Pleasant music overcomes the loss of awareness in patients with visual neglect

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During the past 20 years there has been much research into the factors that modulate awareness of contralesional information in neurological patients with visual neglect or extinction. However, the potential role of the individual's emotional state in modulating awareness has been largely overlooked. In the current study, we induced a pleasant and positive affective response in patients with chronic visual neglect by allowing them to listen to their pleasant preferred music. We report that the patients showed enhanced visual awareness when tasks were performed under preferred music conditions relative to when tasks were performed either with unpreferred music or in silence. These results were also replicated when positive affect was induced before neglect was tested. Functional MRI data showed enhanced activity in the orbitofrontal cortex and the cingulate gyrus associated with emotional responses when tasks were performed with preferred music relative to unpreferred music. Improved awareness of contralesional (left) targets with preferred music was also associated with a strong functional coupling between emotional areas and attentional brain regions in spared areas of the parietal cortex and early visual areas of the right hemisphere. These findings suggest that positive affect, generated by preferred music, can decrease visual neglect by increasing attentional resources. We discuss the possible roles of arousal and mood in generating these effects.

attention | brain damage | neuropsychology | positive affect | vision

Lesions to the parietal cortices, usually in the right hemisphere, can lead to spatial neglect. In this syndrome, patients are unaware of information presented on the side of space contralateral to their brain lesion, as indexed by an inability to make an explicit response to contralesional stimuli. This is a serious clinical disorder affecting as many of 60% of patients after a right hemisphere stroke (1), and it is associated with poor functional outcome (2). This loss of awareness for contralesional stimulation may be particularly evident when a competing stimulus is presented at the ipsilesional site, a phenomenon known as visual extinction. The loss of awareness can be attributed to a spatial imbalance between contralesional and ipsilesional information for access to higher-level processing (3), which in turn can be associated with a pathological bias to orient toward, and problems in disengaging attention from, ipsilesional stimuli (4–6).

Given the clinical importance of the neglect syndrome, many studies have examined the factors that modulate the strength of contralesional deficits in patients with neglect and extinction. The results demonstrate that neglect and extinction can be influenced by grouping between contralesional and ipsilesional stimuli (7, 8), alerting by means of auditory stimulation (9, 10), spatial cuing to the contralateral side of space (4, 5), matches between the current contents of working memory and the visual array (11), and emotional factors associated with the stimulus (i.e., happy or angry faces in the contralesional visual field are extinguished less than neutral faces) (12). However, the potential role of the individual's own emotional state in modulating awareness has been largely overlooked. The aim of the present study was to assess whether positive affect, induced by playing pleasant music, increased awareness of neglected stimuli in patients with chronic deficits. Finding positive evidence would imply that attentional functions in patients with visual neglect can be modulated by the emotional state of the individual. This has important implications for attempts to remediate this clinically important disorder and, more generally, for understanding the interplay between attention and emotional states.

Evidence from healthy individuals indicates that changes in positive affect can modify the efficiency of cognitive processing in a variety of tasks. For example, positive affect has been shown to enhance flexibility in problem solving (13), along with the scope of memory recall in word association tasks (14, 15). Furthermore, there is also evidence that positive affect can modulate visual attention in healthy individuals. Rowe et al. (16) induced mood changes in their participants by means of happy and sad music before the execution of a flanker paradigm that required participants to focus on a central target and to ignore the irrelevant flankers. They found that positive affect enhanced flanker interference from the more distant flankers, suggesting that positive affect increased the breadth of the attentional focus (16, 17). Further research has shown that positive affect can reduce the "attentional blink," perhaps by increasing attention resources (18).

Here, we assessed the performance of 3 neglect patients in visual tasks sensitive to neglect and extinction as they listened to music. Särkämö et al. (19) have recently reported that a general acute stroke population showed greater improvement in verbal memory and focusing attention when listening to music compared with listening to audio books or working in silence. However, they did not assess potential differences between music conditions that varied in emotional valence; they did not evaluate the potential role of arousal; they did not examine specific cases of visual neglect; and they did not explore the neural substrates of any beneficial effect. These factors were examined in our study.

Consistent with the common intuition that music conveys emotion and influences the quality of our mood and feelings, we elicited a positive affective response in our patients through music listening. Given that music preference is very idiosyncratic, we allowed the patients to choose and listen to pleasant preferred music, because this is the most effective way to induce a positive emotional response (20). Emotional responses to music have been categorized according to the valence of a piece (i.e., pleasant/unpleasant) and/or its effect on arousal (21). Accordingly, the preferred and unpreferred status of the music selected in the study was operationalized along a continuum of pleasantness. Moreover, effects of music listening

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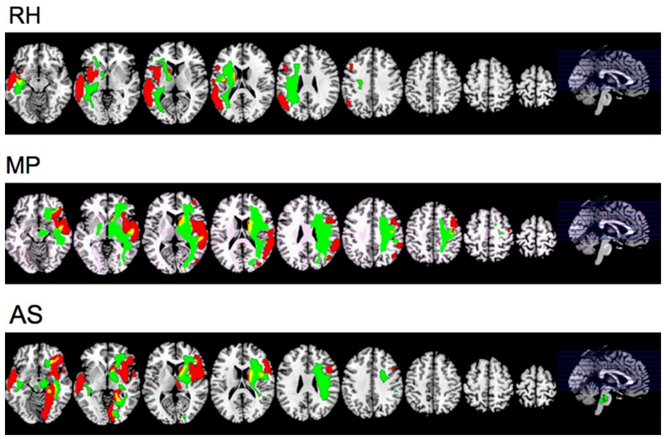

Fig. 1. Lesion reconstructions in the patients from MRI scan (see the *Lesion Reconstruction* section in the *SI Methods* for further details). Left of the slice represents the left hemisphere.

on arousal were assessed by recording the heart rate and the galvanic skin responses of patients—measures which have been used previously in studies of musically induced arousal (22, 23). We note that cognitive effects of arousal have been related to a facilitation of decision-level processes when responding to relevant behavioral targets (24), and also related to improvements in attentional orienting (25, 26). Importantly, there is evidence that alerting patients with visual neglect through auditory stimulation can improve their awareness of the contralesional side of space (9, 10). In addition to this, the valence of the music stimulation may lead to mood changes. Prior evidence from healthy populations indicates that pleasant music can be a powerful tool to induce positive emotions (16, 20), and it may even improve mood in neurological patients after stroke (19). It has been argued that neglect in particular is associated with underactivation of the norepinephrine system supporting arousal (27), and there is evidence that introduction of a noradrenergic agonist to overcome this underactivation reduces the degree of neglect (28). Increased arousal and positive mood induced by preferred music could modulate neglect by increasing neurotransmitter release, and this in turn may boost the cognitive resources available to patients. From a neural point of view, we hypothesized that stimulation by preferred music should lead to the recruitment of areas involved in emotion (i.e., in midbrain structures and the anterior prefrontal cortex) (20), and that emotional brain systems should modulate brain activity in attention and visual areas (i.e., parietal and visual cortices). We predicted an enhancement of activity in areas concerned with attentional processes within the damaged hemisphere when preferred music was played, which may facilitate the selection of contralateral targets. This was tested in a functional neuroimaging study. To confirm that music influenced emotion, the effects of preferred/unpreferred music listening were assessed on visual analog scale (VAS) ratings of enjoyment, mood, and arousal. VAS ratings were taken after completion of the experimental studies to preclude patients from generating any hypothesis about the aims of the study.

Results

VAS Ratings. Three patients with aspects of visual neglect participated in the study. Fig. 1 depicts the lesion reconstructions in the patients from MRI scan. Further patient details are provided in the *SI Methods*. VAS scores were analyzed by means of nonparametric Kruskal–Wallis tests with music as a factor (see *Statistical Analyses* in the *SI Methods* for a justification of the choice of statistical tests). In the case of MP, ratings of musical enjoyment and mood were more positive with preferred music compared with unpreferred music [$\chi^2(1) = 6.94, P = 0.008$, and $\chi^2(1) = 6.9, P = 0.009$], whereas arousal ratings were highest in the unpreferred music condition [$\chi^2(1) = 6.86, P = 0.009$]. Patient RH rated a higher musical enjoyment and mood with preferred music compared with unpreferred music [$\chi^2(1) = 5.33, P = 0.02$, and $\chi^2(1) = 5.4, P = 0.02$], whereas his arousal ratings were highest with preferred music [$\chi^2(1) = 5.33, P = 0.021$]. In the case of AS, musical enjoyment and mood ratings were more positive with preferred music compared with unpreferred music [$\chi^2(1) = 6.81, P = 0.009$ and $\chi^2(1) = 6.86, P = 0.009$], whereas there were no significant differences on arousal ratings across conditions [$\chi^2(1) = 1.33, P = 0.249$]. This pattern shows consistent effects of preferred music on positive affect but inconsistent effects on arousal responses across patients. A single VAS rating for mood and arousal was also taken from each of the patients in a neutral condition, without music (Table 1).

Table 1. VAS ratings of music enjoyment, mood, and arousal (from 0 to 10)

Musical enjoyment	Preferred music	Unpreferred music	Silence
MP	9.78	0.18	
RH	7.87	0.39	
AS	8.52	1.59	
Mood			
MP	9.70	0.14	5.2
RH	7.24	0.75	5.5
AS	7.66	1.68	5.3
Arousal			
MP	0.19	4.85	0
RH	4.02	0.69	0.8
AS	3.45	4.70	5.7

We also assessed whether the preferred pleasant music influenced enjoyment, mood, and arousal differently across the patients. The results indicated that preferred music triggered a higher positive affect response in MP relative to the other patients (*Supporting Analyses* in the *SI Methods*). With regard to the arousal ratings, these were higher for patients RH and AS relative to MP.

Study 1: Behavioral Experiments. ***Perceptual report task.*** Patients were required to report different colored geometric shapes (i.e., "blue square," "green triangle," etc.) presented in the left or right visual field either one at a time or in pairs on a computer screen (see *SI Methods* for details). Performance was assessed when each patient listened either to his preferred music, to unpreferred music, or in silence. The means for each patient's performance for each of the 4 blocks of trials collected within each music session were treated as independent observations (29). A 3 (patient) × 3 (music: preferred vs. unpreferred vs. silent) × 2 (number of targets: 1 vs. 2) × 2 (visual field: contralesional vs. ipsilesional) ANOVA was conducted. The pattern of results appears in Fig. 2*A*. There was an overall effect of music ($F_{2,18} = 15.54, P = 0.0001$), with higher target identification when there was preferred compared with unpreferred music ($P = 0.0001$) and with preferred music compared with silence ($P = 0.011$). Performance was better on single- rather than on 2- object trials ($F_{1,9} = 148.6, P = 0.0001$) and also for ipsilesional relative to contralesional targets ($F_{1,9} = 134.34, P = 0.0001$). The effect of the number of targets present interacted with the positions of the targets in the visual field ($F_{1,9} = 81.66, P = 0.0001$). This demonstrates an extinction effect, with identification of contralesional targets being greater on single- compared with 2-object trials. Interestingly, music modulated the effect of visual field ($F_{2,18} = 11.45, P = 0.002$), and the 3-way interaction between music, visual field, and number of objects was also significant ($F_{2,18} = 4.24, P = 0.036$). Posthoc *t* tests showed that the identification of single contralesional targets increased with

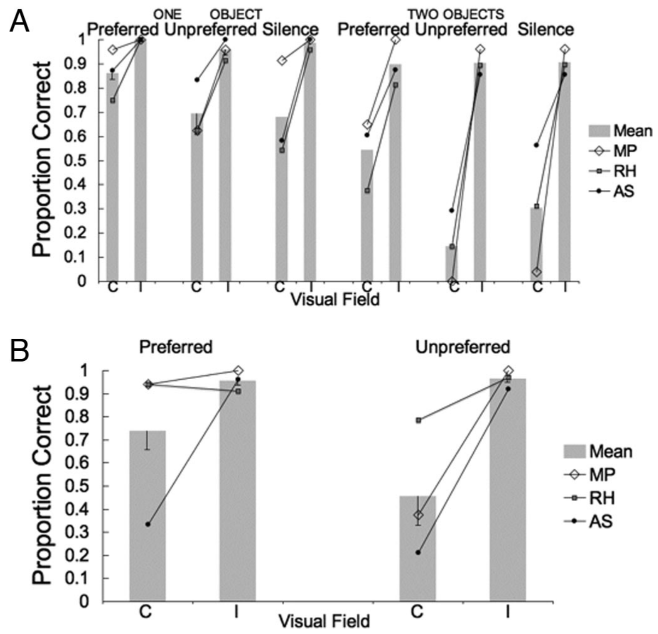

Fig. 2. Behavioral data from Study 1. (*A*) Proportion of correct identification responses in the different music conditions as a function of the number of targets and their position in the visual field. (*B*) Proportion of correct detections as a function of the visual field and the music conditions. C, contralesional; I, ipsilesional.

preferred music relative to both unpreferred music [$t(11) = 2.17$, $P = 0.052$] and silence [$t(11) = 3.2$, $P = 0.008$]. Contralesional performance in the 2-object condition was also better with preferred music than with both unpreferred music [$t(11) = 5.3$, $P = 0.0001$] and with silence [$t(11) = 2.15$, $P = 0.055$]. In addition, performance on 2-object trials was worse with unpreferred music than with no music [$t(11) = -3.31$, $P = 0.007$]. There were no significant effects of music on the identification of ipsilesional targets. We also note that the 3-way interaction was also modulated by patient ($F_{2,18} = 3.43$, $P = 0.036$). The benefits of preferred music on patient MP were larger than for the other patients (AS and RH). Importantly, however, the analyses led to a very similar pattern with MP omitted (see *Supporting Analyses* in *SI Methods*).

Detection task. Here, we required patients merely to detect the onset of a red target by means of a key button press (and to withhold responses to green targets). Patients MP and RH performed 2 sessions, each containing 2 different blocks on each of the music conditions. Patient AS performed 3 sessions. Responses on catch trials were withheld as instructed. A 2 (music) × 2 (target visual field) ANOVA was conducted on the means for each patient (with performance on each session treated as independent observation). The main effect of music was marginal ($F_{1,6} = 5.67$, $P = 0.076$). There was impaired detection of contralesional targets compared with ipsilesional targets ($F_{1,6} = 17.45$, $P < 0.014$). The effect of visual field was modulated by music ($F_{1,6} = 10.11$, $P < 0.034$); neglect of contralesional targets reduced in the preferred music condition relative to the unpreferred music condition (Fig. 2*B*).

We also assessed music effects on the reaction times taken to detect the target, to examine whether preferred music listening enhanced overall readiness to react. Because of the low number of correct responses to contralesional targets, reaction time data from both contralesional and ipsilesional fields were combined. A paired *t* test showed no significant differences in reaction times (RT) between preferred music (mean = 707 ms) and unpreferred music (mean = 711 ms) [$t(6) < 1$, $P = 0.7$]. The same pattern emerged when only reaction times for ipsilesional targets were considered.

Table 2. Percentage of star cancellation responses with unlimited time for the task and with a limited time window

Time	Preferred music: Contralesional	Preferred music: Ipsilesional	Unpreferred music: Contralesional	Unpreferred music: Ipsilesional
Unlimited time				
MP	51.7	74	27.6	77.7
AS	86.2	100	89.6	77.7
Limited time, 3 min				
MP	37.9	81.5	27.6	74
AS	93.1	96.3	58.6	92.6

Preferred music listening did not appear to facilitate decision stages of the reaction to the target. The effect of preferred music seems more linked to an enhancement of the patients' awareness.

A further control experiment was carried out with one of the patients (MP) to assess whether the music needed to be played during the task to generate effects or whether music-induced mood before the task would also facilitate awareness. To induce positive emotions before the task, the patient was exposed to a musical video of his favorite artist, and he was asked to retrieve good feelings and memories. The music was not played during the task. The experimental protocol was similar to the above detection task, except that here we included pictures from the International Affective Picture Scale (IAPS) (30) before each trial to "sustain" the positive mood induced before the task. After 1 block on the positive mood condition, the patient was given a break. Subsequently, the experimenter raised a conversation on the current financial crisis to reduce the level of positive emotion. Then, the patient received 2 blocks of trials in the more "negative" mood condition, where each trial was preceded by a "negative" affect picture from the IAPS. Positive and negative pictures differed in their normative ratings of valence [7.3 vs. 3.37 for the more and less pleasant cases, respectively; $t(7) = 11.14$, $P < 0.001$], and they were matched on the dimension of arousal (4.67 vs. 4.51 for the positive and negative pictures, respectively; $t < 1$). The patient was instructed that pictures were irrelevant to the task and that he or she should concentrate on detecting the red target. The session finished in the more positive mood condition, with positive mood again induced by playing a musical video before the task and by asking the patient to retrieve pleasant memories. The results confirm our prior observations. MP did not show any sign of visual neglect in the positive mood condition. Target detection was perfect both for contralesional and ipsilesional targets (32 of 32 trials). In contrast, in the more "negative" mood condition, the patient only detected 9% of contralesional targets (3 of 32), whereas the patient detected 88% of the ipsilesional targets (28 of 32). This finding provides compelling evidence that positive mood induction played a critical role at improving the patient's awareness.

Star cancellation. MP and AS were asked to search for small stars presented along with big stars and letter distractors on a paper sheet and to mark them with a pencil. RH did not show neglect on this task. MP and AS performed the task with (*i*) unlimited time conditions and (*ii*) with a limited time window of 3 min. Note that 3 min is easily long enough for control participants to perform the task. The data averaged across the patients are depicted in Table 2. The data indicate that a contralesional cancellation deficit was apparent under both task durations. Log-linear analyses assessed the number of correct to error trials as a function of the patient, task duration, music type, and visual field. There was a significant interaction between all factors [$\chi^2(1) = 7.023$, $P = 0.008$]. Next, we reanalyzed the data taking only performance under time-limited conditions. There were fewer cancellations in the contralesional than the ipsilesional field [$\chi^2(1) = 28.027$, $P = 0.0001$]. In addition, the number of cancellations increased with preferred compared with unpreferred music [$\chi^2(1) = 5.44$, $P = 0.02$]. Again, preferred music led to enhanced awareness. The results from the log-linear analyses failed to show differential effects of music as a function of visual field, but Table 2 indicates that the effects of preferred music were more evident on the contralesional side. We also note that music effects in MP were stronger with unlimited exposure conditions, whereas patient AS showed stronger music effects under the 3-min limited time window. These results may reflect that MP moved toward a floor effect with time-limited conditions, whereas AS was close to ceiling with unlimited exposures.

Line bisection. This task required the patient to draw a cross at the center of varying numbers of lines presented in random locations on an A4 sheet of paper. Only MP was tested here, because the other patients (RH and AS) did not show neglect on this task, as indicated by our prior neuropsychological assessment. MP bisected 10 of 18 stimuli in the contralesional field when the preferred music was played, and 9 of 18 with unpreferred music. All lines on the ipsilesional side of the page were bisected. His individual bisection judgments, when attempted, were also assessed in the preferred and unpreferred music conditions. With preferred music, MP bisected the lines on average 0.03 cm to the right from the midline—a distance that was not significantly different from zero [$t(27) = 1.43$, $P = 0.16$]. With unpreferred music, a right-side bias of 0.15 cm was found, which differed significantly from both the deviation found with preferred music [$t(26) = 3.38$, $P = 0.002$] and from zero $t(26) = 5.3$, $P = 0.0001$].

Reading test. The task required the patient to read pronounceable nonwords presented in mixed case ("cHuNe," "fotCh"). These items were chosen because they were likely to induce neglect errors, given that parietal patients are sensitive to both lexical status and case mixing (31). Again, only MP was tested. The stimuli were randomly scattered across an A4 sheet. When his preferred music was played, he correctly read nonwords presented on both the contralesional and ipsilesional sides of the page (28 of 28 and 28 of 28 respectively). With unpreferred music, MP almost read all of the nonwords on the ipsilesional side (27 of 29: the 2 errors were due to MP neglecting the initial letter of the string). In addition, he missed 16 of 28 of the nonwords on the contralesional side of the page.

Study 2: Assessing Effects on Arousal. ***Galvanic response data (GSR).*** We assessed the effects of preferred and unpreferred music on arousal by measuring the GSR (22). During the recordings, the patients were asked just to concentrate on the music. Fig. 3*A* depicts the average of the GSRs across slots of 30 s in the different music conditions for each patient [see *Supporting Analyses* (*GSR Data*) in *SI Methods*].

Heart rate (HR) data. Fig. 3*B* depicts the average of the beats per minute across the different 30-s slots and music conditions for each patient [see *Supporting Analyses* (*HR Data*) in *SI Methods*].

There was no consistent pattern of differences in GSR and HR across the patients and across the measurement periods. Note that, if anything, the highest level of arousal appeared with unpreferred music relative to the other conditions, though this pattern did not hold across all of the patients, across the different measurement periods (i.e., RH), or across the different dependent measures (GSR and HR) (see *Supporting Analyses* in *SI Methods* for more details).

Study 3: Neuroimaging of the Music Effect. The neural correlates of the music effect were delineated by fMRI in one of our patients (MP). The behavioral task used was identical to the detection task used in study 1.

The responses on catch trials were withheld (as instructed) on 100% of the trials. We performed a 2 (target field) × 2 (music) ANOVA on the proportion of correct detections, with the mean of each session taken as an independent observation. There was an effect of target field ($F_{1,7} = 579.4$, $P < 0.0001$). Crucially, the effect of target field interacted with the music condition ($F_{1,7} = 131.3$, $P <$

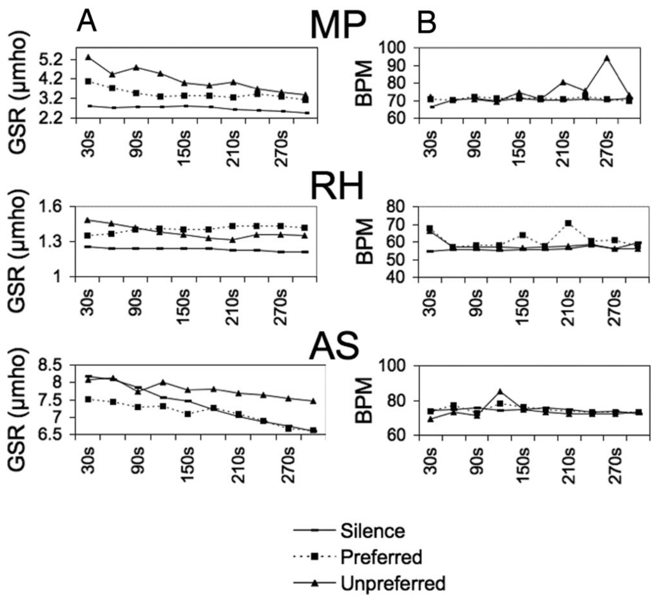

Fig. 3. Psychophysiological data. (*A*) Time course of the GSRs and (*B*) time course of the heart rate [average beats per minute (BPM)] in the 3 patients tested. Solid rectangle, silence conditions; solid square, preferred music; solid triangle, unpreferred music.

0.0001); the amount of contralesional neglect was greatly reduced under preferred music conditions (Fig. 4*A*).

We turn now to the fMRI data. The effect of the target location was clearly seen in the pattern of activations in early visual cortex. Right targets were associated with clusters of activation around left occipital cortex (BA18), whereas left targets activated the right occipital cortex (BA18). This suggests that MP did maintain eye fixation at the center of the display.

We first delineated the brain regions sensitive to the "music enjoyment" by contrasting activity in the preferred vs. unpreferred conditions. We found enhanced activity in the left inferior frontal gyrus (including Broca's area), the left dorsolateral prefrontal cortex, and the cingulate gyrus (Fig. 4*B* and Table S1). The enhancement of awareness of contralesional targets under pleasant music listening conditions was associated with increased activity in

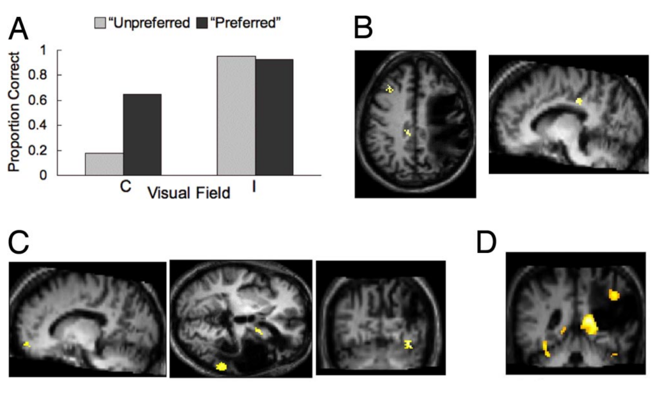

Fig. 4. Functional neuroimaging data. (*A*) Proportion of correct responses as a function of the target visual field and the music conditions. (*B*) The music effect in the fMRI data. (*C*) The interaction between music and awareness of contralesional targets in the fMRI data, reflecting selective increases in activity to contralesional targets when there was preferred music playing. (*D*) PPI results indicating the functional coupling between the OFC and undamaged areas of the right posterior parietal cortex and early visual cortex on hit trials of the preferred compared with the unpreferred music condition.

the left orbitofrontal cortex (OFC) and a network of early visual areas around the lingual gyrus in the right hemisphere that extended to the fusiform gyrus and the middle temporal cortex, and also in the caudate. This pattern of activity was indicated by a contrast that assessed the interaction between music and awareness factors carried out only for targets on the contralesional side (Fig. 4*C* and Table S1). It is also interesting to note that the music effect and its interaction with awareness of contralesional targets also correlated with activation in the amygdala (−20, −8, −16, and −28, −10, −22, respectively) at a more relaxed threshold ($P = 0.01$).

Lastly, a functional connectivity analysis [based on a psychophysiological interaction (PPI)] (32) was performed. The aim of the PPI analysis was to provide evidence that regions involved in positive affect induced by music (i.e., left OFC) were functionally connected with attention and visual brain areas. The results confirmed this prediction. There was increased coupling between OFC (MNI seed: −12, 58, −12) and clusters within undamaged areas of the right posterior parietal cortex (40, −54, 38; $Z = 5.65$, $P = 0.001$) and early visual cortex (left: −10, −76, 8; $Z = 4.64$, $P = 0.001$, and −16, −42, −4; $Z = 4.16$, $P = 0.001$; right: 20, −42, 2; $Z = 6.25$, $P = 0.001$) on hit trials in the preferred compared with the unpreferred music condition (Fig. 4*D* and Table S2). This result indicates a coupling driven by MP listening to pleasant music between emotional brain areas in the left OFC (20) and regions concerned with attentional modulation of visual processes (posterior parietal and early visual cortex). This is consistent with positive affect increasing the attentional resources available for visual perception.

Discussion

Visual neglect was markedly improved when patients listened to their preferred music relative to when they heard unpreferred music and to when the tasks were performed in silence. Preferred music enhanced the identification of contralesional targets in a perceptual report test; it facilitated the simple detection of targets; it led to more accurate midline bisection judgments (overcoming the usual bias to the ipsilesional side); it increased the cancellation of contralesional targets; and it even improved the reading of pronounceable nonwords on the contralesional side of space

Recent research has shown that music can modulate different aspects of performance in stroke populations generally, accelerating overall cognitive recovery (i.e., verbal memory and attentional focusing) and improving mood in the early acute stages following a stroke (19). In line with this, previous research has shown that alerting by means of auditory stimulation (9, 10) and by introducing a noradrenergic agonist (28) can improve awareness of contralesional information in neglect patients. Also, recent research in healthy individuals has shown intense arousal responses (indexed by the GSR) to emotionally powerful music selected by the participants (22). Hence, the music effects may be modulated by increased arousal. However, there are grounds for thinking that increased arousal alone cannot fully account for the findings. First, auditory input was presented both with preferred and unpreferred music, yet costs from unpreferred stimulation were observed relative to the silent condition. Second, the GSR and HR data did not show that arousal was consistently higher with preferred music relative to the other conditions. If anything, the highest level of arousal tended to occur in the unpreferred music condition, although this did not hold across all of the patients and across the measurement period (see RH) or across the different dependent measures (GSR and HR). Also, VAS ratings of arousal did not show consistent music effects across patients, although there were effects on rated positive affect. Moreover, arousal effects on performance have been related to a facilitation of decision-level processes of the response to a target (24); however, we did not find differences in target detection RTs as a function of the music played. It is interesting to note, however, that overall levels of arousal were higher when the music was played relative to silence. There were also some arousal differences between the preferred and unpreferred music conditions. For example, MP and AS showed a higher GSR response with unpreferred than with preferred music. Although patient RH showed no significant differences between preferred and unpreferred music on the GSR, he showed a pattern of HR and VAS ratings consistent with pleasant music enhancing both positive affect and arousal. It is also worth noting that the enhancement of awareness in MP correlated with a medium level of arousal. This result fits a "Yerkes–Dodson" account, according to which medium levels of arousal are associated with optimal performance (33). In line with this, unpreferred music led to a higher amount of contralesional extinction (relative to silent conditions). We speculate that pleasant music may lead to optimal, rather than maximal, levels of arousal, and this can reduce neglect, whereas unpreferred music may increase extinction by overarousing the patients. The reduced awareness of contralesional targets under unpreferred music conditions also fits with evidence that negative affect may lead to a narrowing of the focus of attention (34, 35), which may in turn decrease awareness in patients with visual neglect. Therefore, we do not completely exclude the possibility that musically induced arousal could have contributed to the observed effects. Neglect patients with extensive right-hemisphere lesions, particularly affecting right frontal–parietal circuits, usually present deficits in maintaining alertness (36, 37). It is possible that at least part of the effect of pleasant music stimulation originates from an optimal activation of ascending thalamic–mesencephalic circuits involved in alerting (10, 38, 39).

In contrast with the inconsistent effects on arousal across patients, we found consistent evidence for effects of positive emotion. Music enjoyment and mood ratings were in all cases more positive in the preferred music condition. Moreover, the improved of awareness of contralesional stimuli under pleasant music conditions was strongest in patient MP, who also showed a higher positive affect response relative to the other patients. This finding suggests that the strength of the positive affect response may modulate improvements in visual neglect. Crucially, there was converging evidence from fMRI that preferred music enhanced visual awareness through positive affect. Pleasant music activated brain areas, including the restrosplenial cingulate gyrus and the OFC, both of which have been linked to emotional response to stimuli (40, 41). Our result also fits with evidence that music can activate the substrates of emotional states in paralimbic areas (20, 42), whereas pleasurable responses, induced by listening to pleasant music, may be supported by the activation of subcortical dopamine systems in the ventral tegmental area, the substantia nigra, and the caudate (43). Moreover, in line with our fMRI data, positive affect through "musical enjoyment" have also been associated with activity in the Broca's area (44) and the dorsolateral and orbital parts of the prefrontal cortex, which are also part of a dopaminergic system that receives projections from subcortical substrates (43). Interestingly, functional connectivity analyses showed that emotional regions in the OFC modulated activity of intact attentional brain areas in the intraparietal cortex (45) of the damaged right hemisphere. The enhancement of activation in attention-related parietal systems could help gate the access of visual information to awareness. Increased activity in neural circuits involved in positive emotion may lead to increased availability of neural processing resources in critical brain regions of the damaged hemisphere of patients. Releasing attentional resources through "music enjoyment" may be particularly important for overcoming the "default" tendency of neglect patients to allocate attentional resources to the ipsilesional visual field, and it may even trigger a paradoxical relaxation of attentional control and decreased filtering capacity (16, 46). Our fMRI evidence indicates that any release of resources (through positive effect induced by preferred music) facilitated activation in the peri-lesional area, enabling previously unconscious stimuli to be perceived.

It should be noted that the music used in the study had markedly different acoustical attributes, both within and across the preferred/

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unpreferred pieces, because each patient listened to contrasting pieces played by particular artists. More specifically, music genre and specific music dimensions (i.e., pitch, tempo, lyrics, etc.) varied across the different pieces and even within a piece. This variation in music within and across patients goes against any argument that specific acoustical properties of the music were critical in generating the effects of music on neglect. Instead, the critical factor more likely relates to the preferred status and the more pleasant valence of the music selected by the patients.

Whatever the specific neural mechanism involved, the current findings point to interesting clinical applications that may help the recovery of visual neglect after brain insult. These results imply that attentional function in patients with visual neglect needs to be understood in light of individual emotional factors. Visual neglect may be exacerbated when patients are in a negative emotional state, and it may be improved by inducing positive emotions. In the present case, a pleasant tune was able to reduce contralesional neglect even in chronic patients. Positive emotional responses and optimum arousal induced by pleasant music listening may aid the engagement of the neuroplastic systems that support flexible attentional control.

Materials and Methods

Behavioral computer-based experiments of Study 1 were programmed by using E-Prime (47). Further behavioral testing used typical paper and pencil neuropsychological tests (start cancellation, line bisection) from the Battery Inattention Test (BIT) (48). Further details are provided in the *SI Methods*.

Ratings of enjoyment, mood, and arousal as the patients listened to preferred pleasant music and unpreferred music were taken by using Visual Analogue Scales (*SI Methods*). The preferred and unpreferred status of the music was operationalized along a continuum of pleasantness (21). The patients were asked to choose their preferred pleasant music artists: Kenny Rogers (MP), the Flying Burrito Brothers Band (RH), and Frank Sinatra (AS). The unpreferred music included rock tunes from Sonic Youth (RH) and The Ramones (AS) and hip-hop tunes from Rakim (MP). The unpreferred music was chosen by the researchers following a prior debriefing stage where patients listened to different music samples. We note that patients did not complain when the unpreferred music was played. Patients were debriefed after completion of the study to learn about their feelings during task performance. Further details on the music selection are also provided in the *SI Methods*.

Psychophysiological signals as the patients listened to the music, including the galvanic skin response and heart rate, were recorded by using a Biopac MP150 system and analyzed by using AcqKnowledge software (Biopac Systems Inc.).

Brain imaging data were acquired by means of a Philips 3T Achieva system and analyzed with SPM5 (www.fil.ion.ucl.ac.uk/spm; Wellcome Department of Imaging Neuroscience, London, UK). Further details on fMRI data acquisition and analyses, including the PPI analyses, are provided in the *SI Methods*.

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