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fMRI STUDY OF GRADUATED EMOTIONAL CHARGE FOR DETECTION OF COVERT ACTIVITY USING PASSIVE LISTENING TO NARRATIVES

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Abstract—Detection of awareness in patients with consciousness disorders is a challenge that can be facilitated by functional neuroimaging. We elaborated a functional magnetic resonance imaging (fMRI) protocol to detect covert activity in altered states of consciousness. We hypothesized that passive listening to narratives with graduated emotional charge triggers graduated cerebral activations. The fMRI protocol was designed in healthy subjects for further clinical applications. The emotional charge was graduated using voice familiarity and long-term declarative memory content: low emotional charge, unknown person telling general semantic memory; mean emotional charge, relative telling the same narratives; high emotional charge, same relative telling autobiographical memory. Autobiographical memory was subdivided into semantic autobiographical memory and episodic autobiographical memory. The protocol proved efficient at triggering graduated cerebral activations: low emotional charge, superior temporal gyri and sulci; mean emotional charge, same as low emotional charge plus bilateral premotor cortices and left inferior frontal gyrus; high emotional charge, cingulate, temporal, frontal, prefrontal and angular areas, thalamus and cerebellum. Semantic autobiographical memory revealed larger activations than episodic autobiographical memory. Independent ROI analysis confirmed the preponderant contribution of narratives with autobiographical memory content in triggering cerebral activation, not only in autobiographical memory-sensitive areas, but also in voice-sensitive, language-sensitive and semantic memory-sensitive areas.

Key words: autobiographical memory, disorders of consciousness, semantic memory, speech, voice familiarity.

INTRODUCTION

The detection of awareness in patients with chronic consciousness disorders has attracted a growing interest in the last decade (Fernández-Espejo and Owen, 2013; Giacino et al., 2014; Gosseries et al., 2014). Identifying signs of awareness in severely brain-damaged patients is of upmost importance for the medical staff to set up the care plan in close cooperation with relatives (Graham et al., 2014; Gilutz et al., 2015). In this very particular clinical context, the detection of awareness is a key milestone for the characterization of the state of consciousness, namely vegetative or minimally conscious. Functional brain imaging, particularly functional magnetic resonance imaging (fMRI), makes it possible to reveal covert residual cognitive function (Owen and Coleman, 2008; Monti et al., 2009; Coleman and Pickard, 2011; Laureys and Schiff, 2012; Di Perri et al., 2014): such as speech processing (Coleman et al., 2007; Fernández-Espejo et al., 2008; Bekinschtein et al., 2011) or emotional processing with different stimuli such as the patient's own name (Perrin et al., 2006; Di et al., 2007; Wang et al., 2015), familiar faces (Menon et al., 1998; Sharon et al., 2013) or familiar voices (Machado et al., 2007; Eickhoff et al., 2008; Piperno et al., 2012).

In an effort to improve the detection of covert cerebral activity in clinical settings of severe chronic disorders of consciousness, we aimed to elaborate an fMRI protocol using an emotional trigger, widely empirically used at bedside, for the detection of language-related behavior. We propose an experimental design with graduated emotional charge liable to increase awareness (Tsuchiya and Adolphs, 2007; Perrin et al., 2015). Emotional experience is described by valence (how negative or positive) and arousal (how calming or exciting) (Russell, 1980; Posner et al., 2005). High valence and arousal enhance long-term declarative memory (D'Argembeau et al., 2003; Kensinger, 2004; Buchanan, 2007). Long-term

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Abbreviations: AM, autobiographical memory; BOLD, blood-oxygen-level-dependent; EAM, episodic autobiographical memory; EC, emotional charge; fMRI, functional magnetic resonance imaging; FWE, family-wise error; MNI, Montreal Neurological Institute; ROI, region of interest; SAM, semantic autobiographical memory; SM, semantic memory; SVC, small volume correction.

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declarative memory can be divided into semantic and autobiographical memory. General semantic memory (SM) refers to general knowledge independent of personal experience and the spatiotemporal context in which it was acquired (Tulving, 1972). Autobiographical memory (AM) encompasses both memory for general knowledge about one's life (semantic autobiographical memory, SAM) and memory for personal events embedded within a specific spatiotemporal context (episodic autobiographical memory, EAM) (Tulving, 1985, 2002). For example, "A cat is a small domesticated felid", "Your cat is black and is called Loki" and "You saw Loki for the first time at the RSPCA this last October 22nd" are narratives with SM, SAM and EAM content, respectively. SAM and EAM have been explored in neuropsychological studies of patients with memory disorders (see e.g. Grilli and Verfaellie, 2014), but to our knowledge there are few fMRI studies on the anatomic components of the autobiographical memory (Martinelli et al., 2013; Picard et al., 2013; Araujo et al., 2014; Kalenzaga et al., 2014).

In our study, graduation of emotional charge in narratives was ensured by voice familiarity and long-term declarative memory content: narratives spoken by a relative are more emotionally charged than narratives spoken by an unknown person, and narratives with AM content are more emotionally charged than narratives with SM content.

We used our fMRI protocol in healthy subjects in order to study the impact of graduated emotional charge on the cerebral blood-oxygen-level-dependent (BOLD) signal according to speech, voice familiarity and declarative memory, enabling us to construct a control group. We first focused on the serial graduation of triggers and the location of related cerebral activations, in a whole-brain analysis. We then performed a region of interest (ROI) analysis in four sets of independent regions defined in the literature involved respectively in voice processing, speech processing, semantic memory and autobiographical memory. We hypothesized that passive listening to narratives with graduated emotional charge should trigger graduated cerebral activations: the higher the charge, the larger the recruitment of brain networks engaged in emotional processing and related behavior.

EXPERIMENTAL PROCEDURES

Participants

Twenty healthy adult volunteers participated in the fMRI study as control group to establish reference data for later clinical study. Data from one participant had to be discarded due to discomfort during the scanning, prompting the volunteer to prematurely stop the experiment. The final dataset included 19 participants (10 females; 16 right-handed, 2 left-handed and 1 ambidextrous; age = 27.9 ± 9.6 years).

For each participant, one relative (first degree or partner) was involved for audio recordings of narratives. All participants were French native speakers with no history of neurological or psychiatric disorders. To rule out radiological signs of pathology, a senior consultant in neuroradiology (B.J.) performed assessments of the anatomical scans of each subject. This study followed all legislation governing biomedical research (Ethics Review Board, Sud-Est 6, AU 890; recording number 2011-A00300-41). All participants and relatives provided written informed consent and were compensated for taking part in the experiment.

fMRI paradigm design

The task consisted of passive listening to narratives. The block design was divided into five conditions (Table 1): (1) silence, except the noise of scanner; (2) unintelligible narratives with unfamiliar voice (i.e. narratives as defined in (3), played backward, matching the originals in terms of acoustic characteristics but without phonological properties and linguistic content, as described by Fernández-Espejo et al. (2008); (3) low emotional charge (Low EC), unknown person telling general semantic memory (SM); (4) mean emotional charge (Mean EC), relative telling the same SM narratives; (5) high emotional charge (High EC), same relative telling autobiographical memory (AM).

The full stimulation protocol, including the five conditions, was applied to every subject. The Low EC narratives were the same for all subjects (read by a male French speaker with vivid intonation) and contained neither recall instruction nor subject's forename. All blocks of High EC narratives began with recall instruction and the subject's forename, *e.g.* "Remember, Paul, ...", thus increasing emotional charge. Their content was about either general information on the subject's own life, i.e. semantic autobiographical memory (High EC_SAM, 10 participants, 5 females, age = 27.8 ± 8.7 years) or specific events experienced by the subject at a particular time and place, i.e. episodic autobiographical memory (High EC_EAM, 9 participants, 5 females, age = 28.1 ± 11 years). Memories were chosen by the relative, with the instruction of an emotional charge with positive valence for SAM and positive valence and high arousal for EAM. The gender of relatives was equally distributed in the EAM and SAM groups (3 male speakers for each) to avoid any gender-specific speaker effect potentially influencing the cortical processing of sounds (Sokhi et al., 2005). In the SAM group, the Mean EC condition was subdivided into two subgroups, with and without recall instruction and subject's forename, for further between-group analysis.

All narratives were recorded using a digital voice recorder and post-processed with Audacity (http://audacity.sourceforge.net) for sound volume and length harmonization, as well as to produce reverse narratives. Stimuli were aurally presented with scanner-compatible headphones *via* E-Prime 2.0 (Psychology Software Tools, Inc.).

The experiment was divided into two runs to minimize session duration in an effort to account for further clinical application in patients with disorders of consciousness prone to unanticipated spontaneous movements, which could increase motion-induced data loss. Each run contained the five conditions, with five blocks per condition, at a block length of 12 s and a variable inter-

Table 1. fMRI conditions. Each of the five conditions was applied to the 19 healthy subjects; *n* = number of subjects in each subgroup

Speech type		Voice familiarity	Declarative memory		Recall instruction and subject's forename	Emotional charge	Designation
Silence							Silence (n = 19)
Narratives	Unintelligible	Unfamiliar					Unintelligible (n = 19)
Narratives	Intelligible	Unfamiliar	General semantic (SM)		Without	Low	Low EC (n = 19)
Narratives	Intelligible	Familiar	SM		Without (*n* = 14) With (*n* = 5)	Mean	Mean EC (n = 19)
Narratives	Intelligible	Familiar	Autobiographical (AM)	Semantic autobiographical (high EC_SAM, *n* = 10) Episodic autobiographical (high EC_EAM, *n* = 9)	With	High	High EC (n = 19)

block interval of 0 to 1 s. The order of the 5 conditions and inter-block intervals was randomized. The total length of the two runs was 11 min and 18 s.

MRI acquisition

Images were acquired using a 3 T MRI scanner (GE, Discovery MR750) with a 32-channel head coil. High-resolution T_1-weighted structural images were obtained with a three-dimensional inversion recovery gradient-echo sequence (BRAVO), yielding 288 interleaved slices of 1.4-mm thickness in the axial plane (TR = 8.8 s, TE = 3.6 ms, TI = 400 ms, flip angle = 12°, FOV = 240 mm; resulting voxel size = $0.47 \times 0.47 \times 0.7$ mm^3). Functional MRI acquisition was performed using a whole-brain gradient-echo EPI sequence (interleaved acquisition resulting in 48 contiguous axial slices of 4-mm thickness: TR = 3 s, TE = 30 ms, flip angle = 90°, FOV = 240 mm; resulting voxel size = $3.75 \times 3.75 \times 4$ mm^3), and 113 volumes were acquired on each run.

fMRI data preprocessing

Data preprocessing and statistical analyses were performed using Statistical Parametric Mapping (SPM8, Wellcome Trust Centre for Neuroimaging, www.fil.ion.ucl.ac.uk/spm), implemented in MATLAB R2012a (The Mathworks). The first 5 volumes were discarded as dummy scans. Images were slice-time-corrected with reference to the acquisition time of the middle slice, and spatially realigned. The T1 structural volume was co-registered to the functional data, and spatially normalized onto the Montreal Neurological Institute template. The functional data were spatially normalized using the same parameters. The voxels were resampled at $4 \times 4 \times 4$ mm^3. The fMRI volumes were smoothed using an isotropic 8-mm full-width at half-maximum (FWHM) Gaussian kernel. A voxel-wise analysis of the BOLD signal was computed by applying the general linear model. Within the model, the experiment conditions were used as regressors and the motion parameters determined by realignment were used as covariates. Data were filtered using a high-pass filter (cut-off period of 128 s). After model estimation, *t* contrasts were performed.

Whole-brain analysis

Data analysis was performed according to the following four domains of analysis: emotional gradient, speech processing, voice familiarity processing and declarative memory.

Emotional gradient was assessed using the following contrasts: SM narratives spoken by an unknown person *versus* silence, Low EC > Silence; SM narratives spoken by a familiar voice *versus* silence, Mean EC > Silence; AM narratives spoken by a familiar voice *versus* silence, High EC > Silence.

Speech processing was assessed using the following contrasts: unintelligible narratives *versus* silence, Unintelligible > Silence, segregating regions involved in speech auditory processing; narratives played forward *versus* narratives played backward, Low EC > Unintelligible, for linguistic processing.

Voice familiarity processing was assessed using narratives spoken by a relative *versus* spoken by an unknown person, Mean EC > Low EC.

Declarative memory was assessed using the following contrasts: autobiographical memory (AM) *versus* semantic memory (SM), High EC > Mean EC, probing the AM component; episodic autobiographical memory (EAM) *versus* SM, High EC_EAM > Mean EC, probing the EAM component; semantic autobiographical memory (SAM) *versus* SM, High EC_SAM > Mean EC, probing the SAM component; SM *versus* AM, Mean EC > High EC, probing the SM component.

The one-sample *t* test was used for the contrast analyses, and the probability threshold value was set to 0.05 with family-wise error (FWE) corrected for the whole brain and a minimum cluster extent of two contiguous voxels ($k = 2$). Small volume correction (SVC) using the theory of random fields (Worsley et al., 1996) was used for the contrast between familiar voice *versus* unfamiliar voice (Mean EC > Low EC). The volume of interest was determined within the Automated Anatomical Labeling (AAL) human brain atlas (Tzourio-Mazoyer et al., 2002) and contained bilateral superior, middle temporal gyri and temporopolar areas, in accordance with *a priori* knowledge (Belin et al., 2000; Kriegstein and Giraud, 2004). SVC was also applied to EAM and SAM analyses, using the volume contrasted between AM and SM.

Table 2. ROI-sets. Independent peak coordinates of brain regions forming the four ROI-sets, Voice, Language, SM and AM; coordinates refer to the Montreal Neurological Institute coordinate system (L, left; R, right)

	x	*y*	*z*
Voice ROI_set (Voice-sensitivity maxima from Belin et al., 2000)			
R anterior superior temporal sulcus	64	2	−10
R middle superior temporal sulcus	67	−11	−7
R middle temporal gyrus	55	−18	−8
R posterior superior temporal sulcus	59	−30	2
R posterior superior temporal sulcus	47	−44	2
R precuneus	4	−55	31
L anterior middle temporal gyrus	−63	1	−15
L middle superior temporal sulcus	−66	−12	−5
L planum temporale	−42	−38	11
L posterior superior temporal sulcus	−65	−40	7
Language ROI_set (Meta-analysis of language processing compared with a resting baseline from Ferstl et al., 2008)			
L anterior temporal lobe	−62	3	−15
R anterior temporal lobe	55	11	−23
L superior temporal gyrus / sulcus	−63	−23	3
R superior temporal gyrus / sulcus	62	−17	−6
R superior temporal gyrus / sulcus	51	−33	2
L precentral gyrus	−48	−2	52
L inferior frontal gyrus, pars triangularis	−48	33	−4
R middle frontal gyrus / inferior frontal sulcus	47	17	30
R inferior frontal gyrus, pars opercularis	39	25	−12
L pre-supplementary motor area	−6	3	56
SM ROI_set (Semantic task compared with a control task from Binney et al., 2010)			
L inferior prefrontal cortex	−54	24	3
L posterior middle temporal gyrus	−66	−42	3
R occipital lobe	15	−87	−6
AM ROI_set (Meta-analysis of autobiographical memory data from Spreng et al., 2009)			
L and R posterior cingulate cortex	−3	−55	17
L hippocampus / parahippocampal cortex	−27	−25	−21
L temporo-parietal junction	−47	−63	25
L, R medial prefrontal cortex / rostral anterior cingulate cortex	−3	52	0
L middle temporal gyrus / superior temporal sulcus	−59	−5	−20
L ventrolateral prefrontal cortex	−48	29	−9
R parahippocampal cortex	24	−30	−19
L and R middle frontal gyrus	−4	8	63
R temporo-parietal junction	48	−61	27
L posterior lateral prefrontal cortex	−46	2	48
L lateral frontal pole	−40	49	15
R hippocampus	24	−11	−22
R temporal pole, superior temporal sulcus	52	−2	−20
L occipital lobe	−37	−85	30
L dorsolateral prefrontal cortex	−49	25	21
L medial frontal pole	−11	58	20
R thalamus	4	−8	2
L rostral anterior cingulate cortex	−5	35	24
L posterior cingulate cortex	−7	−39	35
L superior frontal sulcus	−28	6	56

Between-group analysis was performed to isolate recall instruction and subject's forename-specific activations, interfering with the analysis of voice familiarity and declarative memory: Mean EC_with > Low EC *versus* Mean EC_without > Low EC. The two-sample *t* test was used in this between-group analysis.

Thresholded SPM clusters were exported to the MRIcron software package (http://www.mccauslandcenter.sc.edu/mricro/mricron/index.html) (Rorden et al., 2007) to enable visualization of significant voxels in a T1 template (ICBM 2009b Nonlinear Asymmetric) (Fonov et al., 2009) and a Brodmann template, both within the Montreal Neurological Institute (MNI) coordinates.

ROI-set analysis

We also estimated the graduation of the BOLD signal on different ROI-sets (Poldrack, 2007) using the MarsBaR toolbox (Brett et al., 2002). In order to avoid circularity (Kriegeskorte et al., 2009), the ROI-sets were created using independent data. Four ROI-sets were built from peak coordinates of previously published fMRI studies or reviews exploring the cerebral regions associated with: voice processing (Belin et al., 2000), Voice ROI-set; language processing (Ferstl et al., 2008), Language ROI-set; semantic memory (Binney et al., 2010), SM ROI-set; and autobiographical memory (Spreng et al., 2009), AM ROI-set (Table 2). Talairach coordinates were converted to MNI coordinates using the MNI2Tal atlas available online via the BioImage Suite at Yale University (http://bioimagesuite.yale.edu/mni2tal/; Lacadie at al., 2008). Eight-mm radius spheres were drawn around each set of peak coordinates and combined into a ROI-set. Voxels without BOLD signal across the 19 subjects were removed from analysis.

Mean beta weights were extracted from the ROI-sets for the five regressors used in the general linear model, i.e. the five conditions (Silence, Unintelligible, Low EC, Mean EC and High EC). Beta weights correspond to the regression slope and quantify the contribution of each condition of the experimental paradigm in explaining the observed time course of BOLD signal, i.e. parameter estimates (Friston et al., 1995). In the case of multiple linear regression, beta weights can be over 1 in absolute value. A negative beta weight corresponds to a decrease in BOLD signal, while a positive beta weight corresponds to an increase. A random effects analysis was run to compute *t* statistics with Bonferroni's correction within each ROI-set in the group of 19 subjects.

RESULTS

Recall instruction and subject's forename

Recall instruction and subject's forename did not trigger detectable cerebral activation, even at a less restrictive statistical threshold without FWE correction (uncorrected $p < 0.001$, $k = 2$). We thus assumed that recall was implicit, occurring even in the absence of recall instruction, and that hearing one's own forename once was not sufficient for BOLD-detectable variations.

For the four domains of analysis, location and volume of activation clusters are reported in Table 3.

Emotional gradient. Low EC (*versus* Silence) elicited the bilateral middle and superior temporal gyri, particularly in the left hemisphere (larger clusters and higher T-scores), including higher order associative auditory cortices (Fig. 1A).

Mean EC (*versus* Silence) elicited the same regions as Low EC, as well as bilateral premotor cortices and left inferior frontal gyrus (Fig. 1B).

High EC (*versus* Silence) triggered a large bilateral pattern of activation encompassing the middle and superior temporal gyri, the temporopolar areas, the posterior cingulate and retrosplenial cortices, the medial temporal lobes, the medial frontal lobes, the middle and inferior frontal gyri, the thalami, the cerebellum, particularly in the left hemisphere (larger clusters and higher T-scores) except for the cerebellum. Left angular gyrus activation was also observed (Fig. 1C).

Speech processing

Listening to unintelligible narratives (*versus* Silence) elicited bilateral activation of the superior temporal gyri and sulci, both predominantly in the left hemisphere (Fig. 2A). The contrast between narratives played forward (Low EC) and backward (Unintelligible) revealed activations in the left superior temporal sulcus, the left caudate nucleus body, the bilateral hippocampi and the anterior section of the right collateral sulcus (Fig. 2B). No significant differences were found between right and left-handed subjects ($p < 0.05$, FWE-corrected).

Voice familiarity

We observed bilateral activation in the superior temporal sulci (Fig. 2C), with SVC applied to the contrast between familiar (Mean EC) and unfamiliar (Low EC) voices. No significant differences were found between right- and left-handed subjects ($p < 0.05$, FWE-corrected).

Declarative memory

High EC (*versus* Mean EC) elicited a large pattern of activation encompassing (Fig. 3A): (i) medial regions, the bilateral medial occipital, frontal, prefrontal cortices and the left precuneus; (ii) limbic regions, the bilateral retrosplenial, posterior and anterior cingulate cortices, the hippocampi and the parahippocampal gyri; (iii) temporal regions, the left superior, middle, fusiform and inferior gyri, the right superior temporal sulcus and the left temporopolar area; (iv) lateral frontal regions, the left middle and inferior frontal gyri, the right inferior frontal gyrus; (v) bilateral activations of the thalami, the cerebellum, and the angular gyri.

High EC_EAM (*versus* Mean EC) elicited activation within the right lingual gyrus, but only one significant voxel was found at $p < 0.05$ (FWE-corrected). SVC within the volume-of-interest determined by the previous contrast (High EC *versus* Mean EC) revealed activation in the left retrosplenial and posterior cingulate cortices, the bilateral lingual gyri, the left premotor cortex and the bilateral supplementary motor areas, the left fusiform gyrus, parahippocampal gyrus and hippocampus (Fig. 3B).

High EC_SAM (*versus* Mean EC) elicited activations in the bilateral posterior cingulate cortices, predominantly in the left hemisphere, the left middle temporal and fusiform gyri, the right middle temporal gyrus, the right cerebellum, the right parahippocampal gyrus, the bilateral thalami and the left angular gyrus (Fig. 3C).

As the number of subjects was different between the two groups High EC_EAM ($n = 9$) and High EC_SAM ($n = 10$), a jackknife resampling was done in order to avoid size effect. Statistical analysis in the High EC_SAM group for the 10 subgroups of 9 subjects revealed that even in the worst-case scenario, High EC_SAM remains superior to High EC_EAM in terms of cluster size of significant voxels, i.e. from 66 to 115 voxels *versus* just 1 voxel for High EC_EAM.

Mean EC (*versus* High EC) triggered activation in the right supramarginal gyrus (Fig. 3D).

ROI-set analysis. The beta weights for High EC were greater in the four ROI-sets: Voice ($t = 5.36$; $p = 0.00009$), Language ($t = 4.45$, $p = 0.0006$), SM ($t = 4.72$, $p = 0.0003$) and AM ($t = 7.78$, $p = 0.000001$). In voice and language ROI-sets, beta weights gradually increased from Silence to Unintelligible to Low EC to Mean EC to High EC. In SM ROI-set, Unintelligible did not differ from Silence, contrary to semantically meaningful narratives, i.e. Low EC, Mean EC and High EC. In AM ROI-set, only narratives with autobiographical content, i.e. High EC, differed significantly from Silence. The results are summarized in Fig. 4.

DISCUSSION

Our goal was to use an experimental fMRI paradigm designed for the detection of covert activity in healthy subjects for further clinical application in chronic consciousness disorders. We explored graduated emotional charge, hypothesizing that higher emotional charge, i.e. voice familiarity and autobiographical memory, would recruit larger networks engaged in emotional processing and related behavior. Increasing the emotional gradient extended the recruitment of cerebral areas, from low to high emotional charge, up to cingulate, temporal, frontal, prefrontal and angular areas, thalamus and cerebellum. Speech processing engaged auditory areas and memory-related circuits. Voice familiarity activated the superior temporal sulci. Autobiographical memory elicited the largest pattern of activation, encompassing cingulate, temporal, frontal, prefrontal and angular areas, visual cortex, thalamus and cerebellum. Semantic autobiographical memory revealed larger activations than episodic autobiographical memory. The capacity of high emotional narratives to trigger the greater increase in BOLD signal was confirmed by independent ROI

Table 3. Patterns of activation. Activated regions in emotional gradient, speech and voice processing, and declarative memory analyses. The last four columns (*x*, *y*, *z* and T-score) refer to the main activation peak in the cluster or in the brain structure if clustering is extensive; coordinates refer to the Montreal Neurological Institute coordinate system; L, left; R, right; BA, Brodmann area. See Table 1 for conditions designation. Statistical significance threshold was set to $p < 0.05$ (FWE-corrected) with a minimum cluster extent of two contiguous voxels. *Small volume correction applied. (see *Experimental procedures* for details)

Anatomy	BA	Cluster size (voxels)	*x*	*y*	*z*	T-score
Low EC > Silence (low emotional charge)						
L superior and middle temporal gyri	22, 21	243	−60	−28	4	16.55
R superior and middle temporal gyri	22, 21	161	56	−12	4	11.49
Mean EC > Silence (mean emotional charge)						
L superior and middle temporal gyri	22, 21	310	−60	−28	4	18.85
R superior and middle temporal gyri	22, 21	197	60	−12	0	13.92
R premotor cortex	6	15	52	0	48	9.12
L premotor cortex	6	5	−56	−4	44	7.03
L inferior frontal gyrus (pars opercularis)	44	4	−52	20	16	7.34
High EC > Silence (high emotional charge)						
L superior and middle temporal gyri, temporopolar area	22, 21, 38	1750	−56	−24	4	19.04
L, R retrosplenial and posterior cingulate cortices	29, 30, 23		−4	−56	12	14.07
L inferior frontal gyrus (pars triangularis, pars orbitalis)	45, 47		−48	20	16	12.75
R cerebellum (inferior vermis and posterior lobe)			1	−56	−44	12.19
L, R hippocampus and parahippocampal gyrus			−28	−32	−8	10.51
L angular gyrus	39		−48	−64	20	9.75
L, R thalamus			−4	−8	4	9.40
L, R medial frontal and prefrontal cortices	6, 8, 9, 10	300	4	4	68	13.06
R superior and middle temporal gyri, temporopolar area	22, 21, 38	294	56	0	−8	16.78
L middle frontal gyrus	6, 9	77	−44	0	48	10.33
L cerebellum (posterior lobe)		40	−36	−68	−28	8.29
R middle frontal gyrus	6	19	52	−4	48	8.65
R inferior frontal gyrus (pars orbitalis)	47	12	44	28	−4	8.94
Unintelligible > Silence (speech auditory processing)						
L superior temporal gyrus and sulcus	22, 21, 41, 42	190	−56	−28	4	16.05
R superior temporal gyrus and sulcus	22, 21	152	56	−12	4	13.64
Low EC > Unintelligible (linguistic processing)						
L superior temporal sulcus	21, 22	14	−60	−12	−12	9.18
L caudate nucleus body		10	−20	−8	20	7.75
R hippocampus head, body and collateral sulcus		6	28	−32	−16	7.22
L hippocampus head		2	−32	−16	−16	6.45
*Mean EC > Low EC (voice familiarity processing)**						
R superior temporal sulcus	21, 22	58	52	−20	−8	6.28
L superior temporal sulcus	21, 22	58	−56	−44	4	5.73
High EC > Mean EC (autobiographical component)						
L, R medial occipital lobe	17, 18	1604	−8	−56	12	14.88
L, R retrosplenial and posterior cingulate cortices	26, 29, 30, 23		−4	−60	20	14.47
L middle and superior temporal gyri	21, 22		−60	−4	−12	11.76
L fusiform and inferior temporal gyri L, R thalamus	37, 20		−28	−36	−16	11.42
L fusiform and inferior temporal gyri			−4	−12	8	10.30
L, R thalamus			12	−80	−36	9.84
R cerebellum (posterior lobe)						
L, R hippocampus and parahippocampal gyrus			−28	−28	−12	9.57
L angular gyrus	39		−48	−60	20	9.14
L precuneus	7		−8	−48	40	8.41
L, R medial frontal cortices and anterior cingulate cortex	6, 8, 9, 10, 24, 32	604	−4	8	60	10.90
L, R cerebellum (inferior vermis)		104	0	−60	−44	12.08
R superior temporal sulcus	21, 22	71	60	−4	−8	10.68
L middle frontal gyrus	6, 9	63	−40	8	52	9.11
L inferior frontal gyrus (pars triangularis, pars orbitalis)	45, 47	55	−52	20	16	8.06
L temporopolar area	38	11	−36	12	−12	7.34
R inferior frontal gyrus (pars orbitalis)	47	5	36	24	−4	6.65
R angular gyrus	39	4	56	−68	28	7.01
*High EC_EAM > Mean EC (episodic autobiographical component)**						
L retrosplenial and posterior cingulate cortices	23, 30	19	−4	−60	20	8.69
L, R lingual gyri		11	0	−40	0	9.93

Table 3 (*continued*)

Anatomy	BA	Cluster size (voxels)	*x*	*y*	*z*	T-score
L premotor cortex	6	8	−40	0	56	10.06
L fusiform gyrus		5	−24	−40	−16	9.37
L parahippocampal gyrus			−28	−28	−16	9.00
L, R supplementary motor area	6	4	0	8	60	9.98
L hippocampal body		2	−32	−32	−12	8.42
High EC_SAM > Mean EC (semantic autobiographical component)						
L, R posterior cingulate cortex	23, 30	104	−8	−52	8	21.01
L middle temporal gyrus	20, 21	30	−56	−8	−16	16.16
	21	15	−52	−44	−4	14.94
R cerebellum (inferior vermis, posterior lobe)		21	0	−60	−44	13.46
		8	16	−76	−28	10.93
		5	36	−60	−28	10.78
R parahippocampal gyrus		13	8	−48	0	12.77
		4	8	−32	−4	12.44
R middle temporal gyrus	20, 21	11	64	−8	−12	11.63
L, R thalamus		8	4	−8	0	11.31
L fusiform gyrus	37	4	−24	−32	−20	12.01
L angular gyrus	39	2	−52	−64	20	9.84
Mean EC > High EC (general semantic component)						
R supramarginal gyrus	40	42	52	−40	48	7.99

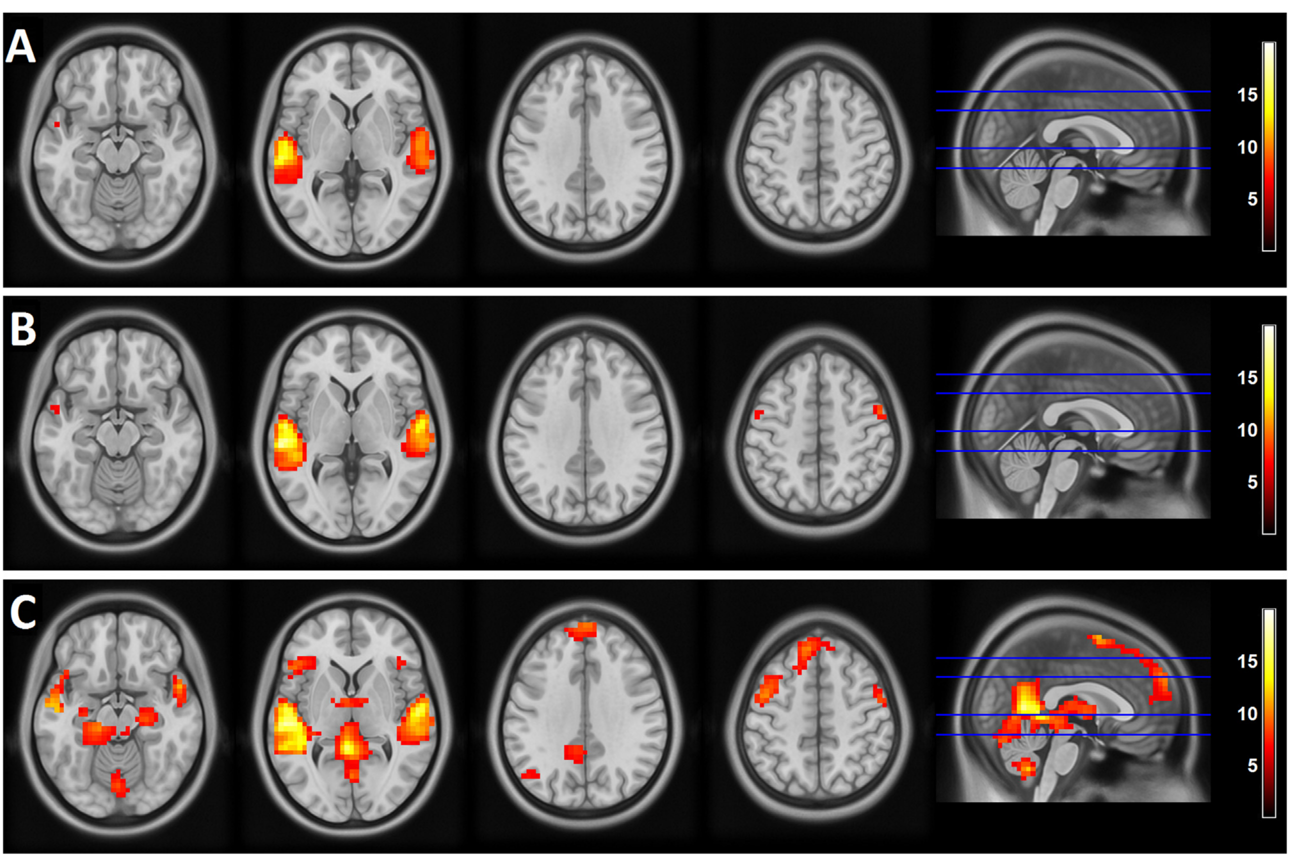

Fig. 1. Emotional gradient. Cerebral activation during passive listening to narratives with low emotional charge (A), mean emotional charge (B) and high emotional charge (C) compared to silence (see Table 3 for an extensive description). Slice MNI coordinates are $z = -15, 2, 34, 50$; $x = 0$; the right hemisphere is on the right side. Statistical significance threshold was set to $p < 0.05$ (FWE-corrected) with a minimum cluster extent of two contiguous voxels.

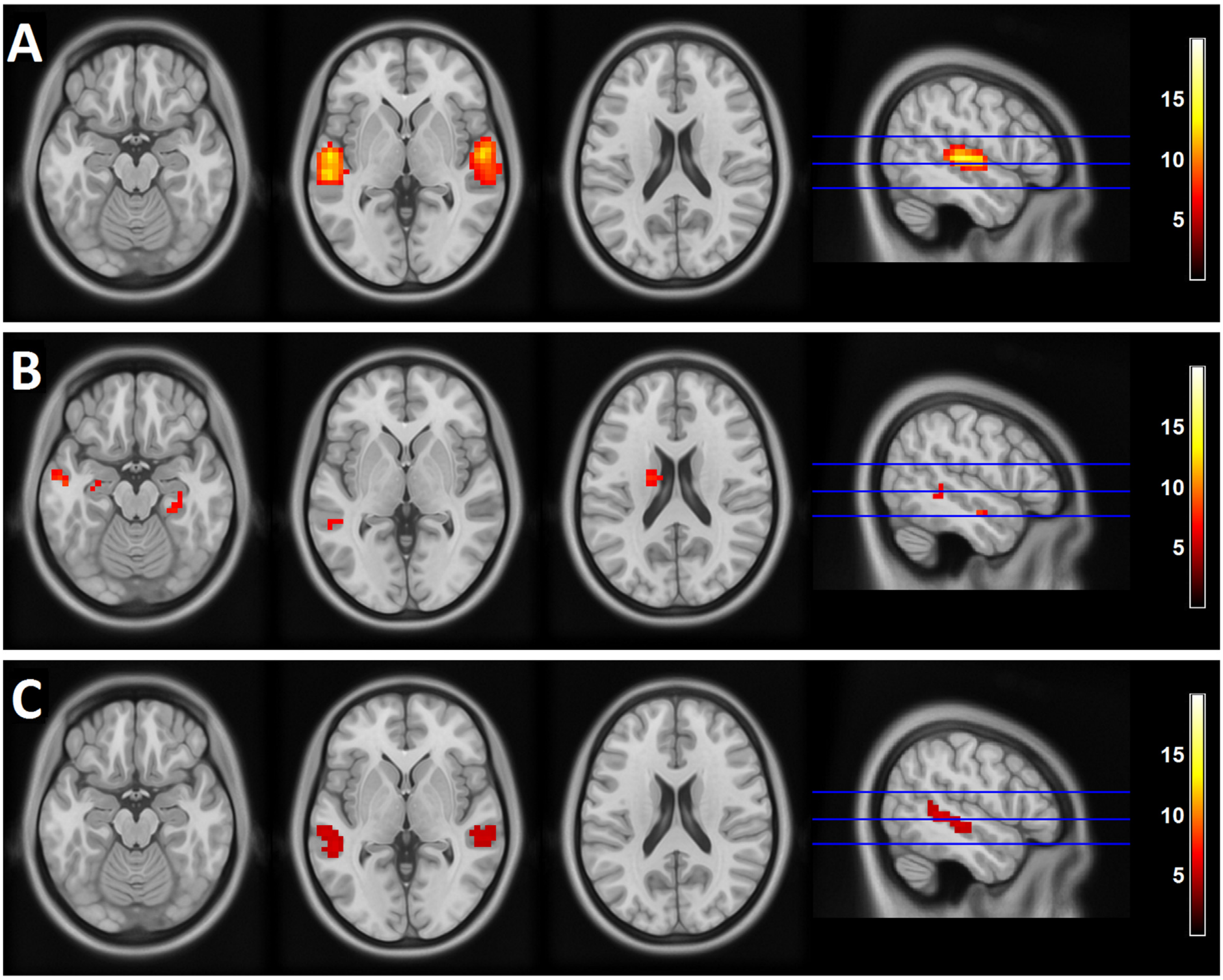

Fig. 2. Speech and Voice familiarity processing. Cerebral activation during passive listening to unintelligible speech rather than silence (A), intelligible speech rather than unintelligible speech (B), and familiar voice rather than non-familiar voice (C) (see Table 3 for an extensive description). Slice MNI coordinates are $z = -18, 0, 20$; $x = -52$; the right hemisphere is on the right side. Statistical significance threshold was set to $p < 0.05$ (FWE-corrected) with a minimum cluster extent of two contiguous voxels. C is presented with small volume correction within bilateral superior, middle temporal gyri and temporopolar areas.

analysis in voice-sensitive, language-sensitive and declarative memory-sensitive areas.

Emotional gradient

Our analysis of the Low EC condition confirmed the involvement of the bilateral superior and middle temporal gyri (Binder et al., 2008).

The Mean EC condition, with the same narratives spoken by a relative, elicited the same activations plus the bilateral premotor cortices and the left *pars opercularis* involved in speech perception (Wilson et al., 2004; Iacoboni, 2008) and auditory attention for speech comprehension (Giraud et al., 2004; Osnes et al., 2011). These prefrontal activations in the Mean EC condition could be explained by enhanced auditory attention while hearing a relative, in the noisy environment of the scanner.

Listening to High EC narratives elicited a large activation pattern partially overlapping with the default mode network (DMN) observed during resting state (Buckner et al., 2008), i.e. posterior cingulate and retrosplenial cortices, medial prefrontal cortices, medial temporal lobes and left angular gyrus. DMN activity is spontaneously generated by internal-self thoughts such as concerns and experiences in everyday life (Andrews-Hanna et al., 2014b; Raichle, 2015). DMN-like activations observed outside resting state have been reported during retrieval of autobiographical memory (Kim, 2010; Spreng and Grady, 2010; Ino et al., 2011; Bado et al., 2014; Andrews-Hanna et al., 2014a). Self-referential processing, which is the process of experiencing stimuli as they relate to one's self, has been associated with greater activity in the cortical midline structures comprising the medial prefrontal cortex, the anterior and posterior cingulate cortices (Kelley et al., 2002; Northoff and Bermpohl, 2004; Northoff et al., 2006), with the medial prefrontal

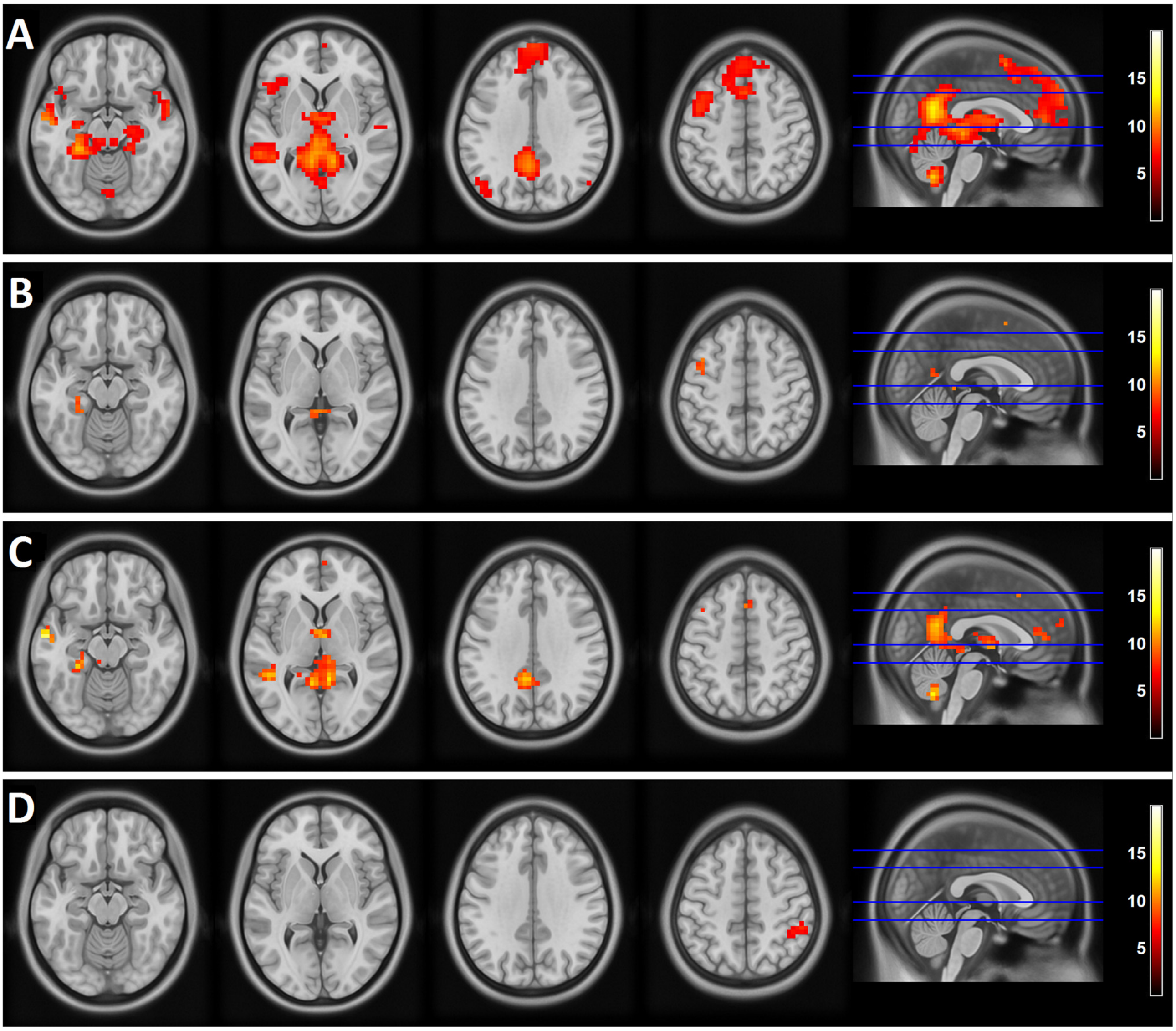

Fig. 3. Declarative memory. Cerebral activation during passive listening to autobiographical (A), episodic autobiographical (B) and semantic autobiographical (C) rather than general semantic narratives, and general semantic rather than autobiographical narratives (D) (see Table 3 for an extensive description). Slice MNI coordinates are $z = -15, 2, 34, 50$ for A, C, D and $z = -15, 2, 34, 51$ for B; $x = 0$; the right hemisphere is on the right side. Statistical significance threshold was set to $p < 0.05$ (FWE-corrected) with a minimum cluster extent of two contiguous voxels. B and C are presented with small volume correction within the volume of contrast A.

cortex playing a pivotal role (Heatherton et al., 2006; Denny et al., 2012). The high solicitation of the self in the High EC condition could thus explain the overlap of the activations with DMN structures (Kjaer et al., 2002; Schneider et al., 2008; Whitfield-Gabrieli et al., 2011).

As expected, we found that a higher emotional charge led to a more widespread pattern of activations, which can practically serve the clinical objective, i.e. the detection of residual covert activity in patients with severe and chronic disorders of consciousness.

Speech and voice processing

The temporal voice areas located in bilateral superior temporal sulci (Belin et al., 2000) were activated during speech auditory, speech linguistic, and voice familiarity processing. Our study also revealed involvement of the left caudate nucleus body and the bilateral medial temporal lobes in linguistic processing, thus confirming their implication in language processing (Meyer et al., 2005; Tomasi and Volkow, 2012; Grönholm et al., 2016).

Declarative memory

Listening to autobiographical (AM) rather than semantic memory (SM) triggered DMN-like activations. Semantic autobiographical memory (SAM) elicited more activations than episodic autobiographical memory (EAM). EAM chosen by the relative may have been more relevant for the relative than for the subject himself. SAM has a more general aspect, relevant for both relative and subject. Furthermore, SAM plays an

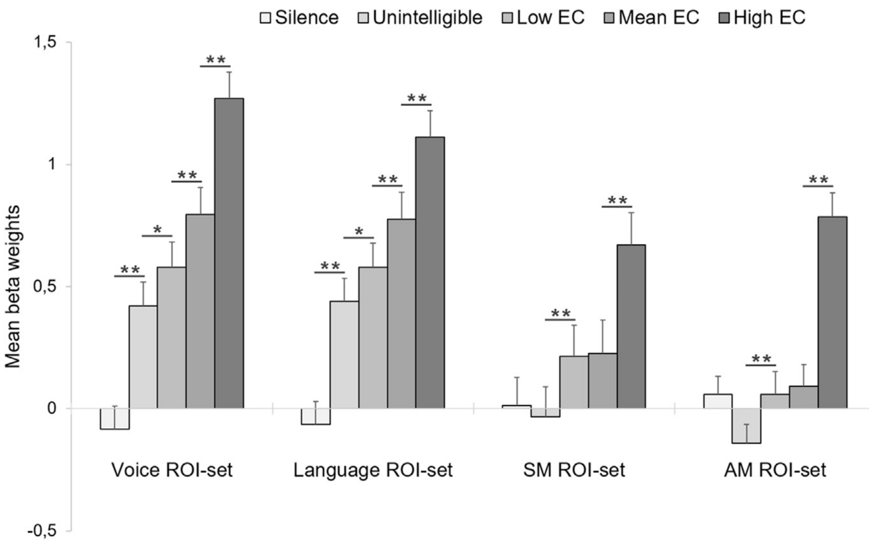

Fig. 4. ROI-set analysis. Mean beta weights extracted from the ROIs for the five conditions: Silence (lighter gray), Unintelligible, Low EC, Mean EC and High EC (darker gray). $^{**}p < 0.005$ (Bonferroni-corrected); $^{*}p < 0.05$ (Bonferroni-corrected). Statistics are only shown for contrasts with the nearest neighbor (horizontal bars). Vertical error bars depict the standard error of the mean.

important role in maintaining the integrity of the self (Haslam et al., 2011) and structuring life stories (Thomsen, 2009).

The SM *versus* AM contrast only revealed the right supramarginal gyrus. The neural basis of SM is generally associated with temporopolar and rhinal cortices (Davies et al., 2009). Those structures were present in the AM condition compared to silence, and consequently may have escaped being made visible by the SM > AM contrast.

ROI-set analysis

Independent ROI analysis confirmed the preponderant contribution of narratives with high emotional charge (i.e. autobiographical content) in triggering cerebral activation, beyond regions specifically involved in autobiographical memory processing: in SM ROI-set, semantically meaningful narratives increased the BOLD signal, and this increase was significantly greater with high emotional charge narratives; in Voice ROI-set and Language ROI-set, there was a positive gradient of BOLD signal as a function of the emotional content of the stimulus.

CONCLUSION

Using a novel fMRI protocol in healthy subjects, we showed that passive listening to narratives with graduated emotional charge led to graduated cerebral activations, with the highest charge triggering the largest recruitment of brain regions. Voice familiarity and autobiographical memory turned out to be efficient as an emotional gradient to trigger serial cerebral activations. Furthermore, the greater effect of high emotional narratives on BOLD signal increase was not only observed in autobiographical memory-sensitive areas, but also in voice-sensitive, language-sensitive and semantic memory-sensitive areas. Priority should be given to semantic autobiographical rather than episodic autobiographical for the selection of relevant memory content by the relative.

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DISCLOSURE OF INTEREST STATEMENT

The authors declare that they have no conflicts of interest to report.

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REFERENCES

Andrews-Hanna JR, Saxe R, Yarkoni T (2014) Contributions of episodic retrieval and mentalizing to autobiographical thought: evidence from functional neuroimaging, resting-state connectivity, and fMRI meta-analyses. NeuroImage 91:324–335. http://dx.doi.org/10.1016/j.neuroimage.2014.01.032.

Andrews-Hanna JR, Smallwood J, Spreng RN (2014) The default network and self-generated thought: component processes, dynamic control, and clinical relevance. Ann N Y Acad Sci 1316:29–52. http://dx.doi.org/10.1111/nyas.12360.

Araujo HF, Kaplan J, Damasio H, Damasio A (2014) Involvement of cortical midline structures in the processing of autobiographical information. PeerJ 2:e481. http://dx.doi.org/10.7717/peerj.481.

Bado P, Engel A, de Oliveira-Souza R, Bramati IE, Paiva FF, Basilio R, Sato JR, Tovar-Moll F, Moll J (2014) Functional dissociation of ventral frontal and dorsomedial default mode network components during resting state and emotional autobiographical recall. Hum Brain Mapp 35:3302–3313.

Bekinschtein TA, Manes FF, Villarreal M, Owen AM, Della-Maggiore V (2011) Functional imaging reveals movement preparatory activity in the vegetative state. Front Hum Neurosci 5:5. http://dx.doi.org/10.3389/fnhum.2011.00005.

Belin P, Zatorre RJ, Lafaille P, Ahad P, Pike B (2000) Voice-selective areas in human auditory cortex. Nature 403:309–312. http://dx.doi.org/10.1038/35002078.

Binder JR, Swanson SJ, Hammeke TA, Sabsevitz DS (2008) A comparison of five fMRI protocols for mapping speech comprehension systems. Epilepsia 49:1980–1997. http://dx.doi.org/10.1111/j.1528-1167.2008.01683.x.

Binney RJ, Embleton KV, Jefferies E, Parker GJM, Ralph MAL (2010) The Ventral and Inferolateral Aspects of the Anterior Temporal Lobe Are Crucial in Semantic Memory: evidence from a Novel Direct Comparison of Distortion-Corrected fMRI, rTMS, and Semantic Dementia. Cereb. Cortex 20:2728–2738. http://dx.doi.org/10.1093/cercor/bhq019.

Brett M, Anton J, Valabregue R, Poline J (2002) Region of interest analysis using an SPM toolbox. In: Proceedings of the 8th International Conference on Functional Mapping of the Human Brain.

Buchanan TW (2007) Retrieval of emotional memories. Psychol Bull 133:761–779. http://dx.doi.org/10.1037/0033-2909.133.5.761.

Buckner RL, Andrews-Hanna JR, Schacter DL (2008) The brain's default network: anatomy, function, and relevance to disease. Ann N Y Acad Sci 1124:1–38. http://dx.doi.org/10.1196/annals.1440.011.

Coleman MR, Pickard JD (2011) Detecting residual cognitive function in disorders of consciousness. Adv Tech Stand Neurosurg 36:3–16. http://dx.doi.org/10.1007/978-3-7091-0179-7_1.

Coleman MR, Rodd JM, Davis MH, Johnsrude IS, Menon DK, Pickard JD, Owen AM (2007) Do vegetative patients retain aspects of language comprehension? Evidence from fMRI. Brain 130:2494–2507. http://dx.doi.org/10.1093/brain/awm170.

D'Argembeau A, Comblain C, Van der Linden M (2003) Phenomenal characteristics of autobiographical memories for positive, negative, and neutral events. Appl Cogn Psychol 17:281–294. http://dx.doi.org/10.1002/acp.856.

Davies RR, Halliday GM, Xuereb JH, Kril JJ, Hodges JR (2009) The neural basis of semantic memory: evidence from semantic dementia. Neurobiol Aging 30:2043–2052. http://dx.doi.org/10.1016/j.neurobiolaging.2008.02.005.

Denny BT, Kober H, Wager TD, Ochsner KN (2012) A meta-analysis of functional neuroimaging studies of self- and other judgments reveals a spatial gradient for mentalizing in medial prefrontal cortex. J Cogn Neurosci 24:1742–1752. http://dx.doi.org/10.1162/jocn_a_00233.

Di HB, Yu SM, Weng XC, Laureys S, Yu D, Li JQ, Qin PM, Zhu YH, Zhang SZ, Chen YZ (2007) Cerebral response to patient's own name in the vegetative and minimally conscious states. Neurology 68:895–899. http://dx.doi.org/10.1212/01.wnl.0000258544.79024.d0.

Di Perri C, Thibaut A, Heine L, Soddu A, Demertzi A, Laureys S (2014) Measuring consciousness in coma and related states. World J Radiol 6:589–597. http://dx.doi.org/10.4329/wjr.v6.i8.589.

Eickhoff SB, Dafotakis M, Grefkes C, Stöcker T, Shah NJ, Schnitzler A, Zilles K, Siebler M (2008) FMRI reveals cognitive and emotional processing in a long-term comatose patient. Exp Neurol 214:240–246. http://dx.doi.org/10.1016/j.expneurol.2008.08.007.

Fernández-Espejo D, Owen AM (2013) Detecting awareness after severe brain injury. Nat Rev Neurosci 14:801–809. http://dx.doi.org/10.1038/nrn3608.

Fernández-Espejo D, Junqué C, Vendrell P, Bernabeu M, Roig T, Bargalló N, Mercader JM (2008) Cerebral response to speech in vegetative and minimally conscious states after traumatic brain injury. Brain Inj 22:882–890. http://dx.doi.org/10.1080/02699050802403573.

Ferstl EC, Neumann J, Bogler C, von Cramon DY (2008) The extended language network: a meta-analysis of neuroimaging studies on text comprehension. Hum Brain Mapp 29:581–593. http://dx.doi.org/10.1002/hbm.20422.

Fonov V, Evans A, McKinstry R, Almli C, Collins D (2009) Unbiased nonlinear average age-appropriate brain templates from birth to adulthood. NeuroImage 1:S102. http://dx.doi.org/10.1016/S1053-8119(09)70884-5. Organization for Human Brain Mapping 2009 Annual Meeting.

Friston KJ, Holmes AP, Poline JB, Grasby PJ, Williams SC, Frackowiak RS, Turner R (1995) Analysis of fMRI time-series revisited. NeuroImage 2:45–53. http://dx.doi.org/10.1006/nimg.1995.1007.

Giacino JT, Fins JJ, Laureys S, Schiff ND (2014) Disorders of consciousness after acquired brain injury: the state of the science. Nat Rev Neurol 10:99–114. http://dx.doi.org/10.1038/nrneurol.2013.279.

Gilutz Y, Lazary A, Karpin H, Vatine J-J, Misha T, Fortinsky H, Sharon H (2015) Detailed behavioral assessment promotes accurate diagnosis in patients with disorders of consciousness. Front Hum Neurosci 9:87. http://dx.doi.org/10.3389/fnhum.2015.00087.

Giraud AL, Kell C, Thierfelder C, Sterzer P, Russ MO, Preibisch C, Kleinschmidt A (2004) Contributions of sensory input, auditory search and verbal comprehension to cortical activity during speech processing. Cereb Cortex N Y N 1991(14):247–255.

Gosseries O, Zasler ND, Laureys S (2014) Recent advances in disorders of consciousness: focus on the diagnosis. Brain Inj 28:1141–1150. http://dx.doi.org/10.3109/02699052.2014.920522.

Graham M, Weijer C, Peterson A, Naci L, Cruse D, Fernández-Espejo D, Gonzalez-Lara L, Owen AM (2014) Acknowledging awareness: informing families of individual research results for patients in the vegetative state. J Med Ethics. http://dx.doi.org/10.1136/medethics-2014-102078.

Grilli MD, Verfaellie M (2014) Personal semantic memory: insights from neuropsychological research on amnesia. Neuropsychologia 61:56–64. http://dx.doi.org/10.1016/j.neuropsychologia.2014.06.012.

Grönholm EO, Roll MC, Horne MA, Sundgren PC, Lindgren AG (2016) Predominance of caudate nucleus lesions in acute ischaemic stroke patients with impairment in language and speech. Eur J Neurol 23:148–153. http://dx.doi.org/10.1111/ene.12822.

Haslam C, Jetten J, Haslam SA, Pugliese C, Tonks J (2011) "I remember therefore I am, and I am therefore I remember": exploring the contributions of episodic and semantic self-knowledge to strength of identity. Br J Psychol Lond Engl 1953(102):184–203. http://dx.doi.org/10.1348/000712610X508091.

Heatherton TF, Wyland CL, Macrae CN, Demos KE, Denny BT, Kelley WM (2006) Medial prefrontal activity differentiates self from close others. Soc Cogn Affect Neurosci 1:18–25. http://dx.doi.org/10.1093/scan/nsl001.

Iacoboni M (2008) The role of premotor cortex in speech perception: evidence from fMRI and rTMS. J Physiol Paris 102:31–34. http://dx.doi.org/10.1016/j.jphysparis.2008.03.003.

Ino T, Nakai R, Azuma T, Kimura T, Fukuyama H (2011) Brain activation during autobiographical memory retrieval with special reference to default mode network. Open Neuroimaging J 5:14–23. http://dx.doi.org/10.2174/1874440001105010014.

Kalenzaga S, Sperduti M, Anssens A, Martinelli P, Devauchelle A-D, Gallarda T, Delhommeau M, Lion S, Amado I, Krebs M-O, Oppenheim C, Piolino P (2014) Episodic memory and self-reference via semantic autobiographical memory: insights from an fMRI study in younger and older adults. Front Behav Neurosci 8:449. http://dx.doi.org/10.3389/fnbeh.2014.00449.

Kelley WM, Macrae CN, Wyland CL, Caglar S, Inati S, Heatherton TF (2002) Finding the self? An event-related fMRI study. J Cogn Neurosci 14:785–794. http://dx.doi.org/10.1162/08989290260138672.

Kensinger EA (2004) Remembering emotional experiences: the contribution of valence and arousal. Rev Neurosci 15:241–251.

Kim H (2010) Dissociating the roles of the default-mode, dorsal, and ventral networks in episodic memory retrieval. NeuroImage 50:1648–1657. http://dx.doi.org/10.1016/j.neuroimage.2010.01.051.

Kjaer TW, Nowak M, Lou HC (2002) Reflective self-awareness and conscious states: PET evidence for a common midline parietofrontal core. NeuroImage 17:1080–1086.

Kriegeskorte N, Simmons WK, Bellgowan PSF, Baker CI (2009) Circular analysis in systems neuroscience: the dangers of double dipping. Nat Neurosci 12:535–540. http://dx.doi.org/10.1038/nn.2303.

Kriegstein KV, Giraud A-L (2004) Distinct functional substrates along the right superior temporal sulcus for the processing of voices. NeuroImage 22:948–955. http://dx.doi.org/10.1016/j.neuroimage.2004.02.020.

Lacadie CM, Fulbright RK, Constable RT, Papademetris X (2008) More accurate Talairach coordinates for neuroImaging using nonlinear registration. NeuroImage 42:717–725. http://dx.doi.org/10.1016/j.neuroimage.2008.04.240.

Laureys S, Schiff ND (2012) Coma and consciousness: paradigms (re)framed by neuroimaging. NeuroImage 61:478–491. http://dx.doi.org/10.1016/j.neuroimage.2011.12.041.

Machado C, Korein J, Aubert E, Bosch J, Alvarez MA, Rodríguez R, Valdés P, Portela L, Garcia M, Pérez N, Chinchilla M, Machado Y, Machado Y (2007) Recognizing a mother's voice in the persistent vegetative state. Clin EEG Neurosci 38:124–126.

Martinelli P, Sperduti M, Devauchelle A-D, Kalenzaga S, Gallarda T, Lion S, Delhommeau M, Anssens A, Amado I, Meder JF, Krebs M-O, Oppenheim C, Piolino P (2013) Age-related changes in the functional network underlying specific and general autobiographical memory retrieval: a pivotal role for the anterior cingulate cortex. PloS One 8:e82385. http://dx.doi.org/10.1371/journal.pone.0082385.

Menon DK, Owen AM, Williams EJ, Minhas PS, Allen CM, Boniface SJ, Pickard JD (1998) Cortical processing in persistent vegetative state. Wolfson Brain Imaging Centre Team. Lancet Lond Engl 352:200.

Meyer P, Mecklinger A, Grunwald T, Fell J, Elger CE, Friederici AD (2005) Language processing within the human medial temporal lobe. Hippocampus 15:451–459. http://dx.doi.org/10.1002/hipo.20070.

Monti MM, Coleman MR, Owen AM (2009) Neuroimaging and the vegetative state: resolving the behavioral assessment dilemma? Ann N Y Acad Sci 1157:81–89. http://dx.doi.org/10.1111/j.1749-6632.2008.04121.x.

Northoff G, Bermpohl F (2004) Cortical midline structures and the self. Trends Cogn Sci 8:102–107. http://dx.doi.org/10.1016/j.tics.2004.01.004.

Northoff G, Heinzel A, de Greck M, Bermpohl F, Dobrowolny H, Panksepp J (2006) Self-referential processing in our brain–a meta-analysis of imaging studies on the self. NeuroImage 31:440–457. http://dx.doi.org/10.1016/j.neuroimage.2005.12.002.

Osnes B, Hugdahl K, Specht K (2011) Effective connectivity analysis demonstrates involvement of premotor cortex during speech perception. NeuroImage 54:2437–2445. http://dx.doi.org/10.1016/j.neuroimage.2010.09.078.

Owen AM, Coleman MR (2008) Using neuroimaging to detect awareness in disorders of consciousness. Funct Neurol 23:189–194.

Perrin F, Schnakers C, Schabus M, Degueldre C, Goldman S, Brédart S, Faymonville M-E, Lamy M, Moonen G, Luxen A, Maquet P, Laureys S (2006) Brain response to one's own name in vegetative state, minimally conscious state, and locked-in syndrome. Arch Neurol 63:562–569. http://dx.doi.org/10.1001/archneur.63.4.562.

Perrin F, Castro M, Tillmann B, Luauté J (2015) Promoting the use of personally relevant stimuli for investigating patients with disorders of consciousness. Front Psychol 6:1102. http://dx.doi.org/10.3389/fpsyg.2015.01102.

Picard L, Mayor-Dubois C, Maeder P, Kalenzaga S, Abram M, Duval C, Eustache F, Roulet-Perez E, Piolino P (2013) Functional independence within the self-memory system: new insights from two cases of developmental amnesia. Cortex. J Devoted Study Nerv Syst Behav 49:1463–1481. http://dx.doi.org/10.1016/j.cortex.2012.10.003.

Piperno R, Battistini A, Cevolani D, Maffei M, Leonardi M, Agati R (2012) FMRI activation with an "affective speech" paradigm in vegetative and minimally conscious States: applicability and prognostic value. Neuroradiol J 25:289–299.

Poldrack RA (2007) Region of interest analysis for fMRI. Soc Cogn Affect Neurosci 2:67–70. http://dx.doi.org/10.1093/scan/nsm006.

Posner J, Russell JA, Peterson BS (2005) The circumplex model of affect: an integrative approach to affective neuroscience, cognitive development, and psychopathology. Dev Psychopathol 17:715–734. http://dx.doi.org/10.1017/S0954579405050340.

Raichle ME (2015) The Brain's Default Mode Network. Annu Rev Neurosci 38:433–447. http://dx.doi.org/10.1146/annurev-neuro-071013-014030.

Rorden C, Karnath H-O, Bonilha L (2007) Improving lesion-symptom mapping. J Cogn Neurosci 19:1081–1088. http://dx.doi.org/10.1162/jocn.2007.19.7.1081.

Russell JA (1980) A circumplex model of affect. J Pers Soc Psychol 39:1161–1178. http://dx.doi.org/10.1037/h0077714.

Schneider F, Bermpohl F, Heinzel A, Rotte M, Walter M, Tempelmann C, Wiebking C, Dobrowolny H, Heinze HJ, Northoff G (2008) The resting brain and our self: Self-relatedness modulates resting state neural activity in cortical midline structures. Neuroscience 157:120–131. http://dx.doi.org/10.1016/j.neuroscience.2008.08.014.

Sharon H, Pasternak Y, Ben Simon E, Gruberger M, Giladi N, Krimchanski BZ, Hassin D, Hendler T (2013) Emotional processing of personally familiar faces in the vegetative state. PLoS ONE 8. http://dx.doi.org/10.1371/journal.pone.0074711.

Sokhi DS, Hunter MD, Wilkinson ID, Woodruff PWR (2005) Male and female voices activate distinct regions in the male brain. NeuroImage 27:572–578. http://dx.doi.org/10.1016/j.neuroimage.2005.04.023.

Spreng RN, Grady CL (2010) Patterns of brain activity supporting autobiographical memory, prospection, and theory of mind, and their relationship to the default mode network. J Cogn Neurosci 22:1112–1123. http://dx.doi.org/10.1162/jocn.2009.21282.

Spreng RN, Mar RA, Kim ASN (2009) The common neural basis of autobiographical memory, prospection, navigation, theory of mind, and the default mode: a quantitative meta-analysis. J Cogn Neurosci 21:489–510. http://dx.doi.org/10.1162/jocn.2008.21029.

Thomsen DK (2009) There is more to life stories than memories. Mem Hove Engl 17:445–457. http://dx.doi.org/10.1080/09658210902740878.

Tomasi D, Volkow ND (2012) Resting functional connectivity of language networks: characterization and reproducibility. Mol Psychiatry 17:841–854. http://dx.doi.org/10.1038/mp.2011.177.

Tsuchiya N, Adolphs R (2007) Emotion and consciousness. Trends Cogn Sci 11:158–167. http://dx.doi.org/10.1016/j.tics.2007.01.005.

Tulving E (1972) Episodic and semantic memory. In: Tulving Endel, Donaldson Wayne, Bower Gordon H, editors. Organization of Memory. New York: Academic Press. p. 381–403.

Tulving E (1985) Elements of Episodic Memory. Oxford Psychology Series 2.

Tulving E (2002) Episodic memory: from mind to brain. Annu Rev Psychol 53:1–25. http://dx.doi.org/10.1146/annurev.psych.53.100901.135114.

Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B, Joliot M (2002) Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. NeuroImage 15:273–289. http://dx.doi.org/10.1006/nimg.2001.0978.

Wang F, Di H, Hu X, Jing S, Thibaut A, Di Perri C, Huang W, Nie Y, Schnakers C, Laureys S (2015) Cerebral response to subject's own name showed high prognostic value in traumatic vegetative state. BMC Med 13:83. http://dx.doi.org/10.1186/s12916-015-0330-7.

Whitfield-Gabrieli S, Moran JM, Nieto-Castañón A, Triantafyllou C, Saxe R, Gabrieli JDE (2011) Associations and dissociations between default and self-reference networks in the human brain. NeuroImage 55:225–232. http://dx.doi.org/10.1016/j.neuroimage.2010.11.048.

Wilson SM, Saygin AP, Sereno MI, Iacoboni M (2004) Listening to speech activates motor areas involved in speech production. Nat Neurosci 7:701–702. http://dx.doi.org/10.1038/nn1263.

Worsley KJ, Marrett S, Neelin P, Vandal AC, Friston KJ, Evans AC (1996) A unified statistical approach for determining significant signals in images of cerebral activation. Hum Brain Mapp 4:58–73. http://dx.doi.org/10.1002/(SICI)1097-0193(1996)4:1 < 58::AID-HBM4 > 3.0.CO;2-O.

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