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# Early evaluation of the therapeutic effectiveness in children with epilepsy by quantitative EEG: A model of Mozart K.448 listening—a preliminary study

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Received 7 March 2014; received in revised form 3 June 2014; accepted 28 June 2014

Available online 5 July 2014

## KEYWORDS

Mozart K.448;  
Epilepsy;  
qEEG;  
Epileptiform  
discharges

## Summary

**Purpose:** There are many treatments being developed for patients with epilepsy, including anti-epileptic drugs, ketogenic diet and vagus nerve stimulation. To date, there is a lack of valid methods to predict at an early stage the therapeutic effects on patients with epilepsy who receive one of these treatments. Our previous studies revealed that epileptiform discharges which were observed in patients with epilepsy were significantly decreased while listening to Mozart K.448. In this study, we attempted to develop a useful marker by utilizing a quantitative electroencephalogram (qEEG) method in analyzing the features of EEG to early evaluate the effect of the music on children with epilepsy, even without epileptiform discharges.

**Methods:** EEG segments from 19 Taiwanese children who were selected from a large screen study of music effect (eight boys and 11 girls) diagnosed with epilepsy were analyzed. EEG examinations were performed in two parallel periods in each patient; before, and while listening to Mozart K.448's first movement (8 min 22 s) and EEG data were compared by qEEG. EEG segments were classified into music effective/ineffective group. The term "effective" was defined as patient exposure to music resulting in over a 25% reduction in epileptiform discharges. On the contrary, the term "ineffective" was defined as patient exposure to music resulting in less than a 5% reduction in epileptiform discharges.

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**Results:** There were four global feature descriptors selected for the music effective/ineffective classification. Two descriptors, DecorrTime\_avg\_AVG and DecorrTime\_std\_AVG, were related to the EEG feature "decorrelation" whereas the other two descriptors, RelPowGamma\_avg\_SNR and RelPowGamma\_std\_SNR, were related to "relative power of gamma." There were significantly higher RelPowGamma\_std\_SNR ( $0.190 \pm 0.133$  vs.  $-0.026 \pm 0.119$ ,  $p=0.0029$ ), DecorrTime\_std\_AVG ( $0.005 \pm 0.004$  vs.  $0.0003 \pm 0.0016$ ,  $p=0.0055$ ), DecorrTime\_avg\_AVG ( $0.005 \pm 0.005$  vs.  $-0.002 \pm 0.008$ ,  $p=0.0179$ ), and RelPowGamma\_avg\_SNR ( $0.176 \pm 0.219$  vs.  $-0.078 \pm 0.244$ ,  $p=0.0222$ ) in the effective group than in the ineffective group. The precision rate of classification was 0.953.

**Conclusions:** Using qEEG, we have developed a useful model for predicting therapeutic effectiveness of music in patients with epilepsy. Among the limited number of patients, the tool is of potential to predict the effectiveness in patients even without epileptiform discharges. It is worthwhile in the application of other therapeutic model.

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## Introduction

In addition to anti-epileptic drugs, there are several treatments developed for patients with epilepsy, including ketogenic diet and vagus nerve stimulation (Arya et al., 2013; Wang and Lin, 2013). In order to prove the effectiveness of a treatment, patients always need to receive some sort of long-term follow-up. At present, there is lack of a valid method to evaluate in an early way the therapeutic effects of patients with epilepsy who receive one of these treatments.

It is well known that electroencephalogram (EEG) is a commonly used tool in diagnosis and classification of epilepsy. A routine 20-min EEG, however, shows abnormalities in as few as 30–55% of patients with epilepsy, with repeated 20-min studies increasing the yield to a maximum of 77% (Doppelbauer et al., 1993; Marsan and Zivin, 1970). On the other hand, still 30–50% of patients with epilepsy demonstrate no epileptiform discharges in their EEGs. Although EEG experts are able to identify specific EEG abnormalities by visual inspection, some EEG features, including power, frequencies, and complexity cannot be analyzed without computer technology (Cabrerizo et al., 2012). There have been many studies published regarding quantitative EEG (qEEG) by computer analysis that provide additional information for patients with epilepsy (Jouny et al., 2010; Kessler et al., 2011; Tedrus et al., 2009).

Regarding the music effect on epilepsy, Hughes et al. found that the epileptiform discharges reduced during listening to Mozart K.448 in 23 of 29 comatose patients, with status epilepticus or with periodic lateralized epileptiform discharges (PLEDs) (Hughes et al., 1998). Our previous study also reported that epileptiform discharges in patients with epilepsy were significantly decreased during and right after listening to Mozart K.448. The largest decrease in discharges was observed among patients with generalized or central discharges (Lin et al., 2010). In another study, Turner reported that interictal epileptiform discharges decreased in four patients with rolandic seizure when they were listening to Mozart K.448 (Turner, 2004). These studies used the decreases of epileptiform discharges as a marker to evaluate the effectiveness of music. However, there is lack of valid methods available at this time that can be used to evaluate the effect of music in patients with epilepsy who do not

have epileptiform discharges. In this study, we attempted to create a useful prediction model by utilizing a qEEG method to evaluate the immediate music effect on children with epilepsy based on a reduction of epileptiform discharges.

## Materials and methods

### Subjects

EEG segments from 19 Taiwanese children (eight boys and 11 girls) who had been diagnosed with epilepsy selected from a large screen study for music effect were analyzed. These patients received EEG examinations and listened to Mozart K.448 simultaneously and epileptiform discharges were compared. Their EEG segments were classified into music effective group and ineffective group. The term "effective" was defined as patient exposure to music resulting in over 25% reduction in epileptiform discharges (about the value of one standard deviation of decreased epileptiform discharges in the effective group). On the contrary, the term "ineffective" was defined as patient exposure to music resulting in less than a 5% reduction in epileptiform discharges (about further decrease of one standard deviation from 25%). Patients who had 5–25% changes were excluded because the change of epileptiform discharges was not prominent in patients with 5–25% reduction. The numbers of patients in the effective and ineffective classes were 10 and 9, respectively. The mean age for the effective group was 8 years 7 months  $\pm$  3 years 3 month (ranging from 4 years 10 months to 12 years), and for the ineffective group it was 8 years 10 months  $\pm$  3 years 9 month (ranging from 4 years 2 months to 12 years 1 month) (Table 1). The diagnosis of epilepsy was made according to the criteria established by the International League Against Epilepsy (ILAE). Written informed consent was given by a family member or legal guardian in each case. This study was approved by the Institutional Review Board of the Kaohsiung Medical University Hospital (KMUIRB-2012-01-09 (II)).

### Electroencephalogram examinations

The patients in this study received electroencephalogram (EEG) examinations in two parallel periods; before, and

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