Quantitative EEG analysis of REM sleep in children with Down syndrome

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Abstract

Purpose: **The aim was to compare quantitative EEG analysis of REM sleep in children with Down syndrome (DS) and normal age-matched controls.**

Material and methods: **Twenty-one channel EEG of 21 patients with Down syndrome and 21 normal children, with ages ranging from 1 to 8 years, were submitted to quantitative analysis EEG of discharge-free epochs. The signals were recorded using a set of 17 (F3, F4, F7, F8, Fz, C3, C4, Cz, P3, P4, Pz, O1, O2, T3, T4, T5, T6) scalp electrodes. For each child, 20 artifact – free EEG epochs, each of 2 s without epileptiform discharges were selected for spectral analysis to calculate spectral power. Delta, theta, alpha and beta frequency ranges were compared between groups for all electrode positions.**

Results: **Quantitative analysis of the REM sleep from DS group disclosed reduction of the power mainly in the alpha when comparing the healthy group. Beta, theta and delta bands did not differ significantly between the groups.**

Conclusions: **Our findings agree with recent evidences that these children may differ from children normal development.**

Key words: EEG, Down syndrome, quantitative analysis sleep.

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Introduction

Down syndrome (DS) is a chromosomal mutation in which the affected individual has three copies of chromosome 21. The prevalence of DS in the population is therefore almost entirely maintained by mutation [1,2]. The probability that a woman will give birth to a child with DS increases with increasing maternal age, with a steeper rate of increase after about age 34. To date there is no evidence for any racial differences or change over time in the maternal age-specific rates [1,3]. Several studies have reported that the observed DS live birth prevalence has remained steady or increased since the early to mid 1980s despite an increase in the percentage of women using prenatal diagnosis and an increase in the number of DS fetuses detected.

DS is one of the most serious and most frequently reported major congenital malformations among liveborn children, accounting for 25%-35% of severe mental retardation [3,4,5]. The short-term prognosis for a baby born with DS today is much better than it was in the past [5] and life expectancy has also improved [6]. Many authors have analysed the importance of the relationship between REM sleep and learning or memory [7,8,9].

On the other hand a quantitative EEG (power spectra and coherence) provides objective measures in the search for global or focal abnormality which, if present, may signal an underlying organic or non-organic processes [10,11,12,13]. Petit et al. [14] showed that EEG slowing during REM sleep is a more sensitive biological marker of Alzheimer's disease than is EEG slowing during wakefulness. The REM sleep EEG measure allowed complete discrimination of AD patients at mild to moderate stages from age-matched control subjects.

Although quantitative analysis of EEG background activity has been frequently done [15,16], the studies that dealt with this particular aspect on EEGs were rare in children with DS. Most previous studies [15,17,18,19] on EEG in patients with DS were conducted in adult patients or at school age.

However, one theoretical possibility is that quantitative analysis of the background activity could disclose subtle abnor-

malities not detected by visual analysis. This study was done to test this possibility.

Material and methods

Patients

Twenty-one patients aged 1-8 years old with genetically confirmed Down were included in this study. EEGs were recorded from 9.00 to 12.00 during days. Patients did not take any pharmacological agents which could exert effects on sleep or EEG. Patients with seizures or epilepsy were excluded from the study. The control group included twenty-one normal subjects, matched for chronological age and gender.

EEG

EEG recordings were performed while the patients were in a REM sleep during the first 40 minutes. EEG signals were recorded from scalp electrodes (according to the International 10-20 system), all correlated with the vertex reference. The signals were recorded using a set of 17 (F3, F4, F7, F8, Fz, C3, C4, Cz, P3, P4, Pz, O1, O2, T3, T4, T5, T6) scalp electrodes, and amplified and filtered by a Elmiko, Warsaw, Poland. We used Ag/AgCl electrodes, with an impedance less than 5 kΩ. Visual analysis of EEG was performed before the quantitative assessment. For each child, 20 artifact – free EEG epochs, each of 2 s without epileptiform discharges were selected for spectral analysis to calculate spectral power using (the Elmiko software) in according Achermann's and Borbely [16]. The sampling frequency was 240 Hz. Frequencies below 1 Hz and above 70 Hz were eliminated by digital filtering. The respiratory signal was first filtered with a low-pass filter. The channels were recorded relative to a vertex reference. A fast Fourier transformation algorithm of signal processing was used to obtain the power spectrum of each lead. For the statistical evaluation of the EEG phenomena: absolute power spectrum and coherence values were calculated within 4 frequency bands: delta (1-3.99 Hz), theta (4-7.99 Hz), alpha (8-12.99 Hz), and beta (13-30 Hz).

Statistical analysis

Wilcoxon's test was applied to determinate the probabilities in all the groups, in power spectra. Each of the frequency bands was analysed separately. Statistics were obtained using the Statistica 6.0.

Results

Visual analysis of background activity showed no abnormalities in the EEGs from all the subjects of the control children. In children with DS sleep REM was less pronounced as compared to controls. Quantitative analysis of the sleep REM from DS group disclosed reduction of the power mainly in the alpha when comparing the healthy group (*Fig. 1*). Moreover, beta, theta and delta bands did not differ significantly between the groups. In the spectral analysis, we detected significant ($p<0.001$) decrease of alpha bands at occipital derivations (*Fig. 2*).

***Figure 1*. EEG Power spectra of REM sleep in children with Down syndrome (n=21) and controls (n=21). *p<0.001 vs control**

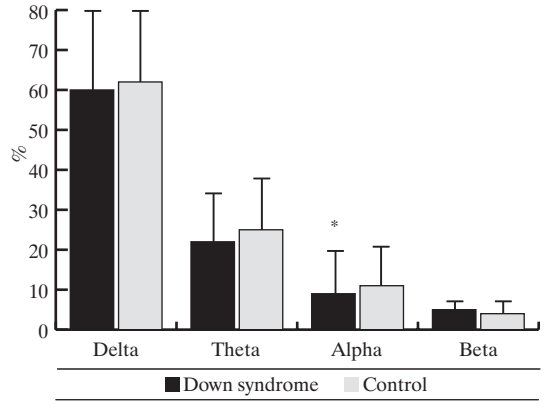
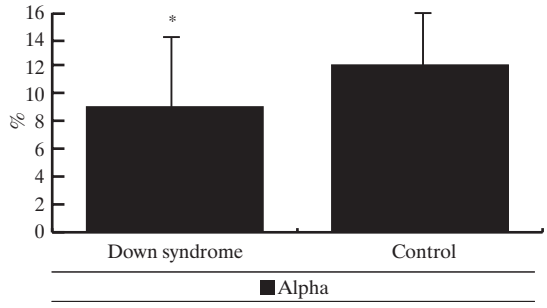


***Figure 2*. Alpha bands at 01 and 02 derivations in patients with Down syndrome (n=21) and control group (n=21) during REM sleep. * p<0.001 vs control**



Discussion

In the present study, we did not find significant differences in the general distribution (delta, theta and beta bands) between children with DS and controls. However, we detected significant decrease of alpha bands at total EEG and at occipital derivations. Our findings are agreement with previous results on EEG in patients with DS [15,17,18,19].

Down's syndrome patients express a neurodegenerative disorder and mental retardation. Partanen et al. [17] studied 32 patients with Down's syndrome and 31 controls for blocking of occipital EEG activity. DS patients and controls showed significant diminution of alpha, beta and theta activity and decrease of EEG frequency with eyes closed/eyes opened. However, there was a significant impairment in DS in the eyes closed/eyes opened ratio in alpha band, compared to controls. They had also significant correlations of the alpha eyes closed/eyes opened ratio and neuropsychological test scores. DS also showed significant differences in resting EEG variables, compared to the controls, even if the conventional EEG showed normal or mildly slowed dominant occipital rhythm in most of the patients.

The EEG may be an important tool in the clinical diagnosis of Alzheimer-type dementia in patients with Down's syndrome and other disorders [18,19,20,21]. Visser et el. [20] analysed the

role of EEG in the diagnosis of Alzheimer-type dementia in patients with Down's syndrome. Almost 197 patients with DS were monitored for 5 to 8 years. EEGs were scored in a blind fashion, and changes in the EEG were compared to changes in cognitive functioning. Cognitive functioning was drastically reduced in 29 patients. The dominant occipital rhythm became slower at the onset of the cognitive deterioration, and eventually disappeared. In 11 of these patients neuropathological examination showed a severe form of Alzheimer's disease. They postulated that changes in the frequency of the dominant occipital rhythm could distinguish between Alzheimer's disease or other causes as underlying the cognitive decline. Slowing of the dominant occipital rhythm seems to be related to Alzheimer's disease in patients with DS, and the frequency of the dominant occipital activity decreases at the onset of cognitive deterioration.

A slowing of alpha rhythm in patients with DS is considered as a manifestation of premature aging [19]. Ono et al. [19] performed spectral analysis of EEG in patients with DS aged 15 to 54 and compared with two control groups; healthy volunteers and mentally retarded people without DS. The frequencies of occipital alpha rhythms of DS patients showed a significant inverse correlation with chronological age, while comparison group did not. The average frequencies of DS were significantly low even in the youngest age-group in comparison with those of control, and also decreased in the age-groups of 35 and older compared with mental retardation.

In another study, the relation of EEG alpha background to cognitive function and cerebral metabolism was evaluated [21]. Patients and control subjects had EEGs, psychometric testing, quantitative computed tomography, and positron emission tomography with fludeoxyglucose. All the control subjects, the 13 young adult patients with Down's syndrome, and the 5 older patients with DS had normal EEG backgrounds. In comparison with the age-matched patients with DS with normal alpha background, older patients with DS with decreased alpha background had dementia, fewer visuospatial skills, decreased attention span, larger third ventricles, and a global decrease in cerebral glucose utilization with parietal hypometabolism. In the young patients with DS, the EEG background did not correlate with psychometric or positron emission tomographic findings, but the third ventricles were significantly larger in those with abnormal EEG background. The young patients with DS, with or without normal EEG background, had positron emission tomographic findings similar to those of the control subjects. The mechanism underlying the abnormal EEG background may be the neuropathologic changes of Alzheimer's disease in older patients with DS and may be cerebral immaturity in younger patients with DS. Quantitative EEG is a sensitive method in the determination brain maturation and reorganization in children with cerebral palsy [22].

Conclusions

In conclusion quantitative analysis of the REM sleep from Down syndrome group disclosed reduction of the power mainly in the alpha when comparing the healthy group. Beta, theta and delta bands did not differ significantly between the groups.

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