Verbal and musical short-term memory: Variety of auditory disorders after stroke

Catherine Hirel [a,b,c,d,*], Norbert Nighoghossian [c,d,e], Yohana Lévêque [a,b,c], Salem Hannoun [c,e], Lesly Fornoni [a,c], Sébastien Daligault [f], Patrick Bouchet [a,c], Julien Jung [a,c,d], Barbara Tillmann [b,c], Anne Caclin [a,c]

[a] INSERM, U1028, Lyon Neuroscience Research Center, Brain Dynamics and Cognition Team, Lyon F-69000, France
[b] CNRS, UMR5292, Lyon Neuroscience Research Center, Auditory Cognition and Psychoacoustics Team, Lyon F-69000, France
[c] University Lyon 1, Villeurbanne F-69000, France
[d] Stroke Department, Hospices Civils de Lyon, Hôpital Neurologique Pierre Wertheimer, Bron F-69000, France
[e] CREATIS, CNRS, UMR5220, INSERM, U1044, University Lyon 1, F-69000, France
[f] CERMEP, MEG Department, Bron F-69000, France

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ABSTRACT

Auditory cognitive deficits after stroke may concern language and/or music processing, resulting in aphasia and/or amusia. The aim of the present study was to assess the potential deficits of auditory short-term memory for verbal and musical material after stroke and their underlying cerebral correlates with a Voxel-based Lesion Symptom Mapping approach (VLSM). Patients with an ischemic stroke in the right (N = 10) or left (N = 10) middle cerebral artery territory and matched control participants (N = 14) were tested with a detailed neuropsychological assessment including global cognitive functions, music perception and language tasks. All participants then performed verbal and musical auditory short-term memory (STM) tasks that were implemented in the same way for both materials. Participants had to indicate whether series of four words or four tones presented in pairs, were the same or different. To detect domain-general STM deficits, they also had to perform a visual STM task. Behavioral results showed that patients had lower performance for the STM tasks in comparison with control participants, regardless of the material (words, tones, visual) and the lesion side. The individual patient data showed a double dissociation between some patients exhibiting verbal deficits without musical deficits or the reverse. Exploratory VLSM analyses suggested that dorsal pathways are involved in verbal (phonetic), musical (melodic), and visual STM, while the ventral auditory pathway is involved in musical STM.

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1. Introduction

1.1. Auditory deficits after stroke

Music and language are present in all human societies. Even though music is not essential for the survival or the reproduction of the human race, it provides benefits for our physical and moral well-being (MacDonald, Kreutz, & Mitchell, 2012). Auditory

cognitive deficits after stroke may affect language and/or music processing (Nicholson et al., 2003; Särkämö et al., 2009), and can also impact the processing of environmental sounds (Vignolo, 2003). Aphasia is more frequent after lesions in the left hemisphere, whereas acquired amusia can appear after lesions in both left or right hemispheres (Särkämö et al., 2009). Amusia is a music agnosia characterized by the inability to recognize music in the absence of sensory, intellectual, verbal and mnesic impairments. Amusia is rarely documented after stroke and remains largely underestimated. In Särkämö et al. (2009), 60% of patients had acquired amusia one week after stroke in the territory of the middle cerebral artery, and 42% remained amusic three months after stroke. In Schuppert, Münte, Wieringa, and Altenmüller (2000), 69% of the stroke patients (tested ten days after stroke) had deficits in perceptual musical functions, whatever the lateralization of the lesions in frontal, temporal and parietal areas. Acquired amusia

may be also associated with musical anhedonia (Hirel et al., 2014), a loss of pleasure in listening to music, which can also arise without any perceptual deficits (Griffiths, Warren, Dean, & Howard, 2004; Satoh, Nakase, Nagata, & Tomimoto, 2011). These studies of musical anhedonia are case reports with diverse lesion locations and the association between amusia and musical anhedonia has not been studied so far in brain-damaged patients at the group level.

After brain damage, music and language deficits do not always co-occur, as evidenced by reported cases of amusia without aphasia (or the reverse) (Griffiths, Flees, & Green, 1999; Griffiths et al., 1997; Peretz, Belleville, & Fontaine, 1997; Peretz et al., 1994). These reported double dissociations suggest that music and language are processed by (at least partly) separate cerebral networks. However, the diagnosis of amusia or aphasia relies on qualitatively different neuropsychological testing: Diagnosing aphasia typically involves tests of language comprehension and production, whereas diagnosing amusia relies on testing the perception of various musical dimensions (e.g., pitch, rhythm) or musical emotions. To allow for a better understanding of auditory deficits after brain damage, music and language disorders needs to be assessed with the same methodological approach. For this aim, our present study tested patients' short-term memory (STM) for auditory material (either verbal or musical) in comparison to visual material with the same experimental paradigm. STM is a basic cognitive ability involved in a wide range of tasks and contexts, and deficits in STM could be associated to or cause various patterns of deficits (see for example Tillmann, Lévêque, Fornoni, Albouy, & Caclin, 2015, for a discussion of how deficits in pitch STM might be central in congenital amusia).

1.2. Auditory short-term memory: behavior and cerebral correlates

Auditory verbal STM refers to a temporary memory store of verbal information for a short period of time (on the order of seconds). Baddeley's model (Baddeley, 2003) posits that auditory verbal working memory has two components: a phonological store, for very brief storage of verbal information, and an articulatory rehearsal component (phonological loop), for refreshing the information and keeping it active. Previous research investigating brain-damaged patients suggests that the left inferior parietal lobe is critical for the phonological store and the left inferior frontal lobe for the articulatory rehearsal component (Baldo & Dronkers, 2006; Leff et al., 2009; Warrington, Logue, & Pratt, 1971).

A Voxel-based Lesion Symptom Mapping (VLSM) study on stroke patients showed that auditory verbal STM is linked to the left middle temporal gyrus, left superior temporal gyrus (including Heschl's gyrus) and left inferior parietal areas (angular gyrus and supramarginal gyrus) (Baldo, Katseff, & Dronkers, 2012). An analysis of the lesions of patients with conduction aphasia highlights the importance of a region in the posterior portion of the left planum temporale, area Spt (Sylvian-parietal-temporal) for phonological STM (Buchsbaum et al., 2011). More generally, the area Spt is a sensory-motor integration area for vocal tract actions (Hickok, Okada, & Serences, 2009).

Functional Magnetic Resonance Imaging (fMRI) and Positron Emission Tomography (PET) studies with healthy participants showed that the left supramarginal gyrus is involved in short-term storage of phonological information (Henson, Burgess, & Frith, 2000; Paulesu, Frith, & Frackowiak, 1993; Salmon et al., 1996). They further suggest that a larger network of cortical areas is operating in verbal STM, including the auditory cortex (notably left superior temporal areas), the (left) premotor cortex, and Broca's area, which supports the articulatory processes.

Taken together, the studies with brain-damaged patients and the neuroimaging studies in healthy participants converge on the implication of temporal posterior, parietal inferior, and frontal inferior regions in auditory verbal STM, with a predominant role for left-hemisphere structures.

In comparison to verbal material, the cerebral correlates of STM processing for tonal (musical) material have been less investigated by neuropsychological and neuroimaging studies. A study on brain-damaged patients (lobectomy for intractable epilepsy) showed that patients with right fronto-temporal lesions had a deficit in the retention of pitch in STM (Zatorre & Samson, 1991). To our knowledge, no research has investigated the anatomical locus of auditory musical STM in stroke patients.

A PET study in healthy participants (Griffiths, Johnsrude, Dean, & Green, 1999) showed that blood flow increased in the posterior superior temporal lobe, inferior frontal regions and the cerebellum when participants compared pitch sequences of six tones (requiring a same/different judgment), a classical STM paradigm. The network was bilateral, but predominant in the right hemisphere. Using fMRI when participants performed a STM task with single tones, Stevens (2004) showed bilateral activation in the supramarginal gyrus, the posterior insula and the posterior inferior temporal gyrus as well as activation in the right IFG. Grimault et al. (2014) showed in a MEG study the implication of superior parietal lobe and pre-central gyrus bilaterally in STM for tones. Other functional imaging studies showed the implication of bilateral parieto-fronto-temporal areas in pitch STM tasks (Gaab, Gaser, Zaehle, Jancke, & Schlaug, 2003; Platel et al., 1997; Stevens, 2004; Zatorre, Evans, & Meyer, 1994), while a tDCS study suggested a causal involvement of the left SMG in non-musicians (Schaal, Williamson, et al., 2015).

Some data sets suggest (at least partly) separate cognitive and neural resources for verbal and musical STM. In control participants, auditory STM seems to be different for words, tones and timbre. In congenital amusia, a selective disorder of auditory STM for tones and timbre has been demonstrated, while verbal STM is intact (Tillmann, Schulze, & Foxton, 2009; Tillmann et al., 2015). The disorder of auditory STM for tones has been confirmed with tonal and atonal sequences, contrasting with normal performance for the verbal digit span (Albouy, Schulze, Caclin, & Tillmann, 2013). For a musical STM task, functional anomalies in a bilateral fronto-temporal network have been reported with MEG data for congenital amusia (Albouy, Mattout, et al., 2013), supporting the view that this fronto-temporal network is involved in non-verbal auditory memory.

The work on congenital amusia thus suggests that the processing and storage of musical stimuli might recruit, at least partly, a different sub-system of STM than speech. However, neuroimaging studies on control participants have uncovered a cortical network for tonal STM that was surprisingly similar to the network for verbal STM (Koelsch et al., 2009; Schulze & Koelsch, 2012). The present study with stroke patients might thus further shed light on whether common or separated neural resources are involved in verbal and musical STM. Furthermore, whereas in congenital amusia compensatory plastic changes over the course of development in infancy might account for normal performance in verbal STM, such plastic changes should be largely reduced in the adult patient population tested here.

1.3. Objectives of the present study

Our present study investigated memory deficits after stroke, in particular verbal and musical auditory STM (in comparison to visual STM), and the cerebral underpinnings of these deficits using an exploratory voxel-based lesion symptom mapping approach. We included patients with focal cortical lesions in regions of interest for auditory STM, i.e., temporo-parieto-frontal areas in the territory of the middle cerebral artery.

2. Materials and methods

2.1. Participants

Twenty patients and fourteen control participants were included in the present study. Stroke patients were recruited from the stroke unit of the neurological hospital in Lyon, France. The main inclusion criterion was the presence of an ischemic stroke in the right or left middle cerebral artery territory, confirmed by MRI. Inclusion criteria also included: age over 18 years, native French-speakers, no other prior neurological or psychiatric disease, no severe cognitive disorder, no severe hearing loss, being able to have an MRI scan and to be tested with various behavioral tests for 2 h. Patients were all tested in the chronic phase of their stroke (4–52 months after stroke). The same inclusion criteria (except criteria related to stroke) were applied to control participants, which were matched to the patients for age, gender, education level and music training. All participants gave written consent. The study was approved by the appropriate French ethics committee on Human Research (CPP Sud-Est III, 2014-050B).

2.2. Neuropsychological assessment

The behavioral measures (audiometry, neuropsychological assessment, STM tasks, and other behavioral tasks beyond the scope of the present report) were run during two sessions of approximately 2 h each. Standard audiometry was performed to exclude severe hearing loss. Series of neuropsychological measures were performed to assess general cognitive abilities (MMSE, Mini Mental State Examination, Folstein, Folstein, & McHugh, 1975) and language deficits, including tests of lexical and categorical verbal fluencies and a short battery of denomination (BARD, Croisile, Astier, Beaumont, & Mollion, 2010).

Music cognition was evaluated as part of the neuropsychological assessment with the MBEA (Montreal Battery of Evaluation of Amusia, Isabelle Peretz, Champod, & Hyde, 2003). The MBEA includes six subtests that measure different components of music cognition. The scale, contour, interval and rhythm subtests comprise 30 pairs of piano melodies, and participants have to judge, on each trial, whether the two melodies are the same or different. In the metric subtest, participants had to categorize melodies as either a waltz or a March and in the memory subtest they had to determine if the melody has been heard during previous trials or not. For each subtest, the maximum score was 30. The MBEA score was calculated as the mean score of the six subtests. This test allowed us to diagnose acquired amusia after stroke.

We also evaluated participants' pitch discrimination thresholds, using a two-alternative forced choice task with two-tone pairs in an adaptive paradigm (Tillmann et al., 2009).

2.3. Short-term memory tasks

Verbal and musical auditory STM performance was measured using delayed matching-to-sample tasks adapted from Tillmann et al. (2009). Participants listened to an auditory sequence (S1), which consisted of four events (words or tones), followed by a 1-s silence, and then a second sequence (S2), in which the four events were the same or different from S1. If the second sequence was different, only one event was changed (i.e., a new word/tone was introduced). The change never occurred in the first or the last element of the sequence. Each event (tone, word) had a duration of 500 ms and the four events in the sequence were presented with a silent inter-stimulus interval of 40 ms. The software Presentation (Neurobehavioral systems) was used to run the experiment and record the responses.

For the musical task, six piano tones were used (C3, D3, E3, F3, G3, and A3, Cubase 5.1 software, i.e., with F0 ranging from 262 to 440 Hz). For the different trials, all the changes between S1 and S2 entailed a change of melodic contour (i.e., a change in the pattern of up and downs created by the intervals). The changed tone in S2 created a pitch change between three and nine semi-tones from S1 and S2. For the verbal task, we used six monosyllabic French words differing only by their initial consonant, and all with the same fundamental frequency: "toux" (/tu/, cough), "bout" (/bu/, end), "loup" (/lu/, wolf), "goût" (/gu/, taste), "mou" (/mu/, flabby), "pou" (/pu/, head louse), spoken by a female voice, semi-synthesized (i.e., natural recordings were edited to equate loudness and F0 – at 230 Hz – across stimuli, see Tillmann et al., 2009, for details). For different trials, we excluded changes of words between S1 and S2 corresponding to minimal phonetic pairs (i.e., changes included at least two phonetics differences), to decrease the difficulty of the verbal task.

In addition, we tested visual STM, to detect general STM disorders, which are not specific to auditory memory. A shape was presented to the participant on a computer screen. This shape was continuously distorted and returned to the initial shape (S1) in 2100 ms (i.e., the duration of the auditory sequences), followed by a blank screen of 1 s, and then the same shape was distorted again (S2), either exactly in the same way or differently (different related to the intensity and speed of the deformation). The shapes were designed with Bezier curves to minimize possible simple verbal labels to remember the shape or its deformation (Tallon-Baudry, Bertrand, Peronnet, & Pernier, 1998).

There was one block for each material type (words, tones, visual). At the beginning of each block, six example trials were presented. Then, for each material type, 32 trials were presented (16 same and 16 different pairs). For each trial, the participant had to choose if the two sequences were the same or different. They had 2 s to provide their answer after the end of S2 and they indicated their answer by a button press (for one 85-year-old patient who had never used a computer the experimenter recorded the answers by button press). The order of the two auditory tasks was counter-balanced across participants, and the visual condition was always presented at the end (Fig. 1). For each material, the trials in each block were presented in a different pseudorandom order for each participant, with the constraint that the same type of trial (same or different) could not be repeated more than three times in a row.

2.4. Statistical analyses for the behavioral data

For the demographical and the neuropsychological data, we first compared patients and controls and then compared patients with left lesions to patients with right lesions with t-tests. Chi2 tests were used to compare sex ratios.

For the STM tasks, we computed d' and c, according to signal detection theory (Macmillan & Creelman, 2005), for each material type for each participant. d' corresponds to the sensitivity of the participant to perceive a difference between S1 and S2, and so to his/her performance at the task. The criterion c corresponds to the response bias. Positive values for c indicate a tendency to answer "same", negative values indicate a tendency to answer "different". The correction of d' and c measures used 1/number of same trials for cases without false alarms and 1–1/number of different trials for the maximum number of hits. d' and c were analyzed with (1) a 2 × 3 ANOVA with Group (patients vs. control participants) as the between-participants factor and Condition (words, tones, visual) as the within-participant factor, and (2) a 2 × 3 ANOVA with Patient group (patients with left lesions vs. patients with right lesions) as the between-participants factor and Condition (words, tones, visual) as the within-participant factor. Post-hoc analyses
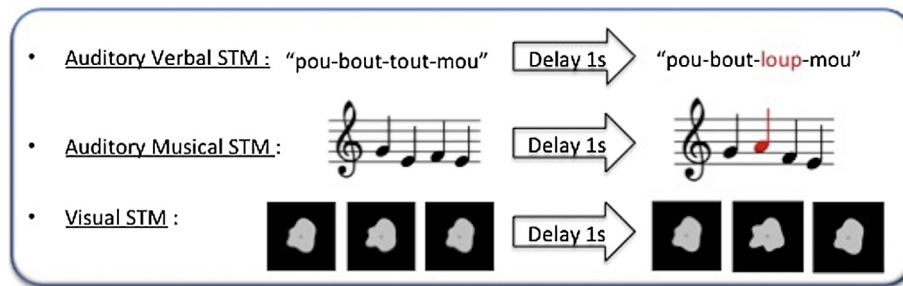
Fig. 1. Neuropsychological assessment for STM. For each task, participant have to indicate if the two sequences are the same or different. All sequences have the same duration (2.1 s).

for significant effects or interactions were carried out using Fisher LSD tests.

We also used multiple regression models to correlate performance on STM tasks with the results of neuropsychological assessment. As we could not collect Pitch Discrimination Threshold data for two patients (P007 and P019), the regression analyses were carried out with 18 patients.

2.5. Lesion analysis

For 19 out of the 20 patients, an anatomical MRI was acquired at the end of the second session of behavioral tests. One patient had cardiac surgery with placement of an implantable defibrillator before the second appointment. The analysis of his lesion was thus conducted on a T2Flair MRI performed 12 months after stroke.

Participant lesions were imaged with 3D MRI scans (Magnetom Prisma Siemens 3T MRI equipped with a 64-channel head/neck coil), with T1, T2 and T2FLAIR sequences (Fluid-Attenuated Inversion Recovery scan: TR = 5000 ms, TE = 349 ms, TI = 1008 ms, FOV = 224 × 224 mm, sagittal acquisition, slice thickness = 0.9 mm, 192 slices). Lesions were drawn manually by a trained neurologist[1] on the individual's T2FLAIR MRI images in native space, using MITK 3M3 (Mint Medical Ins, USA) and then checked against the T1 and T2 images, to be as accurate as possible (see also Dinomais et al., 2015)). Hyper-intense areas on T2FLAIR were defined as part of the lesion because MRIs were done several months after stroke, hence after oedema resorption. MRI images and lesions masks were normalized into the MNI (Montreal Neurological Institute) space, using the standard linear spatial normalization procedure from SPM12 (Functional Imaging Laboratory, London, UK) in Matlab R2014B (Mathworks Inc., Natick, MA, USA).

To get insights into the anatomic correlates of the auditory STM tasks, we used "Voxel-based Lesion Symptom Mapping" (VLSM, Bates et al., 2003, with the toolbox "VLSM2" in Matlab R2014B (Mathworks Inc., Natick, MA, USA)). In VLSM, a *t*-test is used at each voxel to compare performance on a given measure (e.g., musical STM performance) in individuals with a lesion at that voxel versus individuals without a lesion at that voxel (based on the lesion masks created during the previous step). The advantage of the VLSM approach, compared to a ROI-based approach is that it does not make any a priori assumptions regarding relevant subgroups of patients (e.g., patients with temporal lesions vs. patients with frontal or parietal ones, see Supplementary Fig. 1 for such an analysis). As the present study included only 20 patients[2] which is below the

current practice in the VLSM literature, with typically >40 patients tested (e.g., Dovern et al., 2011), the present analysis was exploratory and used a liberal statistical threshold cut-off with alpha set at 0.001 at each voxel. To increase the power of the VLSM analysis we combined the data from both hemispheres by flipping the right lesions on the left hemisphere (see below). The VLSM analysis was run for the d' for the three STM tasks separately.

3. Results

3.1. Participants

Demographic data are presented in Tables 1 and 2. Twenty patients and fourteen control participants were included. Among the 20 patients, ten had lesions in the left hemisphere and ten in the right hemisphere. The delays since stroke varied from 4 to 52 months, for a median of 13 months. The volumes of the residual lesions at distance from the stroke varied from 0.1 to 68.4 mL, for a median of 9.45 mL. There were no significant differences between patients with left and right lesions for the delay since stroke and lesions size.

The three groups were comparable for sex ratio, level of education, number of years of regular musical practice, and audiometry. All participants were right-handed (right writing hand).

3.2. Neuropsychological assessment

The results of neuropsychological assessment are presented in Table 3. Patients had lower MMSE scores than control participants. But with the MMSE cut-off score adapted for age and education, only two patients (P003 and P004) had a mild cognitive disorder. Patients had reduced fluencies (lexical and categorical) when compared to control participants. There were no differences between the two groups of patients for the neuropsychological assessment. All participants obtained the maximal score for the battery of denomination, BARD (10/10).

3.2.1. MBEA
The cut-offs (mean −2SD) were calculated from MBEA scores of 421 participants (http://www.brams.umontreal.ca/plab/publications/article/57#extras) (Peretz et al., 2003). The cut-off score to be considered as amusic is ⩽22.4/30 for participants under sixty years, and ⩽21.6/30 for participants over sixty years.

Based on these criterions, three patients and two control participants were diagnosed as amusics. The three patients (P003, P014 and P015) had lesions in the left hemisphere and their scores were 18.5/30, 17.7/30 and 18.7/30, respectively. They were all older than sixty. The two control participants (congenital amusics) had MBEA scores of 20.5/30 and 20.7/30 and they were both under sixty years old.

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[1] Manual drawing of lesions was also performed by a second rater. We then re-ran the VLSM analysis with this second set of lesion masks, which led to results in agreement with those reported here.

[2] Note however that the current study is one of the largest lesion-led studies in terms of number of stroke patients included in the music cognition domain (with 20 patients as in Ayotte, Peretz, Rousseau, Bard, & Bojanowski, 2000; Schuppert et al., 2000). To the best of our knowledge, only the studies by Särkämö et al. (2009, 2010) were larger in terms of sample size (n = 53).

Table 1
Demographic data of patients and control participants.

	Right lesions (N = 10)	Left lesions (N = 10)	Control participants (N = 14)	p (group effect) Patients (N = 20) vs. Control participants (N = 14)	p (group effect) Left (N = 10) vs. Right (N = 10) lesions
Sex ratio M/F	4/6	7/3	7/7	p = 0.8	p = 0.2
Age (years)	58.8 ± 10.3 (48–74)	62.3 ± 13.2 (37–85)	59.1 ± 10.7 (37–73)	p = 0.7	p = 0.5
Education (years)	10.8 ± 2.9 (5–14)	12.2 ± 4.1 (5–16)	13.4 ± 4 (5–20)	p = 0.2	p = 0.4
Musical practice (years)	0.3 ± 0.9 (0–3)	5.9 ± 15.8 (0–50)	3.7 ± 11.9 (0–45)	p = 0.9	p = 0.3
Time since stroke (months)	18 ± 18 (4–52)	16.6 ± 13.3 (7–50)	NA	NA	p = 0.8
Size of lesion (mL)	16.1 ± 19.7 (0.1–67.6)	21.6 ± 20.1 (1–68.4)	NA	NA	p = 0.5
RE Audiometry (dB)	18.9 ± 12.2 (7.5–46.25)	22.6 ± 8.5 (8.75–36.25)	19.9 ± 9.6 (7.5–42.5)	p = 0.8	p = 0.4
LE Audiometry (dB)	21.1 ± 13.9 (6.25–46.25)	21.5 ± 12.4 (7.5–43.75)	17.4 ± 11.6 (0–42.5)	p = 0.4	p = 0.9

For each parameter the group average, standard deviation and range is reported. Between-group differences were assessed with a chi2 test for the sex ratios and with *t*-tests for the other variables. Musical practice is the number of years of regular music practice. Removing the participants with extreme values on this parameter (one patient with 50 years of musical practice, and one control with 45 years of musical practice) did not change the results of the between-group comparisons (p = 0.9 for the comparison between patients and controls, p = 0.5 for the comparison between patients with left and right lesions). The audiometry is calculated as the average hearing threshold at 500, 1000, 2000 and 4000 Hz for each ear. RE: right ear; LE: left ear.

Table 2
Demographic data of patients.

Patient	Sex	Age (years)	Education (years)	Musical practice (years)	Time since stroke (months)	Laterality of lesion	Size of Lesion (ml)	RE Audio-metry (dB)	LE Audio-metry (dB)
P001	F	69	5	0	10	R	9.4	16.25	8.75
P002	F	62	12	0	10	R	19	16.25	20
P005	F	60	12	0	4	R	0.1	46.25	45
P008	F	49	12	0	52	R	7	22.5	13.75
P009	M	53	11	0	14	R	3.7	11.25	20
P012	M	48	14	3	5	R	4.7	7.5	6.25
P013	M	51	12	0	14	R	26.4	13.75	22.5
P016	F	49	12	0	13	R	9.5	10	15
P019	F	74	6	0	51	R	67.6	33.75	46.25
P020	M	73	12	0	7	R	13.8	11.25	13.75
P003	M	66	14	0	7	L	24.5	23.75	15
P004	M	56	12	0	9	L	7.8	8.75	7.5
P006	M	65	5	50	20	L	8.8	18.75	17.5
P007	M	50	16	0	26	L	68.4	25	26.25
P010	M	56	11	0	13	L	28	17.5	10
P011	M	72	14	0	17	L	11.2	36.25	43.75
P014	F	85	5	0	7	L	6.1	32.5	33.75
P015	M	70	16	0	9	L	38.4	30	33.75
P017	F	66	14	0	8	L	21.7	15	18.75
P018	F	37	15	9	50	L	1	18.75	8.75

R: right; L: left. See Table 1 for details.

Table 3
Neuropsychological assessment for all participants (mean, SD and range for the different parameters tested).

	Right lesions (N = 10)	Left lesions (N = 10)	Control participants (N = 14)	p (group effect) Patients (N = 20) vs. Control participants (N = 14)	p (group effect) Left (N = 10) vs. Right (N = 10) lesions
MMSE (/30)	**27.8 ± 1.8 (25–30)**	**27.3 ± 3.1 (23–30)**	29.2 ± 0.9 (27–30)	**p = 0.02**	p = 0.7
BARD (/10)	10 ± 0	10 ± 0	10 ± 0	NA	NA
Lexical fluencies	**17.1 ± 7.7 (3–25)**	**16.3 ± 8 (6–28)**	22.7 ± 7.1 (13–35)	**p = 0.03**	p = 0.8
Categorical fluencies	**25 ± 6.1 (15–36)**	**26.5 ± 8 (15–35)**	31.9 ± 9.9 (18–53)	**p = 0.04**	p = 0.6
PDT (semi-tones)	1.4 ± 1 (0.15–3.27)	1.5 ± 1.6 (0.16–4.67)	1 ± 1.2 (0.17–4.42)	p = 0.3	p = 0.9
MBEA score (/30)	24.6 ± 1.8 (22.5–27.5)	22.8 ± 3.5 (17.67–26.67)	24.5 ± 2.3 (20.5–27.83)	p = 0.4	p = 0.2

Patients had a lower MMSE score in comparison with control participants (but note that all except two were normal in comparison to age and education-related norm). They also had reduced fluencies (lexical and categorical) in comparison with control participants (scores highlighted in bold).

At the group level, there was no difference between the patients and control participants for the MBEA score (F(1,32) = 0.7; p = 0.4) and between the two groups of patients (left vs. right lesion) (F(1,18) = 2.1; p = 0.2).

3.2.2. PDT

The pitch discrimination thresholds were ranging from 0.15 to 4.67 semi-tones in patients and from 0.17 to 4.42 semi-tones in control participants (see Table 3). PDT inferior to one semi-tone is considered normal in young people, but a decrease of frequency

selectivity was expected with aging (Patterson, Nimmo-Smith, Weber, & Milroy, 1982). There was no significant difference between patients and control participants (F(1,30) = 1; p = 0.3) and between the two groups of patients (F(1,16) = 0.02; p = 0.9).

3.3. Short-term memory tasks

For performance in d' (Fig. 2), the first ANOVA comparing patients and controls revealed a significant main effect of condition (F(2,64) = 7.6; p = 0.001): post hoc analyses showed that d' of the
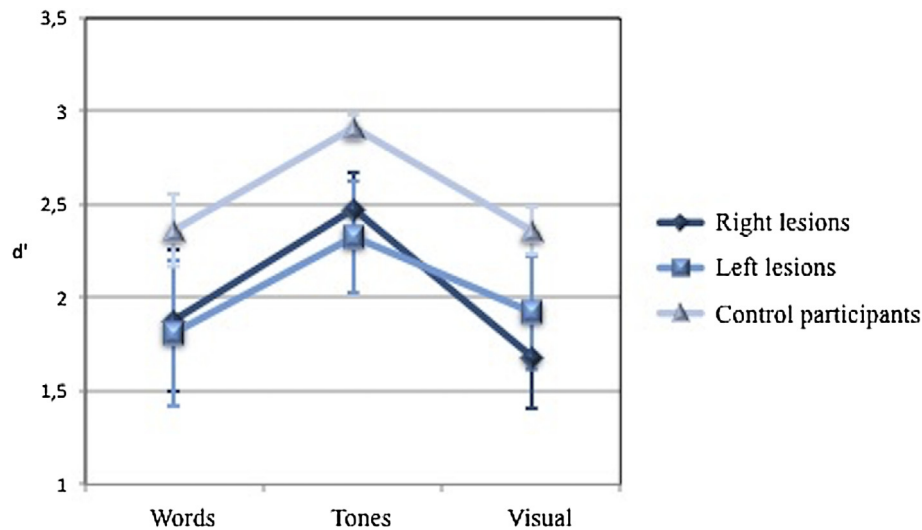
Fig. 2. Performance (d′) for short-term memory tasks presented as a function of material and participant group. d′ for the three groups (patients with left lesions, patients with right lesions, control participants) for the three STM tasks (words, tones, visual). Overall the patients had lower performances in comparison with control participants, regardless of the material to be memorized. The musical task was easier than the verbal and visual tasks for all groups.

auditory musical task (tones) was higher than $d′$ of the auditory verbal task ($p = 0.001$) and the visual task ($p < 0.001$), while $d′$ of verbal and visual tasks did not differ ($p = 0.87$).[3] There was a significant main effect of group ($F(1,32) = 6.2$; $p = 0.02$), with patients having lower performance than control participants. The interaction between the two factors was not significant ($F(2,64) = 0.005$; $p = 0.99$). The second ANOVA comparing the two patient groups confirmed the main effect of condition ($F(2,36) = 3.73$; $p = 0.03$), and showed that there was no difference between the two groups of patients ($F(1,18) = 0.0003$; $p > 0.98$), and no significant interaction between the factors Group and Condition ($F(2,36) = 0.35$; $p = 0.7$).

The same analyses were performed for the criterion c. For the first analysis (patients vs. controls), only the main effect of group was significant: patients had a higher criterion c ($c = 0.21 \pm 0.32$, mean ± SD) in comparison with control participants ($c = 0.06 \pm 0.24$) ($F(1,32) = 4.7$; $p = 0.04$). The main effect of condition and its interaction with group were not significant ($p > 0.1$). For the second analysis (patients with left lesions vs. patients with right lesions), there was no significant effect (all $p > 0.3$).

Overall, analyses of $d′$ and the criterion c in STM tasks revealed that patients had lower performance than controls in all tasks and that this was due to missing differences between S1 and S2 (they answered "same" more often than did control participants). There was no significant difference between patients with left or right lesions as groups for any of the measures of interest.

The individual results (Table 4 and Supplementary Fig. 1) revealed that (1) five patients had deficits in auditory verbal STM (with a cut-off defined as 2SD below the mean of the control participants): three patients with a lesion in the right hemisphere and two patients with a lesion in the left hemisphere; (2) nine patients had deficits in auditory musical STM: four with a right-hemisphere lesion and five with a left-hemisphere lesion; and (3) six patients had deficits in visual STM: three with a left-hemisphere lesion and three with a right-hemisphere lesion.

Among the five patients with deficits in verbal STM, four had also deficits in musical STM, and three of the five also in visual STM. Two of these cases are noteworthy: P009 had verbal, but not musical auditory STM deficits, and P003 had the second largest deficit in verbal STM of patients in the present sample, but he only

Table 4
Individual performance of the patients for the STM tasks.

Patients	Lesion	d' words	d' tones	d' visual
P001	R	**0.887**	**1.308**	1.853
P002	R	2.376	**2.023**	2.023
P005	R	2.326	2.685	2.257
P008	R	3.069	**2.209**	2.209
P009	R	**1.163**	3.069	**1.11**
P012	R	2.602	3.069	3
P013	R	2.685	3.069	**0.993**
P016	R	3.036	2.422	2.038
P019	R	**-0.821**	**1.809**	**-0.294**
P020	R	1.469	3.069	1.692
P003	L	**-0.646**	**2.209**	1.438
P004	L	1.853	3.069	1.639
P006	L	1.825	3.069	**1.349**
P007	L	1.562	2.685	3.069
P010	L	3.069	3.069	3.069
P011	L	**0.25**	**1.659**	**1.163**
P014	L	2.422	**0.075**	1.534
P015	L	1.639	**1.965**	**0.318**
P017	L	3.069	3.069	3.036
P018	L	3.069	**2.376**	2.612
Cut-off		0.9	2.4	1.4
Cut-off without outlier		1.4	NA	NA

The cut-offs are defined as below 2SD from the mean of control participants' performance. Performance below the cut-off are highlighted in bold and with a grey background. For the verbal STM task, one control participant was below the cut-off ($d′ = 0.588$), so we recalculated the cut-off without this data point (last line of the table). Performances below this corrected cut-off are highlighted with a grey background.
L = left; R = right.

had a small impairment for musical STM. In contrast, among the nine patients with deficits in musical STM, four did not have any deficit in verbal and visual STM (we describe the most striking case, P014, below) and one had deficits in musical and visual STM, but not verbal STM. Finally three patients had only a visual STM deficit.

Additionally, we tested the correlations between the performances ($d′$) in the different STM tasks. For patients, $d′$ for the verbal

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[3] Note that the visual task was designed to be slightly more difficult than the auditory tasks to avoid overlooking generalized STM deficits.

task was correlated with d' for the visual task ($r(18) = 0.64$; $p = 0.003$), but not with the musical task ($r(18) = 0.26$; $p = 0.3$), and the d' of the musical and visual tasks did not correlate ($r(18) = 0.32$; $p = 0.2$). For control participants, there was no correlation between the three tasks ($p > 0.17$).

Finally, as some of the participants had elevated PDT, we checked whether these pitch discrimination deficits might hinder the performance in the musical STM task and cause the observed between-group differences. For that purpose, the different trials in the musical STM task were sorted into two classes, corresponding to large changes between S1 and S2 (at least 5 semi-tones) and small changes (3 or 4 semi-tone changes). Each of the two classes contained 8 trials (per participant). Note that the large changes were above the PDT of every participant. d' were recalculated for each class of trials and participant, and analyzed with an ANOVA with Group (Patients vs. Controls) and Size of change as factors. The ANOVA revealed a main effect of Group ($F(1,32) = 4.502$; $p = 0.04$) with controls outperforming patients (as expected from the main analysis), and a main effect of Size of change ($F(1,32) = 8016$; $p = 0.008$) as expected (see also Albouy et al., 2013). However, the critical Group-by-Size of change interaction was not significant ($F(1,32) = 0.511$; $p = 0.5$). The patients' musical STM deficit was thus observed for all sizes of changes, including changes larger than the worst PDT observed.

3.4. Case report of a selective deficit to music

We here discuss the case of P014, an 85-year-old woman without any musical training. She had a stroke in the left hemisphere (resulting in two lesions in frontal and parietal areas) seven months before the present study. The MBEA scores revealed her as amusic: her mean MBEA score was 17.7/30 (cut-off = 21.6/30),

with a score at chance level (15/30) for each of the first three sub-tests. In addition, she had an elevated pitch discrimination threshold at 3.3 semi-tones. Her performance for the musical STM task ($d' = 0.075$) was 9 SD below the cut-off, while her performance for verbal and visual STM tasks was normal ($d' = 2.42$ and $d' = 1.53$ respectively). In sum, the results reveal that she performed at chance level for all musical tasks involving pitch memory (the first three sub-tests of the MBEA, the musical STM task investigated here) and that her deficit was specific to music. Interestingly, the patient had no complaints about potential difficulties with music perception. The patient's auditory deficit would thus have been completely overlooked by standard clinical examination.

3.5. Regression models between the neuropsychological assessments and performance in the STM tasks

Multiple regression models were performed aiming to explain performance on each STM task by the results of neuropsychological assessments for all participants. For the d' of each task, we aimed to explain performance with age, MBEA score, PDT, MMSE score, lexical and categorical fluencies.

For the verbal task, the regression model was marginally significant ($F(6,25) = 2.2$; $r^2 = 0.34$; $p = 0.08$), with lexical fluency as the only significant predictor ($\beta = 0.06$; $p = 0.04$). For the musical task, the model was significant ($F(6,25) = 4.2$; $r^2 = 0.50$; $p = 0.005$), with PDT as the only (marginally) significant predictor of performance ($\beta = -0.20$; $p = 0.07$). For the visual task, the model was not significant ($F(6,25) = 1.7$; $r^2 = 0.29$; $p = 0.16$). The corresponding scatter plots between the performance of the STM tasks and the neuropsychological assessment are shown in Fig. 3.
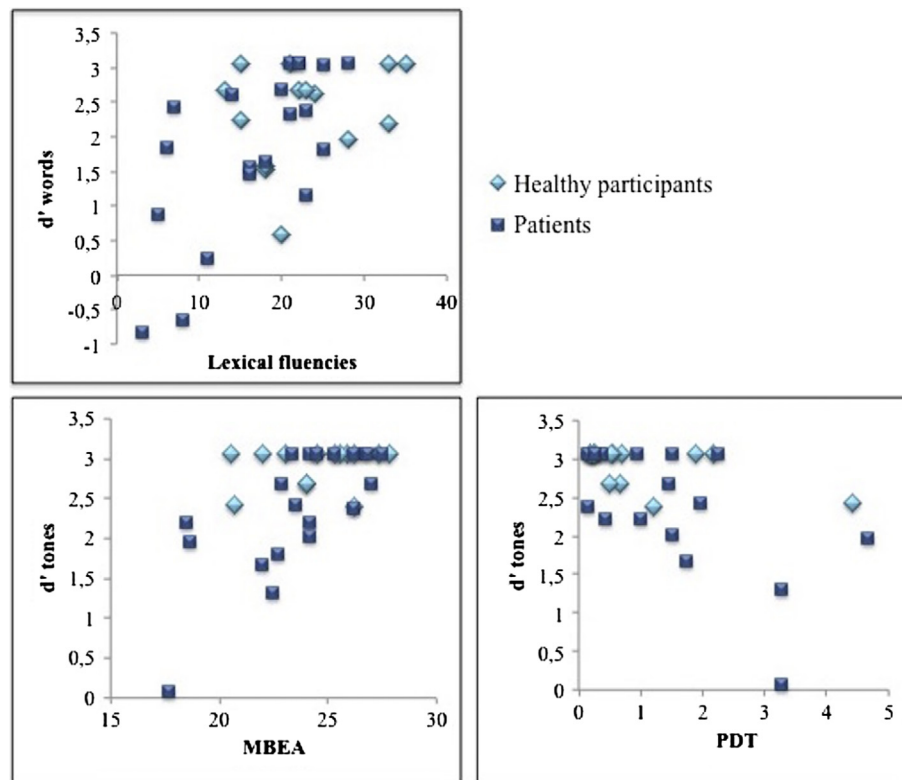

Fig. 3. Scatter plots: Performance (d') in STM tasks as a function of the neuropsychological assessment for all participants. There is a significant relation between the performance for the verbal STM task and the lexical fluencies across all participants (see main text for the results of the regression analysis). There is a significant relation between the performance for the musical STM task and the MBEA in patients and a significant relation between this STM task and the PDT in controls and across all participants. Lexical fluencies are expressed as the number of words produced in 2 min. For the MBEA, the maximum score is 30/30, chance level is 15/30. PDT is measured in semitones.

Table 5
Location of the lesions of the 20 patients.

		Temporal				Insula			Frontal		Parietal		BG
		HG med.	HG lat.	STG (excl. HG)	MTG	Post.	Med	Ant.	Pre-cent.	IFG	Post-cent	SMG	
P001	R					X	X						X
P002	R	X		X		X					X	X	
P005	R					X							
P008	R							X	X	X			
P009	R						X		X				
P012	R		X	X									
P013	R				X						X		
P016	R					X						X	
P019	R					X			X		X	X	
P020	R						X	X	X	X	X		
P003	L					X					X		
P004	L					X						X	
P006	L								X				
P007	L					X					X	X	
P010	L						X	X	X	X			
P011	L					X			X				
P014	L						X		X	X	X		
P015	L							X		X			
P017	L			X									
P018	L									X			

Abbreviations: L = left lesion; R = right lesion; BG = basal ganglia; SMG = supra-marginal gyrus; IFG = inferior frontal gyrus; STG = Superior temporal gyrus; MTG = medium temporal gyrus; HG = Heschl gyrus; med = medial; lat = lateral; excl = excluding; post = posterior; ant = anterior; cent = central.
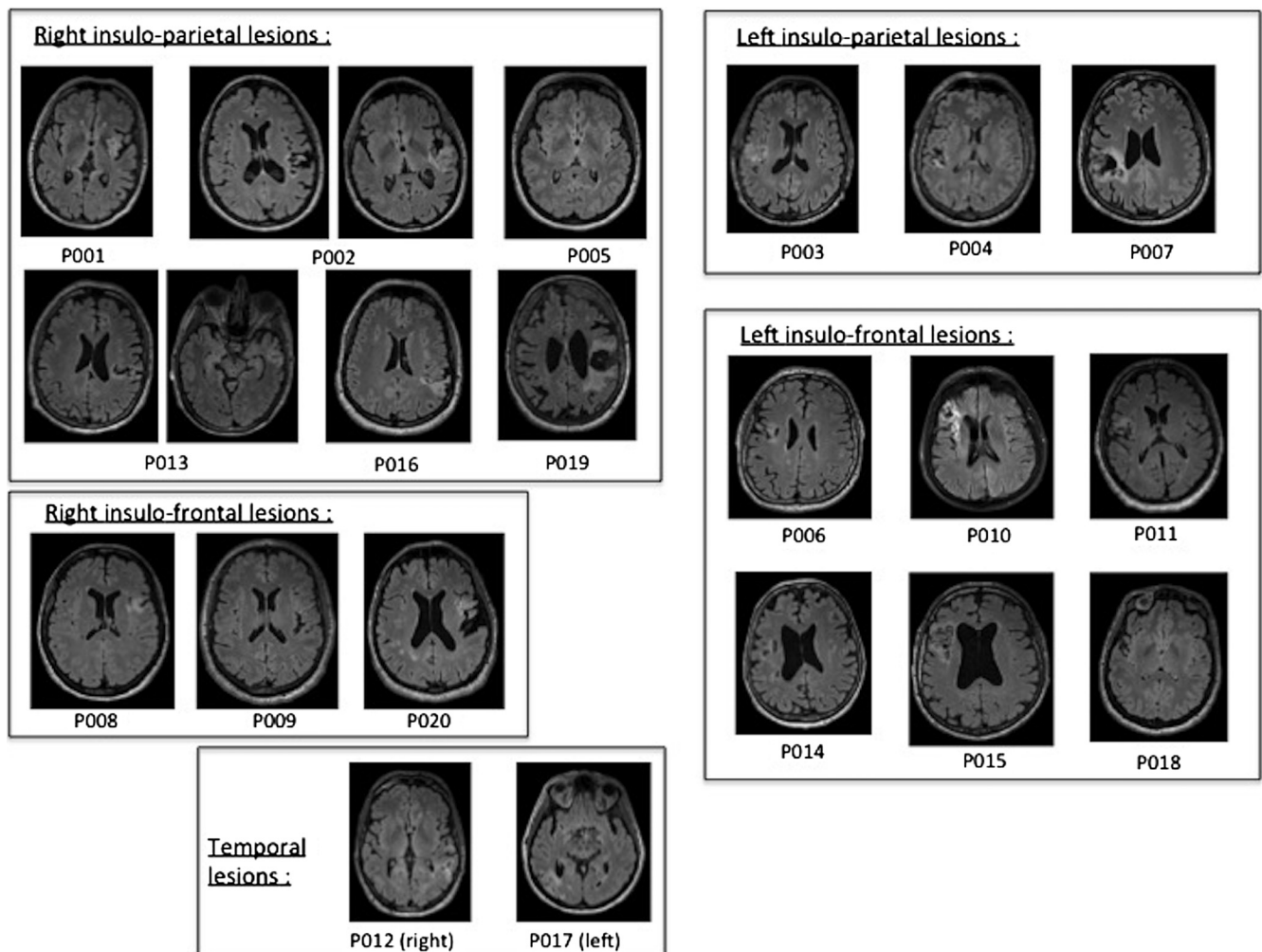
Fig. 4. MRI of the 20 patients. Axial slices, T2Flair sequences, showing the focal brain lesions.

In a second step, we performed these regression analyses separately for each group of participants. For control participants, the model was not significant for the verbal task ($F(6,7) = 0.7$; $r^2 = 0.38$; $p = 0.6$) and the visual task ($F(6,7) = 2.7$; $r^2 = 0.69$; $p = 0.1$), but it was significant for the musical task ($F(6,7) = 4.2$; $r^2 = 0.78$; $p = 0.04$), with PDT ($\beta = -0.25$; $p = 0.005$) and lexical fluency ($\beta = 0.03$; $p = 0.02$) as significant predictors. For patients, we added the size of the lesions as an explanatory factor. Note that none of the performance measure from the neuropsychological tasks and STM tasks was correlated with the size of the lesions ($p > 0.10$). The model was not significant for the verbal task ($F(7,10) = 1.8$; $r^2 = 0.56$; $p = 0.19$) and the visual task ($F(7,10) = 1.1$;

$r^2 = 0.44$; $p = 0.43$), but it was significant for the musical task ($F(7,10) = 4.2$; $r^2 = 0.75$; $p = 0.02$), with only the MBEA score being a significant predictor of performance ($\beta = 0.20$; $p = 0.03$). It is worth mentioning here that MBEA scores exhibited a somewhat greater variability in the patient group than in the control group (see Fig. 3).

3.6. Lesion analysis

The location of all patients' lesions is shown in Table 5 and illustrated on individual T2Flair MRIs in Fig. 4. For each of the STM tasks, we performed VLSM analyses. As performance for the STM
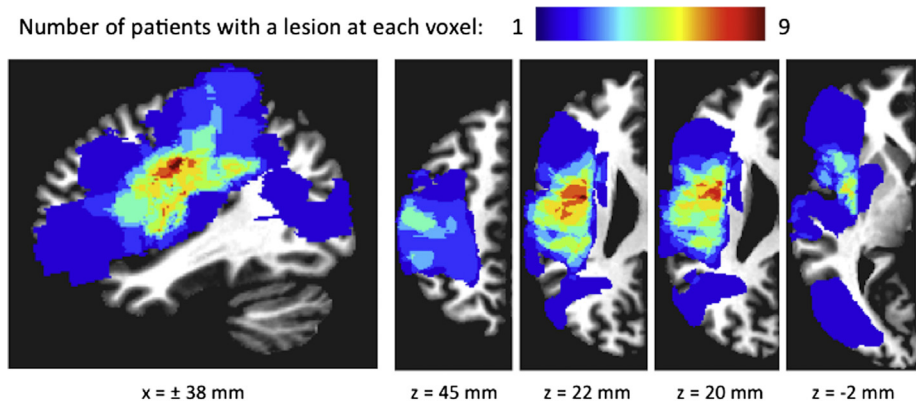

Fig. 5. Overlay of the 20 lesions. The number of patients having a lesion at each voxel is color-coded. The ten lesions in the right hemisphere have been flipped on left hemisphere for the VLSM analysis. There is a maximum of nine patients having a lesion in the same voxel. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 6
Significant clusters for the STM tasks in VLSM analysis.

	Cluster Volume	px	py	pz	cx	cy	cz	Max T	Location
Words	4854	±59	−12	11	±51	−18	31	5.93	Fronto-parietal operculum
	11	±44	0	21	±42	0	21	4.46	Fronto-parietal operculum
	227	±41	−17	40	±46	−18	47	3.68	Post-central gyrus
Tones	14	±32	−5	13	±33	−5	14	5	Insula
	93	±39	−2	−6	±41	−3	−4	4.63	Insula
	18	±54	−5	23	±54	−6	22	4.14	Fronto-parietal operculum
Visual	242	±33	−8	20	±40	−8	20	4.42	Fronto-parietal operculum
	12	±41	−1	21	±43	0	21	4.19	Fronto-parietal operculum
	20	±59	−2	21	±57	−3	21	3.84	Fronto-parietal operculum

The volume of clusters is in mm³. The MNI coordinates of the peak of clusters (px, py, pz) and the MNI coordinates of the center of clusters (cx, cy, cz) are represented. These clusters indicate that a lesion at this location had an effect on STM tasks ($p < 0.001$).
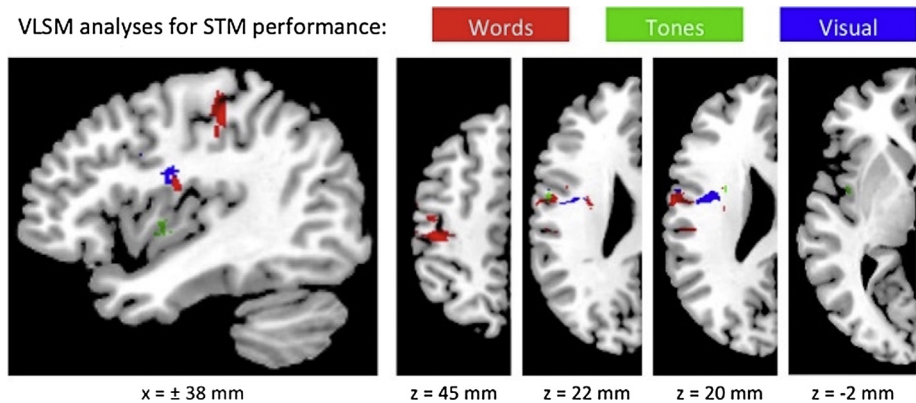

Fig. 6. Results of the VLSM analysis. For d′ in each STM task (words, tones, visual), a VLSM analysis was run on the lesion masks of the twenty patients. Significant clusters ($p < 0.001$, see Table 6 for peak and center coordinates) are depicted with a color for each task (red for words, green for notes and blue for visual). The VLSM analysis highlighted the involvement of dorsal areas for all STM tasks, particularly the words and visual tasks, and of more ventral areas for the musical task. Clusters are superimposed on the MNI template, and MNI coordinates are specified for each slice. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

tasks did not differ depending on the lateralization of the lesion, we combined the data from both hemispheres by flipping the right lesions on the left hemisphere aiming to increase the power of the statistical analysis. It should however be noted that the relative involvement of the left and right hemispheric structures cannot be assessed with this procedure. The overlay of the lesions for the 20 patients showed a maximum overlap of nine lesions in the same voxel (Fig. 5).

The significant clusters resulting from the VLSM analyses are presented in Table 6 and Fig. 6. They were grouped mainly in the central region, parietal lobe, and insula. Lesions in inferior fronto-parietal operculum (rolandic operculum, inferior pre-central and post-central gyrus) were associated with deficits in all three STM tasks. Lesions in the insula were associated to lower performance in the musical task, and parietal lesions with lower performance in the verbal task.

4. Discussion

The present study investigated deficits of verbal and musical auditory STM after stroke, and the cerebral correlates of the observed behavioral deficits using a voxel-based lesion symptom mapping approach. We used STM tasks that were well matched across materials, and we performed a thorough neuropsychological assessment covering peripheral auditory processing, language and music perception. We included patients with focal cortical lesions in regions of interest for auditory STM, i.e., temporo-parieto-frontal areas in the territory of the middle cerebral artery, based on previous findings of neuropsychological and neuroimaging studies. None of the patients had severe aphasia, neither severe functional or cognitive disability.

The two groups of patients (with either right- or left-hemisphere lesions) were matched for demographic data and also with control participants. For neuropsychological assessment and performance in the STM tasks, patients with a right- or a left-sided lesion did not differ. In comparison to the control participants, patients had lower scores on MMSE and verbal fluencies. This result suggests that stroke affected patients' general cognition, including language. STM deficits might contribute to these general cognitive difficulties. However, note that even though they had lower scores than the controls tested here, all patients (except two) were normal on the MMSE when considering age and education-related norms. For the STM tasks, patients had lower performances in comparison with control participants, regardless of the material type (words, tones, visual). The individual data revealed a double dissociation between some patients exhibiting verbal deficits without musical deficits or the reverse. The VLSM analysis showed the importance of inferior fronto-parietal operculum for auditory and visual STM. However, the sample size did not allow us to separate the two hemispheres in the VLSM analysis, and thus although the two patient groups did not differ as a whole, we cannot exclude differences between the two hemispheres regarding the involvement of specific brain structures in auditory and visual STM.

In the following, we discuss the selectivity of STM deficits, in particular with respect to the side of the lesion, the clinical application of our new assessment tool, and the brain correlates of STM as observed with VLSM, and finally, we propose an interpretation of the data within a connectionist framework.

4.1. Short-term memory deficits after stroke

We have studied auditory STM in brain-damaged patients, by comparing performance in the same task-setup applied to tones and to words. We also have studied visual STM, to evidence poten-

tial STM disorders, which were not specific for the auditory modality. The results showed that the musical task was easier than the verbal and visual tasks, which were similar in difficulty. Overall, stroke patients had poorer performance in all STM tasks, in comparison with control participants, regardless of the condition (words, tones, visual). Based on prior neuroimaging studies, we had targeted lesions of the temporal, parietal and frontal lobes.

In contrast to our hypothesis expecting more verbal deficits with left-hemisphere lesions and more musical deficits with right-hemisphere lesions, performance in the STM tasks (for words, tones and visual materials) did not differ between patients having lesions in either right or left hemispheres. Also, there were as many patients with STM deficits with lesions in either hemisphere. Overall, the present data suggest that bilateral networks are involved in verbal, tone, and visual memory.

For musical STM, previous imaging studies had shown the bilateral involvement of brain structures: using positron emission tomography (PET), Zatorre et al. (1994) showed that for short-term pitch retention in control participants, the right fronto-temporal cortex was activated. Using magneto-encephalography, Albouy, Mattout, et al. (2013) showed that bilateral fronto-temporal areas are involved in STM for pitch sequences. Other PET and fMRI studies congruently showed the implication of both hemispheres in auditory musical STM (Griffiths et al., 1999; Schulze, Gaab, & Schlaug, 2009).

For verbal STM, most neuroimaging studies showed predominant activation of the left hemisphere (Henson et al., 2000), but bilateral activation has also been shown, notably in the insula (Salmon et al., 1996), the temporal regions (Burton, Small, & Blumstein, 2000) and the parietal regions (Ravizza, Behrmann, & Fiez, 2005). However, the overall left-hemisphere bias observed in verbal working memory tasks should be taken with caution as most imaging studies use visually-presented verbal stimuli, whereas the activation is more bilateral in inferior parietal areas when auditory verbal stimuli are used (Crottaz-Herbette, Anagnoson, & Menon, 2004; Kirschen, Chen, & Desmond, 2010), as in our study. Furthermore, the verbal STM task used here mostly requires phonological memory with almost no demands on semantic processes and no demands on syntactic processes. Unlike semantic processing which involves the left inferior frontal gyrus, phonological processing does not necessarily recruit frontal areas and is associated to the activation of both hemispheres for fronto-temporal regions (Burton et al., 2000; Poldrack et al., 1999). For visual STM, also both hemispheres have been shown to be implicated (Christophel, Hebart, & Haynes, 2012).

The individual results showed double dissociations between patients exhibiting verbal deficits without musical deficits and the reverse (see Table 4 and supplemental Fig. 1). Also, there was no correlation between performance in the musical STM task and the verbal STM task in the patient group. One main conclusion, which can thus be drawn from the observed data, is that the cerebral networks involved in musical and verbal STM are to some extent distinct, and that the distinction between networks is not the laterality (relative involvement of both hemispheres).

4.2. Clinical application: interest of testing auditory short-term memory after stroke

Until now, classical neuropsychological assessments testing auditory STM use mostly verbal material, and for the testing of music processing, the MBEA is used. We propose a new STM test, which has the advantage to apply the same paradigm setup to different materials: it uses verbal, musical and visual material and is short (about 20 min), what is important to test brain-damaged patients, to limit fatigue and lack of concentration. As discussed

above, the tests also allow for observing selective deficits for the different materials (Schaal, Pfeifer, Krause, & Pollok, 2015).

The multiple regression models showed that performance in the verbal task was correlated with the lexical fluencies for all participants. This is in agreement with previously reported close links between auditory verbal STM and language production (Laures-Gore, Marshall, & Verner, 2011; Martin & Ayala, 2004; Potagas, Kasselimis, & Evdokimidis, 2011). For example, Potagas et al. (2011) showed a strong correlation between aphasia scores and verbal STM performance in aphasic patients.

Performance in the musical STM was correlated with the PDT for all participants and with the MBEA for all patients. Considering the paradigm and material manipulation, we can make the hypothesis that both STM and pitch discrimination play a role for good performance in the musical STM. For the control participants, performance was related to their pitch discrimination threshold. However, for the patients, the STM performance was related to the MBEA score. As four of the six subtests of the MBEA engage auditory STM, in addition to pitch, interval, contour and rhythm discrimination, memory seems to be a critical factor for the patients. The musical short-term memory task involved changes of pitch between three and nine semi-tones. Three patients and one control participant had a higher PDT than three semi-tones (P001, P014, P015, and C009). However as the musical STM deficit of the patient was observed for both small and large changes (above all participants' PDT) between the two tone sequences, this deficit could not be solely explained by the increased PDT of some patients.

Following the diagnosis criteria of the MBEA, three patients and two control participants emerged as amusic, even though none had specific complaints about music. The three patients had lesions in the left hemisphere, but it is important to also consider that the two groups of patients (left vs. right lesion site) did not differ on the MBEA score. This observation is in agreement with previous report showing acquired amusia in brain-damaged patients with lesion in either hemisphere (Peretz, 1990; Schuppert et al., 2000; Särkämö et al., 2009). The three amusic patients also had an auditory musical STM deficit. We reported the case of P014, which had a specific deficit on music with a MBEA score just above chance, an elevated PDT and a performance on musical STM task well under the cut-off. It is worth mentioning here that there are similarities between the current musical STM task and some subtests of the MBEA, notably the Contour subtest: both are delayed-matching-to-sample tasks involving contour changes. However, our test uses a simplified material with shorter isochronous melodies, which makes it adequate for the comparison with verbal STM, whereas the MBEA is designed to assess a wider palette of musical abilities, including rhythm.

The present study showed that different kinds of STM deficits can co-exist (musical, verbal, visual), even when the involved lesions are small and focal. In our study, even patients without cognitive deficit (assessed by MMSE and verbal fluencies) exhibited STM deficits. In a study investigating deficits of stroke patients, patients diagnosed as amusic also had other cognitive deficits, including working memory, semantic fluencies, executive functions and visuo-spatial cognition deficits, in comparison with the patients without acquired amusia (Särkämö et al., 2009, 2010). It therefore seems important to diagnose these associations of deficits, especially those involving language and music, to provide appropriate reeducation. Our STM tasks could be used in neuropsychological assessment after stroke for this purpose.

4.3. Brain correlates of auditory short-term memory

Here, we studied the encoding and maintenance of information in STM, and did not require manipulation of information as in clas-sical working memory tasks. With current tasks settings, participants didn't have time to repeat the sequences. We therefore expected that the parietal lobe would be more strongly involved in the verbal STM task than the frontal lobe, which is involved in the articulatory rehearsal component of working memory and speech production (Baldo & Dronkers, 2006). In line with this hypothesis, the VLSM analysis revealed that lower performance in the verbal STM task was associated to lesions in the inferior fronto-parietal operculum and the post-central gyrus. These results are in agreement with previously reported neuroimaging data: The superior temporal gyrus is involved in speech perception and the parietal lobe is related to the phonological store (Buchsbaum & D'Esposito, 2008; Salmon et al., 1996). The areas recovered by the VLSM analysis were slightly more anterior than the parietal clusters observed in previous neuroimaging studies, a finding that should however be interpreted with caution given the variability in the location of clusters reported in previous neuroimaging studies (see for example Buchsbaum & D'Esposito, 2008) and given the limited sample size in the VLSM analysis.

The VLSM analysis further revealed that lower performance in the musical task was associated to lesions in the insula and the inferior fronto-parietal operculum (clusters in the operculum obtained by VLSM were very close for musical, verbal, and visual performance see Table 6 and Fig. 6). For a task requiring the active retention of pitch, Zatorre et al. (1994) reported activations in inferior frontal and insular cortex, the planum temporale and the supramarginal gyrus. Stevens (2004) have compared STM for tones, voice and words using fMRI. The tone condition produced clusters in posterior insula, in posterior inferior temporal gyrus and supramarginal gyrus. Our results converge with functional neuroimaging studies, showing the involvement of insula and fronto-parietal cortex in auditory musical STM.

Schulze, Zysset, Mueller, Friederici, and Koelsch (2011) have reported a large overlap of neural resources underlying auditory STM for verbal and tonal information (Broca's area, premotor cortex, pre-SMA/SMA, left insular cortex and inferior parietal lobe). Here, we observed an overlap in central areas (inferior fronto-parietal operculum), and the insula seems to be more strongly involved in musical STM and the parietal lobe more strongly involved in verbal STM. Overall, even if the results of the VLSM analysis should be taken with caution given the sample size, they are in keeping with prior findings in particular showing the importance of the parietal lobe for phonological short-term memory and the involvement of fronto-parietal regions in auditory STM in general. They further suggest an involvement of more ventral areas in musical STM, an hypothesis that warrants further testing.

Finally, the VLSM analysis revealed that lower performance in the visual task was associated to lesions in inferior fronto-parietal operculum (rolandic operculum, inferior pre-central and post-central gyrus). These regions were also involved in auditory STM in our data. We assume that these central regions are implicated in the integration of information in STM, be it visual or auditory. Potagas et al. (2011) showed that verbal and visual STM deficits can coexist in aphasic patients, and suggested that this is due to a possible primary deficit in information retention.

4.4. Auditory short-term memory and the dual stream model

In addition to the interpretation focusing on the impact of lesions in specific cortical areas on STM performance (see above), another possible explanation of the deficits is that the lesions are located on pathways connecting frontal and temporal lobes, which induces a disconnection that is responsible for the deficits.

The dual stream model of auditory processing refers to a dorsal pathway and a ventral pathway connecting auditory cortices and frontal areas. The dorsal pathway corresponds to the superior lon-

gitudinal fasciculus, including the arcuate fasciculus. The arcuate fasciculus connects frontal, parietal and temporal lobes. It is involved in language and visuo-spatial processing (Catani & Thiebaut de Schotten, 2008). The ventral pathway includes the extreme capsule fiber system and the inferior longitudinal fasciculus. Kellmeyer et al. (2013) suggest that the dorsal language pathway is a fast path for phonological memory and articulatory network from the left inferior parietal lobule to the left inferior frontal gyrus. The ventral language pathway is important for lexical and semantic processing. In singing, the dorsal pathway is involved in automatic, category-based sound analysis, while the ventral pathway is involved in conscious access to perceptual information (Loui, 2015). The importance of the dorsal pathway for music memory has already been emphasized (Rauschecker, 2014). In keeping with this hypothesis, in congenital amusia, there is a disconnection of the right superior branch of arcuate fasciculus, in tractography (Loui, Alsop, & Schlaug, 2009, but see Chen et al., 2015), causing pitch perception and STM deficits.

In our study, lesions in the inferior fronto-parietal operculum were linked to STM deficits for both auditory and visual materials. The arcuate fasciculus goes through this area. As previous data have shown that the arcuate fasciculus is involved in phonological and visuo-spatial processing, we make the hypothesis that lesions in the fronto-parietal operculum could cause a disconnection in the dorsal pathway, which might explain STM deficits. For the musical (pitch) task, our data suggest that both dorsal and ventral pathways are involved, in keeping with previous findings implicating both pathways in music processing (Musso et al., 2015). Indeed, the ventral pathway goes through the extreme capsule, right next to the insula. Future research should use the methodology of Diffusion Tensor Imaging to further shed light on the involvement of ventral and dorsal pathways in various types of STM, and in music processing in general.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.bandc.2017.01.003.

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