised to reflect processing in the insula, dorsal visual stream and amygdala. The dorsal visual stream is associated with creating images of the environment from a viewer-dependent perspective (egocentric), while appropriate contextual encoding additionally requires allocentric processing (viewer-independent).

In their revised dual representation theory, Brewin and colleagues (2010) presume an amygdala-mediated strengthening of egocentric visual representations during the traumatic moment in the context of a weak hippocampus-dependent allocentric representation. According to this model, intrusive imagery reflects an imbalance between strong emotion-

laden sensory-bound representations and weak contextual representations. In PTSD, sensory cues (e.g. smell or sound) in the environment trigger retrieval of images of the traumatic scene involuntarily, which are experienced without the associated context. Accordingly, the model proposes that strengthening of egocentric processing and/or weakening of allocentric spatial processing ability would result in an increase of intrusions (cf. Bisby & Burgess, 2017).

Empirical support for the dual representation theory stems from studies in healthy individuals as well as in individuals with PTSD. In healthy cohorts, a common approach to investigate intrusive memories is the trauma film paradigm (for review see James et al., 2016), in which participants watch at least one traumatic video and report the experience of intrusive memories or thoughts in a diary over the subsequent days. Researchers have used the trauma film paradigm to manipulate trauma processing either before, during, or after encoding of the traumatic material. Relevant for the present work are findings showing a decrease of intrusive images by deploying a visuospatial task either during encoding (Bourne, Frasquilho, Roth, & Holmes, 2010; Brewin & Saunders, 2001; Holmes, Brewin, & Hennessey, 2004) or directly thereafter (Holmes, James, Coode-Bate, & Deeproose, 2009; Holmes, James, Kilford, & Deeproose, 2010), with preliminary translational evidence in survivors of a motor vehicle accident (Iyadurai et al., 2017). A possible explanation is that visuospatial tasks compete for perceptual resources, which leads to an attenuation of the sensory representation and thus to fewer intrusive memories (cf. Brewin, 2014; Stuart, Holmes, & Brewin, 2006).

Influences on intrusive memory development **may also take the form of** individual cognitive differences. Meyer, Krans, van Ast, and Smeets (2017) tested 81 healthy individuals with a contextual cueing paradigm and found an inverse relationship between memory contextualization learning abilities and visual intrusive memories, but not verbal intrusive thoughts (Meyer et al., 2017). In line with these findings, Bisby, King, Brewin, Burgess, and Curran (2010) deployed the Town Square Task in a healthy cohort ( $n=48$ ) to assess allocentric spatial memory and found that participants' allocentric memory performance correlated negatively with the amount of experienced intrusions in the week after watching traumatic videos. The authors further tested the causal relationship between allocentric spatial processing and intrusive memory formation by administering alcohol (low/high dosage versus placebo), which suppresses allocentric-dependent hippocampal functioning. In line with the

model, a low dosage of alcohol was linked to reduced allocentric spatial memory performance and resulted in the development of more intrusions.

Findings from analogue experiments do not translate directly to clinical populations who have experienced real-life trauma, but some parallels are evident. Reduced hippocampal volume has been reported by numerous studies in PTSD (cf. O'Doherty, Chitty, Saddiqui, Bennett, & Lagopoulos, 2015) and was recently confirmed by the largest neuroimaging study in PTSD today (ENIGMA-PGC consortium study involving 1868 subjects, comparing 794 patients with PTSD to trauma-exposed controls; Logue et al., 2018). Further, a recent meta-analysis on 19 functional neuroimaging studies, which focussed on the reaction to trauma-related stimuli versus a control condition (Sartory et al., 2013), found heightened activation of the retrosplenial cortex and precuneus – structures that have been implicated to play a role in the interaction between egocentric and allocentric representations (e.g. Bisby & Burgess, 2017; Kravitz, Saleem, Baker, & Mishkin, 2011).

Building on these findings, Smith, Burgess, Brewin, and King (2015) investigated allocentric spatial processing, using a topographical recognition task, and allocentric spatial memory ability using the Town Square Task, in 29 patients with PTSD and 30 trauma-exposed controls. The authors found that individuals with PTSD performed significantly worse on both allocentric spatial processing and memory task compared to trauma-exposed controls. The groups did not differ in their egocentric processing performance and non-spatial memory for object lists. Reduced spatial processing abilities in PTSD compared to trauma-controls have also been reported in other work (Gilbertson et al., 2007; Miller, McDougall, Thomas, & Wiener, 2017; Tempesta, Mazza, Iaria, De Gennaro, & Ferrara, 2012). Interestingly, patients phenomenologically experience intrusive memories to lack context, i.e. they reflect isolated moments, disjointed from what happened before or after (Michael, Ehlers, Halligan, & Clark, 2005), which supports the view of intrusions as **consisting of** de-contextualised egocentric representations of the traumatic scene.

In contrast, some cognitive psychologists consider intrusive memories not to be different from other autobiographical memories. They assume the mnemonic process for traumatic and ordinary events are mechanistically equal (Rubin, Berntsen, & Bohni, 2008), making the

etiology of intrusive memories still a controversial issue in the study of PTSD. Moreover, evidence is scarce regarding the association between intrusions and brain morphology as most studies focus on general PTSD symptom severity instead of distinct symptom clusters (cf. Karl et al., 2006). One study has reported reduced volume in bilateral inferior temporal cortex, which is part of the VVS and involved in processing the context of visual objects and scenes, to be associated with increased re-experiencing (Kroes, Rugg, Whalley, & Brewin, 2011). Two others reported negative correlations between re-experiencing symptoms and left hippocampal volume in PTSD (Lindauer, Olf, van Meijel, Carlier, & Gersons, 2006; Villarreal et al., 2002). As reduced hippocampal volume has been associated with childhood abuse (Teicher et al., 2017) as well as cumulative stress exposure (Hanson et al., 2015), it may indicate that individuals with childhood trauma are specifically vulnerable to developing severe intrusive symptomatology.

In sum, good empirical evidence exists for impairments in hippocampus-based contextual memory in patients with PTSD and for an inverse relationship between allocentric spatial memory and intrusive memories in healthy cohorts. Yet, a systematic investigation of the relationship between allocentric spatial memory, brain morphology, and intrusive memories in PTSD is lacking. This may in part be due to the difficulty in quantifying intrusive memories in patients with PTSD. They are generally assessed retrospectively with self-report questionnaires or clinical interviews asking for their frequency in the past month(s). This approach may not be adequate as patients actively avoid exposure to trauma reminders that could trigger intrusive recall (cf. Brewin, 2015). Thus, in the present study, a symptom provocation paradigm triggering intrusive memories will be administered to address the question of whether allocentric spatial memory performance, and morphometric changes in areas of the VVS and the hippocampus, are related to intrusive memory severity in PTSD. Specifically, we will use the script-driven imagery paradigm (Lanius et al., 2002) to elicit intrusions and ask participants to rate the intensity of any experienced intrusive memories directly after symptom provocation<sup>1</sup>. To assess allocentric spatial memory, we will employ the Town Square Task, which enables us to obtain a measure of allocentric spatial memory

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<sup>1</sup> Note that functional imaging data has also been acquired. However, this data set is part of a complex double-blind, placebo-controlled pharmacological challenge paradigm (cf. page 12), which will be published as a whole in a separate article.

while controlling for egocentric spatial processing (cf. King, Burgess, Hartley, Vargha-Khadem, & O'Keefe, 2002). Using a virtual environment, this task presents objects to be encoded in relation to their location. During recall, these objects are then shown either from the same view versus a shifted-view relative to the encoding phase. It is assumed that the same-view condition can be solved using egocentric processing only, whereas in the shifted-view condition additional allocentric processing is required (cf. King et al., 2002). Because this task isolates measurements of egocentric and allocentric processing abilities, it is particularly useful for testing implications of the dual representation model, which proposes that involuntary memory reflects the difference between strong egocentric and weak allocentric encoding. We will further control for general visuospatial ability and working memory performance as potential confounding factors affecting allocentric memory performance.

## **2. Methods**

### **2.1 Participants**

A total of 41 women with a history of childhood trauma were recruited via public advertisements, through mental health in- and outpatient clinics, and in collaboration with private psychotherapists and psychiatrists. Female participants were included in the study if they were diagnosed with current PTSD (see below) and in addition met the following criteria: (1) ages 20 to 60 years; (2) sufficient proficiency in German; (3) MRI compatible; (4) no history of head injury; (5) no incidental finding by the neuroradiologist (examination after the MR scan); (6) no history of substance dependency within the past 6 months; (7) no intake of benzodiazepines or anticonvulsants; (8) no comorbid psychiatric disorders other than secondary depressive and anxiety disorders, borderline personality disorder, eating disorders, and substance abuse disorders, which we allowed to ensure ecological validity. For the same reason, participants taking mild antidepressant medication were included. The study protocol was approved by the ethics boards of the Faculty of Medicine, University of Magdeburg and the Berlin Psychological University. Written informed consent was obtained from all participants and they received a monetary compensation for their participation.

## 2.2 Procedure

### 2.2.1 Clinical diagnostics

Subjects interested in participating in the study received a screening questionnaire via mail. Here, self-report information on MRI incompatibilities, previous head injuries, current medication, and current psychological as well as neurological disorders was acquired and trauma exposure and PTSD symptom severity were assessed via German versions of the Essen Trauma Inventory (Tagay et al., 2006) and the PTSD Checklist for DSM-IV (PCL; Teegen, 1997), respectively. Eligible subjects were invited for a comprehensive psychological assessment by a clinical psychologist (A.M.) who administered German versions of four standardised interviews: The PTSD diagnosis and symptom severity were established using the Clinician-Administered PTSD Scale (CAPS-IV; Schnyder & Moergeli, 2002). The Structured Clinical Interview for DSM-IV (Wittchen, Zaudig, & Fydrich, 1997) was used to assess Axis I disorders. To verify that no primary diagnosis of borderline personality disorder was present, the respective section of the Structured Clinical Interview for DSM-IV Axis II (Fydrich, Renneberg, Schmitz, & Wittchen, 1997) was conducted. Finally, we employed the Structured Clinical Interview for DSM-IV Dissociative Disorders (Gast, Zündorf, & Hofmann, 2000) to exclude patients with dissociative disorders. All participants completed German versions of the following self-report questionnaires for sample characterization: the Beck Depression Inventory (BDI-II, Hautzinger, Keller, & Kühner, 2006), the Cambridge Depersonalization Scale (CDS-30; Michal et al., 2004), the Childhood Trauma Questionnaire (CTQ; Wingenfeld et al., 2010), Dissociative Experiences Scale (DES; Spitzer, Mestel, Klingelhöfer, Gänsicke, & Freyberger, 2003), and the State-Trait Anxiety Inventory (STAI-T; Laux & Spielberger, 2001).

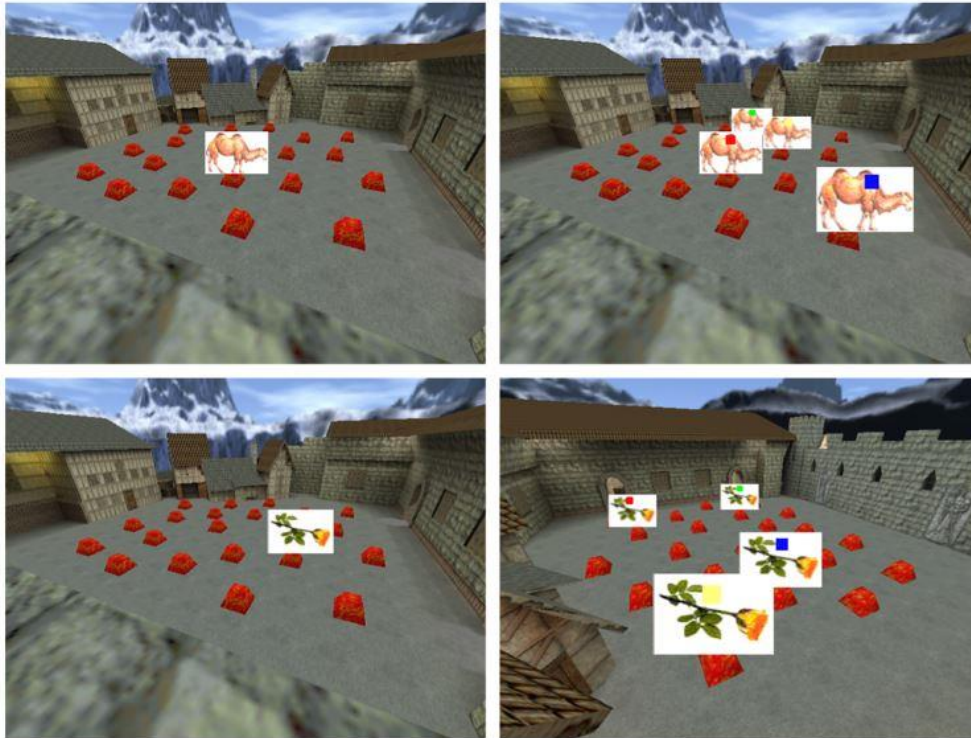
### 2.2.2 Allocentric Spatial Memory – *The Town Square Task*

Allocentric spatial memory was assessed with the Town Square Task, presented on a 14-inch laptop screen. The task consists of a virtual environment depicting a courtyard surrounded by visually distinct buildings. 21 red-coloured placeholders distributed in the courtyard served for the presentation of the stimuli. Subjects were exposed to 32 trials, each consisting of an encoding and a recall phase. To start the trial, participants were asked to navigate along a perimeter wall (left or right) at roof top level towards a traffic cone, which on contact brought them into a standardised view overlooking the courtyard. During the encoding phase, either



three or six targets were presented in a pseudo-randomized order with the constraint that each list length (of either 3 or 6 objects) was not employed more than four times in a row. Images of everyday objects served as targets and appeared on the placeholders one at a time for 3 s each, with a 1 s inter-stimulus interval. Participants were instructed to remember the location (i.e. the specific placeholder) of each object. During the recall phase, the location of these targets was tested either from the same viewpoint as encoding or from a shifted viewpoint (rotated by 140°, cf. Fig. 1).

The same-view condition can be processed using only egocentric strategies, while in the shifted-view condition allocentric processing is necessary in addition to egocentric processes (cf. King et al., 2002). During recall, object locations were tested in a random stimulus order within trials, using multiple choice by placing the correct image (target) on its original placeholder and three copies (foils) on other placeholders. A small, coloured square was superimposed on each image and participants were asked to indicate the location of the target by pressing the corresponding colour-coded button on the keyboard (cf. Fig. 1). The response time was self-paced. Furthermore, task difficulty was matched between same-view and shifted-view conditions by placing the foils always within the nearest five positions to the target in the same-view condition while distributing them evenly across locations in the shifted-view condition. In a healthy cohort, this procedure successfully resulted in comparable performance across conditions (King, Trinkler, Hartley, Vargha-Khadem, & Burgess, 2004).



**Figure 1.** The Town Square Task. The left upper and lower panel display the presentation of items during the encoding phase. The upper right panel displays the location test during the recall phase in the same-view condition while the lower right panel shows the respective location test in the shifted-view condition. During recall, the correct image is placed on its original placeholder and three foils are placed on other placeholders. The superimposed coloured squares are used for participants to indicate their response.

### 2.2.3 Working Memory – *The N-back Task*

Some participants use verbal rehearsal strategies during spatial processing, which draws on working memory resources (cf. Baddeley, 2000). Thus, individual differences in retention span may influence performance on the Town Square Task and need to be controlled for. We employed the n-back paradigm, which is a neurocognitive test commonly used to measure working memory capacity (Kearney-Ramos et al., 2014; Redick & Lindsey, 2013). In this task, participants press a key whenever the current item matches the item that had been presented  $n$  items back (cf. Redick & Lindsey, 2013). We implemented four levels of difficulty, i.e. a 0-back task, 1-back task, 2-back task, and a 3-back task, using a block design. Single capital letters (font style: 'Arial'; font size: 100) were chosen as stimuli and were presented for 1 s in the centre of a 14-inch laptop screen with an inter-stimulus interval of 500 ms. In the 0-back

condition, subjects were asked to hit the response key whenever the letter X appeared on the screen. In the 1-, 2-, and 3-back condition, subjects were instructed to press a marked key on the keyboard if the present letter corresponded to the letter shown 1, 2, or 3 items back, respectively. Each condition consisted of 20 stimuli including six targets and each condition was presented three times throughout the task in a pseudo-randomized order (boundary condition: no direct repetition of the same condition), resulting in 12 testing blocks overall.

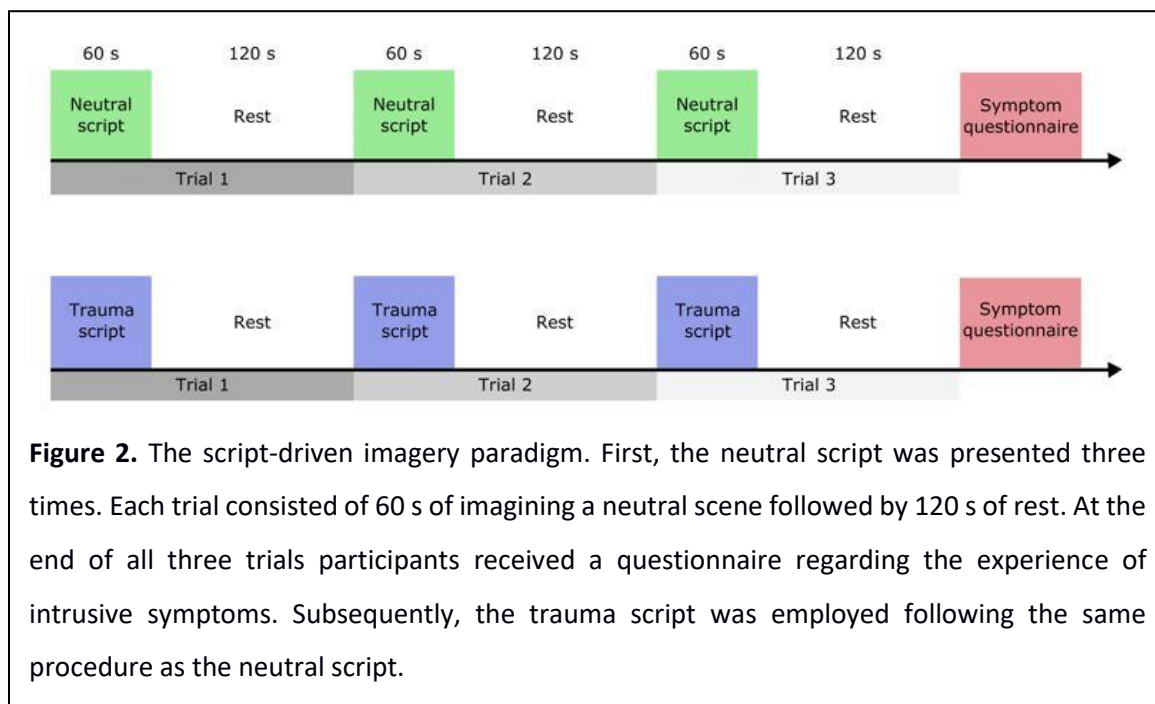
#### 2.2.4 Screening for general visuospatial ability

We implemented a brief measure (12-item) of general visuospatial ability (Raven's Advanced Progressive Matrices: RAPM, Set I; Raven, 1938). The RAPM is a standardised assessment of non-verbal abstract reasoning and visual-spatial problem-solving abilities. Set 1 consists of 12 geometric patterns with a missing piece. Subjects were instructed to pick the correct missing piece from a pool of eight similar pieces. The first item served for practice. If participants chose the correct missing piece they were asked to complete the remaining 11 items. The task was self-paced and subjects were informed that no time limit applies. The number of correct pieces was computed as a measure of general visuospatial ability.

#### 2.2.5 Symptom provocation – script-driven imagery

Following the behavioural assessments, we conducted the script-driven imagery paradigm in the scanner, which is a symptom provocation task commonly used in PTSD research (Daniels, Coupland, et al., 2012; Daniels et al., 2011; Daniels, Hegadoren, et al., 2012). According to the published procedure (Lanius et al., 2002), individualised scripts containing descriptions of one neutral and one traumatic event in the patient's life were created. The neutral autobiographical event served as the control condition and it was ensured that an event was chosen which neither elicited positive nor negative emotions. For the traumatic script, participants were asked to describe scenes from which reminders have triggered intrusive symptoms in the past. Both descriptions were each condensed to a 30 s audio script and recorded for presentation in the MRI environment. During exposure, participants were asked to imagine the events vividly while listening to the 30 s audio script and for 30 s thereafter (i.e. 60 s imagery period) and not to avoid symptoms if they arose. A rest period of 2-minutes was given between trials. Each script was presented three times, with all neutral runs preceding the traumatic ones to avoid carry over effects (cf. Fig. 2). Upon completion of the

three trials per condition, participants first filled out the Response to Script-Driven Imagery Scale (RSDI; Hopper, Frewen, Sack, Lanius, & Van der Kolk, 2007) and then answered six questions assessing the experience of intrusive and dissociative symptoms for each trial. With regards to intrusions, participants were asked “*During Trial X, did you re-experience part of the trauma involuntarily (intrusions)?*”. The response was given on a 7-point-Likert scale from 0 (not at all) to 6 (very strong). This work was conducted within a larger study, which investigates the neurobiology of dissociation in PTSD by using a placebo-controlled, pharmacological challenge paradigm. The present study only considers reported intrusions after trauma exposition under placebo; we ensured with our study design that carry over effects were highly improbable<sup>2</sup>.



**Figure 2.** The script-driven imagery paradigm. First, the neutral script was presented three times. Each trial consisted of 60 s of imagining a neutral scene followed by 120 s of rest. At the end of all three trials participants received a questionnaire regarding the experience of intrusive symptoms. Subsequently, the trauma script was employed following the same procedure as the neutral script.

## 2.2.6 MRI acquisition and Preprocessing

<sup>2</sup> The larger study mentioned here comprised a random alteration between placebo and pharmacological trials. In the pharmacological trial, we administered half a dosage of a noradrenergic agent whose full dosage has a half-life of 72 hours. We ensured that there were always at least 72 hours between placebo and pharmacological trials, which makes the occurrence of any carry-over effects highly improbable.

Structural MR images were obtained on a 3T Siemens Tim Trio scanner equipped with a 12-channel head coil. T1-weighted images were acquired with a magnetization-prepared rapid acquisition with gradient echo sequence using the following parameters: TR=1.9ms, TE=2.52ms, inversion time=900ms, flip angle=9°, FoV=256mm, 192 slices, 1mm isovoxels, 50% distancing factor. Measurements of cortical thickness and volume of cortical and subcortical regions, respectively, were acquired using the default settings of FreeSurfer version v6.0 (<https://surfer.nmr.mgh.harvard.edu/>), which have been described in previous publications (Fischl & Dale, 2000). Important preprocessing steps included intensity normalization and skull stripping, segmentation of subcortical white matter and deep gray matter volumetric structures, and parcellation of the cerebral cortex. Each output was visually inspected for quality insurance. From the Desikan Killany atlas, we selected left and right hippocampus and the following eight bilateral regions of interest as part of the ventral visual stream: lateral occipital gyrus, fusiform gyrus, lingual gyrus, sulcus of the pericalcarine gyrus, middle temporal gyrus, inferior temporal gyrus, temporal pole, and parahippocampal gyrus.

### **2.3 Statistical analyses**

#### *Egocentric and allocentric memory score (Town Square Task)*

To obtain a measure of egocentric memory performance, we computed an overall percentage correct score (number of items correct/total number of items) across trial length for the same-view condition (see Table 2). To obtain a measure of allocentric memory performance, we first calculated an overall percentage correct score for the shifted-view condition and then subtracted the egocentric memory score to isolate allocentric spatial memory performance while controlling for confounding differences in egocentric spatial processing. A log transformation was conducted on the performance scores of the Town Square Task, because their distributions were negatively skewed. After transformation, the data were normally distributed as confirmed by Shapiro-Wilk tests (egocentric memory performance:  $W=.955$ ,  $p=.181$ ; allocentric memory score:  $W=.951$ ,  $p=.141$ ). The data of eight participants were excluded (two as they misinterpreted the instruction and six due to performance below chance level, i.e. <25%), reducing the original sample of  $n=41$  to  $n=33$  for the present analysis.

#### *Working memory (n-back task)*

Working memory performance was computed by averaging the sensitivity index  $d'$  (Macmillan & Creelman, 1990) across all four difficulty levels. Two participants did not complete the n-back task and two participants were excluded after outlier detection, that is, their  $d'$  average score exceeded three times the interquartile range. This left a sample of 31 subjects for whom both allocentric memory and working memory performance were available.

#### *Intrusive memories (symptom provocation task)*

To quantify the severity of intrusive memories during symptom provocation, the mean of the three intensity ratings that participants provided for each trial after the script-driven imagery paradigm (cf. section 2.2.5) was computed. Intrusive severity scores were not normally distributed. We performed a squared transformation which improved the skewness and resulted in normality as confirmed by the Shapiro-Wilk test ( $W=.951, p=.147$ ).

#### *Structural data (MRI)*

Cortical thickness of VVS areas, volumetric measures of the hippocampi, and total intracranial volume were derived from the standard statistical directory of FreeSurfer. To control for inter-individual variability in head size, we normalised hippocampal volume by intracranial volume using the residual approach (cf. Voevodskaya et al., 2014).

#### *Multiple linear regression analysis*

We performed a planned **hierarchical** multiple linear regression analysis. Considering that age, working memory as well as RAPM score may influence allocentric spatial memory performance, we included those variables in the first step of the linear regression model while allocentric spatial memory was added in the final step. Because of a low subject-to-variable ratio, we based our decision on which of the 18 brain regions to include in the second step of the regression model by performing bivariate Pearson's correlations with intrusive symptom severity. Thus, the relationship between left and right hippocampal volume as well as cortical thickness measurements of bilateral VVS (16 regions) with intrusive severity scores was tested while correcting for multiple comparisons using the false discovery rate (FDR; Benjamini & Hochberg, 1995). The regression model was considered significant at the statistical threshold

of  $p < .05$ . The statistical analyses were performed in R version 3.5.1 (R Core Team, 2018) as well as SPSS version 25 (SPSS, IBM Corp. in Armonk, NY).

### **3. Results**

#### **3.1. Population characteristics**

Demographics and psychometric scores of the sample are presented in Table 1. Participants had a mean age of 39.7 and an average CAPS score of 68.73. Age at index trauma was on average 15.24. All participants reported childhood trauma, which they did not always specify as their index trauma. Age at first trauma was not acquired. Almost all participants ( $n=32$ ) displayed comorbid disorders, mainly secondary anxiety disorders ( $n=30$ ), borderline personality disorder ( $n=9$ ), and mood disorders ( $n=7$ ). For further details on comorbidity see the Appendix, Table A.1. Two patients used the antidepressant medication Valdoxan and Escitalopram, respectively.

#### **3.2. Experimental results**

##### *Descriptives*

Descriptive statistics of performance and intrusive memory severity are shown in Table 2. Participants reported significantly higher intrusive memory severity after listening to the trauma script than to the neutral script (paired sample t-test:  $t(32)=-11.60$ ,  $p < .001$ , cf. Fig 3A). Participants performed significantly better in the same-view than in the shifted-view condition  $t(32)=-5.83$ ,  $p < .001$ ). The mean allocentric memory score for this sample was  $-.16$ .

**Table 1**

Sample characteristics.

Variable	<i>n</i>	<i>Min.</i>	<i>Max.</i>	<i>Mean</i>	<i>SD</i>
Age	33	23	58	39.67	10.16
Est. age at index trauma*	33	3	49	15.24	10.05
Est. years since index trauma*	33	2	48	24.21	12.84
BDI-II	30	1	53	22.07	14.16
CAPS re-experiencing subscale	33	8	30	20.18	5.75
CAPS avoidance subscale	33	12	43	27.15	8.64
CAPS hyperarousal subscale	33	12	31	22.82	4.75
CAPS total	33	41	95	68.73	15.23
CDS-30	30	0	80	28.73	21.58
CTQ	28	65	112	86.71	14.53
DES	33	3	62	28.80	16.20
PCL	33	25	50	39.12	6.49
STAI-T	30	37	75	56.70	11.10

BDI=Beck Depression Inventory; CAPS=Clinician-Administered PTSD Scale; CDS=Cambridge Depersonalization Scale; CTQ=Childhood Trauma Questionnaire; DES=Dissociative Experiences Scale; Est.=Estimated; PCL=PTSD Checklist for DSM-IV; STAI-T=State-Trait Anxiety Scale, trait version. \*Note that descriptives for age at and years since index trauma are estimates as some participants indicated a time range instead of a specific age; in these cases, the beginning of the reported time period was chosen as the estimated age at index trauma.



**Table 2**

Descriptive statistics of behavioural performance and intrusive memory severity.

Variable	<i>n</i>	<i>Min.</i>	<i>Max.</i>	<i>Mean</i>	<i>SD</i>
RAPM	33	7	12	10.61	1.44
N-back d'	31	-2.09	1.31	.14	.84
TSQ Performance total	33	.35	.87	.68	.14
TSQ Performance egocentric condition	33	.40	.93	.75	.13
TSQ Performance allocentric condition	33	.26	.83	.60	.16
Allocentric memory score	33	-.33	.03	-.16	.10
Trauma script - Intrusive memory severity Trial 1	33	0	6	3.58	1.64
Trauma script - Intrusive memory severity Trial 2	33	0	6	3.81	1.78
Trauma script - Intrusive memory severity Trial 3	33	0	6	4.36	1.85
Trauma script - Mean intrusive memory severity	33	0	6	3.92	1.56
Neutral script - Mean intrusive memory severity	33	0	4.67	.73	1.10

Allocentric memory score=difference between egocentric and allocentric spatial memory performance;

RAPM=Raven's Advanced Progressive Matrices, Set I; SD=standard deviation; TSQ=Town Square Task.

Participants rated the intensity of intrusive symptoms experienced during trauma exposition on a 7-point-Likert scale.

### Multiple linear regression analysis

Bivariate correlations did not reveal any significant correlation between neural morphometric measurements (VVS structures, left and right hippocampus) and intrusive severity scores after correcting for multiple comparisons (cf. Appendix Table A.2). We found a trend indicating a negative association between cortical thickness of left lingual gyrus and intrusive symptom severity ( $r=-.428$ ,  $p_{FDR}=.055$ ). Congruently, there was a trend between higher allocentric memory scores and greater cortical thickness of the left lingual gyrus ( $r=-.379$ ,  $p_{FDR}=.098$ ). However, given these non-significant findings, only age, RAPM scores, working memory scores, and allocentric memory performance were entered as predictors into the **hierarchical** linear regression model. Note that the sample was reduced to 31, as working memory scores were only available for 31 participants. At step 1, age ( $\beta=.168$ ,  $p=.386$ ), RAPM scores ( $\beta=-.064$ ,  $p=.712$ ), and working memory scores ( $\beta=-.292$ ,  $p=.085$ ) did not significantly predict intrusive memory severity. At step 2, higher allocentric memory score ( $\beta=.404$ ,  $p=.024$ ) significantly predicted lower intrusive memory severity ( $R^2=.164$ ,  $F(2,29)=5.671$ ,  $p=.024$ ). Observation of the standardized residuals for this **hierarchical** regression indicated that the residuals formed a normal distribution (residual statistic: *minimum*: -2.30, *maximum*: 1.861, *mean*=.000, *standard deviation*=.983).

**Table 3**

Results of the **hierarchical** linear regression analysis ( $n = 31$ )

	Predictor	$\beta$	$t$	$p$
<b>Step 1</b>	Age	.168	.880	.386
	RAPM score	-.064	-.373	.712
	Working memory score	-.292	-1.783	.085
<b>Step 2</b>	Allocentric memory performance	.404*	2.381	.024
Final model	$F(29)$	5.671		
	$R^2$	.4164		
	Adjusted $R^2$	.135		

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\*Note that the parameter estimates for allocentric memory performance are reversed (positive instead of negative), because allocentric memory ability is measured as the difference score between same and shifted-view condition to control for egocentric processing. Thus, a higher difference score indicates lower allocentric memory ability.

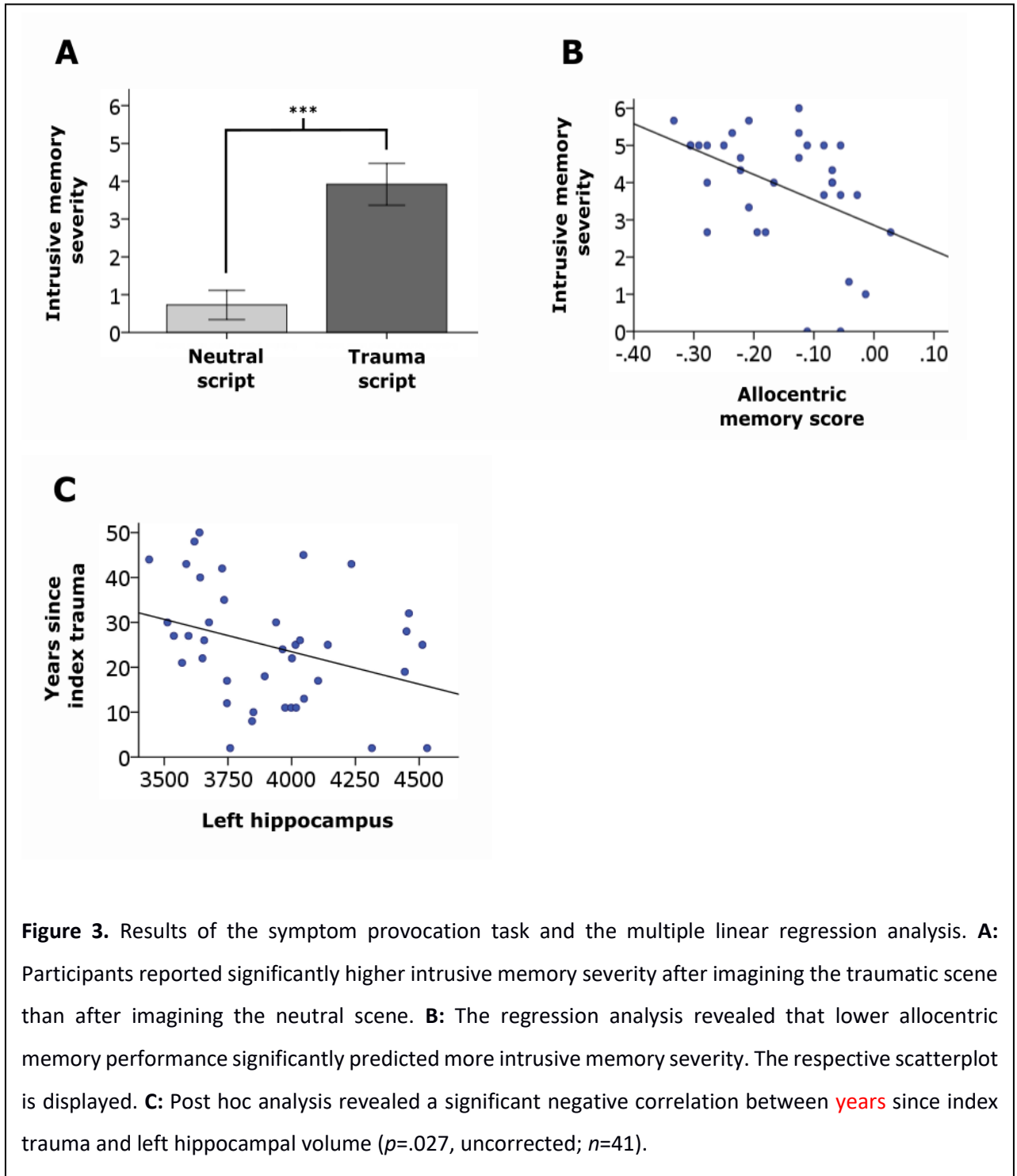
### *Post hoc analyses*

First, considering the high comorbidity of mood and anxiety disorders in our sample (see the Appendix Table A.2), we ran post hoc partial correlational analyses between the allocentric memory score and intrusive memory severity, controlling for age, depressive symptom severity (BDI-II scores), and trait anxiety (STAI-T scores), which were available for 30 participants. The negative correlation between the allocentric memory score and intrusive memory severity stayed significant ( $r=-.43, p=.025$ ).

Second, the allocentric memory score was computed by subtracting egocentric memory performance (same view condition) from the performance score in the shifted-view condition. To rule out the possibility that the association between the allocentric memory score and intrusive memory severity arose due to variability in egocentric memory processing and not allocentric processing, we subjected egocentric memory performance to partial correlational analysis with intrusive symptom severity. When controlling for age and RAPM score, there was a significant correlation between higher egocentric memory performance and higher intrusive symptom severity ( $r=.38, p=.030$ ). However, this association disappeared when additionally controlling for depression and anxiety scores ( $r=.13, p=.505$ ).

Third, to identify whether the association between intrusive symptom severity and allocentric memory performance is also evident if symptoms are not provoked, we correlated allocentric memory performance with naturally occurring symptom severity as measured by the CAPS. We did not find any significant association either with the total score or with any sub-scores (intrusion, avoidance, and hyperarousal symptoms). Moreover, the symptom severity rating of the provoked intrusive memories was not associated with the intrusion sub-scores on the CAPS ( $r=.168, p=.358$ ).

Finally, to test for potential effects of duration of symptoms, we performed Pearson's correlation between years since index trauma, intrusive memories, and brain morphology. No association was found between years since index trauma and intrusive memory severity or cortical thickness of VVS structures, respectively. A significant negative correlation was found between years since index trauma and left hippocampal volume ( $r=-.36$ ,  $p=.027$ , uncorrected;  $n=41$ , cf. Fig. 3C).



## 4. Discussion

### 4.1. Allocentric spatial memory, intrusive memories and brain morphology

We investigated the capacity of allocentric spatial memory performance, cortical thickness of ventral visual stream (VVS) structures, and hippocampal volume to predict intrusive memory severity in patients with PTSD. In a **hierarchical** multiple linear regression model, higher allocentric memory performance significantly predicted lower intrusive memory severity. This relationship could not be accounted for by age, general visuospatial ability, egocentric memory performance, working memory, depression or anxiety scores. Our results complement previous studies, which reported a selective impairment of allocentric spatial memory in PTSD (Gilbertson et al., 2007; Smith et al., 2015) and stronger allocentric processing to be associated with fewer intrusive memories in healthy subjects following an analogue trauma (Bisby et al., 2010).

To our knowledge, this is the first study to provide the missing link by showing an association between lower allocentric memory performance and more frequent intrusive memories in a clinical population. Previous studies which investigated allocentric memory in PTSD have not measured or considered intrusive memory severity (Astur et al., 2006; Gilbertson et al., 2007; Smith et al., 2015). Our findings further support the dual representation model which emphasizes the role of allocentric spatial memory for contextualizing mental imagery in PTSD.

Specifically, the model proposes a distinction between lower-level sensory representations of the negative items of the event, which involve egocentric memory, and hippocampal-dependent representations of the associations between items and the context of the person experiencing the event, which involve allocentric memory (Brewin & Burgess, 2014). The dual representation theory further implies that strengthening of egocentric representations would increase intrusions while strengthening of allocentric representations would decrease intrusions (Bisby & Burgess, 2017). Congruently, we did find both in our PTSD sample - an association between lower allocentric memory and higher intrusive memory severity as well as a significant correlation between stronger egocentric memory scores and higher intrusive memory severity. Interestingly, the significance of the latter association (egocentric memory

and intrusive severity) disappeared when controlling for depression and anxiety symptoms whereas the first (allocentric memory and intrusions) remained significant after controlling for these variables. Considering that other forms of intrusive recollection are evident in trauma-exposed individuals who develop different anxiety disorders and depression (Brewin et al., 2010), these findings strongly support the notion that impaired allocentric memory is specific to the development of intrusive memories in PTSD (cf. Brewin, 2015; Smith et al., 2015).

Due to our cross-sectional study design, we can only speculate whether impaired allocentric memory ability presents a risk factor for the development of posttraumatic intrusive memories or is a consequence of traumatic stress. Our sample comprised women with childhood abuse, albeit not all participants reported their childhood trauma as their index trauma. Allocentric processing is assumed to be hippocampal-dependent (Hartley et al., 2007; King et al., 2002) and reduced hippocampal volume has been associated with childhood abuse (Teicher et al., 2017) as well as cumulative stress exposure (Hanson et al., 2015). Congruently, we found a negative correlation between left hippocampal volume and years since index trauma. However, no association between hippocampal volume and allocentric spatial memory performance or intrusive memory severity was detected.

We hypothesized that structures of the VVS predict intrusive memory severity and found a trend indicating an association between reduced cortical thickness of the left lingual gyrus and higher intrusive memory severity. Yet, as cortical thickness of the left lingual gyrus was also positively associated with allocentric memory performance, it might be worth considering its role in mnemonic processing of affective stimuli. It has previously been linked to visual as well as crossmodal spatial attention (Driver & Spence, 2000; Macaluso, Frith, & Driver, 2000) and has been associated with visual memory (Bogouslavsky, Miklossy, Deruaz, Assal, & Regli, 1987). Studies in women with PTSD due to childhood abuse reported reduced cortical thickness in the right lingual gyrus compared to trauma controls (Tomoda, Navalta, Polcari, Sadato, & Teicher, 2009) and increased blood flow during re-experiencing (Bremner et al., 1999). Also, altered connectivity between the bilateral lingual gyrus and the left dorsal anterior cingulate cortex has been associated with resilience to childhood maltreatment (van der Werff et al., 2013). Hence, it might be possible that traumatic experiences during sensitive

times in childhood restrict the development of areas necessary for declarative memory formation and thus for the creation of a coherent spatio-temporal context for an event, which may present a vulnerability factor for the development of posttraumatic intrusive memories.

~~Interestingly, our findings comprise alterations solely in the left hemisphere as opposed to the right. This is in line with Teicher's work (2002), which emphasizes the impact of childhood maltreatment on the left hemisphere. His team reported an equally developed right hemisphere in 104 abused patients (regardless of primary diagnosis) compared to controls, but detected extensive abnormality throughout the left hemisphere in patients, with the temporal regions being the most affected (Ito et al., 1993). An influential hypothesis about hemispheric specialization proposes that the left hemisphere is specialized for approach responses, whereas the right hemisphere is linked to avoidance responses (Fetterman et al., 2013). Repeated suppression of approaching trauma memories versus activation of avoidant strategies when trauma memories are activated may lead to morphometric alterations in the left instead of the right hemisphere.~~ However, having not obtained data on age at first trauma, we cannot substantiate these speculations, while our cross-sectional design and lack of power further restrict any causal inferences. Future studies should investigate the role of age at trauma onset in the contextualization of mental imagery further using a longitudinal design in larger samples.

#### **4.2. Limitations**

The following limitations need to be considered: First, our sample comprised solely women who experienced childhood trauma. Our results cannot be generalized to a male clinical population or to individuals who experienced a different type of trauma. Second, our assessment of visual intrusions only related to a brief time period. Third, we instructed participants to image the event vividly and may have only assessed visual intrusive memories. Thus, we cannot draw any conclusions regarding the effect of allocentric spatial memory on intrusive thoughts or other sensory intrusions. Fourth, as our findings are based on correlational analyses, no directionality can be inferred. Lastly, our assessment of provoked symptom severity has not been validated and intrusive symptom severity ratings did not correlate with naturally occurring intrusive symptomatology of the CAPS. However, it needs



to be considered that patients actively avoid exposure to trauma reminders that trigger intrusive recall in everyday life, which may result in retrospective reporting bias as demonstrated using ambulatory assessment (Priebe et al., 2013). We postulate that using a symptom provocation paradigm assesses the severity of intrusive memories more accurately as avoidant strategies are less likely to be applied.

#### **4.3. Clinical implications**

Our findings have relevant clinical implications for psychological intervention, specifically for trauma-focused therapy in PTSD (cf. Ehlers & Clark, 2000). Patients are typically asked to relive their trauma via imagery and update negative appraisals. According to most standard procedures, patients imagine the traumatic scene in front of their eyes, i.e. reconstructing their egocentric representation (Bisiach & Luzzatti, 1978). The dual representation theory proposes that strengthening the allocentric representation, e.g. by imagining the scene from a different perspective as done for example in screen techniques (Sachsse, 2009), facilitates the integration of contextual details and thus reduces intrusive re-experiencing. Our finding of an inverse relationship between allocentric spatial memory performance and intrusive memory severity suggests that patients with severe intrusive memories will have more difficulty creating an allocentric representation and may need specific guidance. To date there are case studies that support this approach (Kaur, Murphy, & Smith, 2016). Further trials should investigate whether such a module would be effective at reducing the frequency and intensity of intrusive memories and how strengthening an allocentric representation may be implemented effectively. Our findings may also imply that a strong premorbid allocentric memory ability could present a resilience factor for the development of posttraumatic intrusive memories, which is particularly relevant for populations who are at greater risk for traumatic exposure, such as first responders or soldiers. Further studies testing this implication are warranted.

## **5. Conclusion**

This is the first study to report a significant association between allocentric spatial memory and intrusive memory severity in patients with PTSD. Our work accentuates the crucial role of allocentric spatial memory for the contextualization of mental imagery in PTSD. Psychological therapies may benefit from additional elements comprising allocentric re-encoding of the traumatic scene to specifically treat visual intrusive memories in posttraumatic psychopathology.

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