International Journal of Bifurcation and Chaos, Vol. 26, No. 1 (2016) 1650001 (9 pages)

DOI: 10.1142/S0218127416500012

Modulation of EEG Theta Band Signal Complexity by Music Therapy

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Received November 14, 2011; Revised April 2, 2012

The primary goal of this study was to investigate the impact of monochord (MC) sounds, a type of archaic sounds used in music therapy, on the neural complexity of EEG signals obtained from patients undergoing chemotherapy. The secondary goal was to compare the EEG signal complexity values for monochords with those for progressive muscle relaxation (PMR), an alternative therapy for relaxation. Forty cancer patients were randomly allocated to one of the two relaxation groups, MC and PMR, over a period of six months; continuous EEG signals were recorded during the first and last sessions. EEG signals were analyzed by applying signal mode complexity, a measure of complexity of neuronal oscillations. Across sessions, both groups showed a modulation of complexity of beta-2 band (20–29 Hz) at midfrontal regions, but only MC group showed a modulation of complexity of theta band (3.5–7.5 Hz) at posterior regions. Therefore, the neuronal complexity patterns showed different changes in EEG frequency band specific complexity resulting in two different types of interventions. Moreover, the different neural responses to listening to monochords and PMR were observed after regular relaxation interventions over a short time span.

Keywords: EEG; complexity; oscillations; theta band; music therapy; PMR.

1. Introduction

The human brain is often considered as the most complex object in the known universe, and music, with all its complexities and richness, is considered as one of the most unique characteristics of our species. Music is present in all cultures, and listening to (and performing) music is consistently rated as one of the most pleasurable experiences in our lives [Vuust & Kringelbach, 2010]. Listening to music can engage a multitude of brain regions including anterior cingulate cortex, hippocampal formation, and dopaminergic neural networks [Koelsch, 2010]. In particular, changes in brain activity were shown during strong emotional experience induced by the listener's most preferred music, and this phenomenon, termed as "chill sensation", is perceived as an intensely positive or peak experience. Intensity of the chill experience was positively

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Author Contributions: JB developed the complexity index and performed data analysis; EJL performed data collection; JB and EJL wrote the paper.

correlated with activations of right thalamus, anterior cingulate cortex, supplementary motor area, and insula, and negatively correlated with activations of right amygdala, left hippocampus/amygdala, and ventral medial prefrontal cortex [Blood & Zatorre, 2001]. Listening to music also alters the dynamical brain responses, i.e. oscillatory component(s) of the electroencephalogram (EEG) signals, particularly theta frequency band (3.5–7.5 Hz). For instance, pleasant music elicits an increase of the frontal midline theta power [Sammler *et al.*, 2007], and listening to classical music causes an increase in posterior theta power [Chan *et al.*, 2008], whereas the relaxation effects of music are associated with a change in the total theta power [Kabuto *et al.*, 1993]. Further, broadband EEG complexity as measured by the correlation dimension increases with increasingly complex music and with musical sophistications [Birbaumer *et al.*, 1996]. Furthermore, EEG responses for music with fractal or self-similar scaling properties were associated with reduced correlation dimension and largest Lyapunov exponent than for music without scaling properties [Jeong *et al.*, 1998].

It is therefore important to consider to what extent the results from neurophysiological and neurophenomenological studies on the effects of listening to music are significant for the clinical usage of music. Previously, only a few neurobiological studies have demonstrated the positive effect of music (listening or playing) in a clinical context, including in the music therapeutic context, such as improvements for tinnitus sufferers [Okamoto *et al.*, 2010], cognitive rehabilitation after a stroke [Sarkamo *et al.*, 2008], improvement in fine as well as gross motor skills after a stroke [Altenmuller *et al.*, 2009], or improvement of speech in patients suffering from Broca's aphasia [Schlaug *et al.*, 2009]. Apart from functional improvements, music has also been used in various clinical contexts to positively influence patients' psychological and physiological states by reducing pain [Nilsson *et al.*, 2003; Tan *et al.*, 2010], anxiety [Singh *et al.*, 2009], and by promoting relaxation [Nilsson, 2009]. Typically, in oncological context, music has been shown to be effective by reducing anxiety [Burns *et al.*, 2008; Sabo & Michael, 1996] and side effects [Ezzone *et al.*, 1998] in patients undergoing chemotherapy.

Despite such success with musical intervention in clinical settings, the underlying neurophysiological responses have rarely been studied, yet neural correlates to these changes caused by music can provide deeper insights into the effect of music in patients. Moreover, these insights can be used as neuroscientific evidence towards the broader acceptance of musical intervention and further establish the evidence-based use of music and music therapy as a scientifically supported therapeutic method in the clinical context [Hillecke *et al.*, 2005]. It is therefore necessary to investigate the neural changes accompanying not only functional improvement but also psychological and physical support (i.e. the anxiolytic, analgesic, or relaxing effects) achieved by listening to music.

The current study aims to fill this gap between the music psychological, music physiological (neurophysiological), and music therapeutic approaches to analyzing how patients benefit from the receptive use of music with a particular focus on listening to monochord sounds. Monochord is an ancient music instrument with approximately 30 strings tuned on the same tone with many induced overtones, and has been shown to improve the psychological and physiological states of patients [Rose & Weis, 2008]. Unlike the excerpts of familiar music used in music therapy [Khalfa *et al.*, 2003], monochord is rather unfamiliar, and contains minimal musical parameters, thereby minimizing the involvement of different music psychological factors (subjective preference, arousal, etc).

This study focused on neurophenomenological patterns and on changes in the mode complexity values in standard EEG frequency bands during relaxation induced by monochord sounds and compared them to those induced by the progressive muscle relaxation (PMR) method. PMR is a widely established technique for relaxation by alternately tensing and relaxing the muscles [Jacobson, 1938]. Using a recently proposed index, signal mode complexity, it is possible to quantify the complexity of EEG signals by investigating the constituent oscillatory components within standard EEG frequency bands [Bhattacharya & Pereda, 2010].

2. Materials and Methods

This randomized clinical study has been conducted at the Women's Hospital, University of Heidelberg, Germany. A total of 43 female patients with gynaecological cancer receiving chemotherapy were recruited into the study. Of these, 22 patients were randomly assigned to the monochord group (MC) (mean age: 49, range: 27–55) and 21 patients to the PMR group (mean age: 51, range: 31–56). During both relaxation treatments, patients were lying down, awake but with eyes closed. Both groups received the recorded intervention (either monochord sounds or instructions for PMR) for 25 min after a period of verbal introduction (4 min). Each session was in sync with the onset of chemotherapy. Patients received individual relaxation treatment sessions — a total of four times over a span of six months.

During the first and the last treatment sessions, EEG signals were recorded with 23 Ag/AgCl electrodes attached to the scalp (Fp1, Fp2, F3, F4, F7, F8, C3, C4, T1, T2, T3, T4, T5, T6, P3, P4, O1, O2, Fz, Cz, Pz, A1, A2) according to the International 10–20 electrode placement system [Jasper, 1958]. All electrode impedances were kept below 10 KΩ. The sampling frequency was 128 Hz. The EEGs were re-referenced offline to the algebraic mean of the two earlobe electrodes. During EEG recording, participants were awake but their eyes were closed.

Data from five patients were excluded due to excessive artefacts, and the data of a total of 38 patients were analyzed (MC: $n = 20$, PMR: $n = 18$). EEG signal at each electrode location was bandpass filtered in six standard frequency bands: delta (< 3 Hz), theta (3.5–7.5 Hz), alpha (8–12 Hz), beta 1 (12–19.5 Hz), beta 2 (20–29 Hz), and gamma (> 30 Hz); in this study, we strategically focused our analysis on theta, alpha and beta-2 bands based on our earlier analysis (unpublished observation). The EEG analysis concentrated on two 5 min long periods within each treatment session: *Begin* period (from the beginning phase of a treatment session) and *End* period (from the final phase of a treatment session). These periods were chosen so that the within-session effect of each relaxation treatment could be reliably assessed. Within each period, the data were divided into 30 nonoverlapping epochs of 10 sec. Epochs with maximum absolute amplitude larger than 75 μV were considered as artefacts and eliminated from subsequent complexity analysis. The complexity values were computed for individual epochs.

The procedure of calculating signal mode complexity is described briefly as follows. Consider an EEG time series, $\{x(k), k = 1, 2, \ldots, N\}$, which is normalized to zero mean and unit variance. We form a $m \times n$ matrix,

$$\mathbf{A}_n = \begin{bmatrix} x(1) & x(2) & \cdots & x(n) \\ x(n+1) & x(n+2) & \cdots & x(2n) \\ \vdots & \vdots & \ddots & \vdots \\ x(n(m-1)+1) & x(n(m-1)+2) & \cdots & x(mn) \end{bmatrix}$$

and calculate its singular values ($\sigma_1, \sigma_2, \ldots, \sigma_p, p = \min(m, n)$) [Golub & Van Loan, 1996]. By varying the row length (n), new matrices are formed, and their singular values are subsequently calculated. For each configuration of $\mathbf{A}_n$, the singular values are linearly mapped to R normalized singular values but preserving the total energy spanned by the sum of squares of singular values. This way all the singular values for each matrix configuration were considered and the associated singular value profiles were made linearly equivalent to each other. Hence for M different values of row length n, M sets of R singular values are obtained:

$$\{\sigma_{i,j} : i = 1, 2, \ldots, M; j = 1, 2, \ldots, R\}.$$

An average singular value profile is obtained as:

$$\hat{\sigma}_j = \frac{1}{M}\sum_{i=1}^{M} \sigma_{ij}.$$

Earlier we have shown that this average profile could distinguish chaotic time series from a random one, and further could be used to characterize physiological signals.

The signal mode complexity, C_S, is computed as:

$$C_S = \frac{\sum_{j=1}^{R} j^2 \hat{\sigma}_j}{\sum_{j=1}^{R} j^2}.$$

The lower the C_S value, the higher the likelihood of regularly occurring pattern of synchronized oscillations. C_S is found to be able to detect changes in the complexity of the signal that is very similar to the changes in the largest Lyapunov exponent, a hallmark of chaotic complexity. Further, C_S is a measure with high reliability that can be applied to small data sets, and further the method is assumption-free. See [Bhattacharya & Pereda, 2010] for further details.

The complexity values were log-transformed prior to statistical analysis. A mixed factorial ANOVA was performed with between-subject factors, *group* (2 levels: MC and PMR), and within-subject factors, *session* (2 levels: Pre and Post), *time* (2 levels: Begin-period and End-period), and *region* (two levels: anterior (Fp1, Fp2, F3, F4, F7, F8, T1, T2, Fz), and posterior (T5, T6, P3, P4, Pz, O1, O2)). The statistical significance was set at $p < 0.05$. All statistical analyses were performed using SPSS (version 16.0).

3. Results

First, we investigated the C_S differences across sessions. Figure 1 shows the C_S values at 21 electrode regions in three standard EEG frequency bands (theta, alpha, and beta-2) for both groups during the first (designated as Pre) and last (designated as Post) sessions of treatment. At first glance, the spatial profiles of C_S values appeared to be similar between Pre and Post within each group, and further the scalp distribution of differences in C_S values (Pre–Post) were quite similar across frequency bands within each group. However, upon closer inspection, several interesting features emerged. The theta band complexity in the MC group was

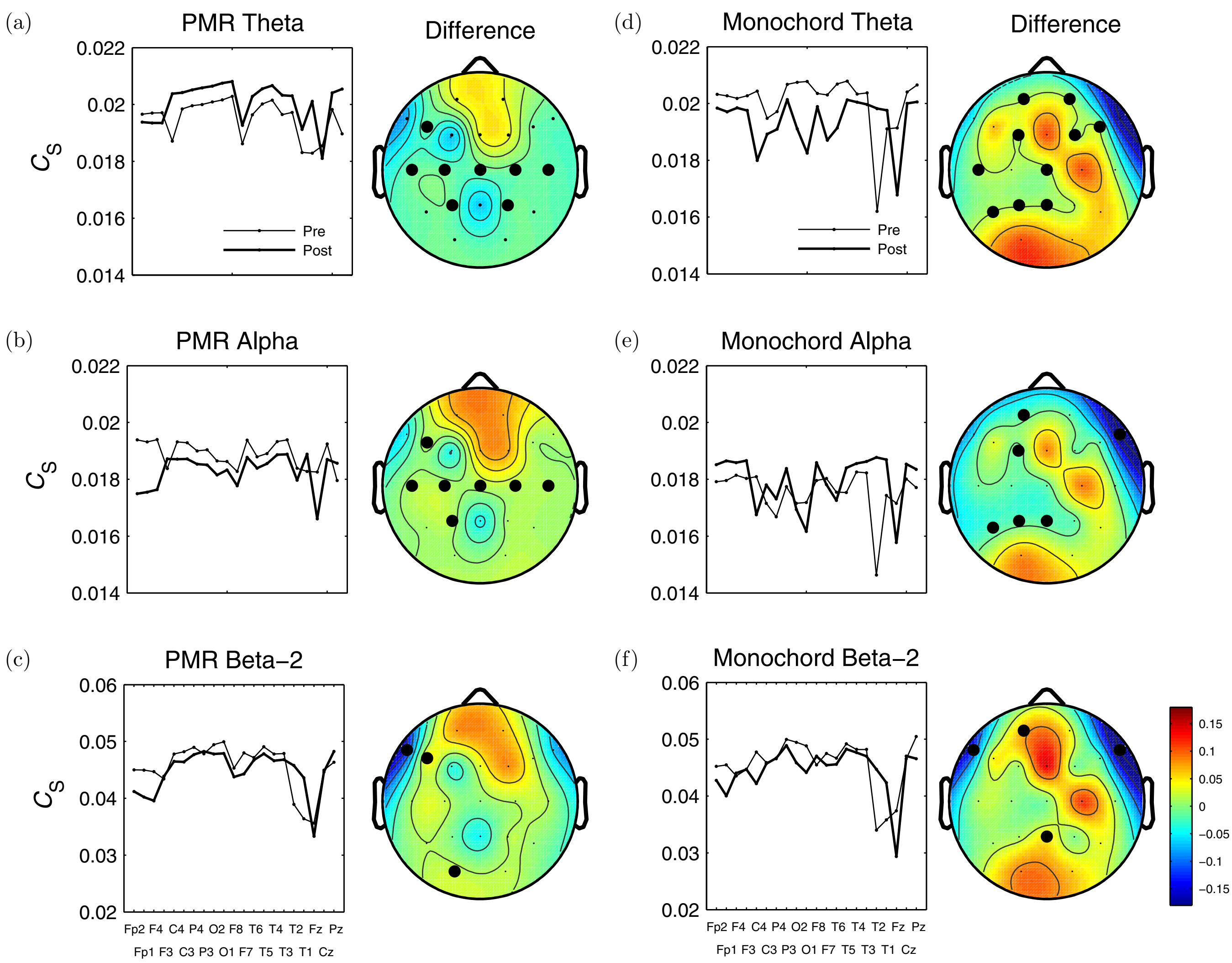

Fig. 1. Signal mode complexity (C_S) of three frequency bands (theta, alpha and beta-2) at 21 scalp electrodes in the first (Pre) and the last (Post) treatment sessions for (a)–(c) the PMR and (d)–(f) the MC groups. Results were averaged across two periods (*Begin* and *End*, see text) within a session. Scalp map adjacent to each plot describes the topographical distribution of difference (Pre–Post) C_S values. Red color indicates a decrease in C_S in the last session compared to the first session. Electrodes showing statistically significant ($p < 0.05$, Bonferroni corrected) changes are shown by bigger filled circles.

considerably lower in the last session compared to the first session over a multitude of electrode regions [Fig. 1(d)], but with a stronger emphasis in the posterior region ($F(1, 19) = 5.15$, $p = 0.03$). Interestingly, the PMR group displayed an opposite trend: theta band complexity increased in the last session compared to the first one over many brain regions except frontopolar and midfrontal regions showing the reverse pattern [Fig. 1(a)]. The alpha band complexity in the MC group was rather similar between first and last sessions but a trend towards decreased complexity was found in midfrontal (Fz), right temporal (T4, T2, T1) and occipital (O1, O2) electrode regions [Fig. 1(e)]. In beta-2 band, C_S value in midfrontal electrode region was significantly lowered in the last session compared to the first session in the MC group ($F(1, 19) = 5.66$, $p = 0.02$). The results in the PMR group were quite similar across frequency bands and the midfrontal region showed consistently decreased complexity.

Next, we studied the within session C_S differences. Figure 2 shows the general tendencies of the change in theta band complexity values between *Begin* (5 min period from the beginning phase of a session) and *End* (5 min period from the end phase of a session) periods within both first (Pre) and last (Post) sessions. Within a session, the PMR group showed very similar distributions without any significant difference between the two periods [Figs. 2(a) and 2(b)], whereas the MC group showed large significant differences between the two periods in both anterior ($F(1, 19) = 5.69$, $p = 0.02$) and in posterior ($F(1, 19) = 8.80$, $p = 0.00$) electrode regions. In both sessions, C_S values decreased in the *End* period from its values in the *Begin* period, and the effect was larger in the anterior region in the last session than in the first session. Regarding alpha band complexity, the MC group showed robust significant differences between the two periods in both anterior ($F(1, 19) = 13.03$, $p = 0.00$) and posterior ($F(1, 19) = 7.28$, $p = 0.01$) regions, where the complexity value was decreased during the *End* period compared to the *Begin* period.

Figure 3 shows the within session C_S differences for beta-2 frequency band. Both MC and PMR groups showed a robust increase of C_S in the frontopolar and midfrontal electrode regions during the *End* period as compared to the *Begin* period ($p < 0.00$). Scalp maps were quite consistent across both periods within individual groups.

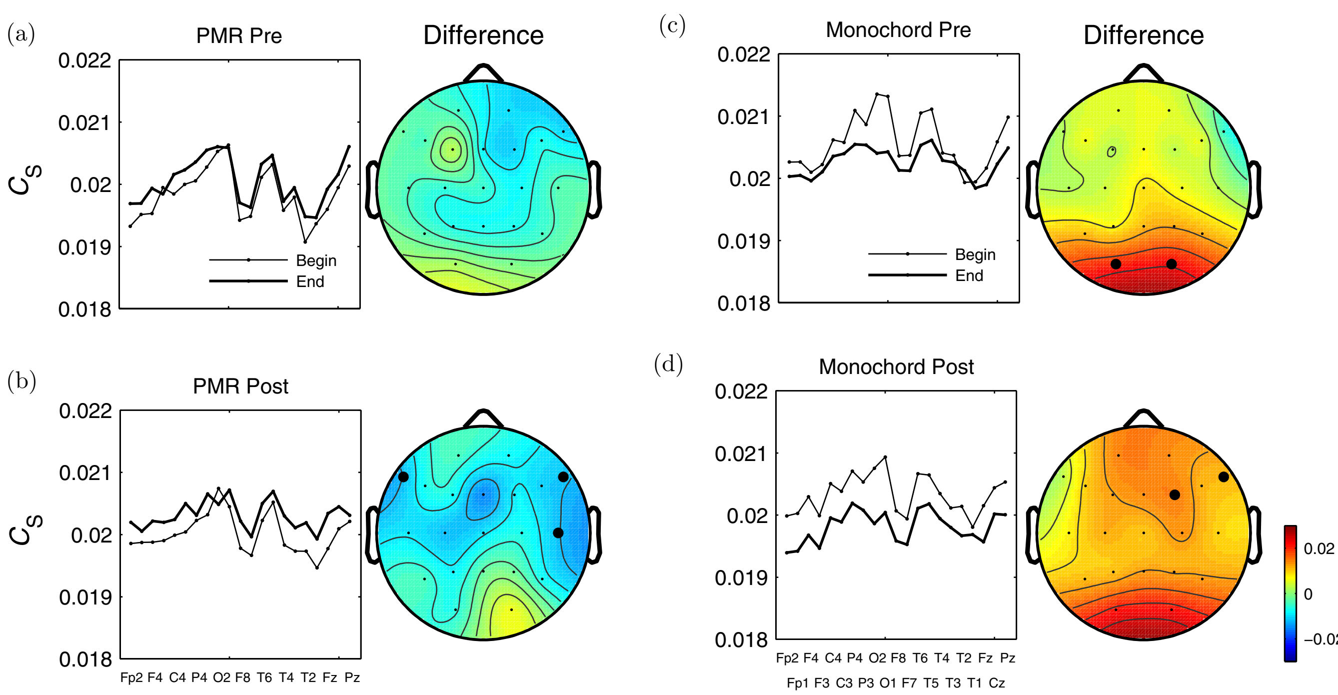

Fig. 2. (a) Signal mode complexity (C_S) of theta frequency band at 21 scalp electrodes shown separately for *Begin* and *End* period for the first session of PMR group. Scalp map shows the topographical distribution of difference (*Begin–End*) C_S values. (b) Same as in (a) but for the last session of the PMR group. (c)–(d) Same as in (a)–(b) but for the MC group. Electrodes showing statistically significant ($p < 0.05$, Bonferroni corrected) changes are shown by bigger filled circles.

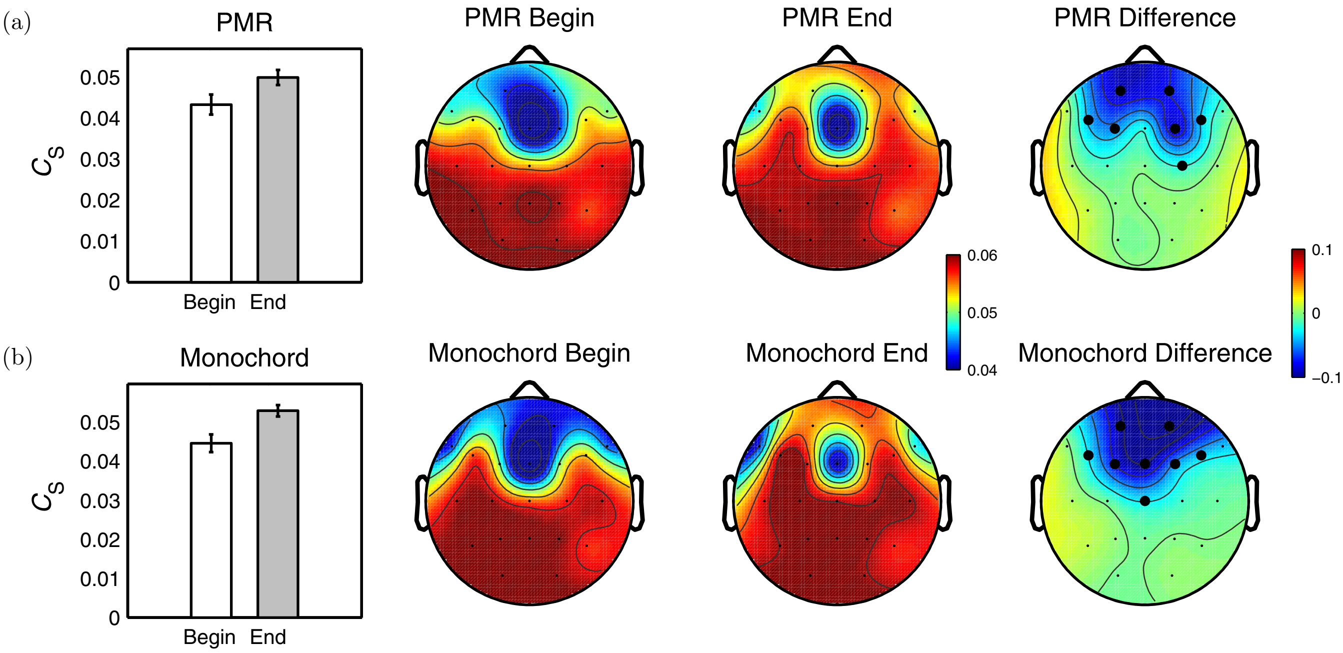

Fig. 3. Signal mode complexity (C_S) of beta-2 band at frontopolar and midfrontal electrode regions (Fp1, Fp2, F3, F4, Fz) for *Begin* (empty bar) and *End* (gray bar) period for (a) PMR and (b) MC groups. Results were averaged across sessions (first and last). Scalp maps on the right of each bar plot show the topographical distribution of C_S for *Begin* and *End* period within each group. Electrodes showing statistically significant ($p < 0.05$, Bonferroni corrected) changes are shown by bigger filled circles.

4. Discussion

Listening to monochord sounds or practising PMR to induce relaxation during chemotherapy produced different complexity profiles of electrical brain responses of gynaecological patients in oncology. The difference was most conspicuous in the theta frequency band: in the MC group, theta band complexity decreased both within a session and across sessions, while no such decrease was observed in the PMR group. Both groups showed an increase of beta-2 band complexity within a session.

EEG signals are neither fully deterministic nor fully stochastic, but rather a mix of both processes [Lehnertz *et al.*, 1999]. As the degree of stochasticity or randomness increases or decreases, C_S increases or decreases [Bhattacharya & Pereda, 2010]. Therefore, a decrease of C_S at an electrode region suggests an increase of orderliness or regularity in the oscillatory component of the time series recorded by that electrode. Emergence of locally synchronized oscillations is one candidate of such enhanced patterned regularity. Hence, in the MC group, the theta band spectral power was likely to be enhanced at the end of a session compared to its beginning and also at the last session compared to the first session. This is in line with earlier studies showing that the posterior theta band oscillation is an effective indicator of induction of relaxation [Hari & Naukkarinen, 1977; Williams & Gruzelier, 2001]. This clearly suggests that monochord sounds were quite effective as an inducer of relaxation even within one session. Interestingly, the difference in midfrontal and frontal theta complexity between *End* and *Begin* period was larger in the second session than in the first session [Figs. 2(c) and 2(d)]. This possibly reflects a training effect of the monochord method. Theta oscillations over midfrontal region are shown to be modulated by various meditational techniques [Aftanas & Golocheikine, 2002; Baijal & Srinivasan, 2010]. Training related changes in the MC group were found also over other brain regions [Fig. 2(d)]. Decrease of signal mode complexity over multiple brain regions is usually associated with an increase of neuronal synchronization over these distant brain regions [Bhattacharya & Pereda, 2010]; therefore one could infer that the gradual intervention by monochord sounds elicited a dense functionally connected network.

While theta band effect was exclusive to the MC group only, beta-2 band complexity was increased in both MC and PMR groups. The dimensional complexity of EEG during meditation is negatively correlated with theta and positively correlated with beta frequency band [Aftanas & Golocheikine, 2002]. Therefore, if our earlier relationship between signal mode complexity and synchronized oscillation holds, one expects a reduction of beta band oscillations with both relaxation methods. Note that the largest increase of beta band complexity was found over frontal regions [Figs. 3(a) and 3(b)], suggesting an anxiolytic response common to both groups as frontal beta oscillations are inversely correlated with the degree of anxiety [Begic *et al.*, 2001; Chen *et al.*, 1989].

This is also the first study which has systematically analyzed the dynamic brain responses to monochord sounds in a clinical context. Previously, only two pilot studies investigated the effects of body monochord using EEG [Fachner & Rittner, 2004; Sandler *et al.*, 2008]. These studies demonstrate altered states of consciousness induced by the body monochord which was associated with an increase of theta and beta-2 band spectral power [Fachner & Rittner, 2004]. Both of these studies are purely exploratory and involve very few healthy participants. Consequently, no neurophysiological account is available on the effect of monochord sounds used in clinical context. Future studies need to assess whether the relaxing effect or the altered states as mentioned above in a specific clinical context could offer similar therapeutic effects to patients.

We acknowledge certain limitations of this study. Firstly, the current study did not include a control group. However, it was difficult to conduct a comparison with a control group, given that this was a clinical study with gynaecologic cancer patients who were burdened both physically and psychologically with their illness. For obvious ethical reasons, it was questionable to measure EEG, especially because these female patients were already suffering from alopecia (a condition of hair loss due to chemotherapy) and attaching electrodes would therefore mean additional emotional burden. It would nevertheless be scientifically interesting to make a comparison with a control group, provided that a study can be designed without adding stress to the patients. Secondly, the length of the intervention method should be investigated more systemically. The process of relaxation and the patterns of becoming relaxed are situational and differ across individuals. It will be necessary to track the changes in complexity (or in other suitably chosen features) of brain responses over the course of the intervention to find out the most effective and efficient length of time for the relaxation intervention and to develop an optimal and individually adapted music relaxation treatment. Thirdly, one could consider investigating the post effect after listening to monochord sounds, potentially increasing the applicability of music in the clinical context. Fourthly, the current study did not cover the entire EEG frequency spectrum; it strategically focused on three preselected frequency bands after previous studies, yet other EEG frequency bands like gamma ($> 35\,\mathrm{Hz}$) are also shown to be modulated by varied states of alertness [Aftanas & Golosheykin, 2005; Sebastiani *et al.*, 2005; Tei *et al.*, 2009]. Therefore, future research should attempt to establish a relationship between music mediated relaxation and signal complexity of higher EEG frequency bands. Finally, any quantifier of complexity, be it C_S or any other, is, after all, a mathematically derived index. In order to establish its prognostic value in determining the efficacy in predicting the success of an individual relaxation method, it would be essential to demonstrate that such a quantifier is systematically related to behavioral measures, thereby establishing a link between neural and behavioral responses. In the similar vein, it would also be relevant, for future studies, to correlate changes in signal mode complexity with peripheral or other physiological measures (e.g. heart rate, respiration) related with relaxation.

In summary, this is the first neuroscientific study of the effect of listening to archaic sounds (monochord) in patients that demonstrates the changes in complexity in brain oscillation patterns in comparison with PMR.

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