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Who am I really? The ephemerality of the self-schema following vmPFC damage

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ABSTRACT

We studied the role of the ventromedial prefrontal cortex (vmPFC) in supporting the self-schema, by asking vmPFC patients, along with healthy and brain-damaged controls, to judge the degree to which they (or another person) were likely to engage in a series of activities, and how confident they were in their responses. Critically, participants provided their judgments on two separate occasions, a week apart. Our underlying assumption was that a strong self-schema would lead to confident and stable self-related judgments. We observed that control groups exhibited higher across-session consistency for self-related compared to other-related judgments, while this self-advantage was absent in vmPFC patients. In addition, regression analyses showed that in control groups the level of confidence associated with a specific (self- or other-related) judgment predicted the stability of that judgment across sessions. In contrast, vmPFC patients' confidence and rating consistency were aligned only for other-related judgments. By contrast, self-related judgments changed across sessions regardless of the confidence level with which they were initially endorsed. These findings indicate that the vmPFC is crucial to maintaining the self-schema and supporting the reliable retrieval of self-related information.

1. Introduction

Personal preferences, idiosyncrasies, and little quirks of personality are what makes us uniquely ourselves. We know that we take our coffee black, are always late, like diving but hate when others take pictures of us. These instances of personal semantic knowledge are part of the self-schema, an articulated set of beliefs about oneself, generally deriving from the repeated categorization and subsequent evaluation of one's behavior, which defines our identity and drives our behavior (Markus, 1977). How do we know who we are?

Personal semantic knowledge is a memory system at the border between episodic memory, our ability to recollect personal experiences within their unique spatio-temporal context (e.g., 'the first time I tried black coffee I liked it'), and semantic memory, our (culturally shared) knowledge of facts and concepts by now detached from the context of acquisition (e.g., 'black coffee contains more caffeine'), as it is personal but relatively devoid of context (Renoult et al., 2012, 2016), although different domains of personal semantic memories differ in their relation to semantic and episodic memory (see also Grilli and Verfaellie, 2014). Self-knowledge is the most extensively studied instance of personal semantic memory; it has been classically operationalized as knowledge of one's own personality traits or, less frequently, personal preferences (e.g., I am shy; I prefer dogs to cats; Renoult et al., 2012; Craik et al., 1999; Kelley et al., 2002; Martinelli et al., 2013; Wank et al., 2022). Personal semantic memory, however, also contains information that is less abstract and more directly related to (or inferable from) events (Grilli and Verfaellie, 2014, 2015), such as autobiographical facts (e.g., I have a female dog) and repeated events (e.g., I smoke everyday while walking my dog) that all contribute to shape the self-schema (Markus, 1977 , (Markus, 1983).

Past work has demonstrated that judging the self-relevance of a personality trait does not influence the time required to subsequently recollect an event in which one displayed that personality trait (episodic memory), or to define that trait (semantic memory; Klein and Loftus,

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1993; Klein and Lax, 2010), suggesting some degree of functional independence between self-knowledge and semantic and episodic memory. Moreover, there is neuropsychological evidence that preserved self (trait) knowledge can withstand impairments in semantic and episodic memory (Klein and Lax, 2010; Renoult et al., 2012). Tulving (1993) first reported that the severely amnesic patient KC could describe his personality accurately and reliably. KC's self-reported personality traits were consistent between testing sessions (78% agreement) and in line with those provided by his mother (see also Klein et al., 1996; Klein et al., 2002a; Klein et al., 2002b). Self-trait knowledge can remain intact even in the presence of profound semantic memory deficits (Westmacott et al., 2001; Klein et al., 2002b, Klein et al., 2003; Picard et al., 2013; Duval et al., 2012), such as in late-stage Alzheimer's disease (Klein et al., 2003) or semantic dementia (Duval et al., 2012). However, other results have challenged these findings (see Charlesworth et al., 2016; Tanguay et al., 2018; Wank et al., 2022), for example questioning the accuracy/completeness of self-knowledge in patients with episodic and semantic memory deficits (Klein et al., 2003). More in general, recent findings call for a qualification of the relation between the personal semantic and episodic memory systems reflecting the heterogeneity of the former (Renoult et al., 2012; Grilli and Verfaellie, 2014). For example, autobiographical facts that are 'experience-near' and not completely devoid of spatio-temporal information (e.g., I was involved in sports in high school) have been found to depend on the integrity of the medial temporal lobe (Grilli and Verfaellie, 2015, 2016; see also Wank et al., 2022; Sawczak et al., 2022).

What are the neural bases of personal semantic memory? There is converging evidence that the medial prefrontal cortex (mPFC) is associated with self-knowledge. In functional neuroimaging (fMRI) studies, mPFC is more active for self (trait) judgments rather than general semantic evaluations (Johnson et al., 2002; Schmitz et al., 2004; D'Argembeau et al., 2010a; D'Argembeau et al., 2010b). Zysset et al. (2002) reported a functional dissociation between mPFC and the inferior precuneus, which proved more engaged by self-trait judgments and autobiographical memory retrieval, respectively (see also Sajonz et al., 2010). Also, mPFC is at the basis of the self-reference effect (SRE; Rogers et al., 1977; Symons and Johnson, 1997). This region is indeed more active when participants judge the self-relevance of personality traits (e.g., are you an extrovert?) compared to their phonemic or semantic properties, or their descriptiveness of another individual (Kelley et al., 2002; Moran et al., 2006; D'Argembeau et al., 2007; Sui and Humphreys, 2015). Moreover, activity in mPFC predicts the level of enhanced memory for personality traits encoded with respect to the self than to another individual (Moran et al., 2006). Importantly, Philippi et al. (2012a) and Stendardi et al. (2021) reported a drastic reduction of the SRE in patients with lesion in mPFC, especially in its ventral sector (vmPFC; Stendardi et al., 2021). In these studies, vmPFC patients did not show a memory advantage for items encoded with respect to the self compared to another individual, suggesting that vmPFC is necessary to support the self-schema or to impart a mnemonic advantage to items relevant to the self-schema.

Although previous studies revealing a virtual absence of the SRE in vmPFC patients point to a crucial role of vmPFC in self-knowledge (Philippi et al., 2012a; Stendardi et al., 2021), in those studies the status of self-knowledge is inferred from performance in an episodic (anterograde) memory task. Because vmPFC patients may have anterograde memory impairments that go beyond their self-knowledge deficits (Della Sala et al., 1993; Kopelman et al., 1999; Ciaramelli et al., 2006; Ciaramelli et al., 2009; Ciaramelli and di Pellegrino, 2011; Ciaramelli et al., 2019; Bertossi et al., 2016;Bertossi et al., 2017 De Luca et al., 2018), it is not clear the degree to which the reduction of the SRE following vmPFC damage is due to degraded self-knowledge or impaired self-referential encoding in these studies. Ideally, tests with low demands on anterograde episodic memory would be better suited to capture the status of the self-schema. Two single case studies adopted this approach. Marquine et al. (2016) required J.S., a patient with a bilateral (mostly right-lateralized) mPFC damage, to provide (the same) self-related judgments (e.g., "are you an introvert?") on two different testing sessions, under the assumption that a preserved self-schema should support highly consistent self-related judgments across sessions. J.S. was highly inconsistent in self-related judgments across sessions, despite a normal performance in other-related judgments, suggesting impaired self-knowledge. Philippi et al. (2012b) reported the case of a patient with bilateral (mostly right-lateralized) mPFC lesion, R., who was instead highly consistent between sessions. However, his judgments did not match his mother and sister's judgements, suggesting again an impairment of trait self-knowledge, though of a different kind. Although case studies are important to illuminate brain-behavior relations, they have inherent limitations, and therefore it would be important to confirm these findings in a group study of patients with focal lesions to vmPFC.

Note, also, that most previous studies have focused on the role of mPFC in trait knowledge, and therefore it is not clear whether mPFC would also support different instances of personal semantic memory. The mPFC is consistently engaged by self-referential processing (Northoff et al., 2006; Jenkins and Mitchell, 2011). Renoult al. (2012), indeed, pointed out that mPFC regions are generally more engaged by self-knowledge, autobiographical facts, and repeated events than by general semantic knowledge. Paulus and Frank (2003) found that vmPFC activity was crucially linked to personal preferences, and Mitchell et al. (2011) showed that vmPFC was engaged while individuals predicted the probability with which they would enjoy a series of events.

The aim of this work is twofold. First, we aimed to confirm the role of vmPFC in personal semantic memory probing the domain or personal preferences and activities, instead of the most extensively studied self-trait knowledge (Philippi et al., 2012a, 2012b; Marquine et al., 2016; Stendardi et al., 2021). Moreover, we aimed to use a test that does not make heavy demands on anterograde memory, as was the case in previous studies (Philippi et al., 2012a; Stendardi et al., 2021). To this aim, we asked a sample of patients with focal lesions to the vmPFC (vmPFC patients), control patients with lesions outside vmPFC, and healthy controls to judge the likelihood with which they (or a close friend) engaged in a series of activities (e.g., "going to work on foot", "eating a croissant"; "sleep more than 7 h a night"). Preferences and activities tap a more concrete aspect of self-knowledge than trait-knowledge, and with greater commonality with other domains of personal semantic memory, such as autobiographical facts and repeated events. Participants rated the same stimuli on two separate occasions, a week apart. We predicted that vmPFC patients would show inconsistent self-related (but not necessarily other-related) judgments, indicative of an impaired self-schema. In addition, we investigated the confidence associated with self-related judgments. The vmPFC is thought to generate confidence signals resulting from the match between incoming information and the self-schema (Hebscher and Gilboa, 2016). If vmPFC patients have an impaired self-schema, as we predict, they should show a generally reduced confidence in self-related (but not necessarily other-related) judgments. Gathering confidence ratings also allowed us to explore whether the vmPFC patients were aware of the expected impairment in self-related knowledge.

2. Methods

2.1. Participants

Twenty-nine healthy participants (healthy controls; 9 females; mean age = 58.34 years, sd = 5.7, range = 47–74; mean education = 13.34 years, sd = 4.1, range = 5–22), 6 patients with lesions to vmPFC (vmPFC patients; 1 female; mean age = 55.7 years, sd = 5.04, range = 48–61; mean education = 11.33 years, sd = 2.6, range = 8–13) and 8 patients with lesions outside vmPFC (control patients; 3 females; mean age = 52.6, sd = 18.2 years, range 28–78; mean education = 12.6 years, sd =

6.9, range = 5–22) participated in the study (see Table 1 for patients' demographic and clinical data). Patients were recruited at the Centre for Studies and Research in Cognitive Neuroscience, Cesena, based on their lesion site, as documented by MRI or computerized tomography (CT) scans. VmPFC patients' lesions resulted, in all cases, from the rupture of an aneurysm of the anterior communicating artery (ACoA). They were bilateral in all cases, although predominantly right lateralized for one patient.

The other 8 (control) patients had lesions caused by ischemic or haemorrhagic stroke, traumatic brain injury or brain tumour and were unilateral in seven cases (four right-lateralized, three left-lateralized), and bilateral in one case. Control patients' lesion sites involved the fronto-temporal area (three cases), the occipital cortex (one case), the occipito-parietal area (one case), the occipito-temporal cortex (one case), the temporo-parietal cortex (one case), and the thalamus (one case). There was no significant difference in mean lesion volume between vmPFC and control patients (53.7 cc vs 28.2 cc., $p = 0.052$). All patients were in the stable phase of recovery (at least 3 months post-morbid). VmPFC patients' general cognitive functioning was generally preserved, as indicated by scores within the normal range at the Raven Standard Matrices, phonemic and semantic fluency, the prose passage recall, and the digit span test, and their performance was comparable to the controls' (all $ps > 0.09$; see Table 1). VmPFC patients did not show clinical evidence of confabulation.

Healthy participants were matched to patients on age ($F_{2,40} = 1.28$, $p = 0.29$), education ($F_{2,40} = 0.5$, $p = 0.61$), and females/males ratio ($\chi^2 = 0.79$, $p = 0.67$). Participants gave written informed consent to participate in the experiment, which was performed in agreement with the Declaration of Helsinki, and approved by the Bioethical Committee of the University of Bologna and the Ethical Committee of Area Vasta (CEIIAV) of Emilia Romagna.

2.2. Lesion analysis

Patients' individual lesions derived from the most recent MRI or CT scans were manually drawn by a trained neuroscientist (not involved in the study) directly on each slice of the normalized T1-weighted template MRI scan from the Montreal Neurological Institute provided with the MRIcro software (Rorden and Brett, 2000). The standard template provides various anatomical landmarks to help experts plot the size and localization of the lesion using structural features such as sulci and gyri as guides. This manual procedure combines segmentation (identification of lesion boundaries) and registration (to a standard template) into a single step, with no additional transformation required (Kimberg et al., 2007). Manual segmentation/registration procedures have the limit to rely greatly on anatomical expertise, and to be subjective in nature. On the other hand, they circumvent problems frequently encountered by automated normalization procedures, such as (1) warping scans from individuals with brain injury, which may be affected by structural distortions related to the lesion and not easily compensated for (e.g., ventricular enlargement, large regions of atypical voxel intensity values, artifacts induced by the presence of metallic clips), and combining subjects scanned with different imaging modalities (e.g., MRI vs. CT) (see also Bertossi et al., 2016; Kimberg et al., 2007).

The MRIcro software was used to estimate lesion volumes (in cc) and generate lesion overlap images. Fig. 1 shows the extent and overlap of brain lesions in vmPFC patients. The Brodmann areas (BAs) mainly affected were BA 11, BA 10, BA 32, BA 25, and BA 24. The maximal lesion overlap occurred in BA 11 (M = 20.6 cc, s.d. = 9.01), BA 10 (M = 11.03 cc, s.d. = 7.26) and BA 32 (M = 8.29 cc, s.d. = 5.39).

2.3. Materials and procedure

The experimental procedure was articulated in two testing sessions. In the first testing session, participants were first asked to select one of their friends, someone they felt they knew very well, but with whom they had never lived. We required participants to select a friend they had never lived with to minimize the possibility that they engaged (or had engaged) in a series of everyday activities together, and therefore participants could answer about the other merely reiterating the answers about themselves. Participants were then administered a task requiring to answer questions about themselves and the friend they had selected. During the task, a list of 100 activities (e.g., "read a novel", "play sudoku", "walk to work"; adapted from Kaplan and Friston, 2019), were presented, one at time, on the computer screen. In the Self condition, for each activity, participants had to rate on a Likert scale how likely they were to engage in that activity from 1 (= not likely at all) to 9 (= extremely likely). They then answered the same question about their friend (Other condition), rating how likely the friend was to engage in each of the same series of activities.

After each (self-related and other-related) judgment, participant also rated their confidence associated with the judgment on a Likert scale from 1 (= not sure at all) to 5 (= absolutely sure). During the second testing session, which was run about 1 week apart, participants were administered the same task, with the exception that confidence ratings were not collected.

3. Results

3.1. Judgment consistency across sessions (Δ)

For each participant, we computed a score change (Δ) as the difference between the ratings given to each activity in the first session and the second session (in absolute value), and then averaged it across activities, separately for the Self and Other conditions (see Fig. 2). High Δ values represent low rating consistency between sessions. We then ran a mixed repeated measure ANOVA, with Δ as the dependent variable, and Group (Healthy controls, vmPFC patients, Control Patients) and Condition (Self, Other) as predictors. Both the main effects of Group ($F_{2,40} = 24.6$, $p < 0.0000001$, $\eta_p^2 = 0.55$) and Condition ($F_{1,40} = 8.8$, $p = 0.005$,

Table 1
The table reports, for each vmPFC patient (p) and control patient (cp), scores corrected for age, education and **sex** according to normative samples (Spinnler and Tognoni, 1987). An impaired performance (percentile score <5) is signalled by an *.

	vmPFC patients						Control patients							
Sex	p. 1	p. 2	p. 3	p. 4	p. 5	p. 6	cp.1	cp. 2	cp. 3	cp. 4	cp. 5	cp. 6	cp.7	cp.8
	M	M	F	M	M	M	F	M	M	F	M	F	M	M
Age (years)	51	58	61	48	59	57	28	73	41	52	78	52	64	33
Education (years)	13	8	13	13	8	13	13	5	9	5	21	22	8	18
Raven Standard Matrices (cut-off = 15)	33	33.5	35.75	32.5	33.5	27	31.5	26.75	37.5	10.25	22	29.5	24	31.5
Phonemic Fluency (cut-off = 17)	34	27	25	21	36	32	–	15	36	20	31	56	41	48
Semantic Fluency (cut-off = 25)	31	37	42	40	61	35	36.5	25	54	28	33	54	57	75
Short term memory - Digit span (cut-off = 3.75)	6.75	5	5.75	6.5	5	5.75	5.44	4.5	6	3	4.5	5.25	5	8.25
Long-term memory - Prose passage recall (cut-off = 4.75)	2.5*	5	19	13	8.5	13.5	–	11.9	18	7.5	10.5	7	19.5	6.9
Chronicity (months)	14	198	25	73	118	91	10	5	3	15	84	72	4	84
Lesion size (cc)	31	55	74	40	52	69	16	16	33	64	6	14	7	69

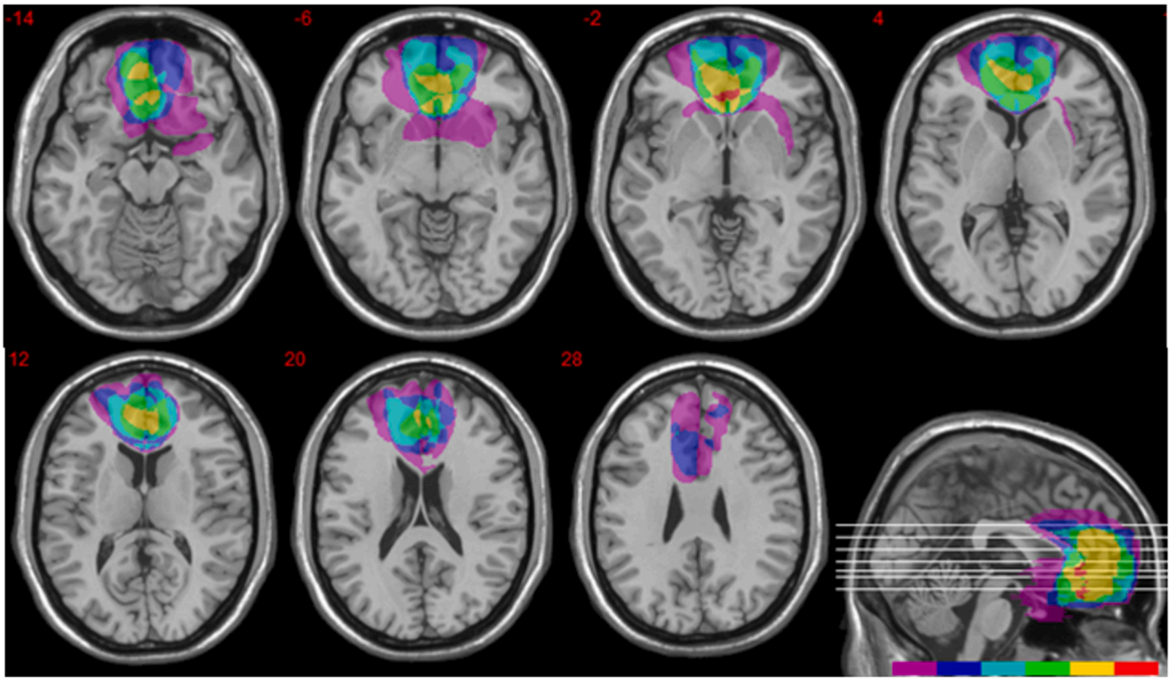

Fig. 1. Extent and overlap of vmPFC patients' brain lesions. Lesions are projected on the same seven axial slices of the standard Montreal Neurological Institute brain. The white horizontal lines on the sagittal view are the positions of the axial slices. Numbers above the axial views represent the z-coordinates of each slice. The color bar indicates the number of overlapping lesions, from 1 (purple) to 6 (red). Maximal overlap occurs in BA 11, 10 and 32. The left hemisphere is on the left side.

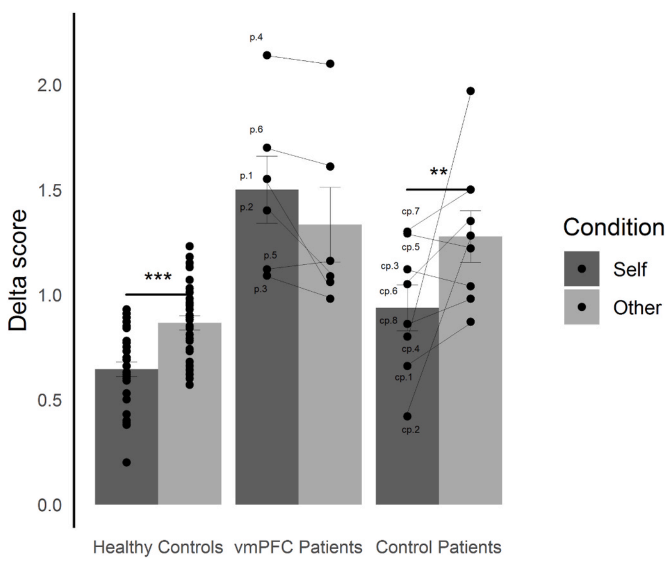

Fig. 2. Mean score change between testing sessions (Δ score) by participant group and experimental condition. Bars represent standard errors. Labels denote individual vmPFC patients (p) and control patient (cp). ** = $p < 0.01$; *** = $p < 0.001$.

$\eta_p^2 = 0.18$) were significant. There was also a significant Group × Condition interaction ($F_{2,40} = 9.1$, $p = 0.0006$, $\eta_p^2 = 0.31$). Post-hoc Bonferroni tests revealed that in the Self condition vmPFC patients' Δ was higher than that of both healthy (vmPFC patients: 1.50 vs. Healthy controls: 0.64, $p < 0.00001$) and brain-damaged controls (vmPFC patients: 1.50 vs Control patients: 0.94, $p < 0.01$), with no difference between the control groups (Control patients: 0.94 vs Healthy controls: 0.64, $p = 0.08$). In the Other condition, vmPFC displayed a higher Δ score compared to healthy controls (vmPFC patients: 1.33 vs Healthy controls: 0.86, $p = 0.001$) but comparable to that of control patients (vmPFC patients: 1.33 vs Control patients: 1.28, $p = 1$). Crucially, whereas both control groups exhibited lower Δ scores in the Self condition vs. the Other condition (Healthy controls: 0.64 vs 0.86, $p < 0.001$; Control patients: 0.94 vs 1.28, $p < 0.01$), meaning that their self-related judgments were more robust (stable) than their other-related judgments, this self-advantage was not present in vmPFC patients (1.50 vs 1.33, $p = 1$), who showed a numerically higher Δ in Self compared to the Other condition, suggestive of more stable other-than self-related judgments.

Control analysis. To verify that the results were not driven by vmPFC patients p1, who had very low episodic memory scores (see Table 1), we ran again the ANOVA excluding p1's data. We confirmed our findings. The effect of Group ($F2,39 = 22.8$, $p < 0.000001$, $\eta p2 = 0.54$), Condition ($F1,39 = 11.2$, $p < 0.01$, $\eta p2 = 0.22$), and the Group × Condition interaction ($F2,39 = 6$, $p < 0.01$, $\eta p2 = 0.24$) were significant: in the Self condition, vmPFC patients' Δ in was higher than that of both control groups (vmPFC patients: 1.49 vs. Healthy controls: 0.64, $p < 0.00001$; vmPFC patients: 1.49 vs Control patients: 0.94, $p < 0.01$), with no difference between the control groups (Control patients: 0.94 vs Healthy controls: 0.64, $p = 0.09$). In the Other condition, vmPFC patients showed Δ scores higher than healthy controls' (vmPFC patients: 1.39 vs Healthy controls: 0.86, $p = 0.001$) but comparable to control patients' (vmPFC Patients: 1.39 vs Control Patients: 1.28, $p = 1$). Both control groups had lower Δ scores in the Self compared to the Other condition (Healthy controls: 0.64 vs 0.86, $p < 0.0001$; Control Patients: 0.94 vs 1.28, $p < 0.01$), but this self-advantage in judgment stability was absent in vmPFC patients (1.49 vs 1.39, $p = 1$).

Intra-Class Correlation (ICC). As an additional measure of rating consistency, we calculated the two-way mixed effect (absolute

Table 2
Mean confidence ratings (and SD) by participant group and condition.

	Condition	
Group	Self	Other
Healthy controls	4.69 (0.3)	4.14 (0.5)
vmPFC patients	4.07 (0.8)	3.85 (0.7)
Control patients	4.79 (0.3)	4.11 (0.4)

agreement) ICC for each group, separately for self- and other-related judgments (see Table 2; Koo and Li, 2016). According to the classification by Koo and Li (2016), ICC values lower than 0.5 are indicative of poor reliability, values between 0.5 and 0.75 of moderate reliability, values between 0.75 and 0.9 of good reliability, and values higher than 0.90 of excellent reliability. According to this classification, vmPFC patients exhibited poor reliability in the Self condition (ICC = 0.48; 95% CI [0.29; 0.77]) and higher (moderate) reliability in the Other condition (ICC = 0.52; 95% CI [0.32; 0.80]), whereas control patients showed good reliability in the Self condition (ICC = 0.75; 95% CI [0.57; 0.92]) and lower (moderate) reliability in the Other condition (ICC = 0.63; 95% CI [0.43; 0.86]). Healthy participants exhibited good reliability across conditions (ICC Self = 0.87; 95% CI [0.76 0.96], ICC Other = 0.79; 95% CI [0.63; 0.93]). These findings confirm that whereas the control groups have more reliable self-related than other-related judgments, vmPFC patients exhibit the opposite tendency.

3.1.1. *Confidence*

A repeated measure ANOVA, with confidence ratings as the dependent variable, and Group (Healthy controls, vmPFC patients, Control Patients) and Condition (Self, Other) as predictors revealed a significant main effect of Group ($F_{2,40} = 3.4$, $p = 0.04$, $\eta_p^2 = 0.15$) and a significant effect of Condition ($F_{1,40} = 47.1$, $p < 0.000001$, $\eta_p^2 = 0.54$), with no interaction ($F_{2,40} = 2.4$, $p = 0.1$). Post-hoc Bonferroni tests indicated that vmPFC were generally less confident in their judgments than healthy participants ($p = 0.049$), and, though only numerically, control patients ($p = 0.09$), with no difference between the control groups ($p = 1$). All groups showed more confident judgments in the Self compared to the Other condition ($p < 0.000001$; see Table 2).

3.1.1.1. Relation between Δ and confidence. We investigated the relation between confidence ratings (in the first testing session) and score changes (Δ) from the first to the second session, under the assumption that more confident judgments would tend to remain stable from the first to the second session. To this aim, we ran a full factorial linear mixed effect model on Δ with repeated measures (here Δ represents the score change for each trial, leading to 100 data points per participant) with Confidence, Group and Condition as fixed effects, and Subject as a random effect. The model allowed estimating both a random intercept, and random slopes for the Confidence and Condition predictors, as specified by the lmer formula in R (Bates et al., 2014):

$$\Delta \sim \text{Group} * \text{Confidence} * \text{Condition} + (1 + \text{Confidence} + \text{Condition} \mid \text{Subject})$$

There were significant main effects of Group ($\chi^2 = 34.4$, $p < 0.0000001$) and Confidence ($\chi^2 = 130.2$, $p < 0.000000001$), a significant Group × Confidence interaction ($\chi^2 = 7.6$, $p = 0.03$), a significant Condition × Confidence interaction ($\chi^2 = 3.9$, $p = 0.048$), and a significant Group x Confidence × Condition interaction ($\chi^2 = 7.8$, $p = 0.02$). The estimates of the regression coefficient β (and the 95% CI) for the variable Confidence are displayed in Table 3. As shown in Table 3, all β estimates were below 0, indicating a negative relation between the confidence associated with an answer and the score change for that answer in the second session. As expected, the more confident healthy and brain-damaged controls were in a judgment, the less that judgment changed in the second session (see Fig. 3). This pattern of performance was also apparent in vmPFC patients, but only in the Other condition (β = −0.18, CI [−0.33, −0.03]). By contrast, in the Self condition there was no evidence for a significant relation between confidence and score change between sessions in vmPFC patients (β = −0.07, CI [−0.23, 0.08]; see Fig. 3), indicating that the change in self-related judgments across sessions did not depend on the level of confidence with which the judgment was endorsed in the first session.

Table 3
β coefficient and 95% confidence intervals for the variable Confidence, for each group and each condition. SE = Standard error; CI = 95% Confidence Interval.

Group	Condition	Estimate (β)	SE	CI Lower	CI Upper
Healthy controls	Self	−0.41	0.05	−0.51	−0.32
	Other	−0.29	0.03	−0.36	−0.22
vmPFC patients	Self	−0.07	0.08	−0.23	0.08
	Other	−0.18	0.08	−0.33	−0.03
Control patients	Self	−0.49	0.10	−0.69	−0.28
	Other	−0.29	0.06	−0.40	−0.17

4. Discussion

The self-schema maintains relatively stable information about one's personality and preferences that are at the core of one's identity. In the present study, we investigated the causal role of the vmPFC in supporting the self-schema by having patients with vmPFC lesions and controls provide judgments about the likelihood for them (vs. another person) to engage in a series of activities, on two separate occasions. To the extent that self-related judgments rely on a stable set of knowledge (self-schema), these judgments should prove relatively stable across testing sessions. This should not necessarily apply to other-related judgments, which supposedly rely on fewer or less strong memories or schemata.

As predicted, we found that healthy participants and control patients were consistent in their endorsement of self-related activities across sessions and were significantly more consistent for self-compared to other-related information. This consistency advantage for self-related judgments was not apparent in vmPFC patients, who displayed comparably unstable judgments about the self and the other. This finding confirms and extends previous single case observations of impaired (stability of) self-trait knowledge in patients with lesions to the mPFC (Marquine et al., 2016; Philippi et al., 2012b), pointing to the generalizability of these findings to different vmPFC patients and to other domains of self-knowledge (activities and personal preferences).

Before discussing this finding further, it is important to emphasize that the inconsistency in self-related judgments displayed by vmPFC patients cannot be ascribed to an unspecific effect of brain lesions in reducing cognitive functioning or the sense of self (Ciaramelli et al., 2019), as it was not observed in (control) patients with lesions not including vmPFC. Additionally, vmPFC patients' performance is unlikely to be reflective of erratic responding or poor compliance with the task because these patients were as consistent as control patients when

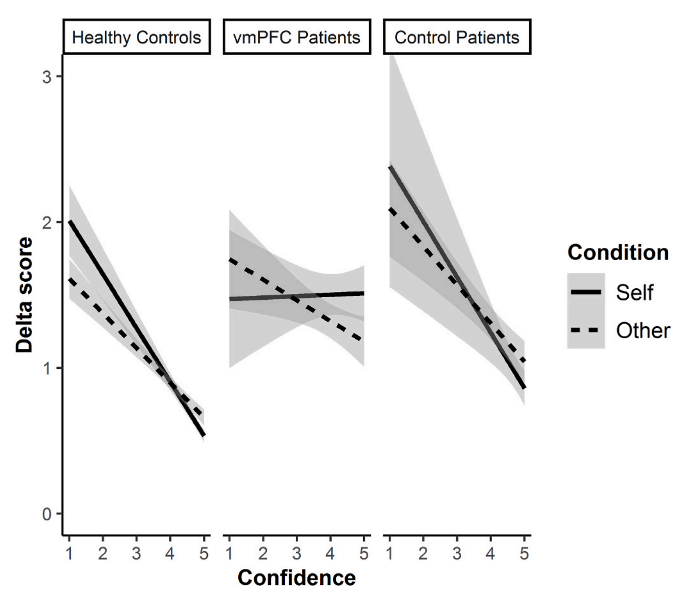

Fig. 3. Relation between Δ (score change) and confidence ratings for each group in the two conditions (Self, Other).

judging other-related knowledge, suggesting a more prominent impairment in self-related knowledge. There is another aspect of our results that underlines the selective impairment in self-related compared to other-related knowledge in vmPFC patients, which pertains to the confidence levels associated with vmPFC patients' judgments. First, vmPFC patients were generally less confident in their answers than were healthy controls (see also Barron et al., 2015; Lebreton et al., 2015; Hebscher and Gilboa, 2016; Gherman and Philiastides, 2018), though they were not significantly less confident than control patients. Most importantly, in the brain-damaged and healthy control groups confidence levels associated with both self-related and other-related judgments (at the first testing session) predicted the consistency of these judgments from the first to the second session. That is, unsurprisingly, judgments associated with high confidence tended to change less between sessions. In vmPFC patients, the expected relation between confidence and consistency was only present for other-related judgments. By contrast, vmPFC patients' confidence levels and score change for self-related information were completely unrelated: their judgments about themselves and the typical activities they engaged in fluctuated over time, regardless of whether the judgments were associated with high or low confidence. Thus, while not all judgments are unreliable in vmPFC patients, self-related judgments are. It is self-related- and not other-related- knowledge that proves inconsistent and disconnected from confidence in vmPFC patients, whereas both self- and other-related knowledge are tied to confidence in the control groups.

Together, these findings point to a selective degradation of the self-schema following vmPFC damage, which is consistent with fMRI studies and meta-analyses showing an involvement of the medial prefrontal cortex in self-vs. other-related processing (D'Argembeau et al., 2007; D'Argembeau et al., 2014; Jenkins et al., 2008; Wagner et al., 2012), with a ventral-to-dorsal gradient, with vmPFC mostly associated to self-related processing, and dorso-medial prefrontal cortex (dmPFC) with other-related processing (Denny et al., 2012; see also Lieberman et al., 2019). Neuropsychological evidence from patients with medial prefrontal damage is also consistent with this. We have shown (Stendardi et al., 2021), as have others (Philippi et al., 2012a), that vmPFC damage abolishes the self-reference effect (SRE), that is, the increase in memory for information encoded with (as opposed to without) reference to the self. These tasks, however, inherently tap anterograde memory abilities, and therefore the absence of the SRE could be (at least in part) explained by vmPFC patients' encoding deficits. Here, we confirm an impairment in the self-schema in vmPFC patients in a task with no anterograde memory demands, in line with previous evidence (Philippi et al., 2012b; Marquine et al., 2016). Moreover, we extend previous evidence on impaired self (trait) knowledge in vmPFC patients probing knowledge about one's preference and common activities, which is a form of personal semantic less abstract than self-trait summaries, and more likely to be tied to autobiographical facts and events (e.g., did I ever go bungee jumping? Grilli and Verfaellie, 2014). Together, our current results and those of previous studies probing self (trait) knowledge (Philippi et al., 2012a, 2012b; Marquine et al., 2016; Stendardi et al., 2021) reinforce the view of an impairment of the self-schema following vmPFC damage. One important follow up of this study would be to manipulate the closeness of the other, hence the strength of other-related schemata, to verify whether vmPFC patients' impairment is selective for self-related k8owledge or rather extends to other types of schema-related knowledge (see Aron et al., 1991; Kim and Johnson, 2014.

Although the vmPFC patients involved in the present study do not show evidence of confabulation, confabulation is a common consequence of vmPFC damage, and therefore our findings speak to current theories on the role of vmPFC in confabulation. According to Gilboa and his colleagues, confabulation arises as a failure of the "feeling of rightness" (FOR), a pre-conscious monitoring process mediated by vmPFC at the basis of the confident endorsement (or rejection) of information based on the automatic intuition of its veracity (Gilboa, 2004; Gilboa et al., 2006; Hebscher and Gilboa, 2016; Gilboa, 2010). The intensity of FOR is deemed to depend on the match between incoming information and schematic knowledge, with strong schemata, such as the self-schema, giving rise to the strongest confidence signals (Gilboa, 2004, 2010; Hebscher and Gilboa, 2016). On this view, a damage to vmPFC should lead to an inability to filter our self-relevant yet false information, and to high confident false memories (see also Gilboa and Verfaellie, 2010; Kopelman, 2019; Ciaramelli and Spaniol, 2009). To test this hypothesis, Gilboa et al. (2006) tested confabulating and non-confabulating vmPFC patients in an autobiographical recognition memory task involving true statements about their past, plausible lures, and implausible lures that were blatantly inconsistent with vmPFC patients' life history. Confabulating compared to non-confabulating vmPFC patients showed significantly more false recognitions of implausible lures and were highly confident in their (false) memories. This finding is consistent with an impairment of the FOR and the self-schema in (confabulating) vmPFC patients, and makes contact with our current finding of impaired self-knowledge and untied confidence and consistency of self-related knowledge following vmPFC damage.

To conclude, we have shown that vmPFC patients have an impairment in self-related knowledge, which proved highly unreliable across testing sessions, as if retrieved from, or through, a degraded self-schema. In addition, we found that the confidence levels accompanying self-related judgments were not reflective of their consistency, a finding reminiscent of confabulatory behavior, and that applied selectively to self-related but not other-related judgments. These findings indicate that the vmPFC is crucial to maintain the self-schema and support the reliable retrieval of self-related information.

Author contributions

Debora Stendardi: Methodology, Software, Formal analysis, Investigation, Data Curation, Writing - Original Draft, Writing - Reviewing and Editing. Luca Giacometti Giordani: Investigation, Data curation. Silvia Gambino: Resources, Investigation. Raphael Kaplan: Conceptualization, Supervision, Writing - Reviewing and Editing. Elisa Ciaramelli: Conceptualization, Writing - Original Draft, Writing - Reviewing and Editing, Supervision, Project administration, Funding acquisition.

Declaration of competing interest

The authors declare no competing financial interests.

Data availability

Data will be made available on request.

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