Leveraging Prior Knowledge to Support Short-term Memory: Exploring the Role of the Ventromedial Prefrontal Cortex

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Abstract

■ It is well established that the ventromedial prefrontal cortex (vmPFC) plays a critical role in memory consolidation and the retrieval of remote long-term memories. Recent evidence suggests that the vmPFC also supports rapid neocortical learning and consolidation over shorter timescales, particularly when novel events align with stored knowledge. One mechanism by which the vmPFC has been proposed to support this learning is by integrating congruent information into existing neocortical knowledge during memory encoding. An important outstanding question is whether the vmPFC also plays a critical role in linking congruent information with existing knowledge before storage in long-term memory. The current study investigated this question by testing whether lesions to the vmPFC disrupt the ability to leverage stored knowledge in support of short-term memory. Specifically, we investigated the visuospatial bootstrapping effect, the phenomenon whereby immediate verbal recall of visually presented stimuli is better when stimuli appear in a familiar visuospatial array that is congruent with prior knowledge compared with an unfamiliar visuospatial array. We found that the overall magnitude of the bootstrapping effect did not differ between patients with vmPFC lesions and controls. However, a reliable bootstrapping effect was not present in the patient group alone. Post hoc analysis of individual patient performance revealed that the bootstrapping effect did not differ from controls in nine patients but was reduced in two patients. Although mixed, these results suggest that vmPFC lesions do not uniformly disrupt the ability to leverage stored knowledge in support of short-term memory. ■

INTRODUCTION

It is well established that prior knowledge can influence the incorporation of novel events into long-term memory (LTM; Bartlett, 1932). Events that align with existing knowledge structures, or schemas, are typically better remembered than events that are inconsistent with existing knowledge (Kumaran, 2013; Staresina, Gray, & Davachi, 2009; Tse et al., 2007). Neurobiological theories propose that the ventromedial prefrontal cortex (vmPFC) supports this ability to leverage stored knowledge in support of new learning by promoting the rapid assimilation of congruent events into existing neocortical memories (Gilboa & Marlatte, 2017; Ghosh & Gilboa, 2014; McClelland, 2013; Preston & Eichenbaum, 2013; van Kesteren et al., 2013; van Kesteren, Ruiter, Fernandez, & Henson, 2012; Tse et al., 2007, 2011). In the animal literature, evidence for this proposal comes from the upregulation of early genes in the rodent medial prefrontal cortex (mPFC) when animals encode novel events congruent with prior knowledge as well as the impairment of LTM for knowledge-congruent events following pharmacological inactivation of the mPFC (Tse et al., 2011). In the human literature, functional neuroimaging and neuropsychological studies also suggest that the vmPFC plays a key role in the consolidation and later LTM retrieval of information that is consistent with prior knowledge (Bonasia et al., 2018; Liu, Grady, & Moscovitch, 2017; Brod, Lindenberger, Werkle-Bergner, & Shing, 2015; Spalding, Jones, Duff, Tranel, & Warren, 2015; van Buuren et al., 2014; Warren, Jones, Duff, & Tranel, 2014; Preston & Eichenbaum, 2013; van Kesteren et al., 2012, 2013).

Whereas prior research has firmly established that the vmPFC plays a key role in the ability to use prior knowledge as a scaffold to support LTM, whether the vmPFC plays a similar role in the domain of short-term memory (STM) remains an open question. Although the vmPFC is not typically included in traditional models of working memory, it is well established that preexisting or recently acquired information stored in LTM can influence performance on immediate recall tasks (Yousif, Rosenberg, & Keil, 2021; Starr, Srinivasan, & Bunge, 2020; Calia, Darling, Havelka, & Allen, 2019; Kaiser, Stein, & Peelen, 2015; Oberauer, Jones, & Lewandowsky, 2015; Baddeley, Allen, & Vargha-Khadem, 2010; Jackson & Raymond, 2008; Bor, Cumming, Scott, & Owen, 2004). For example, immediate serial recall of digits is enhanced when digits are presented within a highly familiar visuospatial array (typical keypad) compared with an unfamiliar visuospatial array (atypical

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keypad; "visuospatial bootstrapping effect"; Darling, Havelka, Allen, Bunyan, & Flornes, 2020; Calia et al., 2019; Allan, Morey, Darling, Allen, & Havelka, 2017; Race, Palombo, Cadden, Burke, & Verfaellie, 2015; Darling, Parker, Goodall, Havelka, & Allen, 2014; Darling, Allen, Havelka, Campbell, & Rattray, 2012; Darling & Havelka, 2010). Similarly, objects presented in familiar spatial arrangements consistent with real-world regularities (e.g., mirror above a sink) are better remembered on tests of visual STM compared with objects presented in unfamiliar spatial arrangements (e.g., mirror below a sink; Kaiser et al., 2015). Whereas such findings support theories suggesting that STM and LTM interact (Postle, 2006; Ranganath & Blumenfeld, 2005; Cowan, 1999; Ericsson & Kintsch, 1995), which brain regions support these interactions, and the contribution of the vmPFC in particular, remain an open question (Race et al., 2015).

The current study used a lesion-deficit approach to investigate whether the vmPFC plays a necessary role in the ability to leverage stored knowledge in support of STM. Specifically, extending from the findings in the domain of LTM, we hypothesized that lesions to the vmPFC would abolish the immediate recall benefit typically observed for digits presented within a congruent (typical) versus an incongruent (atypical) keypad array. In Experiment 1, we first confirmed that patients with vmPFC lesions have access to familiar visuospatial knowledge about a typical keypad by testing whether they have faster RTs when entering digits into a typical versus an atypical keypad array (RT congruency effect). Experiment 2 then investigated whether patients can leverage this stored visuospatial knowledge to enhance STM by testing whether immediate digit recall is superior when digits are presented in a typical versus atypical keypad array (STM congruency effect). If the vmPFC plays a critical role in the ability to leverage stored knowledge in support of immediate recall, STM congruency effects should be reduced in patients with vmPFC lesions compared with healthy controls. Alternatively, if regions outside the vmPFC can support this function, STM congruency effects should be present in both vmPFC patients and controls.

EXPERIMENT 1: KEYPAD KNOWLEDGE TASK

Methods

Participants

The study sample consisted of 11 patients with vmPFC lesions due to aneurysm of the anterior communicating artery (ACoA) and 16 control participants. Sample size was determined based on previous studies investigating prior knowledge effects in patients with vmPFC lesions (Giuliano, Bonasia, Ghosh, Moscovitch, & Gilboa, 2021; Spalding et al., 2015) and previous neuropsychological studies of the visuospatial bootstrapping effect (Race et al., 2015). Demographic and neuropsychological characteristics for the vmPFC patients are provided in Table 1. Intellectual function was generally preserved in vmPFC patients, as indicated by performance within the normal range for Wechsler Adult Intelligence Scale, third edition (WAIS-III) verbal IQ (mean = 105.6) and Working Memory Index (mean = 102.5) scores. Memory performance was variable in these patients, mirroring the pattern typically observed among patients with vmPFC damage secondary to ACoA aneurysm because of the variability in lesion profile and possibility of damage to the basal

Table 1. Demographic and Neuropsychological Characteristics of Participants with Lesions of the Ventromedial Prefrontal Cortex (vmPFC)

				WAIS, III			*WMS, III*		
Patient	*Etiology*	*Age*	*Edu*	*VIQ*	*WMI*	*DSF*	*GM*	*VD*	*AD*
P01	ACoA aneurysm	73	12	92	90	4	72	88	58
P02	ACoA aneurysm	68	16	112	109	6	111	103	111
P03	ACoA aneurysm	59	16	106	104	7	111	118	105
P04	ACoA aneurysm	67	18	118	109	7	91	100	89
P05	ACoA aneurysm	63	12	97	88	5	63	68	58
P06	ACoA aneurysm	34	16	110	106	6	83	75	89
P07	ACoA aneurysm	64	12	97	99	7	62	62	64
P08	ACoA aneurysm	22	12	93	92	6	49	68	46
P09	ACoA aneurysm	71	12	105	108	7	66	65	67
P10	ACoA aneurysm	68	16	134	113	7	96	88	99
P11	ACoA aneurysm	70	12	98	109	7	112	109	114

Age = Age (years); Edu = Education (years); VIQ = Verbal IQ; WMI = Working Memory Index; DSF = Longest Digit Span Forward; WMS, III = Wechsler Memory Scale, III; GM = General Memory; VD = Visual Delayed; AD = Auditory Delayed.

forebrain or white mater pathways between the basal forebrain and hippocampus (Ghosh & Gilboa, 2014; Gilboa, Alain, He, Stuss, & Moscovitch, 2009). Lesions were manually drawn onto the standard Montreal Neurological Institute brain using MRIcro software (Rorden & Brett, 2000) for nine of the ACoA patients for whom scans were available. For the remaining two patients, vmPFC pathology was inferred on the basis of etiology and presence of confabulation (Moscovitch, 1989). Lesions in the vmPFC patients involved Brodmann's areas (BAs) 4, 5, 6, 8, 9, 10, 11, 23, 24, 25, 32, 38, 46, 47, and 48, but additionally involved basal forebrain in several patients. The extent of patients' lesions as well as lesion overlap across patients is displayed in Figure 1. The maximal overlap of lesions was in BA 25, BA 10, and BA 11. The average amount of lesion in vmPFC was 16.8%, calculated by superimposing individual scans on a template of vmPFC based on identified landmarks (Mackey & Petrides, 2014). Lesions were bilateral in six patients and limited to the right hemisphere in the remaining three patients. One patient had an additional lesion in left ventrolateral PFC (P03), another patient had an additional lesion extending from the right putamen dorsally into premotor/motor areas (P02), and another patient had an additional lesion extending into the right caudate (P09).

Sixteen healthy control participants with no history of neurological or major psychiatric illness were matched to the patient group in terms of age (mean = 64.9 years), education (mean = 15.5 years), and verbal IQ (mean = 108). All participants were paid for their participation and provided informed consent in accordance with the procedures of the institutional review board at the VA Boston Healthcare System.

Procedure

Sets of three nonrepeating digits were concurrently presented on a computer screen, and participants had to enter the digits as quickly as possible into an external numeric keypad that had either (i) a typical keypad layout or (ii) an atypical keypad layout (in which digits were arranged in a pseudorandom pattern so that the digit-location mapping was unfamiliar; Figure 2A). Importantly, the spatial position and distance between digits was

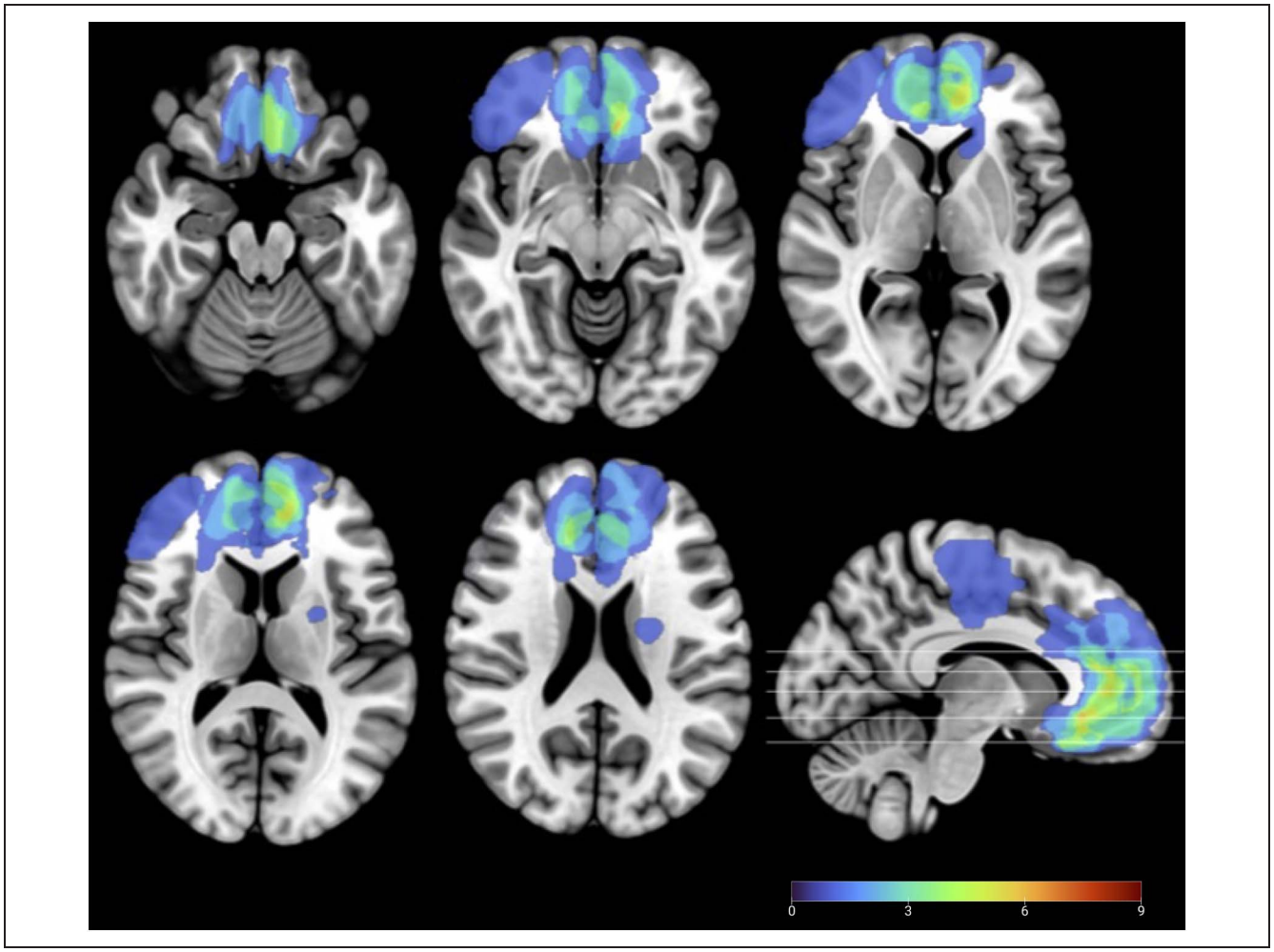

Figure 1. Location of brain lesion overlap in nine ventromedial prefrontal cortex (vmPFC) patients. Five axial slices display lesions projected according to neurological convention at locations indicated on sagittal slice. The color bar indicates the number of overlapping lesions.

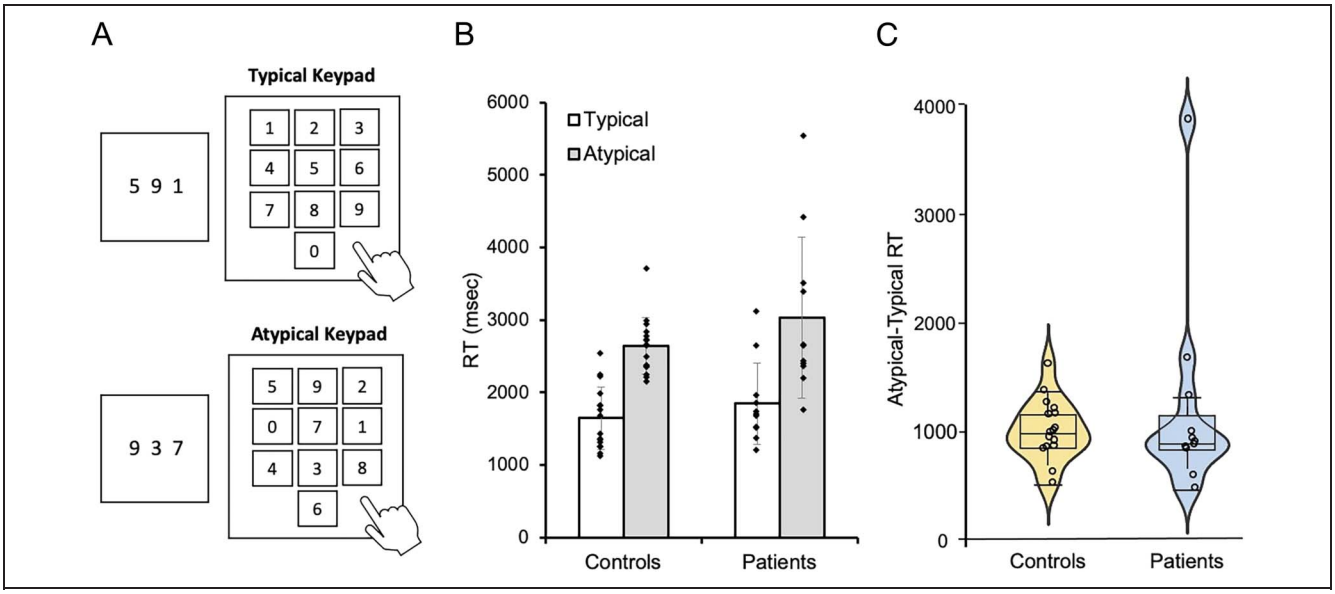

Figure 2. Experiment 1 methods and results. (A) Example digit stimuli and keypad layouts used in Experiment 1. (B) Mean RTs when digits were entered into a typical (white bar) versus an atypical (gray bar) keypad. (C) RT facilitation (typical−atypical RT) for controls (left) and patients (right). Boxplot within violin plot displays median value (horizontal black bar) and interquartile range.

matched across the typical and atypical keypad number sets so that motor movements were equivalent across conditions. Participants performed 42 trials of the typical keypad condition and 42 trials of the atypical keypad condition, with the order of conditions counterbalanced across participants, and RTs and accuracy were collected. RTs were calculated as the total time to enter the three digits into the keypad. In the atypical keypad condition, the layout of the atypical keypad changed every 14 trials to reduce potential effects of digit-location learning across trials in controls. If the long-term representation of a typical keypad is intact in patients, and they can access this representation as well as controls, patients and controls should demonstrate similar RT facilitation when entering digits into a typical versus an atypical keypad.

Statistical Approach

Results were first analyzed using ANOVA to compare the performance of the vmPFC patient group to the control group, with Keypad Context as a within-subject variable and Group as a between-subjects variable. In addition, because of heterogeneity among the vmPFC patients, we also utilized a post hoc multiple case study approach (Rosenbaum, Gilboa, & Moscovitch, 2014) to compare the performance of each individual patient to the control group, using modified *t* test for single cases (Crawford & Howell, 1998).

Results

Both groups were highly accurate when entering digits into the typical and atypical keypads (accuracy > 98% across conditions in both groups). When mean accuracy was entered into a 2 (Group) × 2 (Keypad Context) ANOVA, there was not a main effect of Context, $F(1, 25) = 1.36, p = .26, \eta_p^2 = .05$; group, $F(1, 25) = 2.53, p = .12, \eta_p^2 = .09$; nor a Group × Keypad Context interaction, $F(1, 25) = .16, p = .69, \eta_p^2 = .006$. Analysis of RTs (Figure 2B), performed on log transformed data, revealed that there was a main effect of Keypad Context, $F(1, 25) = 127.15, p < .001, \eta_p^2 = .84$, and both groups were faster to enter digits into the typical keypad compared with the atypical keypad (control RT benefit in the typical vs. atypical keypad condition = 993 msec, patient RT benefit in the typical vs. atypical keypad condition = 1183 msec). There was no main effect of Group, $F(1, 25) = 1.36, p = .25, \eta_p^2 = .05$. Importantly, the RT advantage for the typical keypad did not differ across groups, $F(1, 25) = .03, p = .86, \eta_p^2 = .001$, and there was no difference in the percent improvement in RTs for the typical versus atypical keypad across groups, $t(25) = .22, p = .83, d = .09$. A reliable RT benefit for the typical versus atypical keypad was also present within each of the groups (controls: $t(15) = 10.44, p < .001, d = 2.61$; patients: $t(10) = 6.11, p < .001, d = 1.84$). Post hoc analysis of the individual cases confirmed that for 10 of the vmPFC patients, the magnitude of the RT advantage for the typical keypad did not differ from that in controls, $ts(15) < 1.62, ps > .15$ (Table 2). In the remaining patient (P01), the RT advantage for the typical keypad was greater than that in controls, $t(15) = 3.56, p < .005$. These results indicate that patients with vmPFC lesions have intact access to stored visuospatial knowledge about a typical keypad.

EXPERIMENT 2: STM TASK

Methods

Participants

Participants included the same group of vmPFC patients who participated in Experiment 1 (run in a separate session)

Table 2. Task Performance in Experiment 1 and Experiment 2 for Patients with Lesions of the Ventromedial Prefrontal Cortex (vmPFC)

	RTs (Experiment 1)				*Memory Accuracy (Experiment 2)*			
	Typ	*Atyp*	*A-T*	*t*	*Atyp*	*Typ*	*T-A*	*t*
Patient								
P01	1700	5547	3847	3.56	0.54	0.57	0.03	−0.37
P02	1519	2362	843	−0.27	0.73	0.82	0.09	0.89
P03	1379	2200	820	−0.16	0.82	0.83	0.01	−0.65
P04	1528	2431	903	−0.16	0.80	0.88	0.08	0.61
P05	3120	4417	1297	−0.81	0.49	0.53	0.05	0.06
P06	1205	1764	559	−0.59	0.91	0.94	0.03	−0.22
P07	1962	2402	440	−1.51	0.88	0.91	0.03	−0.41
P08	1685	2651	966	−1.62	0.74	0.77	0.03	−0.22
P09	2646	3513	868	−1.08	0.85	0.72	−0.12	−3.43
P10	1734	3398	1664	0.97	0.97	1.00	0.03	−0.22
P11	1859	2665	805	−0.65	0.92	0.83	−0.10	−2.90
Control Mean	1646	2639	993	–	0.87	0.91	0.05	–

RTs reported in msec; Memory accuracy reported as mean proportion of digits correctly recalled in the appropriate serial position in each sequence. Mean task performance for healthy controls is also displayed for comparison. Typ = Typical Keypad; Atyp = Atypical Keypad; A-T = Atypical − Typical; T-A = Typical − Atypical; *t* = t values from single-case analysis comparing performance of individual patients to healthy control group.

and a new group of 19 healthy controls whose mean age (62 ± 10.0 years), education (15 ± 2.5 years), and verbal IQ (110 ± 12.7) did not differ from that of the patient group. In addition, this new control group was matched to the patient group with respect to forward digit span (7.1 ± 1.3; 6.3 ± 1.0, respectively) given the STM demands of the task. Sample size was determined based on previous studies investigating prior knowledge effects in patients with vmPFC lesions (Giuliano et al., 2021; Spalding et al., 2015) and previous neuropsychological studies of the visuospatial bootstrapping effect (Race et al., 2015).

Stimuli

The experimental stimuli and procedure were modeled on the studies of Darling and colleagues (2012, 2014) and Race and colleagues (2015). Sequences of six digits were created in which the digits 0–9 were randomly sampled without replacement. In the typical keypad condition, the digits were presented in the format of a traditional telephone keypad. In the atypical keypad condition, the digits appeared within the same grid as in the typical keypad condition, but the digits were arranged in a pseudorandom pattern so the digit-location mapping was unfamiliar (Figure 3A). The layout of the atypical keypad changed every eight trials to reduce potential effects of digit-location learning across trials (Darling et al., 2012). The spatial position and distance between digits were matched across the typical and atypical digit sequences to ensure that eye movements would be equivalent across memory conditions.

Procedure

Participants performed two blocks of immediate serial digit recall, with 24 trials per block (Race et al., 2015). In one block, digits were presented in the context of a typical keypad array, and in the other block, digits were presented in the context of an atypical keypad array, with the order of blocks counterbalanced across participants. Sequences of digits were indicated by sequentially highlighting the background of individual digits in the keypad arrays in green. Each digit was highlighted for 1000 msec with a 250-msec delay between digits, and participants were instructed to remember the digits in the order in which they were presented. At the end of the sequence a command prompted the participant to verbally recall the sequence in the correct order.

Statistical Approach

Like Experiment 1, results were first analyzed using ANOVA to compare the performance of the vmPFC patient group to the control group, with Keypad Context as a within-subject variable and Group as a between-subjects variable. In addition, because of heterogeneity among

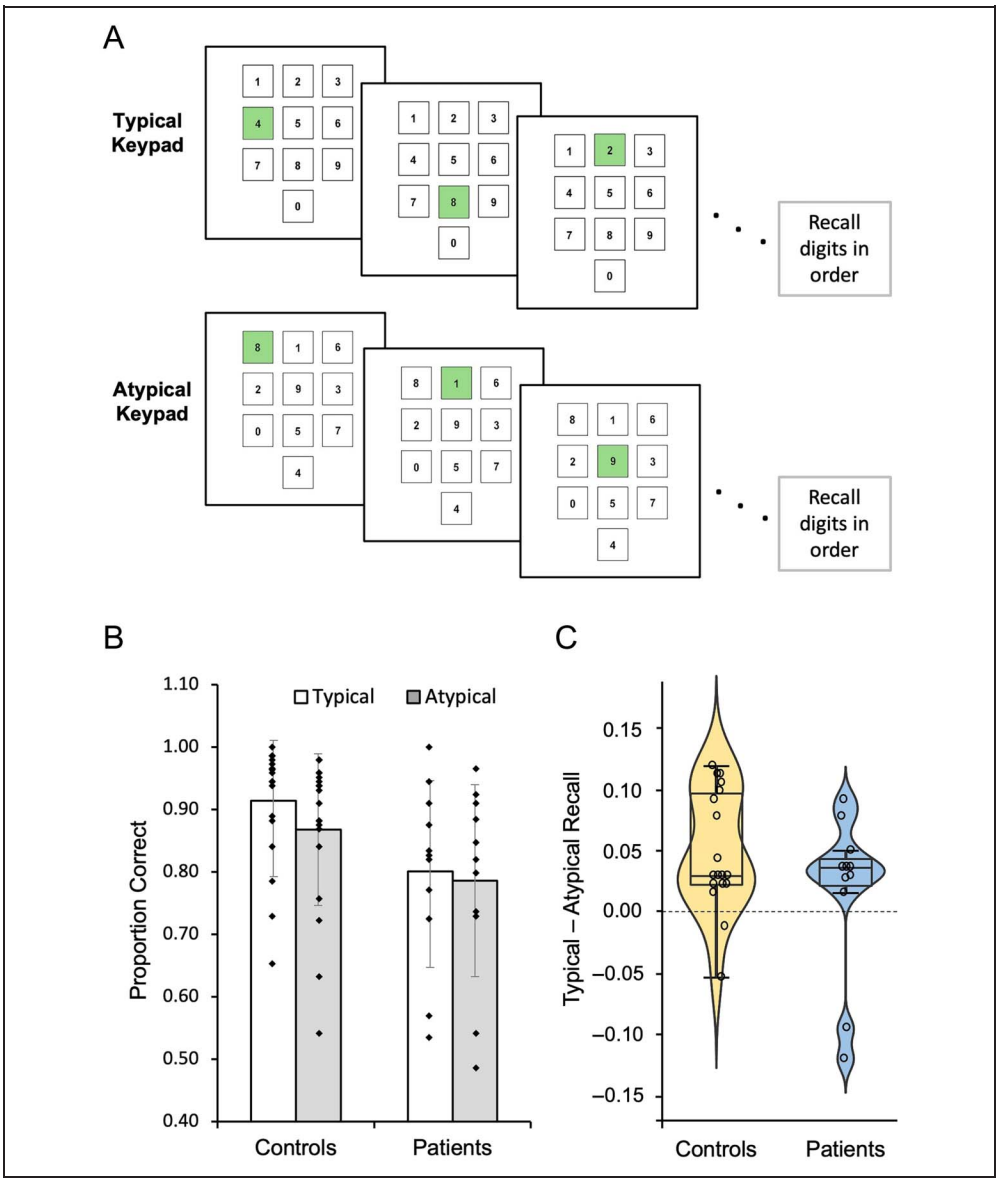

Figure 3. Experiment 2 methods and results. (A) Example keypad displays used in Experiment 2. (B) Proportion of digits correctly recalled when digits were presented in the context of a typical (white bars) or atypical (gray bars) keypad. (C) Recall advantage in the context of a typical keypad (typical−atypical recall) for controls (left) and patients (right). Boxplot within violin plot displays median value (horizontal black bar) and interquartile range.

the vmPFC patients, we also utilized a post hoc multiple case study approach (Rosenbaum et al., 2014) to compare the performance of each individual patient to the control group, using modified *t* test for single cases (Crawford & Howell, 1998).

Results

Memory recall performance is presented in Figure 3B. Recall accuracy was calculated as the mean proportion of digits correctly recalled in the appropriate serial position in each sequence. This analysis approach mirrors that used in Experiment 1 and follows the approach used by Allen, Havelka, Falcon, Evans, and Darling (2015).[1]

Recall accuracy was entered into a 2 × 2 ANOVA with factors of Group (patient, control) and Keypad Context (typical, atypical). There was a main effect of Keypad Context, reflecting higher digit recall accuracy in the typical than the atypical keypad condition, $F(1, 28) = 8.13$, $p < .01$, $\eta_p^2 = .23$. Although overall recall performance was higher in controls than in patients, $F(1, 28) = 4.41$, $p = .045$, $\eta_p^2 = .14$, the magnitude of the typical keypad advantage did not differ across groups, $F(1, 28) = 2.41$, $p = .13$, $\eta_p^2 = .08$. However, follow-up analysis revealed a reliable typical keypad advantage present in the control group, $t(18) = 4.15$, $p < .001$, $d = .42$, but not in the vmPFC group, $t(10) = .69$, $p = .51$, $d = .09$. Post hoc analysis of individual patient performance indicated that the magnitude of the typical keypad advantage did not differ from that in controls in nine of the vmPFC patients, $ts(18) < .89$, $ps > .38$, but did differ in two patients (P09 and P11; $ts(18) > 2.90$, $ps < .003$; Figure 3C) who did not demonstrate a typical keypad advantage despite having access to stored visuospatial knowledge about a typical keypad (indicated by an RT advantage for the typical vs. atypical keypad in Experiment 1).

DISCUSSION

A large body of research suggests that the vmPFC plays a key role in the ability to leverage stored knowledge in support of memory formation (Gilboa & Marlatte, 2017; Ghosh & Gilboa, 2014; Preston & Eichenbaum, 2013; van Kesteren et al., 2012; Tse et al., 2007, 2011). To date, this research has primarily focused on LTM and the benefits that occur when novel information aligns with existing knowledge structures (congruency effects in LTM). In the current study, we used a neuropsychological approach to investigate whether the vmPFC also plays a similar role in STM. Specifically, we examined whether vmPFC lesions affect the immediate recall advantage observed for knowledge-congruent events before storage in LTM (congruency effects in STM). In Experiment 1, we first confirmed that vmPFC lesions do not disrupt the representation or on-line use of stored knowledge about a typical keypad: Patients with vmPFC lesions demonstrated faster RTs when entering digits into a typical keypad array compared with an atypical keypad array. In Experiment 2, we then tested whether vmPFC patients can leverage this stored knowledge about a typical keypad to support immediate recall of digit sequences ("visuospatial bootstrapping effect"; Darling & Havelka, 2010). The magnitude of the immediate recall advantage for digits appearing in a typical compared with an atypical keypad array did not differ across groups (No Group × Keypad Context interaction). However, a reliable typical keypad advantage was present in the control group but not in the patient group. Post hoc inspection of individual patient performance revealed that whereas the magnitude of the typical keypad advantage did not differ from controls in nine of the vmPFC patients, the magnitude of the typical keypad advantage differed from that in controls in two of the vmPFC patients. These results reveal that whereas the vmPFC plays a critical role in the ability to use prior knowledge to benefit LTM, lesions of the vmPFC do not uniformly prevent the ability to leverage stored visuospatial knowledge in support of STM.

The mixed results from Experiment 2 can be interpreted in several different ways. First, we focus on the results that suggest that vmPFC lesions do not disrupt visuospatial bootstrapping (i.e., absence of a Group × Context interaction and similar performance compared with controls in 9 out of 11 patients), which diverged from our hypothesis. One interpretation of these results is that performance benefits in the context of the typical keypad reflect new within-task learning rather than vmPFC-mediated use of long-term knowledge. Although the visuospatial bootstrapping effect is typically taken to reflect a STM benefit derived from preexisting visuospatial knowledge stored in LTM (Darling, Allen, & Havelka, 2017), recent evidence suggests that within-task learning about spatial structure (e.g., consistent mappings between to-be-remembered stimuli and spatial locations within a task) can also improve STM for sequences of objects without support from preexisting knowledge (Yousif et al., 2021). However, this interpretation is unlikely given prior evidence that the visuospatial bootstrapping effect depends on the presence of an LTM representation: When digits are presented in a novel keypad array of random digits, there is no STM advantage, even when that array is static across trials and could presumably support within-task learning, compared with when it changes from trial to trial (Darling et al., 2012). Furthermore, the visuospatial bootstrapping effect is absent in 6-year-old children before long-term knowledge about the layout of a typical keypad has been established (Darling et al., 2014), and remains intact in amnesic patients who have severe deficits in new learning but preserved access to long-term visuospatial knowledge of a keypad (Race et al., 2015). These findings strongly suggest that STM benefits observed in the current study reflect the ability to draw upon long-term visuospatial knowledge rather than within-task visuospatial learning.

A second interpretation of the finding that vmPFC lesions did not always disrupt the visuospatial bootstrapping effect is that prior knowledge may impact performance through multiple mechanisms, not all of which depend on the vmPFC. For example, the contribution of vmPFC may depend on the nature of the prior knowledge being represented and maintained. The vmPFC may be particularly critical for the representation and use of *schemas*, which can be defined as networks of prior knowledge that are adaptable, associative, extracted over multiple episodes, and lack unit detail (Giuliano et al., 2021; Ghosh & Gilboa, 2014; Bartlett, 1932). Schemas are characterized by contextual diversity, involving objects and relations that are dispersed through space and time (Davis, Altmann, & Yee, 2020). In contrast, stored knowledge about the layout of a keypad likely reflects more static conceptual knowledge (e.g., about digits and their typical spatial relationships) that is less adaptable and does not require the integration of information across situations. It is possible that the activation and maintenance of this more concrete conceptual knowledge may depend on regions outside the vmPFC. In line with this proposal, Giuliano and colleagues (2021) recently found that vmPFC lesions had a dissociable effect on neural representations of schemas and semantic category knowledge, and that oscillatory activity in the vmPFC is only associated with the former. Thus, the type of prior knowledge supporting performance may be an important factor determining vmPFC contributions to prior knowledge effects in both the memory and nonmemory domains (Kan, Rosenbaum, & Verfaellie, 2020; Liu et al., 2017). An important outstanding question is whether leveraging prior knowledge to support STM depends on vmPFC mechanisms when that prior knowledge is more schematic in nature.

A third possibility is that prior knowledge effects in STM and in LTM reflect distinct cognitive mechanisms, and only the latter rely on the vmPFC. In the domain of LTM, prior knowledge effects are thought to reflect the assimilation of novel information into established knowledge structures

(Gilboa & Marlatte, 2017). The vmPFC is thought to support this integrative process by strengthening neocortical connections between novel information and existing knowledge representations (van Kesteren et al., 2012). In the case of STM, such assimilation may not be necessary given that events need to be held in mind only temporarily and performance does not require the construction of a durable memory trace. Rather, benefits of prior knowledge may be because of reduced demands on attentional and working memory resources when prior knowledge can support performance. Indeed, the benefits of prior knowledge in the case of the visuospatial bootstrapping effect have been previously attributed to a reduced reliance on verbal working memory when preexisting spatial–verbal associations can support verbal recall (Allen et al., 2015). By this interpretation, the vmPFC may only be necessary when there are demands on assimilating information into LTM. In support of this proposal, activity in the human vmPFC is not consistently observed in neuroimaging studies during the on-line processing of knowledge-congruent events, before encoding in LTM (McAndrews, Girard, Wilkins, & McCormick, 2016; Bonhage, Fiebach, Bahlmann, & Mueller, 2014; Staresina et al., 2009; Bor et al., 2004).

Importantly, the interpretations described above need to be tempered by the finding that a reliable bootstrapping effect was not present in the patient group alone and the finding that two of the patients did not demonstrate a memory advantage for digits appearing in the familiar keypad array. As is typically the case following ACoA aneurysm, the vmPFC lesions in our patients were incomplete, and variability in performance could result from heterogeneous lesion locations within the vmPFC across patients. This leaves open the possibility that only specific subregions of vmPFC are critical for STM congruency effects. Although we note that P09's vmPFC lesion falls within the same BAs as was the case for the group as a whole (BA 10, 11, 24, 25, 32; scans were not available for P11 such that precise lesion localization was not possible), future studies of larger cohorts of vmPFC patients will be needed to allow for more comprehensive lesion-symptom mapping.

An alternative possibility is that impairments in visuospatial bootstrapping occur in the presence of additional damage outside the vmPFC. For example, CT scan of one of the patients who did not demonstrate a bootstrapping effect (P09) indicated the presence of an additional lesion in the right caudate and review of clinical records revealed that the other patient who did not demonstrate a bootstrapping effect (P11) also had a documented lesion in the caudate (no such lesions were identified or reported for any other patient). Although this interpretation is speculative, future work could investigate whether the ability to leverage stored visuospatial knowledge in support of immediate verbal recall depends on the caudate, potentially through its role in the on-line maintenance or manipulation of spatial information (Postle & D'Esposito, 1999, 2003; Wager & Smith, 2003; Levy, Friedman, Davachi, & Goldman-Rakic, 1997) or the gating of information into working memory (O'Reilly & Frank, 2006; Ashby, Ell, Valentin, & Casale, 2005). If this is the case, one might predict that lesions to the caudate nucleus (e.g., in Parkinson's disease) might disrupt the visuospatial bootstrapping effect.

It is also likely that some of the vmPFC patients have additional damage to the basal forebrain that impacts their LTM, which is a limitation of the current study. Indeed, as can be seen in Table 1, memory performance was variable across the patient group. Variable memory performance is a pattern typically observed among patients who have vmPFC damage secondary to ACoA aneurysm, and it is likely that low memory performance in some patients was because of basal forebrain damage. However, it is important to note that any impairments in LTM should have little impact on the results of the current study given that bootstrapping performance was not uniformly impaired in the patient group.

To conclude, the current study demonstrates that vmPFC lesions do not uniformly impair STM visuospatial congruency effects. We found that patients with vmPFC lesions could represent prior knowledge about a typical keypad (evident in the RT benefit for digits presented in the typical versus atypical keypad array) and that the ability to use this prior knowledge to support immediate digit recall did not differ between the vmPFC patient group and controls. However, the STM results were mixed across patients and a typical keypad advantage was not uniformly present in the patient group. Important outstanding questions are whether potential contributions of the vmPFC to congruency effects reflect the nature of the prior knowledge supporting performance (e.g., the use of schema), demands on assimilation (e.g., storage in LTM), or the functions supported by specific subregions of the vmPFC. To gain leverage on these questions, future studies should use the same types of stimuli to examine congruency effects in both STM and LTM (Darling et al., 2020) and should examine larger cohorts of patients to determine whether there is a relationship between specific profiles of neural damage and behavioral performance.

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Data Availability Statement

Data and materials can be obtained from the author upon request.

Author Contributions

Elizabeth Race: Conceptualization; Project administration; Supervision; Visualization, Writing—Original draft; Writing—Review & editing. Hope Tobin: Data curation; Project administration. Mieke Verfaellie: Conceptualization; Project administration; Supervision; Writing—Review & editing.

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Diversity in Citation Practices

Retrospective analysis of the citations in every article published in this journal from 2010 to 2021 reveals a persistent pattern of gender imbalance: Although the proportions of authorship teams (categorized by estimated gender identification of first author/last author) publishing in the *Journal of Cognitive Neuroscience* (*JoCN*) during this period were M(an)/M = .407, W(oman)/M = .32, M/W = .115, and W/W = .159, the comparable proportions for the articles that these authorship teams cited were M/M = .549, W/M = .257, M/W = .109, and W/W = .085 (Postle and Fulvio, *JoCN*, 34:1, pp. 1–3). Consequently, *JoCN* encourages all authors to consider gender balance explicitly when selecting which articles to cite and gives them the opportunity to report their article's gender citation balance.

Note

1. Previous investigations of the visuospatial bootstrapping effect have also analyzed mean proportion of trials on which all items were successfully recalled in the correct order (e.g., Darling et al., 2012; Darling & Havelka, 2010). When the current data were analyzed using that method, the pattern of results remained the same.

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