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# Improving left spatial neglect through music scale playing

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The study assessed whether the auditory reference provided by a music scale could improve spatial exploration of a standard musical instrument keyboard in right-brain-damaged patients with left spatial neglect. As performing music scales involves the production of predictable successive pitches, the expectation of the subsequent note may facilitate patients to explore a larger extension of space in the left affected side, during the production of music scales from right to left. Eleven right-brain-damaged stroke patients with left spatial neglect, 12 patients without neglect, and 12 age-matched healthy participants played descending scales on a music keyboard. In a counterbalanced design, the participants' exploratory performance was assessed while producing scales in three feedback conditions: With congruent sound, no-sound, or random sound feedback provided by the keyboard. The number of keys played and the timing of key press were recorded. Spatial exploration by patients with left neglect was superior with congruent sound feedback, compared to both Silence and Random sound conditions. Both the congruent and incongruent sound conditions were associated with a greater deceleration in all groups. The frame provided by the music scale improves exploration of the left side of space, contralateral to the right hemisphere, damaged in patients with left neglect. Performing a scale with congruent sounds may trigger at some extent preserved auditory and spatial multisensory representations of successive sounds, thus influencing the time course of space scanning, and ultimately resulting in a more extensive spatial exploration. These findings offer new perspectives also for the rehabilitation of the disorder.

Patients suffering from unilateral spatial neglect fail to report, respond to, and orient towards stimuli and events occurring in the side of space contralateral to the damaged cerebral hemisphere (contralesional), and to explore that side of space. Spatial neglect is

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more frequent and severe in brain-damaged patients with lesions in the right hemisphere and involves the left, contralesional, side of space (Heilman & Valenstein, 2011; Vallar & Bolognini, 2014). The deficit of physical exploration of personal and peri-personal space severely impairs patients with spatial neglect in several activities of their daily life. For example, patients may fail to eat the food on the left half of their plate, even though they complain of being hungry. Neglect patients may ignore the contralesional side of their body, shaving or applying make-up only to the non-neglected side. These patients may frequently collide with objects or structures such as doorframes on the side being neglected.

The mental representation of space is believed to share a common coding of magnitude information with several other domains, such as time (DeLong, 1981; Vicario *et al.*, 2008), numbers (Cattaneo, Fantino, Mancini, Mattioli, & Vallar, 2012; Cutini, Scarpa, Scatturin, Dell'Acqua, & Zorzi, 2012), and auditory pitch (Lidji, Kolinsky, Lochy, & Morais, 2007; Rusconi, Kwan, Giordano, Umiltà, & Butterworth, 2006; for reviews, see Walsh, 2003 and Winter, Marghetis, & Matlock, 2015). Owing to this commonality, the impaired spatial exploration of patients with neglect could be improved by the ancillary use of non-spatial feedback, so long as a common magnitude coding is implied. In music therapy settings, sounds are frequently used to support spatial awareness, leveraging on various mechanisms such as the combined spatial–auditory mapping offered by musical instruments, the increase of arousal due to auditory stimulation, and the positive effect on cognitive performance of positive emotions elicited through music (see Guilbert, Clément, & Moroni, 2014 for a review). For example, a recent study has provided evidence of improvement in spatial neglect following a 4-week music therapy intervention: Patients practiced scales and melodies on a custom chime-bar instrument, in which the spacing between the bars could be progressively enlarged, thus inviting increasingly wide exploration (Bodak, Malhotra, Bernardi, Cocchini, & Stewart, 2014). The present paper deals with the specific mechanisms through which sounds may facilitate spatial exploration in patients with spatial neglect. An interesting candidate is the well-known phenomenon by which pitch height is mapped onto an internal representation of space (Spatial-Musical Association of Response Codes, SMARC effect, Rusconi *et al.*, 2006). For example, it has been shown that individuals are faster and more accurate in providing a manual response in a relatively higher region of the space when primed by a high-pitch note, compared to a low-pitch note (Lidji *et al.*, 2007; Rusconi *et al.*, 2006). A musical keyboard, in principle, offers the opportunity for a spatial–auditory mapping along the horizontal dimension (left-to-right): This is directly relevant for the lateral impairment that characterizes spatial neglect. In this way, low pitches could be used to facilitate movement towards the left, neglected, space. However, the transfer from the vertical to the horizontal dimension of the spatial–music associations is not straightforward. While a horizontal spatial–auditory mapping is found in individuals with years of training on a horizontal music keyboard like pianists (Lidji *et al.*, 2007; Rusconi *et al.*, 2006), its existence in non-musicians and even in non-pianist musicians is still controversial (Lega, Cattaneo, Merabet, Vecchi, & Cucchi, 2014; Trimarchi & Luzzatti, 2011). Auditory pitch has yet another property that could potentially support a spatial mapping, even for participants without musical training: The possibility of being organized in predictable sequences, like music scales.

There is some evidence that producing a continuous and regular sequence may improve the spatial exploration of the contralesional side of space by right-brain-damaged patients with left neglect. Ishiai *et al.* (1990) tested the effect of counting targets in a cancellation task, rather than simply cancelling them: They found that numbering significantly improved search and reduced left neglect, compared to simple cancellation. As counting involves the production of a continuous, regular sequence, the motivation to continue searching may have been boosted by the expectation of the subsequent number (Ishiai *et al.*, 1990). A limitation of this interesting study is however the absence of control participants, particularly for non-specific effects, due to a greater general activation (cognitive, attentional non-spatial, see Corbetta & Shulman, 2011), which prevents drawing more definite conclusions as for the precise mechanisms involved.

This study aimed at assessing the hypothesis that auditory sequences with predictable features may bring about an improvement of left spatial neglect. Specifically, we investigated whether scale playing with an audible regular diatonic pitch sequence promotes a more thorough exploration of a standard musical instrument keyboard, compared to no sound or random pitches. The sounds of the Western major music scale constitute a structured pattern that is profoundly ingrained in the auditory representation of Western individuals, including non-musicians. Western listeners have been shown to be sensitive to the statistical structure of Western musical scales (Krumhansl & Kessler, 1982). This sensitivity increases for individuals with greater musical experience, but it is also found in naïve listeners (Krumhansl & Shepard, 1979). For example, when asked to rate how well different tones complete a standard seven-tone major scale, listeners faithfully reproduce the hierarchy that underlies the construction of the scale, assigning highest ratings to the tonic tone, followed by the third and fifth scale degrees, the remaining scale degrees, and, finally, the sounds not pertaining to the scale (Krumhansl & Shepard, 1979). Non-musicians use the structure of the music scale when asked to transpose pattern of sounds (Attneave & Olson, 1971), and remember better sound sequences that are conforming to the tonal sequence, compared to random sequences (Dewar, Cuddy, & Mewhort, 1977). The discrimination of sounds that do not belong to the reference music scale appears as early as in 7-year-old children (Trainor & Trehub, 1994). On a more general level, sequences of sounds structured in a musical form are known to be a powerful trigger for movements (see Maes, Leman, Palmer, & Wanderley, 2013 for a review) and therefore could aid spatial exploration in brain-damaged patients with left spatial neglect. In particular, music and movement appear to share a dynamic structure (e.g., in terms of rate and direction of change, degree of smoothness) that would represent a common mechanism for the universal expression of emotions (Sievers, Polansky, Casey, & Wheatley, 2013). In the light of these findings, it has been argued that

> tonal scales constitute one of the most durable families of perceptual-motor schemata that have been observed in psychology, ranking perhaps only after the schemata of natural language in their stability and resistance to change in adult life. (Dowling, 1978, p. 345)

Here, we exploited the strength of the representation of the music scale, to promote spatial exploration in right-brain-damaged patients with left spatial neglect and without prior musical training. Patients actively played C major music scales by pressing in an ordered sequence the white keys of a 61-key piano keyboard, starting from the rightmost key (i.e., C6, the highest pitch on the keyboard), down to the leftmost key (C1, the lowest pitch, see Latham, 2002). By performing this task, the lateral right-to-left spatial direction is discretely mapped onto the auditory array of the descending C major music scale. We hypothesized that the musical representation of the descending scale would aid the spatial scanning of the contralesional space, when patients play the keyboard from right to left, resulting in a greater number of notes played.

A condition in which no sounds were produced on key press controlled for the role of descending music pitch for space exploration, while a random sound condition, in which the keyboard was programmed to produce a random pitch each time participants struck a key, controlled for any non-specific effect of musical tones on arousal (e.g., Robertson, Mattingley, Rorden, & Driver, 1998). Furthermore, a keyboard bisection task was performed to compare relatively more local versus global influences of the sound on space representation. In fact, Gallace, Imbornone, and Vallar (2008) have shown that right-brain-damaged patients with left neglect are able to perform segmentation tasks in both the ipsilesional and the contralesional side of the stimulus, provided that the segmentation unit is sufficiently short ('local' level of spatial processing). However, the spatial deficit becomes increasingly evident as the segmentation unit increases in size and the task approximates bisection ('global' level of spatial processing). In the present experiment, the integrity of local spatial processing was probed with the music scale task, performed in different auditory feedback conditions. Conversely, the integrity of global spatial processing was probed by asking participants to indicate the central key on the keyboard (i.e., a bisection task), immediately following each scale trial. Were the feedback of the music scale favouring both local and global spatial processing, we expect both sequential exploration and keyboard bisection to improve. On the other hand, it is possible that music scales will only improve the local level of spatial processing, where each key gets directly mapped onto a sound, leaving unaltered the defective performance at the bisection task.

## Method

### *Participants*

Twenty-four patients with right hemisphere lesions were initially included in the study. None of them had professional experience with music keyboards or any other musical instrument or singing. One patient with left spatial neglect was subsequently dropped from the study because she repeatedly failed to comply with the instruction of playing the keys only from right to left (see Procedure). The final sample included 23 patients (15 males, mean age $\pm$ standard deviation, *SD*: 70.91 $\pm$ 6.97, range: 57–82, mean education 11.13 $\pm$ 4.3 years, range 3–18). Nineteen patients had a cerebrovascular accident (10 ischaemic, nine haemorrhagic) and four a brain tumour. All lesions were confined to the right hemisphere. Brain lesions were imaged by CT or MRI scans. All patients were right-handed, with no history or evidence of previous neurological and psychiatric disorders, as well as of cognitive impairment (Mini-Mental State Examination, Grigoletto, Zappalà, Anderson, & Lebowitz, 1999; verbal reasoning task, Spinnler & Tognoni, 1987). One patient (P4) presented with a defective score in the task assessing global cognitive functions (Mini-Mental State Examination), but the examiner verified that his comprehension during the experimental manipulation was adequate. Motor, somatosensory, and visual half-field defects contralateral to the side of the hemispheric lesion (contralesional) were evaluated by a standard neurological examination (Bisiach & Faglioni, 1974). Anosognosia for neurological deficits was also assessed (Bisiach, Vallar, Perani, Papagno, & Berti, 1986).

The patients' demographic and neuropsychological data are reported in Table 1. Based on their performance in baseline visuo-spatial tasks, patients were subdivided into two subgroups: 11 patients with (N+) and 12 patients without (N−) left spatial neglect. The presence of left spatial neglect was determined on the basis of defective scores in at least one cancellation task (considering Letter, Bell, and Star cancellation tests), or in the

**Table 1.** Demographic and neuropsychological information of 23 right-brain-damaged patients

| Patient | Group | Sex/Age | Education (years of schooling) | Duration of disease (months) | Aetiology/lesion site/lesion volume (cc) | Neurological deficit | | | Anosognosia for neurological deficit | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | M | SS | V | M | SS | V |
| Pt1 (S.R.) | N+ | F/77 | 3 | 3.6 | I/P-ic-th/65.44 | +++ | +++ | +++ | +++ | +++ | +++ |
| Pt2 (A.S.) | N+ | F/82 | 10 | 5.2 | I/FP-in (Sylvian)/ 195.07 | +++ | +++ | +++ | – | ++ | ++ |
| Pt3 (G.F.) | N+ | F/75 | 8 | 20.8 | H/F/– | +++ | ++ | +++ | + | + | +++ |
| Pt4 (N.D.) | N+ | M/71 | 13 | – | N/F/70.17 | +++ | + | e | – | – | +++ |
| Pt5 (M.P.S.) | N+ | M/72 | 7 | – | N/bg/110.11 | +++ | +++ | +++ | – | ++ | ++ |
| Pt6 (F.E.) | N+ | F/77 | 5 | 1.3 | I/FTP/239.96 | +++ | +++ | +++ | ++ | +++ | +++ |
| Pt7 (M.A.) | N+ | M/59 | 13 | 1 | I/Sylvian/241.4 | +++ | +++ | ++ | – | +++ | +++ |
| Pt8 (V.A.) | N+ | M/70 | 8 | – | N/T/– | + | – | +++ | + | n.a. | ++ |
| Pt9 (DG.F.A.) | N+ | M/75 | 8 | 2 | H/TO/136.36 | +++ | e | + | + | ++ | ++ |
| Pt10 (C.G.) | N+ | M/68 | 13 | 1.1 | I/FTP/398.97 | +++ | +++ | +++ | – | +++ | +++ |
| Pt11 (B.I.) | N+ | M/64 | 18 | 16.5 | H/FT/127.44 | +++ | +++ | +++ | – | – | + |
| Pt12 (C.M.) | N– | M/68 | 13 | – | N/F/38.08 | – | + | – | n.a. | – | n.a. |
| Pt13 (A.G.) | N– | F/75 | 18 | 1.2 | H/F/– | + | + | – | – | – | n.a. |
| Pt14 (B.G.) | N– | M/65 | 13 | 12.2 | H/th/4.04 | +++ | +++ | – | – | – | n.a. |
| Pt15 (S.B.) | N– | F/57 | 13 | 5.8 | H/bg/19.98 | +++ | e | – | – | – | n.a. |
| Pt16 (C.G.) | N– | M/73 | 5 | 1 | I/bg-ic/10.19 | +++ | – | – | – | n.a. | n.a. |
| Pt17 (P.G.) | N– | M/81 | 13 | 1.1 | I/bg-in/3.27 | + | – | – | ++ | n.a. | n.a. |
| Pt18 (M.A.) | N– | F/67 | 5 | 1 | I/F-in-ec/5.58 | + | – | – | – | n.a. | n.a. |
| Pt19 (P.e.g.) | N– | M/76 | 18 | 1.5 | H/th-ic/4.25 | + | – | – | ++ | n.a. | n.a. |
| Pt20 (R.G.) | N– | M/75 | 13 | 27.6 | H/bg-ic-cr/7.71 | + | – | – | – | n.a. | n.a. |
| Pt21 (P.E.) | N– | M/76 | 13 | 3.7 | I/cr/23.64 | +++ | + | – | – | – | n.a. |
| Pt22 (B.C.) | N– | F/71 | 13 | 1.1 | I/bg-ic-cr/37.84 | +++ | e | – | – | – | n.a. |
| Pt23 (A.G.R.) | N– | M/57 | 13 | 1.2 | H/FT-in/115.48 | +++ | ++ | – | – | – | n.a. |

*Note.* N+/N– = presence/absence of left unilateral spatial neglect; F/M = female/male; I/H/N = ischaemic/hemorrhagic/neoplastic lesion; F = frontal; P = parietal; T = temporal; O = occipital; in = insula; ic = internal capsule; ec = external capsule; th = thalamus; bg = basal ganglia; cr = corona radiata; M/SS/V = left motor/somatosensory/visual half-field deficits; –/+ = absence of/mild; ++ = moderate; +++ = severe impairment; e = extinction of the left-sided stimulus after double simultaneous stimulation. n.a. = not assessed because the motor/somatosensory/visual field functions were normal.
Duration of disease is reported only for stroke patients.

line bisection task, with reference to available norms (see Table 2 and Appendix S1 for more details).

The N+ and N− groups' lesions were drawn on a standard MRI template with a 1-mm slide distance using MRIcro software (Rorden & Brett, 2000). Lesion mapping was performed by RR and LZ, and checked by GV (see Figure 1). The average lesion volumes were 176.1 cc (*SD* 106.15; range 65.44–398.97) for N+ and 24.55 cc (*SD* 32.84; range 3.27–115.48) for N− patients. Overall, lesions were more extensive in the N+ group, a finding in line with previous evidence (Cattaneo *et al.*, 2012; Hier, Mondlock, & Caplan, 1983a,b; Leibovitch *et al.*,1998). Twelve neurologically unimpaired healthy controls (group HC), matched for age, gender, and years of education (five males, mean age ± *SD*: 78.42 ± 7.94, range: 67–92, mean education 9.42 ± 5.26 years, range 5–18) were recruited to serve as controls. Musical processing abilities were assessed using the scale-violation test from the Melodic Organization section of the Montreal Battery of

**Table 2.** Baseline neuropsychological assessment for extra-personal and personal left spatial neglect

| | | | Target cancellation | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Letter | | Bell | | Star | | | |
| Patient | Group | Line bisection (%) | Total | L-R | Total | L-R | Total | L-R | Complex drawing | Personal neglect |
| P1 (S.R.) | N+ | +83.2[a] | 102/104 | 4[a] | n.a. | n.a. | 48/56 | 12[a] | 9.5[a] | 15[a] |
| P2 (A.S.) | N+ | +37.6[a] | 95/104 | 9[a] | 31/35 | 5[a] | 48/56 | 12[a] | 7[a] | 17[a] |
| P3 (G.F.) | N+ | +52.8[a] | 102/104 | 4[a] | 33/35 | 1 | 31/56 | 1 | 6.5[a] | 18 |
| P4 (N.D.) | N+ | +2.6 | 102/104 | 4[a] | 30/35 | 6[a] | 38/56 | 16[a] | 5.5[a] | n.a. |
| P5 (M.P.S.) | N+ | +77.5[a] | 100/104 | 6[a] | n.a. | n.a. | 49/56 | 11[a] | 7[a] | 18 |
| P6 (F.E.) | N+ | +38.5[a] | 100/104 | 6[a] | n.a. | n.a. | 49/56 | 11[a] | 10[a] | 18 |
| P7 (M.A.) | N+ | −2.8 | 6/104 | 6[a] | 4/35 | 4[a] | 16/56 | 14[a] | 1[b] | 17[a] |
| P8 (V.A.) | N+ | +89.2[a] | 99/104 | 7[a] | 34/35 | 2 | 51/56 | 9[a] | 8[a] | 18 |
| P9 (DG.F.A) | N+ | +30.4[a] | 42/104 | 18[a] | 23/35 | 7[a] | 39/56 | 5[a] | 3[a] | 18 |
| P10 (C.G.) | N+ | +25.4[a] | 97/104 | 9[a] | 30/35 | 6[a] | 51/56 | 9[a] | 9.5[a] | 18 |
| P11 (B.I.) | N+ | +2.8 | 50/104 | 48[a] | 14/35 | 8[a] | 2/56 | 2 | 10[a] | 18 |
| P12 (C.M.) | N− | −1.4 | 0/104 | 0 | 0/35 | 0 | n.a. | n.a. | 0 | n.a. |
| P13 (A.G.) | N− | −3.4 | 0/104 | 0 | 1/35 | 1 | 0/56 | 0 | 0 | n.a. |
| P14 (B.G.) | N− | −2.2 | 0/104 | 0 | 0/35 | 0 | 0/56 | 0 | 0 | 18 |
| P15 (S.B.) | N− | +0.2 | 0/104 | 0 | 0/35 | 0 | 0/56 | 0 | 0.5[b] | 18 |
| P16 (C.G.) | N− | +2.4 | 2/104 | 2 | 2/35 | 2 | 1/56 | 0 | 1[b] | 18 |
| P17 (P.G.) | N− | +2.2 | 2/104 | 2 | 3/35 | 1 | 5/56 | −3 | 0.5[b] | 18 |
| P18 (M.A.) | N− | +6 | 1/104 | 0 | 8/35 | 0 | 5/56 | 1 | 0.5[b] | 18 |
| P19 (P.e.g.) | N− | +6.2 | 0/104 | 0 | 16/35 | 0 | 1/56 | −1 | 1.5[c] | n.a. |
| P20 (R.G.) | N− | +6 | 0/104 | 0 | 2/35 | 2 | 0/56 | 0 | 0 | 18 |
| P21 (P.E.) | N− | n.a. | 0/104 | 0 | n.a. | n.a. | 0/56 | 0 | 0 | n.a. |
| P22 (B.C.) | N− | +2.8 | 18/104 | 0 | 5/35 | 1 | 2/56 | −2 | 0 | 18 |
| P23(A.G.R.) | N− | +4 | 1/104 | 1 | 3/35 | 1 | 0/56 | 0 | 0 | 18 |

*Note.* n.a. = not assessed; N+/− = see Table 1.
Scores. Line bisection: Per cent deviation of the participants' mark from the objective mid-point. Cancellation tasks: Omission errors (total) and difference between omissions on the two sides of the sheet (left-sided *minus* right-sided). Complex drawing: Omission errors. Personal neglect: Correct responses.
[a]Defective scores, according to available norms.
[b]Omissions bilateral or localized on the right-hand side of the element(s).
[c]P19 scored 1.5: Bilateral partial omissions in the central element, namely the house (score = 1), plus one omission scored 0.5 on the left-hand side of one element.

Evaluation of Amusia (MBEA) (Peretz, Champod, & Hyde, 2003) (see Appendix S1 and Table S1). All participants gave their written informed consent to participate in the study and to the video recording. The study was approved by the Review Board of the Hospital Ethical Committee.

### *Materials*

Figure 2 illustrates the arrangement of the set-up. A Roland A-800 PRO 61-key (five octaves) music keyboard was employed for the testing sessions. This keyboard has 36 white keys and 25 black keys, with the leftmost key producing the note with the lowest pitch, C1, and the rightmost key producing the note with the highest pitch, a C6 (both are white keys; see also Figure 4). Thus, playing the white keys in a spatially ordered sequence starting from the leftmost or rightmost key produces the C major scale (ascending if playing from left to right, descending if playing from right to left). Participants sat comfortably in front of the keyboard with their body midline aligned with the centre of the instrument. This corresponds to the space between the F3 and G3 (notice that the 31st key, which would be the central key given the total number of keys, is in fact slightly at the left of the centre, due to the asymmetrical disposition of the black keys relative to the white keys). The keyboard was connected through the USB port to a laptop. The performances were recorded as MIDI files using the software Sonar LE (Cakewalk, Boston, MA, USA). The software Max/MSP (Cycling ′74, San Francisco, CA, USA) was used to control the keyboard and to create a standard (Music condition), a random (Random condition), and a no-sound (Silence condition) key-to-pitch mapping. The pitches produced in the Random condition were within the keyboard range and utilized the same

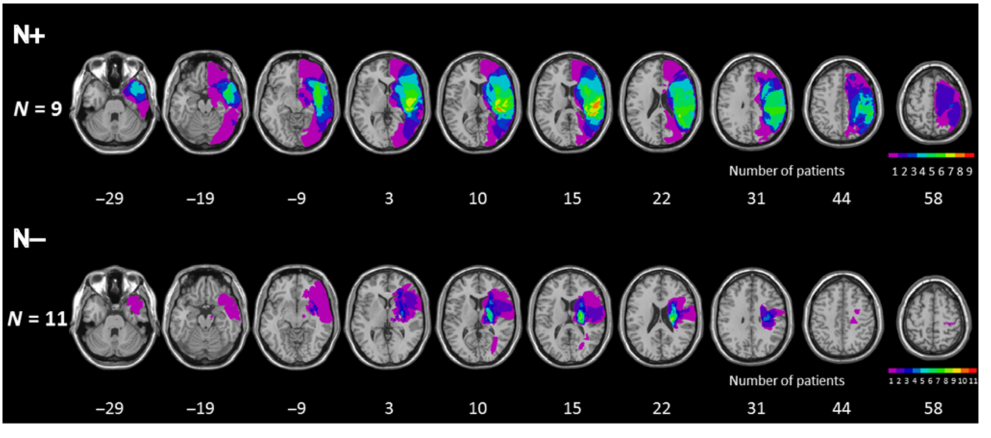


**Figure 1.** Overlay lesion localization. N+: Patients with right hemisphere lesions and left spatial neglect (bottom row: Frequencies of overlapping lesions, from dark violet, $n = 1$, to red, $n = 9$); lesions mainly overlapped ($n = 8$) in the superior temporal and in the Heschl gyri, and in the underneath white matter, with a marginal involvement of the posterior insula and the rolandic operculum of the right hemisphere. N−: Patients with right hemisphere lesions without left spatial neglect (bottom row: Frequencies of overlapping lesions, from dark violet, $n = 1$, to red, $n = 11$); lesions mainly overlapped ($n = 9$) in the white matter under rolandic operculum, with a marginal involvement of thalamus and putamen. Montreal Neurological Institute (MNI) Z-coordinates of each transverse section are reported.

standard piano timbre employed for the Music condition. The duration of the sound generated by each key was set to 1 s. The sound was delivered using a set of two loudspeakers positioned at the centre of the keyboard. The mono port was used, such that no differences in sound lateralization occurred as participants played progressively lower pitches. This set-up was chosen because the focus of the investigation was the effect of the orderly sequenced pattern of the music scale on the extent of spatial exploration, rather than the lateral orienting of spatial attention by lateralized sound stimuli.

### *Procedure*

Participants first familiarized with the keyboard and with the task. Before each of the subsequent three scale-playing tasks (Silence, Music, Random), each participant received the following instruction:

> Please press one after the other all the white keys, using your right index finger, starting from the rightmost key, till the end of the keyboard. Press each key once, without repeating, reversing the direction or skipping any key.

Because of the configuration of the 61-key keyboard, following this instruction in the Music condition produced a descending C major scale (see Paragraph Materials for details). In addition to this instruction, each participant received information about the auditory feedback response by the keyboard for that particular trial ('the keyboard will not produce any sound', '. . .normal sounds', or '. . .mixed sounds'). A metronome was sounded with a pace of 57 beats/min, and participants were encouraged to adjust their execution to this pace. Participants were not asked to synchronize precisely with the beat, and the metronome was employed as a gross reference, just to avoid extremely slow or fast executions. Because we were interested in exploring the participants' spontaneous timing behaviour, the metronome was maintained only for the first five notes of each trial and then turned off.

### *Design*

Participants were tested on two different days. On each day, they performed each of the three experimental conditions twice, following one of two counterbalanced orders of

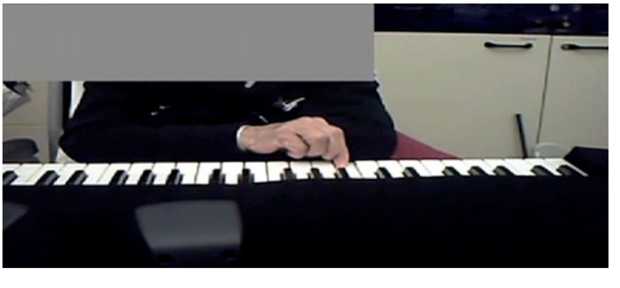

**Figure 2.** Experimental set-up. Participants sat comfortably in front of the keyboard with their body midline aligned with the centre of the instrument. The left arm was kept resting in a comfortable position in the lap. The participant is shown as she progresses through the left side of the keyboard in the Music scale condition.

presentation, ABCCBA and ACBBCA: (1) *Silence-Music-Random-Random-Music-Silence*, or (2) *Silence-Random-Music-Music-Random-Silence*. Each condition was, therefore, repeated four times. Half of the participants started with the first block sequence on the first day and half with the second. The design was therefore fully randomized to control for fatigue, practice effects, or both (Fleet & Heilman, 1986; Weintraub & Mesulam, 1988), and for block order effects. The repetition of the protocol on the second day also allowed testing for potential learning effects.

In addition to scale playing, we assessed participants' performance on a 'keyboard bisection' task, which required to press first the central key of the keyboard, followed by the rightmost and finally the leftmost keys, in the absence of sounds. Patients only received the instruction to press the three keys, without feedback about their performance or without any further guidance. This bisection task was performed following each experimental condition, for a total number of 12 bisection trials (six on each day).

We also sought to control for any effect of the keyboard in itself in modulating patients' performance. The possibility may be entertained that the keyboard *per se* could act as a particularly interesting and motivating object, as compared, for example, with a standard cancellation task, resulting in a better exploration performance (see Russell, Li, & Malhotra, 2013, for a review on the role of motivational factors in modulating spatial unilateral neglect). To this aim, on a separate day, participants were tested in a newly developed cancellation task ('modified H cancellation task'), designed with a rationale similar to the letter cancellation task of Diller and Weinberg (1977). Participants were presented with a 86-cm (i.e., the size of the keyboard) paper sheet with 36 capital H letters printed along the horizontal axis, spaced 1.5 cm from one another (i.e., the same distance separating the central axis of the keyboard keys), such that the spatial distribution of the targets held the same pattern of the keys in the music keyboard. Participants were required to mark with a pencil all the letters, starting with the rightmost one, and progressing from right to left. Were the use of the keyboard *per se* sufficient to improve left neglect, a greater spatial exploration would be expected in the Silence scale-playing task, compared to the modified cancellation task.

Finally, a vertical line bisection task was introduced, to check the presence of 'altitudinal neglect', namely a deficit in attending to stimuli in the upper or lower half of the space (Rapsack, Cimino, & Heilman, 1988). This task was devised as scales may have a 'high' to 'low' dimension, referred to 'pitch' (Rusconi *et al.*, 2006), that may be affected by the possible presence of altitudinal neglect. More details may be found in Appendix S1 (see Table S1 for scores in the modified cancellation task, the vertical line bisection, and the MBEA).

### *Dependent variables*

Data analyses were performed through custom routines written in MATLAB (version 2010b; The Mathworks, Natick, MA, USA). We quantified spatial exploration in two ways: First, we identified the leftmost key pressed at the end of each trial. This score was converted in percentage relative to a complete exploration, reaching the leftmost white key (i.e., the 36th, note C1, see Figure 4; e.g., playing up to the 18th key would had resulted in an exploration score of 50%), and reflected the extension of the leftward space explored. Second, we counted the number of keys missed by participants in the course of the exploration, without taking into account the keys after the last key pressed. This score was expressed in terms of 'number of missed keys' and reflected the thoroughness of the exploration. Both measurements were averaged between the two repetitions of the same condition within each day, while the data from the 2 days of testing were kept separate in the statistical analyses. For an account of the differences between repetitions of the same condition within each day, see the Appendix S1.

The timing of the exploration was quantified with reference to the inter-onset interval (i.e., time between onsets of two subsequent notes, IOI). The mean IOI was employed as an indicator of performance speed, while the *SD* of the IOIs was considered an indicator of timing variability. Means and *SD*s of the IOIs were averaged between the two repetitions of the same condition within each day, while the data from the 2 days were kept separate.

The spatial gradient of exploration speed was also calculated, in order to look at how the different experimental conditions influenced the tendency of N+ patients to move progressively slower and slower leftwards (Manly *et al.*, 2009). To this end, we computed the coefficients of the linear fit of the IOI time series, separately for each scale of each participant in each condition. The first coefficient, expressing the slope of the linear fit, was employed as an indicator of the time gradient. Slopes were averaged between the two repetitions of the same condition within each day, while the data from the 2 days were kept separate.

Before all analyses, a preliminary removal of the notes with IOIs smaller than 5% of the suggested metronome rhythm (i.e., shorter than 53 ms) was applied, to eliminate notes produced by mistake by the simultaneous press of two neighbour keys. An average of $0.19 \pm 0.07$ notes (mean $\pm$ standard error, *SE*) was removed in this way for each scale for the N+ group, $0.18 \pm 0.16$ for the N− group, and $0.08 \pm 0.06$ for the HC group, with no significant differences between groups, ANOVA: $F(2, 32) < 1$, conditions, $F(2, 64) < 1$, day of testing, $F(1, 32) < 1$, and no significant interactions, Group by Day: $F(2, 32) = 1.47$, $p = .25$; Condition by Group: $F(4, 64) = 1.19$, $p = .33$; Group by Day by Condition: $F(4, 64) < 1$.

Performance at the keyboard bisection task was quantified as the number of keys between the actual centre of the keyboard (F or G notes of the central octave, given the even number of white keys and the absence of a unique middle key) and the key pressed by the participant. The bisection data were averaged between the two repetitions of the task following the same condition (Silence, Music, or Random) within each day, while the data from the 2 days were kept separate.

## Results

Statistical analyses were performed using the software STATISTICA (version 6.1; StatSoft Italia srl, Vigonza, Italy). Spatial and timing data were separately submitted to a mixed three-way analysis of variance (ANOVA) with Condition and Day as within-subjects factors (Condition, three levels: Silence, Random, Music; Day, two levels: Day 1, Day 2) and Group as a between-subjects factor (three levels: N+, N−, HC). *Post-hoc* tests were computed using the Newman–Keuls correction for multiple comparisons.

### *Spatial exploration*

#### *Missed keys*

The 'number of missed keys' throughout each full exploratory trial was analysed, to assess whether participants had performed the task according to the instruction 'without skipping any key'. On each trial, N+ patients omitted an average of $0.24 \pm 0.13$ keys (mean ± *SE*), range 0–5, N− patients omitted 0.03 ± 0.02 keys, range 0–3, and HC omitted 0.02 ± 0.01, range 0–2. A repeated-measures ANOVA showed that the main effects of Group, $F(2, 32) = 2.96$, $p = .07$, $\eta_p^2 = .16$, power = .54, Scale conditions, $F(2, 64) < 1$, and Testing days, $F(1, 32) = 1.86$, $p = .18$, $\eta_p^2 = .1$, power = .26, were not significant, as well as all interactions, Day by Group: $F < 1$; Condition by Group: $F(4, 64) < 1$; Day by Condition: $F(2, 64) = 2.95$, $p = .06$; Group by Day by Condition: $F(4, 64) = 1.9$, $p = .12$. Also, the number of keys missed by the N+ group did not differ from 0, $t(10) = 1.87$, $p = .091$. In sum, patients performed the task according to the instructions, and warranted the use of the leftmost key pressed as an indicator of the leftward extent of space explored.

### *Leftward exploration*

Figure 3 shows the average per cent leftward exploration scores of N+ patients. N− and age-matched HC participants scored 100% correct (not shown). In all the three conditions (Silence, Random sound, Music scale), N+ patients explored the keyboard significantly less than the two control groups, main effect of Group: $F(2, 32) = 10.73$, $p < .001$, $\eta_p^2 = .4$, power = .99; *post-hoc* tests: Both $p < .001$; in fact, both control groups explored the whole keyboard in all conditions, with no variability. Accordingly, we analysed the effects of Condition and Day on the extent of spatial exploration in the N+ group alone. As shown in Figure 3, the N+ group explored a larger portion of the keyboard in the Music scale condition, compared to both the Silence and the Random sound conditions. The ANOVA showed a significant main effect of Condition, $F(2, 20) = 8.05$, $p = .003$, $\eta_p^2 = .45$, power = .92; *post-hoc* tests showed that exploration in the Music scale

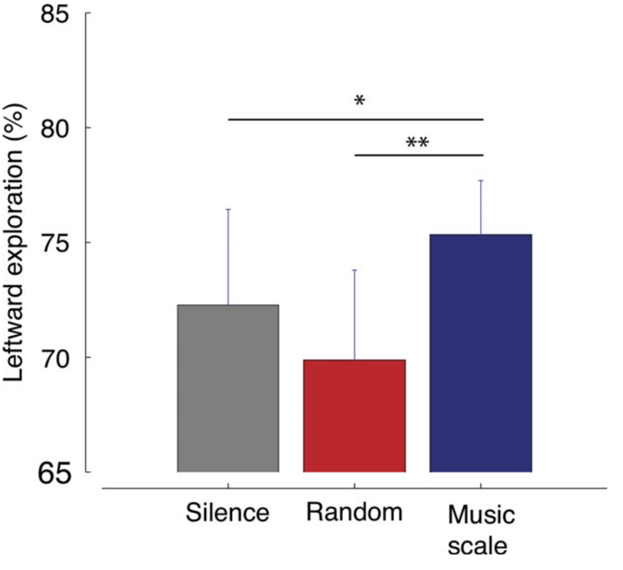


**Figure 3.** Keyboard exploration by neglect patients. Bars: Mean per cent of the keyboard explored (±average *SE* across the four repetitions of each condition), corresponding to the leftmost key pressed by N+ patients in the three experimental conditions. A largest portion of the keyboard was explored in the Music scale condition, as compared to both the Silence and the Random sound conditions. Both N− and healthy control groups performed at 100% in all conditions. *$p < .05$, **$p < .005$.

condition was greater compared to both the Silence ($p$ = .037) and the Random sound ($p$ = .002) conditions, whereas the Random sound condition showed a non-significant trend in reducing exploration compared to the Silence condition ($p$ = .093). The main effect of the day of testing was not significant, $F(1, 10) < 1$, as well as the Condition by Day interaction, $F(2, 20) < 1$. Figure 4 depicts the probability of concluding the exploration at each specific key of the instrument. Probabilities were computed from the pool of data of the 11 N+ patients, each contributing with four trials (for each condition, $n$ = 44). The Music scale condition increases the probability of terminating the exploration at the leftward end of the keyboard. It can be also noticed a pattern such that the Music scale condition tends to shift towards the left-hand side the peaks of exploration conclusion. For example, it can be noticed in Figure 4 that all participants successfully explore the first four keys (probability of stopping = 0, flat curves). The most severely impaired of our participants concluded the exploration in the Silence condition as early as key #5 (see on Figure 4 the slight increase in the black curve at the right-hand side). However, all N+ patients were able to explore at least up to key #7 during the Music scale condition. In other words, the sounds of the music scale helped participants to slightly extend the exploration into the leftward space, thus shifting the first peak of exploration conclusion towards the left (see keys 34–35 for a similar example). We assessed this effect statistically, by computing the cross-correlation between the grand-averaged time series of probabilities for pairs of conditions within a time window of ±5 keys around the lag 0 point (the last data point of each curve was preliminarily removed, as it artificially inflates the correlations given that the exploration cannot continue beyond that point). A maximum correlation at lag 0 would indicate that the peak of exploration conclusion happens at the same keys for, for example, the Music scale and the Silence conditions. On the other hand, a high correlation found at lags increasingly >0 would indicate that the two curves peak at increasingly distant keys, while retaining a similar overall shape.

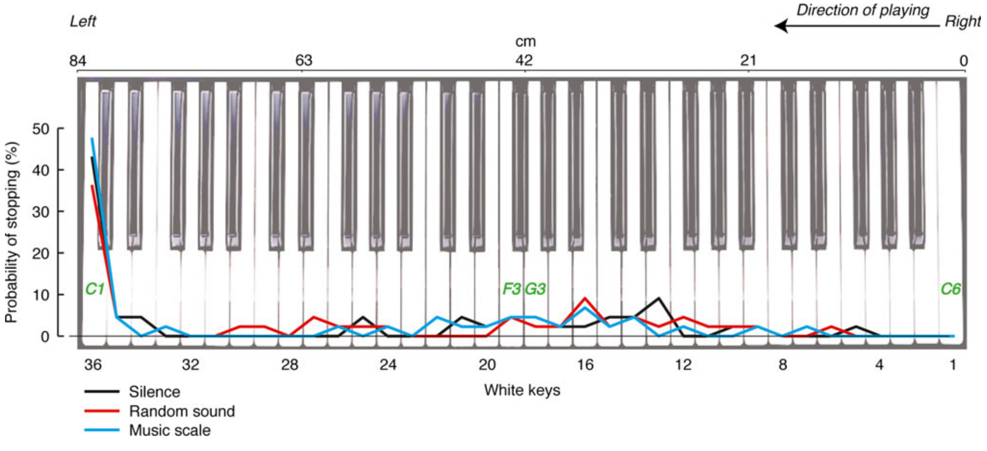


**Figure 4.** Probability of concluding the exploration at each key. The traces represent the probability of terminating the exploration at each given key on the instrument, for the N+ patients. The Music scale condition (cyan trace) increases the probability of terminating the exploration at the left-hand side of the keyboard. A frequent breakdown point can be noticed at about key 15 (from right to left), corresponding to the second octave. It can be also noticed that the peaks of exploration interruption in the Music scale condition tend to be shifted towards the left-hand side, in particular compared to the Silence condition (black trace), indicating greater exploration into the neglected space.

Consistently with an effect of facilitation in the Music scale condition, the peak of cross-correlation between the Silence condition and the Music scale condition was found at lag 1 (lag 1: $r = .65$; lag 0: $r = .27$). This indicates that the probability of concluding the exploration at a given key could be predicted from the probability distribution in the Silence condition shifted by one key towards the left-hand side. The probability of stopping at a certain key in the Random sound condition also showed a left-shifted peak of correlation with the Silence condition, but this relationship was substantially weaker (lag 1: $r = .39$), despite a similar correlation at lag 0 ($r = .26$).

No significant differences were observed in the N+ group between the scale task in the first Silence condition of the first day and the modified H cancellation task (paired-samples *t*-test: $t(10) = -1.5, p = .17$), although some trend favoured the Silence scale exploration over cancellation (exploration in the Silence scale, mean ± *SE*: 69 ± 10%; modified cancellation task: 53 ± 11%).

### *Bisection*

As shown in Figure 5, N+ patients set the mid-point of the keyboard more rightwards than N− patients and HC participants. Also, N+ patients reduced this error on the second day of testing. The ANOVA showed significant main effects of Group, $F(2, 29) = 25.74$, $p < .001$, $\eta^2_p = .64$, power = 1, and of Day, $F(1, 29) = 9.6$, $p = .004$, $\eta^2_p = .25$, power = .85, and a significant Group by Day interaction, $F(2, 29) = 3.66$, $p = .038$, $\eta^2_p = .2$, power = .63. Newman–Keuls tests showed that, on both days, the error scores of N+ patients were greater than those of both N− patients and control participants (all $p < .001$), with the scores of the two latter groups being comparable (all $p > .3$). In the N+ group, the error in the bisection task significantly decreased (i.e., patients set the mid-point of the keyboard closer to the centre) on the second day of testing ($p < .001$). Keyboard bisections following different experimental conditions did not differ one from

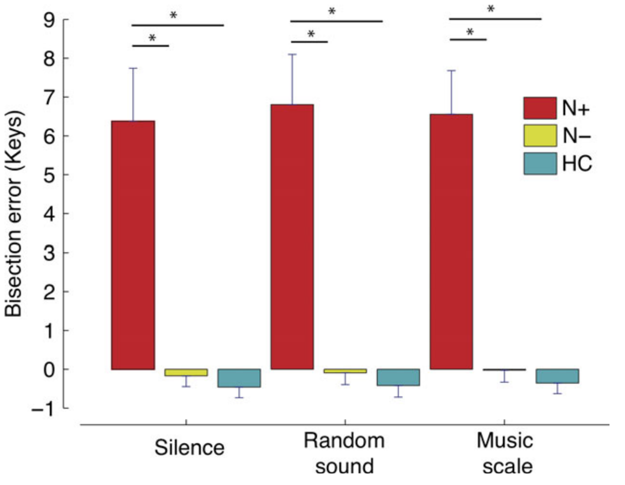


**Figure 5.** Keyboard bisection task. Bars: Average place of bisection (±*SE*), expressed in number of keys away from the actual centre of the keyboard. Positive numbers indicate an error at the right of the centre. N+ patients bisected the keyboard more rightwards, as compared to the other two groups. No differences were found between the Silence, Random sound, and Music scale conditions. *$p < .001$. N+/N−: See captions to Figure 1; HC, healthy controls.

each other, neither as a main effect of Condition, $F(2, 58) = 1.1$, $p = .34$, nor in interaction, Condition by Group: $F(4, 58) < 1$; Condition by Group by Day: $F(4, 58) = 1.01$, $p = .41$. Following the bisection, all N+, N− patients, and HC correctly pressed the rightmost key, except one N+ patient, who in two occasions missed it by one key (once following a Music scale, the other following a Random sound). When subsequently asked to press the leftmost key, all N− patients, and HC performed the task correctly in all trials; therefore, their data were not submitted to statistical analyses. Only three N+ patients could detect the leftmost key in all trials. On average, N+ patients missed the leftmost key by 10 keys (mean ± *SE* for the post-Silence scale: 9.8 ± 3.6; post-Random sound: 10 ± 3.9; post-Music scale: 9.8 ± 3.8), with no effect of Condition, $F(2, 18) < 1$, day of testing, $F(1, 9) < 1$, or Day by Condition interaction, $F(2, 18) < 1$.

### *Timing*

*Inter-onset intervals*

Table 3 reports a synthesis of the timing data. N+ patients differed from the two control groups mainly in terms of higher variability of the IOIs. Conversely, the average duration of IOI was broadly similar between groups, with N− patients being slightly faster than N+ patients, and N+ patients increasing their speed on the second day of testing. In all groups, exploration was faster in the Silence condition, compared to the two conditions with auditory feedback.

The ANOVA on the average IOIs duration revealed a main effect of Condition, $F(2, 64) = 4.73$, $p = .012$, $\eta_p^2 = .13$, power = .77. *Post-hoc* comparison showed that exploration was faster during the Silence condition, compared to both the Random sound ($p = .009$), and the Music ($p = .049$) conditions, whereas the difference between the Random sound and Music conditions was not statistically significant ($p = .29$). No

**Table 3.** Exploration timing data

| | Mean IOI (s) | | | | | |
|---|---|---|---|---|---|---|
| | Silence | | Random | | Music scale | |
| | Day 1 | Day 2 | Day 1 | Day 2 | Day 1 | Day 2 |
| N+ | 0.845 | 0.705* | 0.875 | 0.738* | 0.844 | 0.735* |
| N− | 0.563 | 0.546 | 0.637 | 0.589 | 0.630 | 0.569 |
| HC | 0.688 | 0.727 | 0.742 | 0.740 | 0.721 | 0.734 |
| | **Variability of IOIs (standard deviation) (s)** | | | | | |
| | Silence | | Random | | Music scale | |
| | Day 1 | Day 2 | Day 1 | Day 2 | Day 1 | Day 2 |
| N+ | 0.326 | 0.157* | 0.289 | 0.210* | 0.331 | 0.227* |
| N− | 0.090 | 0.062 | 0.097 | 0.100 | 0.087 | 0.063 |
| HC | 0.059 | 0.049 | 0.067 | 0.044 | 0.053 | 0.041 |

*Note.* N+/− = see Table 1; HC = age-matched healthy controls; IOI = inter-onset interval.
N+ patients showed greater variability of IOIs, than N− and HC participants ($p < .001$), and significantly reduced mean and variability of IOIs on Day 2 versus Day 1 ($*p < .005$).

Condition by Group interaction was found, $F(4, 64) < 1$. The significant main effects of day of testing, $F(1, 32) = 8.38$, $p = .007$, $\eta_p^2 = .21$, power = .8, and of Group, $F(2, 32) = 3.49$, $p = .042$, $\eta_p^2 = .18$, power = .61, and the significant Day by Group interaction, $F(2, 32) = 5.65$, $p = .008$, $\eta_p^2 = .26$, power = .83, showed that N+ patients significantly reduced on the second day the IOI duration, compared to the first day ($p < .001$), while no changes in the IOIs duration were observed for the N− and HC groups. Also, N− patients on the second day were significantly faster than N+ on the first day ($p = .013$). No significant Day by Condition, $F(2, 64) = 1$, $p = .37$, or Group by Day by Condition, $F(4, 64) < 1$, interactions were found.

The ANOVA on the variability of the IOIs revealed a main effect of Group, $F(2, 32) = 20.62$, $p < .001$, $\eta_p^2 = .56$, power = 1, a main effect of day of testing, $F(1, 32) = 22.46$, $p < .001$, $\eta_p^2 = .41$, power = .99, and a significant Day by Group interaction, $F(2, 32) = 10.28$, $p < .001$, $\eta_p^2 = .39$, power = .98. *Post-hoc* comparison showed that, on both days, timing variability was significantly greater in the N+ patients compared to both control groups (all $p < .001$). Also, N+ patients significantly reduced on the second day the variability of the IOIs, compared to the first day ($p < .001$), while no changes were observed for the N− and HC groups. No effects of Condition were found, both as a main effect, $F(2, 64) < 1$, and in interaction with the Group, $F(4, 64) < 1$, with the Day, $F(2, 64) = 1.02$, $p = .36$, and with the Group and Day, $F(4, 64) < 1$, main factors.

*Gradients of exploration timing*

Figure 6 shows the grand-averaged time series of the IOIs. N+ patients slowed down their exploration while moving towards the left side. The ANOVA revealed a main effect of Group, $F(2, 32) = 6.82$, $p = .003$, $\eta_p^2 = .3$, power = .89. *Post-hoc* comparisons revealed significant differences between the time series of N+ patients and those of both N− ($p = .006$) and HC ($p = .003$) participants, who showed an opposite tendency, namely accelerating in the course of the leftward exploration (N− and HC were similar to each other: $p = .87$). The main effect of Condition was significant, $F(2, 64) = 4.1$, $p = .022$, $\eta_p^2 = .11$, power = .71: Timing gradients differed depending on the feedback from the keyboard. In fact, the Music scale and the Random sound conditions were associated with a stronger deceleration pattern, compared to the Silence condition (*post-hoc* comparison: $p = .044$ and $p = .027$, respectively). In the N− and HC groups, these deceleration patterns took the form of a weaker acceleration, given the tendency of these participants to accelerate (instead of decelerate) in the Silence condition. Deceleration was maximal in the Music scale condition, although not to a degree significantly higher than the Random sound ($p = .85$). The main effect of day of testing, $F(1, 32) < 1$, and the Group by Condition, $F(4, 64) = 2.29$, $p = .07$, Day by Group, $F(2, 32) < 1$, Day by Condition, $F(2, 64) = 1.18$, $p = .31$, and Group by Day by Condition, $F(4, 64) = 1.6$, $p = .18$, interactions were not significant.

***Vertical line bisection and amusia***

N+ and N− patients showed a comparable accuracy in vertical line bisection, with an independent samples *t*-test showing no differences (N+: $-2.9 \pm 3.9$; N−: $-0.4 \pm 1.3$; $t(13.3) = -0.59$, $p = .56$). Eight of 11 N+ patients either showed pathological scores at the Melodic Organization test ($n = 5$), or failed to comply with the testing procedure ($n = 3$), indicating that the majority of N+ patients had deficits in musical processing, as

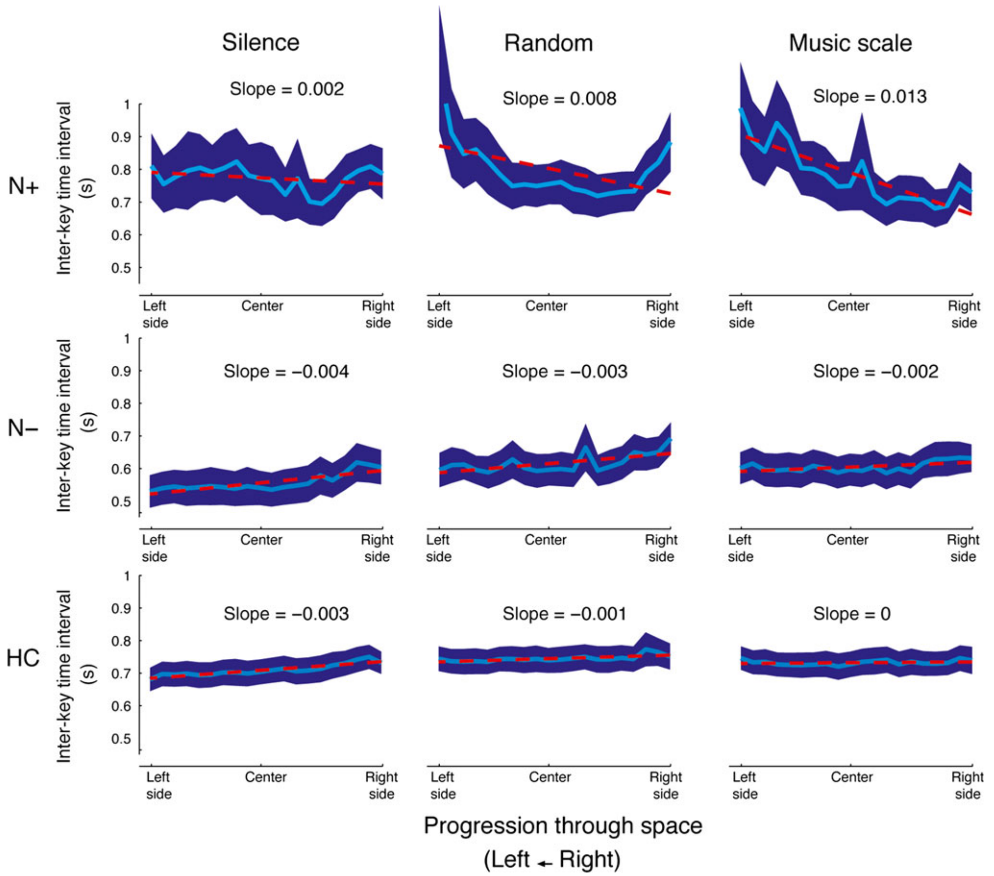


**Figure 6.** Gradients of exploration timing. Grand averages (±*SE*) of the time series of the inter-onset intervals, with all time series normalized to 100 points, before grand averaging, for visualization purposes. Linear fits superimposed in red, with indication of the slope of the grand-averaged time series, by group (N+, N−, HC), and experimental condition (Silence, Random sound, Music scale). N+ patients slowed down exploration while moving leftwards, significantly more in the Music scale and Random sound conditions, compared to the Silence condition. N− and HC groups exhibited an opposite tendency, increasing speed while moving leftwards; this tendency was reduced in the Music scale and Random sound conditions. N+/N−/HC: See captions to Figures 1 and 5. HC, healthy control.

measured with this test (see Table S1). A qualitative screening of the exploration data indicated that these three categories of N+ patients (namely those with pathological scores for amusia, those who failed to comply with the testing procedure, and those with non-pathological scores) had a similar pattern of benefit from the Music scale condition, in terms of greater exploration of the keyboard.

## Discussion

The exploration of a music keyboard by right-brain-damaged patients with left spatial neglect improves when the pressed keys produce the sounds of the music scale, as compared to a silent keyboard or a keyboard producing randomly ordered pitches. Recent investigations have been increasingly considering the potential of sounds and music for ameliorating left spatial neglect (Guilbert *et al.*, 2014 for a review). So far, sounds have been shown to be effective in reducing spatial neglect through two main mechanisms. One may involve an increase of arousal: The presence of auditory stimulation during (Hommel *et al.*, 1990; Tsai *et al.*, 2013) or immediately before (Robertson *et al.*, 1998) the spatial task may result in improved attentional orienting and, therefore, in a higher performance level in spatial tasks (Callejas, Lupiàñez, Funes, & Tudela, 2005; Fuentes & Campoy, 2008). This effect is not specific to music, as both white noise (Hommel *et al.*, 1990) and random pitches (Robertson *et al.*, 1998) are capable of producing similar effects. A second mechanism may operate by improving mood: Listening to preferred music improves spatial performance, as a result of increased positive effect, and the engagement of the mesolimbic dopaminergic reward system (Chen, Tsai, Huang, & Lin, 2013; Salimpoor, Benovoy, Larcher, Dagher, & Zatorre, 2011; Soto *et al.*, 2009). This effect is specific to preferred music, as white noise, or non-preferred music, does not yield the same effects.

In addition to inducing changes in arousal and mood, a third important property of musical sounds is that of being organized in *predictable sequences*. The potential of sequences in improving exploration by right-brain-damaged patients with left spatial neglect has been documented so far in the domain of numbering: Ishiai *et al.* (1990) showed that numbering targets improved search, compared to simple cancellation. The present study investigated whether the sequencing property of sounds could result in similar benefits. Here, we show that the predictable sounds of the music scale improve spatial exploration, compared to silent exploration. This facilitation is not solely due to increased arousal. When patients explored the keyboard with a random sound feedback, there was no improvement of spatial neglect, despite the fact that the level of arousal and phasic alerting was presumably the same in the Music and Random sound conditions. The organization of sounds in a structured sequence appeared to be a necessary component for the improvement reported here. Although it is possible that the music scale was perceived as more pleasant than the random piano pitches (Menon & Levitin, 2005), we suggest that positive emotions (Soto *et al.*, 2009) only played a limited role to shape the observed pattern of results, for two reasons. First, compared to the pleasant music utilized in the previous studies (e.g., Bach, Vivaldi, Frank Sinatra), the music scale we employed represents a substantially more neutral stimulus, one that is unlikely to be capable to elicit the emotional reactions known to activate the mesolimbic dopaminergic system (Salimpoor *et al.*, 2011). Second, the appreciation of music is known to be highly subjective: Accordingly, previous studies required participants to choose their own preferred versus unpreferred music (Soto *et al.*, 2009). However, in our study, the music scale and the experimental protocol were identical for all participants, likely resulting in a cancelling-out of subjective appreciations within the sample. The main factor underlying the improvement of spatial exploration is likely to be the structural organization of the sounds in the music scale. Playing the keys in the music scale condition allows patients to use an auditory reference frame to support spatial exploration. This frame is constituted by the sequence of predictable sounds of the descending Music scale. Once initiated, this sequence suggests its own indefinite continuation towards the lower pitches. As these pitches are situated in the left space, the greater exploration towards the left is made possible by the auditory representation of the notes' sequence. It can also be hypothesized that the auditory reference improves spatial exploration because it taps into a network for the representation of magnitude that is shared between spatial and auditory information (Walsh, 2003). A likely neural basis for this integration is the intraparietal sulcus, a region that has been shown to be involved in comparisons of size, luminance, numbers (Pinel, Piazza, Le Bihan, & Dehaene, 2004), and auditory pitch (Foster & Zatorre, 2010).

A footprint of this auditory framework can be noticed in the timing gradients: Playing the keyboard under the Music scale condition slowed down the execution, compared to the Silence condition. In the neglect group, this was observed in the form of a stronger deceleration pattern, enhancing the natural tendency of these patients to slow down exploration into the left, neglected side (Manly *et al.*, 2009). In brain-damaged patients with no neglect, as well as in HCs, this was observed in the symmetric form of a weaker acceleration pattern, reducing a natural tendency to speed up the performance. Remarkably, a qualitative inspection of the data reveals that HCs generated under the Music condition the only occurrence of a perfectly steady-tempo execution. Altogether, these results suggest that playing the keyboard under the Music scale condition involves the reference to the cognitive representation of the music scale. This is a more structured task, and perhaps even more complex, than merely pressing the keys one after the other. The reference to this structure would influence the timing dynamic, and, in the neglect group, would boost a wider, although increasingly slower, spatial exploration. The Random sound condition seemed also to induce a similar slowing down pattern, possibly due to the attempt to structure the incoming sound into a melodic template of reference. However, the unpredictability of the sounds in this condition is likely to have cancelled out entirely the beneficial effect on spatial exploration.

An important feature of the results reported here is that the music scale seems to be able to bypass the anosognosia for spatial neglect, namely the lack of awareness of the neglect disorder (Vallar & Bolognini, 2014). It is known that spatial neglect shows a strong association with neglect anosognosia, which is considered one of the main factors undermining the attempts to rehabilitate neglect (Kerkhoff & Schenk, 2012). Anosognosia for spatial neglect was not directly measured in our study (see Ronchi *et al.*, 2014, for an example of how it can be quantified). However, the clinical observation of the patients' belief of having explored the whole keyboard, despite failing to do so, and their behaviour at the other standardized tests, suggest that all the N+ patients in our sample were affected. The benefit of the music scale in our study was seen despite the fact that participants were not told to attend the sound of the notes. This suggests that the improvement in spatial exploration with the music scale does not require an explicit strategy, in order to overcome the spatial impairment. In this respect, the mapping of space on the music scale can be conceived as a bottom-up process similar to prism adaptation, which improves spatial exploration without requiring voluntary attention to the left-sided deficit, therefore bypassing the damaged awareness (Jacquin-Courtois *et al.*, 2013). On the other hand, framing exercises for the rehabilitation of spatial neglect in a musical context could also benefit from the engagement of top-down processes unrelated to spatial representation, like melody and lyrics retrieval and emotional engagement.

Although we observed a systematic reduction of left spatial neglect during the scale-playing task in the Music scale condition, no improvements were observed in the keyboard bisection task that immediately followed. This finding may be interpreted as an indication that the music scale operates at a relatively 'local' level of spatial processing (Gallace *et al.*, 2008), where each key can be embedded in a specific tile of the descending sound structure. The relatively more 'global' aspects of spatial processing, as those involved in the bisection task, would instead be unaltered and manifest the neglect symptoms. This result further differentiates the sequencing mechanism described here from a relatively less specific effect of positive emotions induced by music, as the latter have been shown to improve the performance of neglect patients in both bisection and cancellation tasks (Soto *et al.*, 2009).

It is worth noticing the presence in the neglect group of several patients obtaining pathological scores at the Melodic Organization test for the evaluation of amusia, whereas all patients without left neglect scored in the normal range. A definite diagnosis of amusia cannot be formulated on the basis of this single test. However, these defective scores, combined with the presence of brain damage in the right auditory cortex for several of the neglect patients, may suggest that their defective performance in the Melodic Organization test could have indeed been caused by amusia, and not simply by a domain-general cognitive deficit (see Särkämö *et al.*, 2010 for more details about the relationship between amusia and lesions in the right auditory cortex). As interesting as it is, this issue is outside the scope of this study. What matters here is that although, in principle, the presence of amusia could have prevented our patients to benefit from the Music scale condition, this proved to be not the case. The degree of musical sophistication, and global cognitive processing required to score in the normal range at the Melodic Organization test, is likely much higher than what is required to appreciate the presence of the music scale in our experiment. Also, participants in our study were actively producing the sounds, and the whole scale generation was self-paced, which probably constitutes a significant facilitation over a computer-delivered test with relatively complex and fast melodies. This result suggests that the scale-playing procedure we described is a feasible intervention tool for training even for patients with relatively severe impairments of music processing.

Music therapy has been shown to be a useful tool in various domains of neuropsychological rehabilitation, such as speech fluency (Wan, Zheng, Marchina, Norton, & Schlaug, 2014), memory (Särkämö *et al.*, 2008), executive functions (Bugos, Perlstein, McCrae, Brophy, & Bedenbaugh, 2007), and motor control (Schneider, Schönle, Altenmüller, & Münte, 2007). The present study has implications for the rehabilitation of patients with spatial neglect, as it provides the rationale for implementing active music-making rehabilitation protocols. Horizontal displays of devices generating sounds (e.g., piano, drums, xylophones, computer-controlled pads) can be effectively used to promote leftward explorations. Several degrees of exercise difficulty can be designed, leveraging on a virtually infinite repertoire of training melodies with varying degrees of complexity and stretch into the leftward space. Descending arrays of pitches could be compared with ascending arrays (e.g., Noto, Fumiko, Amimoto, Sugimoto, & Futaki, 1999), to investigate whether one could facilitate exploration better than the other. The auditory feedback of pitch could be enriched by verbal information (e.g., segments of lyrics) to provide additional non-spatial cueing. Furthermore, the modular nature of several 'horizontal' instruments (e.g., xylophones, computer-controlled pads) allows extending already well-learned melodies to progressively wider space areas (e.g., Bodak *et al.*, 2014). The well-documented potential of auditory and musical stimuli in sustaining arousal and positive emotions could be used not only as a background support to the training. Music *itself* would become the training, in the form of an active rehabilitation procedure, as outlined in the concept of neurologic music therapy (Thaut & Hoemberg, 2014). This would incorporate the standard features of classical rehabilitation approaches, such as movement repetition and progressive exercise shaping (Miltner, Bauder, Sommer, Dettmers, & Taub, 1999), and add the unique features of music-supported trainings, such as auditory–motor integration, adherence to individuals preferences, motivation, arousal, positive emotions, and sound sequencing. In recent years, the effectiveness of similar approaches has been positively assessed for the recovery of motor function following stroke (Amengual *et al.*, 2013; Schneider *et al.*, 2007; Wittwer, Webster, & Hill, 2013). A recent study by Bodak *et al.* (2014) has also provided evidence that a 4-weekly music intervention involving sequential chime bars playing in the neglected space may improve spatial exploration as measured by standardized tests in patients with spatial neglect (see also Abiru, Mihara, & Kikuchi, 2007; Noto *et al.*, 1999). In this study, we did not investigate the extent to which the benefit of the exercises with the music scale might generalize to standard tests for the assessment of neglect, or to daily activities. This is a question of great importance that will have to be addressed in future studies, involving a prolonged training under the Music scale condition. The present study has rather provided a rationale for developing such future protocols. In fact, we employed a randomized design in which, in the absence of extended training, the music scale immediately appeared to advantage exploration compared to silence or to random sounds. Altogether, the present and these previous studies indicate that spatial neglect could be a fruitful area of application of the principles of neurologic music therapy.

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## Supporting Information

The following supporting information may be found in the online edition of the article:

**Table S1.** Additional experimental tasks: N+ and N− patients' scores.
**Appendix S1.** Additional experimental tasks. Scores of N+ and N− right brain-damaged patients.