Neuroscience Letters 275 (1999) 222–226

Neuroscience Letters

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Analysis of music–brain interaction with simultaneous measurement of regional cerebral blood flow and electroencephalogram beta rhythm in human subjects

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Received 30 August 1999; accepted 16 September 1999

Abstract

To elucidate the neural substrates of the receptive aspect of music, we measured regional cerebral blood flow (rCBF) with positron emission tomography (PET) and simultaneously recorded the electroencephalogram (EEG) in eight normal volunteers. Compared with the rest condition, listening to music caused a significant increase in EEG beta power spectrum (13–30 Hz) averaged over the posterior two third of the scalp. The averaged beta power spectrum was positively correlated with rCBF in the premotor cortex and adjacent prefrontal cortices bilaterally, the anterior portion of the precuneus and the anterior cingulate cortex in both the rest and the music conditions. Listening to music newly recruited the posterior portion of the precuneus bilaterally. This may reflect the interaction of the music with the cognitive processes, such as music-evoked memory recall or visual imagery. © 1999 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Positron emission tomography; Electroencephalogram; Beta rhythm; Cerebral blood flow; Music

Listening to music is a purely personal experience influenced by many factors. Although music shares cognitive functions and operations with other mental activities, such as language as a form of expression and communication, the experience of listening to music, for most people, is primarily of a receptive nature [17]. The arousal of feeling by music and the aesthetic appreciation of music are essentially the interaction of the musical piece with the emotional and mental state of the listener [17]. Without the overt expression of this receptive process, exploration of its neuroanatomical substrate is difficult. However, the interaction of music with the brain state may be reflected in changes in brain electrical activity, recorded by the electroencephalogram (EEG). Brief exposure to music leads to a short-lived improvement in spatial task performance [13], which is correlated with changes in EEG power spectrum [14]. These findings suggest that music facilitates specific changes in the brain state that mediate improved performance and that EEG power spectrum is an indicator of music's effect.

The purpose of the present study was to elucidate the neural substrates of the receptive aspect of music. As the site from which the EEG originates is uncertain, we combined EEG with a functional brain mapping technique to localize neural activities that are correlated with EEG power spectrum [16]. We analyzed regional cerebral blood flow (rCBF) with positron emission tomography (PET) as an indirect measure of local neuronal activity and simultaneously recorded the EEG as an indicator of brain state during the rest and music-listening conditions. In a previous study [16], we focused on the analysis of alpha rhythm in relation to rCBF changes irrespective of the condition. In the present study, we further analyzed the same data to characterize neural substrates for the music effect. The effects of a task (music listening) condition and a rest condition on rCBF, alpha power and beta power

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PII: S0304-3940(99)00766-1

were compared and the results showed an effect of 'condition' on beta power. Therefore, interaction between the correlational change in rCBF with beta power and the condition effect was analyzed to localize the neural substrates responsible for the change in brain state effected by listening to music.

The detailed experimental settings and subjects are described in an earlier report [16]. In brief, the subjects were eight right handed normal volunteers (three women and five men), aged 24–37 years (mean 29.9). The protocol was approved by the Ethical Committee of Fukui Medical University and all subjects gave their written informed consent for the study. During PET scanning, the subjects lay in a supine position with their eyes open and their heads immobilized with an elastic band and sponge cushions. Electrodes were applied to 12 scalp sites according to the international 10–20 system of electrode placement, with linked earlobe electrodes used as a reference and a filter setting of 1–60 Hz. The experiment consisted of three PET studies performed on the eight subjects at 6-month intervals. For each study, each subject had ten consecutive PET scans with a 10-min interval between scans. A complete session consisted of two scans in the 'rest condition' and eight scans in the 'music condition'. For the rest scans, subjects lay quietly while looking at a static picture on a board in front of them. The subjects were instructed not to move or close their eyes during the scan. Spontaneous eye blink was allowed. For the music condition, subjects listened to traditional Indonesian Gamelan music. The music began approximately 50–90 s before the start of the scan and continued for 200 s. The subjects were asked to make no response during the music-listening session. The EEG was continuously recorded throughout the approximately 90 min of each PET study.

PET scanning was performed with a General Electric Advance tomograph (Milwaukee, WI) with the interslice septa retracted. Images of cerebral blood flow were obtained by summing the activity occurring within the 90-s period following the initial increase in cerebral radioactivity after an intravenous bolus injection of 10 mCi of ^{15}O-labeled water [15]. Contamination of tissue activity images of the brain by the radioactivity of the extracranial structures, such as extraocular muscles, was denied by visual inspection.

Due to technical problems of EEG recording, seven PET scans were omitted from analysis and therefore, 233 sets of CBF images and simultaneously recorded EEGs were analyzed. To eliminate artifacts caused by eye movement, only data from the posterior two thirds of the scalp (seven electrodes: C_3, C_4, T_5, T_6, P_z, O_1, O_2) were selected. EEG data were obtained from 120 s of recording beginning approximately 30 s before the start of each PET scan. EEG data from each electrode position in the time domain were first transformed into the Fourier domain in every 2-s epoch and the mean amplitudes of two frequency bands, alpha (8–13 Hz) and beta (13–30 Hz), were calculated and averaged over 60 epochs. The temporally averaged alpha and beta amplitudes of the seven electrodes were then spatially averaged. The temporally and spatially averaged alpha and beta amplitudes for each condition in each subject were normalized with respect to the mean value across all conditions in all three studies in each subject to eliminate intersubject differences. Analysis of variance (ANOVA) was used to evaluate the effects of 'condition' and 'subjects' on EEG power.

The PET and EEG data were analyzed with statistical parametric mapping (SPM95 and 96) [3]. The PET scans from each subject's three studies were realigned, with the first image used as a reference. After realignment, all images were transformed into a standard stereotaxic space [19]. Each image was smoothed by the use of a Gaussian filter ($\mathrm{FWHM}x \times \mathrm{FWHM}y \times \mathrm{FWHM}z = 20 \times 20 \times 20$ mm) to account for variations in normal gyral anatomy.

After the appropriate design matrix was specified, the effect of the condition, subject and covariate (i.e. amplitude of the beta wave) was estimated according to a general linear model at each and every voxel, assuming a linear relationship between the rCBF and the covariate. The effect of global CBF was eliminated by proportional scaling. The statistical model at each voxel k was

$$Y^k_{qji} = \alpha^k_q + \rho^k_q\left(S_{qij} - S_{q\cdot}\right) + r^k_i + \epsilon^k_{qji}$$

where Y^k_{qji} is the rCBF of ith subjects ($i = 1,\ldots,8$) for the jth measurement under condition q ($q = 1, 2$), P^k_q is the covariate effect of EEG power s in condition q, r^k_i is the subject effect and ϵ^k_{qji} is an error term. S_{qij} is the beta power of subject i in condition q and $\mathrm{S}_{\mathrm{q}}.$ is the averaged beta amplitude in condition q over the subjects and the measurements. The q subscript of the covariate effect ρ indicates different slope for each condition. The simple condition effect and covariate effect with EEG power were assessed by linear contrasts (Table 1). Contrast weight CR = (0, 0, 1, 0) (contrast 3, Table 1) expresses evidence against the null hypothesis that there is no covariate effect in the rest condition ($\rho_1 = 0$), assessing evidence for the one-sided alternative hypotheses ($\rho_1 > 0$: rCBF increases with beta power during the rest condition). Similarly, contrast weight CM = (0, 0, 0, 1) (contrast 4, Table 1) assesses the positive covariate effect in the music condition.

Common positive covariate changes in rCBF with beta power, in the rest and music conditions, were assessed by conjunction analysis [12] (Table 1). With this approach, two contrasts were tested, asking whether the covariate changes under the two conditions were equally significant. Conjunction analysis has two processes [12]. The first is the elimination of regions that show significant differences between the simple effects by the F-test with an appropriate threshold ($P < 0.05$, uncorrected for multiple comparisons). The second is the statistical inference test for the main effect with use of the standard procedure based on the theory of Gaussian random fields [3]. To explore the regions where there was positive covariance of rCBF with beta power

Table 1
Linear contrasts for comparisons[a]

Contrasts for simple effects

Contrast	Condition		EEG effect		rCBF
	Rest	Music	Rest	Music	
1	−1	1	0	0	Activation during music
2	1	−1	0	0	Deactivation during music
3	0	0	1	0	Positive correlation with EEG power during rest
4	0	0	0	1	Positive correlation with EEG power during music
5	0	0	−1	0	Negative correlation with EEG power during rest
6	0	0	0	−1	Negative correlation with EEG power during music
7	0	0	1	−1	More positive correlation during rest than music
8	0	0	−1	1	More positive correlation during music than rest

[a] Main effects of conjoint expression of simple contrasts: 3&4: positive correlation during both rest and music; 5&6: negative correlation during both rest and music; 4&8: positive correlation during music only, without change during rest; 6&7: negative correlation during music only, without change during rest; ampersand (&) indicates conjunction analysis [12].

during the music condition, but not during the rest condition, contrasts CM = (0, 0, 0, 1) (contrast 4, Table 1) and (CM–CR) = (0, 0, −1, 1) (contrast 8, Table 1) were tested jointly with conjunction analysis. This approach eliminated the voxels that showed covariate change (either positively or negatively) during the rest condition, but retained the voxels that showed a significant positive covariate during the music condition. This is because, if contrasts CM and (CM–CR) are equally significant, the effect of the rest condition should be null. The statistical threshold was $P < 0.05$ of a corrected P-value [3].

There was a significant effect of condition ($F_{1,185} = 6.401$, $P = 0.0122$) on beta power. Beta power was significantly higher during the music condition than during the rest condition ($P = 0.00001$, Scheffe's post-hoc test). There was no significant effect of condition ($F_{1,185} = 1.723$, $P = 0.191$) on alpha power.

Compared with resting, listening to music caused an increase in rCBF in the temporal regions bilaterally (Table 2). There was a positive correlation of rCBF with beta power in the premotor cortex and adjacent prefrontal cortices, the anterior and medial portions of the precuneus and the anterior cingulate cortex in both the rest and the music conditions, but the difference in activation between the conditions was not significant. Listening to music newly recruited the posterior portion of the precuneus bilaterally, where rCBF showed a positive correlation with beta power only during the music condition (Table 3 and Fig. 1).

Beta power spectrum was higher during the music condition than during the rest condition. Beta rhythm is a measure of cortical integrity, because it is diminished in the presence of cortical injury and because loss of beta activity, whether diffuse or focal, indicates compromised cortical function [8]. As mental arithmetic, linguistic tasks and other cognitive efforts augment beta rhythm [8], beta rhythm has been used as an indicator of cognitive function. Hence, augmentation of beta power spectrum during music listening may indicate the interaction of music with cognitive processes.

An increase in rCBF in the bilateral superior temporal gyri, including the primary and secondary auditory cortices, is presumably related to sound processing. Neuronal activities in the superior aspect of the temporal lobe are responsive to external auditory stimulation.

To localize the neural substrates with which the perception of music interacts, we adopted parametric designs that correlate neural activities, such as a change in rCBF, with EEG amplitude. The assumption here is that the neural substrates involved in a correlational change in EEG amplitude are in some way related to the neural process affecting the EEG amplitude. This assumption is valid, because it has been shown that the alpha amplitude is negatively correlated with rCBF changes in the visual cortices, which is consistent with the well-known reactivity of the alpha amplitude [16]. As the EEG measures only concerted activity of large-scale cell assemblies [20], changes in the synchronization of a neuronal population can occur without significant changes in the mean neuronal firing rates and thus without changes in blood flow and metabolism [5]. Hence, a positive correlation between EEG amplitude and rCBF allows us to localize

Table 2
Increase in regional cerebral blood flow during music listening compared with rest

Cluster level		Talairach coordinates				Area[b]
P	Size	x	y	z	Z (P[a])	
<0.001	3480	−46	−20	4	8.42 (<0.001)	L,GTt (41)
<0.001	2939	38	−30	8	8.22 (<0.001)	R,GTt (41)

[a] The significance of activation is corrected for multiple comparisons at the voxel level. [b]L, left side, R, right side. Numbers in parentheses refer to Brodmann area [19]. GTt, transverse temporal gyrus.

Table 3
Positive correlation between regional cerebral blood flow and EEG beta power

Cluster level		Talairach coordinates				Area[b]
P	Size	*x*	*y*	*z*	*Z* (*P*[a])	
Rest and music conditions						
<0.001	7296	56	0	24	6.77 (<0.001)	R, GPC (6)
		−40	0	44	6.61 (<0.001)	L, GPC (6)
		16	0	44	5.56 (<0.001)	R, ACG (24)
		46	16	36	5.38 (<0.001)	R, GFm (9)
		−32	2	−4	4.89 (0.001)	L, Claustrum
		−6	−48	44	4.78 (0.002)	L, Pcu (7)
		−32	0	48	4.63 (0.003)	L, GFs (6)
		32	0	48	4.33 (0.011)	R, GFs (6)
Music condition only						
0.009	696	0	−68	48	4.38 (0.007)	Pcu (7), posterior

[a] The significance of activation is corrected for multiple comparisons at the voxel level; [b]L, left side, R, right side. Numbers in parentheses refer to Brodmann area [19]. ACG, anterior cingulate gyrus; GFm, middle frontal gyrus; GFs, superior frontal gyrus; GPC, precental gyrus; PCu, precuneus.

information processing that may be caused mainly by modulation of neuronal synchrony, with a small change in energy expenditure compared with the change in EEG power.

Irrespective of the conditions, large areas of premotor and adjacent prefrontal cortices, as well as the anterior cingulate cortex extending posteriorly to the medial portion of the precuneus, showed a positive correlation of rCBF with beta power spectrum. In non-human primates, the premotor cortex and posterior parietal lobe (especially area 7b) appear to form a system for the coding of near-extrapersonal space for guidance of movement within that space [4]. Functional neuroimaging studies in humans suggest that the premotor-posterior parietal connections are not only for motor control but also for cognitive processes. A mental object-construction task activated the bilateral premotor and parieto-occipital regions [10]. Coupled activations of the parietal and premotor cortices have been reported in visuospatial tasks, which involve spatial working memory implicitly [6] or explicitly [7]. Exchange of information between the premotor and parietal areas appears to be necessary when the visuospatial stimulus is processed even only mentally and hence, without the execution of motor activity and independent of perceptual modalities [10]. Mellet et al. [10] speculated that the exchange of information between the premotor and posterior parietal regions is a general feature of spatial processing: execution of the encoding of a spatial environment in its descriptive and behavioral aspects. Therefore, the positive correlation of rCBF in the premotor cortex and the posterior parietal regions with beta power is consistent with the concept that beta rhythm is an indicator of cognitive processes.

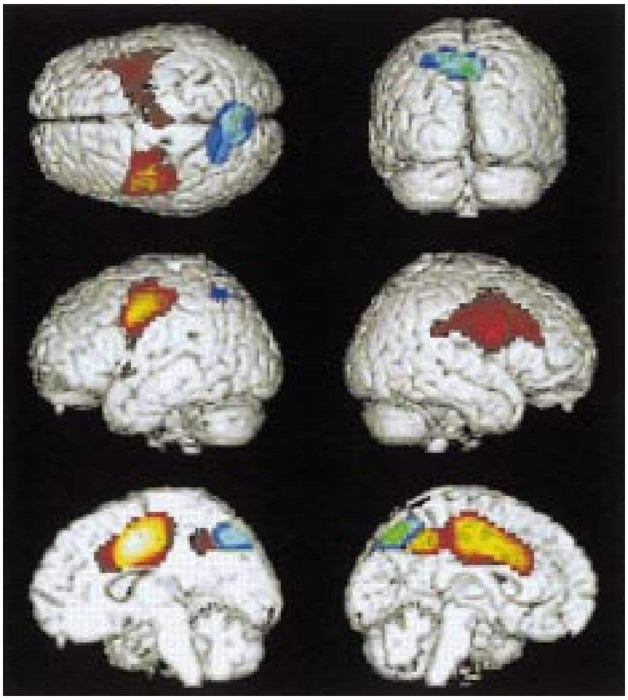

Fig. 1. Statistical parametric maps of the positive correlation between rCBF and EEG beta amplitude, superimposed on surface-rendered, high-resolution MRIs of the brain. Maps show areas in which positive correlations were found during both the rest and the music conditions (red) and during the music condition only (blue). Areas of $Z > 3.09$, with cluster level significance of $P < 0.05$ corrected for multiple comparisons, are shown.

During the music-listening condition, areas with a positive correlation between rCBF and beta power extended into the posterior portion of the precuneus, close to the parieto-occipital sulcus. The increase in beta power during the music condition, compared with the rest condition, suggests that the neural substrates responsible for the correlational change with beta power may be related to the music–brain interaction. This finding may be interpreted within the conceptual framework of premotor-posterior parietal connections. Activation of the cuneus and precuneus on the left side was observed in a pitch discrimination task [11] and in the reading of a musical score by musicians

[18]. Although the present study failed to show an increase in rCBF in this area, the premotor-parietal network may include the precuneus as a part of the neuronal substrate for music perception. Thus, there may be an overlap of the neural networks for musical and spatial processing. Brief exposure to music led to a short-lived improvement on spatial task performance [13]. EEG power correlated with enhanced spatial performance following exposure to music [14]: a lower alpha2 (10.5–11.97 Hz) and a higher beta1 (12.02–17.97 Hz) frequency were associated with greater improvement on the spatial task. Work on a neuronal model [9] suggests that there may be a common neural firing pattern between musical and spatial processing. Considering the role of premotor-parietal networks for spatial processing and the possible overlap between musical and spatial processing, music listening may cause priming of the posterior portion of the precuneus, which may work to the advantage of a subsequent spatial task.

Recruitment of the posterior precuneus during music listening may reflect the interaction of the music with the mental state, such as in music-evoked memory recall or visual imagery. Activation of this area during memory retrieval [1] and through visual imagery as a mnemonic [2] has been reported.

The authors thank B.J. Hessie, ELS, for skillful editing. This study was supported, in part, by a research grant (JSPS-RFTF97L00203) for the 'Research for the Future' program from the Japan Society for the Promotion of Science.

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