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Title: Increased mesiotemporal delta activity characterizes virtual navigation in humans

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Abstract: Hippocampal theta or rhythmic slow activity (RSA) occurring during exploratory behaviors and rapid-eye-movement (REM) sleep is a characteristic and well-identifiable oscillatory rhythm in animals. In contrast, controversy surrounds the existence and electrophysiological correlates of this activity in humans. Some argue that the human hippocampal theta occurs in short and phasic bursts. On the contrary, our earlier studies provide evidence that REM-dependent mesiotemporal RSA is continuous like in animals but instead of the theta it falls in the delta frequency range. Here we used a virtual navigation task in 24 epilepsy patients implanted with foramen ovale electrodes. EEG was analyzed for 1-Hz wide frequency bins up to 10 Hz according to four conditions: resting, non-learning route-following, acquisition and recall. We found progressively increasing spectral power in frequency bins up the 4 Hz across these conditions. No spectral power increase relative to resting was revealed within the traditional theta band and above in any of the navigation conditions. Thus the affected frequency bins were below the theta band and were similar to those characterizing REM sleep in our previous studies providing further indication that it is delta rather than theta that should be regarded as a human analogue of the animal RSA.

Highlights

Mesiotemporal EEG activity was assessed during a spatial task in epilepsy patients.

Low frequency spectral power increased during all three navigation conditions.

There was no change during task performance in the theta frequency band.

Delta rather than theta should be regarded as a human analogue of animal theta.

Abstract

Hippocampal theta or rhythmic slow activity (RSA) occurring during exploratory behaviors and rapid-eye-movement (REM) sleep is a characteristic and well-identifiable oscillatory rhythm in animals. In contrast, controversy surrounds the existence and electrophysiological correlates of this activity in humans. Some argue that the human hippocampal theta occurs in short and phasic bursts. On the contrary, our earlier studies provide evidence that REM-dependent mesiotemporal RSA is continuous like in animals but instead of the theta it falls in the delta frequency range. Here we used a virtual navigation task in 24 epilepsy patients implanted with foramen ovale electrodes. EEG was analyzed for 1-Hz wide frequency bins up to 10 Hz according to four conditions: resting, non-learning route-following, acquisition and recall. We found progressively increasing spectral power in frequency bins up the 4 Hz across these conditions. No spectral power increase relative to resting was revealed within the traditional theta band and above in any of the navigation conditions. Thus the affected frequency bins were below the theta band and were similar to those characterizing REM sleep in our previous studies providing further indication that it is delta rather than theta that should be regarded as a human analogue of the animal RSA.

Key words: rhythmic slow activity, hippocampus, learning, memory

Introduction

Hippocampal rhythmic slow activity (RSA) or theta is a prominent electroencephalographic (EEG) pattern recorded from the hippocampus in many mammalian species during rapid-eye-movement (REM) sleep, exploratory behaviors and movements (Jouvet et al., 1959; Grastyán & Karmos, 1961; Vanderwolf, 1969; Whishaw & Vanderwolf, 1973). Recently there has been much progress in understanding the role of theta oscillations in organizing neuronal activity in animals (O'Keefe & Dostrovsky, 1971; O'Keefe & Recce, 1993; Skaggs et al., 1996; Skaggs & McNaughton, 1996; Nádasdy et al., 1999; Huerta & Lisman, 1993; Montgomery et al., 2008). This knowledge resulted in functional theories implicating theta in memory and other cognitive processes. There was also a tendency to transfer animal-based theories to humans. However, there is still no general consensus whether hippocampal theta really exists in humans or whether theta seen in humans is a functional analogue of that in animals. This is an important issue since in the human literature there is abundant data on theta that was found during virtual navigation (Kahana et al., 1999; de Araújo et al., 2002; Bischof & Boulanger, 2003; Ekstrom et al., 2005) working memory tasks (Tesche & Karhu, 2000; Raghavachari et al., 2001; Schauseng et al., 2004) and REM sleep (Cantero et al., 2003). These studies report theta appearing in short and phasic bursts instead of continuous activity typically seen in animals. In contrast Bódizs et al. (2001a) reported REM-dependent mesiotemporal RSA that was continuous like in animals but instead of the theta it fall in the delta (1.5-3 Hz) frequency range. This initial work was followed by others demonstrating delta activity also during wake-sleep transition a state characterized by several REM-like features (Bódizs et al., 2005, 2008). The presence of hippocampal delta activity during REM sleep as well as wakefulness was also demonstrated by other investigators using stereo-EEG recordings (Moroni et al., 2007, 2012; Ferrara et al., 2012) while another study reported a phase-locking of single-neuron

activity to hippocampal delta activity while patients performed a virtual navigation task (Jacobs et al., 2007). In a recent study we demonstrated a phase-coupling of high-frequency activity with the 1.5-3 Hz mesiotemporal delta oscillations during REM sleep (Clemens et al., 2009). Such a phase coupling closely resembles that seen between theta and gamma in animals. Given the known electroencephalographic similarity between REM sleep and exploration in animals we conjectured that increased delta activity should also characterize spatial exploration in humans. In order to test this assumption mesiotemporal EEG was recorded and analyzed while epilepsy patients performed a virtual navigation task.

Materials and methods

Patients

The study included 24 consecutive epilepsy patients (twelve females and twelve males) who as part of their presurgical evaluation underwent long-term video-EEG monitoring with foramen ovale (FO) electrodes between 2004 and 2012. They were between the ages of 17 and 51 (mean±SD: 33.6±8.2 years). Epilepsy duration was between 1 and 34 years (mean±SD: 15.2±10 years). Eight patients exhibited solely unilateral while six bilateral seizure onset. In eight patients seizures originated from outside the temporal lobe. One patient had both extratemporal and mesiotemporal onset seizures while seizure onset was uncertain in another patient. Mesiotemporal structural alteration evident on magnetic resonance imaging (MRI) scans (hippocampal sclerosis or mesiotemporal dysgenesis) was present in thirteen patients unilaterally and in one patient bilaterally. MRI was normal in eight patients. Unilateral insular structural alteration was present in one patient and another patient had both mesiotemporal and extratemporal structural alterations. All had normal IQ. As part of the

presurgical evaluation protocol, the patients' antiepileptic medication was gradually reduced to be able to record their seizures. Experimental procedures for this study complied with the Code of Ethics of the World Medical Association (1964 Declaration of Helsinki). The study was approved by the local ethics committee and patients gave written informed consent to participate in the study. Patients were video-EEG monitored for a period ranging from 3 to 12 days. We scheduled the virtual navigation task for the early days of the monitoring period in order to minimize the negative cognitive effects of the reduction of antiepileptic medication and seizures. In the early days of monitoring we generally experienced lower frequency of interictal epileptic spikes and better patient compliance. In addition testing was carried out at least six hours away from the last clinical or subclinical seizure in order to avoid possible contamination with postictal EEG activities or seizure-related fatigue.

Testing

Navigation was tested within a realistic and large-scale virtual environment designed and constructed by the second author using a 3D computer program. Subjects could maneuver by pressing the four arrow keys on a keyboard. Navigation was tested according to three conditions: an acquisition, a recall and a non-learning route-following condition (Fig. 1). In order to get acquainted with the testing situation and the use of the arrow keys patients were first asked to perform a practice run according to the route-following condition (see below). So it could be ascertained that the patient could use the arrow keys properly. This practice run was not included in the analysis. During the acquisition phase subjects were given 15-20 minutes to explore the virtual town comprising several streets, various buildings and places such as a school, football ground, playground, park, lake etc. Patients were instructed to navigate through all streets and to learn the position of hallmark locations and the route between them. Following acquisition, recall trials were given. This time subjects were asked

to navigate between different locations in the town. At the beginning of each recall trial a target location appeared in the right bottom corner of the screen and the subject was instructed to navigate to this target using the most direct route and as quickly as possible. Once the location was reached the subject was presented with a new target to be reached. Altogether eight target locations were presented in four blocks each containing two targets. No more than five minutes was allowed for each trial. For the EEG analysis, recordings corresponding to different recall trials were combined into one dataset for each patient. After finishing the recall session, patients were asked to perform a non-learning route-following task. This time subjects were presented with new virtual environments and were asked to follow red arrows placed on the ground without learning the route. Patients had to perform three route-following trials each through different tracks. For the EEG analysis, these recordings were also combined into one dataset. Before starting the virtual navigation tasks itself five minutes of resting with eyes opened was sampled. This time patients were asked to sit quietly and not to move. For an additional analysis video-EEG recordings (continuously recorded through several days) were screened for each patient to select epochs of resting with eyes closed of 3-10 minutes in order to enable a comparison between resting with eyes opened and closed.

EEG recording

EEG monitoring with combined scalp and FO electrodes was carried out using the Brain Quick System 98 or Plus (Micromed, Mogliano Veneto, Italy). Implantation of FO electrodes allows a semi-invasive technique to record mesiotemporal corticography without opening the scull (Wieser et al., 1985). FO electrodes are stainless steel (or platinum) wires of 0.65 mm diameter with four contacts of 2 mm length each separated by 5mm (between contact centres). The electrodes were introduced bilaterally through the foramen ovale such that they are placed in the subarachnoidal space of the cisterna ambiens parallel with the long axis of the

hippocampal formation. Contacts are designated (from posterior to anterior) as FO1-4 on the right side and as FO5-8 along the left side. The exact location of the electrodes was confirmed by X-ray and in some cases by MRI (Fig.2).

In addition to FO electrodes, scalp electrodes were placed (according to the International 10–20 System) together with electrooculogram (EOG), electromyogram (EMG) and electrocardiogram (ECG) electrodes. All signals were recorded to a vertex reference. Signals from all channels were prefiltered at 0.3 Hz. Sampling rate was 1024 Hz in 17 patients, 512 Hz in four patients and 256 Hz in three patients. AD conversion was 22-bit.

EEG analysis

EEG analysis was carried out using Spike2 software (Cambridge Electronic Design, Cambridge, UK). FO signals were analyzed as originally recorded in monopolar montage with vertex reference. FO recordings were first visually inspected for 4 s long epochs to exclude those epochs containing interictal epileptic spikes or movement artifacts in any of the FO channels. Then Fast Fourier Transformation with Hanning windowing was carried out to calculate power spectra for 4-s long epochs with 0.25 Hz resolution. For statistical calculations 0.25 Hz frequency bins were averaged for 1 Hz-wide bins up to 10 Hz. Frequency bands were defined by their upper limits. Given the built-in high-pass headbox prefilter at 0.3 Hz the first frequency bin was defined as between 0.5 and 1 Hz.

Statistical analysis

Since integrated spectral power values may not follow normal distribution, spectral power values for the 1Hz wide frequency bins were subjected to log(10) transformation. Then log-transformed values for each patient (hemisphere) and frequency bins were z-transformed across the four conditions. This was necessary due to the considerable variability of spectral

power values across patients. Repeated measure one-way ANOVA with four levels was performed separately for each frequency bin as dependent variable to assess main effects. Then paired t-tests were applied to perform statistical comparisons for all condition pairs in the collapsed dataset (n=47). Due to the exploratory nature of our investigations we did not apply Bonferroni correction for multiple comparisons.

Results

Overall results for the four FO channels within the same side were nearly identical. Thus, to avoid redundancy we report here, as in our previous studies (Clemens et al., 2007, 2009, 2011) analyses performed on the two anterior channels (FO4 and FO8). In one patient posterior channels (FO1 and FO5) were used because of strong artefacts in the other ones. A patient exhibiting continuous spike activity in all contacts of the left FO electrode is represented only by his right hemisphere in the present sample. The statistical sample thus comprised 47 datasets (24 patients, 47 hemispheres).

Median times (across patients) for completing the recall trials were between 53 and 203 s. There were five patients who performed six or seven recall trials only (instead of eight) due to technical reasons or subjective complaints (nausea, headache).

Visual inspection of recordings indicated a shift toward low-frequency components upon task commencement which remained sustained throughout entire task sessions (Fig. 3 and 4). Repeated measure one-way ANOVA with four levels indicated significant within-subject main effects for the 1 Hz ($F(3,114)=5.31$; $p<0.002$), 2 Hz ($F(3,114)=5.96$; $p<0,001$), 3 Hz ($F(3,114)=2.71$; $p=0.049$), 4 Hz $F(3,114)=7.25$; $p<0.0002$), 8 Hz ($F(3,114)=13.04$; $p<0.000001$), 9 Hz ($F(3,114)=8.09$; $p<0.01$) and 10 Hz ($F(3,114)=10.11$; $p<0.00001$)

frequency bins. Group-level averages (n=47) and SD of the log(10)-transformed and normalized power spectral values for each frequency bin and condition are graphed in Fig. 6. Significant comparisons of post-hoc paired-t-tests are highlighted. Given the exploratory nature of our study we did not apply a correction for multiple comparisons. A Bonferroni correction should have resulted in a loss of significant comparisons of $p>0.008$. Therefore comparisons designated as having a significance level of $p<0.001$ in Fig. 6 should be regarded as main outcome of the study. A comparison of mean power spectral values across conditions and frequency bins indicated different distribution for lower and higher frequency bins (Fig. 5 and 6). The main pattern of results consisted of a progressive increase across resting, non-learning, recall and acquisition in the low frequency bins (up to 4 Hz) and a U-shaped relationship across the same conditions in the high frequency bins (7 Hz and above). No significant difference was revealed for any condition pair in the 5 and 6 Hz bins.

For the low frequency bins paired t-tests revealed 12 significant comparisons. In each of the low frequency bins highest level of significance was found for the comparison with acquisition: in the 1 Hz ($p=0.0009$) and 4 Hz ($p=0.002$) frequency bins comparisons peaked between acquisition and resting while in the 2 Hz ($p=0.0005$) and 3 Hz bins ($p=0.04$) comparisons peaked between acquisition and non-learning. (All significant comparisons are highlighted in Fig. 6.) Thus engagement in the tasks and especially acquisition resulted in a clear increase of activities belonging to the frequency band traditionally referred to as delta. However, in spite of the significantly increased delta activity, a clear delta spectral peak was present only in about half of the cases (in 24/47 cases during resting and in 25/47 cases during acquisition).

For the higher frequency bins (7 Hz and above) 16 significant comparisons were found. Spectral power during resting in the 7 Hz, 8 Hz, 9 Hz and 10 Hz bins significantly exceeded that during non-learning and recall and in the 8 Hz bin also that during acquisition.

Spectral power during acquisition significantly exceeded that during recall and non-learning in the 8 Hz, 9 Hz, 10 Hz bins and exceeded that during non-learning in the 7 Hz bin (Fig. 6). The overall decrease of the 7-10 Hz activity with task performance and its high rhythmicity (as evidenced by rhythmic sinusoid oscillations in the raw EEG and a corresponding peak in the spectral power) suggested this to be analogue with the eyes-closed resting state alpha activity (Fig. 4 and 5). However higher activity during acquisition as compared to non-learning may seem to contradict this. In order to resolve this discrepancy and to determine whether the mesiotemporal 7-10 Hz activity is task- or resting-related we performed an additional analysis to compare EEG properties during resting with eyes opened and closed. Visual EEG analysis and power spectra indicated striking 6-10 Hz mesiotemporal activity in 38/47 cases during resting with eyes closed. This activity appeared concurrently with the occipital alpha upon eye-closure and both fluctuated simultaneously in amplitude. However the two activity significantly ($p=0.03$) differed in their peak frequency: out of those cases where the 6-10 Hz activity was present in both FO and occipital channels (n=37) the FO activity was of lower frequency in 18 cases and the opposite was true only in two cases. In 17 cases no difference was present in the peak frequency between FO and occipital channels. On average mesiotemporal alpha was of 8.45±1.61 Hz and the occipital of 9.19±1.27 Hz frequency. Confirming our visual impression statistical comparison of the normalized power also indicated significantly higher values for the eyes-closed state in the frequency bins within but not lower than the 7-10 Hz range (Fig. 7A). All these features convinced us that the mesiotemporal 7-10 Hz activity indeed reflects resting-related rather than task-related activity.

Discussion

The main finding of this study is that engagement in a virtual navigation task results in increased mesiotemporal activity in the low-frequency range including the 1 Hz, 2 Hz, 3 Hz and 4 Hz bins that is in the traditional delta frequency band. Increase relative to resting was present during each navigation condition with a tendency of non-learning<recall<acquisition. Visual inspection of recordings indicated that increased low-frequency activity started with commencement of the task and was present tonically throughout the entire task sessions without clear signs of burst-like activity in any frequency range.

In contrast to our finding of increases clearly in the delta band, several studies reported theta activity in epilepsy patients performing similar tasks (e.g. Kahana et al., 1999, Caplan et al., 2003, Ekstrom et al., 2005). There may be three possible factors accounting for this discrepancy. First, some studies selectively looked at theta while disregarding other frequency bands. A few studies used bipolar montage while others do not report whether bipolar or monopolar montage was used. Since RSA is highly synchronous across neighboring mesiotemporal contacts slow oscillation cycles are extinguished when using bipolar derivation (Bódizs et al., 2001a,b; Clemens et al., 2009). Third, the majority of studies used recordings from the scalp or various neocortical sites but only three studies looked directly at the hippocampus during virtual navigation tasks. In fact a comparison limited to these three studies is much less contrasting. The study by Ekström et al. (2005) found that the reported theta bursts are related to movements rather than exploration per se. Jacobs et al. (2007) reported delta oscillations in the hippocampus as well as a more tight coupling of neuronal activity to delta than theta oscillations. Thirdly Watrous et al. (2011) reported that the majority of navigation-related hippocampal oscillation changes occur in the theta as well as in the delta band. Regarding the affected frequencies our data closely resembles those in the study by Lega et al. (2011) reporting predominating hippocampal oscillations at ~3 and ~8 Hz with the former positively while the latter negatively correlating with successful episodic

memory encoding. In the present study we found highest task-related power increases in the 1 Hz frequency bin thus of somewhat lower frequency than the 1.5-3 Hz range that we previously found for REM sleep (Bódizs et al., 2001; Clemens et al., 2009). However here we did not analyze REM sleep so we cannot exactly determine how task-related and REM-related slow activity increases are linked within the same patient.

There are a branch of studies with direct medial temporal lobe recording reporting various theta-related phenomena such as theta reset and theta/gamma interaction during a word recognition task (Mormann et al., 2005), pre-stimulus theta predicting successful memory encoding and stimulus-triggered theta related to subsequent recall (Sederberg et al., 2003; Fell et al., 2011), phase-coupling of gamma (Axmacher et al., 2010) and single neuronal activity (Rutishauser et al., 2010) to theta. Despite the diversity of paradigms and electrophysiological measures used in these studies theta power increase was generally not found however this would be the most parsimonious measure to justify that theta is indeed a correlate of cognition. At the same time those studies not limited to the traditional theta band showed spectral power or other electrophysiological changes outside the theta band (Ekstrom et al., 2005; Sederberg et al., 2007; Mormann et al., 2008; van Vugt et al., 2010; Watrous et al., 2011).

The remaining support for hippocampal theta in memory processes comes from studies relying on source analysis methods. These report reconstructed sources of theta within hippocampal (or parahippocampal) structures during task performance (Tesche & Karhu, 2000; Cornwell et al., 2008). Given that source reconstruction models suffer from important limitations in detecting sources in deep brain structures with a close geometry (Alarcon et al. 1994; Wiederin et al. 1999) these results are unconvincing.

Our data show increased activity in the delta but not theta frequency band during task performance. The trend of resting<non-learning<recall<acquisition in delta activity probably

reflects gradual increase in cognitive challenge. Moderate increase in delta activity during the non-learning condition might be due to unintentional learning or increased level of sustained attention. Since recall and acquisition were associated with even higher levels of delta activity it is unlikely that delta reflects sensorimotor integration alone. Instead it might be a reflection of increased memory and/or attention demands. Notably no significant increase relative to resting was observed in the traditional theta band in any of the navigation conditions. At the same time significant differences emerged for each frequency bin above 6 Hz. As compared to resting activity in this range was markedly reduced in all three navigation conditions in accordance with the well-know attenuation of alpha activity during cognitive strain (e.g. Gevins et al., 1997). Interestingly the distribution of alpha drop across conditions did not exactly mirrored the increase of delta: during acquisition alpha remained relatively high as compared with the two other navigation conditions. Since the route-following condition was designed to serve as a non-learning control, higher alpha activity during acquisition as compared to non-learning was unexpected and raised the possibility that mesiotemporal alpha reflects learning after all. Such an interpretation would be supported by two studies by Jensen et al. (2002a,b) reporting scalp-recorded alpha power proportionally increasing with memory load. At the same time Lega et al. (2011) reported decreased ~8 Hz hippocampal activity during successful memory encoding. In order to clarify the nature of mesiotemporal alpha we visually and statistically compared mesiotemporal and occipital EEG during resting with eyes opened and closed. Visual analysis disclosed parallel changes in mesiotemporal and occipital electrodes and a clear increase in the 7-10 Hz frequency bins during resting with eyes-closed as compared to eyes-opened. This was also confirmed by a statistical comparison across the whole dataset (n=47) indicating a highly significant increase in each of the frequency bins above 6 Hz during resting with eyes closed. Thus the trend of resting eyes-closed>resting eyes-opened>acquisition in alpha power clearly showed that mesiotemporal 7-10 Hz activity

follows the classical direction of alpha reactivity and therefore it is unlikely to be a correlate of learning. As a remaining explanation for relative alpha excess during acquisition we suggest that the longer time (20 min) spent in the acquisition phase might have given rise to lapses in attention possibly contributing to increased alpha activity. Alternatively, increased alpha activity may reflect inhibitory control a prerequisite for focused attention as suggested by Klimesh et al. (2007). Another intriguing finding is the lower frequency of the mesiotemporal alpha as compared to the occipital one. This finding can be paralleled with lower frequency of mesiotemporal than parietal sleep spindles (Clemens et al., 2011) with both differences possibly reflecting similar anatomical differences in the neuronal loops underlying these oscillations. Difference in the peak frequency also indicates that mesiotemporal alpha is generated locally and is not volume conducted from occipital sources nor stems from the reference electrode. Lastly, our finding of smaller increases in the low frequency activity during recall as compared to acquisition together with more alpha activity during the latter may be explained by the use of the anterior FO electrodes. Such an assumption would be compatible with findings coming from an fMRI study (Iaria et al. 2007) which revealed complementary roles of the anterior and posterior hippocampus in navigation with the former being involved in the formation of a cognitive map while the latter in using it. In the present study timing of the task during the day varied across patients given the clinical setting which posed several constraints. Thus we were not able to control for a circadian effect which might have introduced some variability in the level of consciousness and EEG reactivity.

Altogether navigation-related increase in mesiotemporal delta activity affected similar frequency bins as did REM sleep in our previous studies with FO electrodes (Bódizs et al., 2001a; Clemens et al., 2009). Although as compared with REM sleep, navigation-related delta

appeared to be less salient and organized and did neither consistently resulted in a low-frequency spectral peak in all navigation conditions and patients.

In lower mammals (Jouvet et al., 1959; Grastyán & Karmos, 1961; Vanderwolf, 1969; Whishaw & Vanderwolf, 1973; O'Keefe & Nadel, 1978) hippocampal theta represent a common EEG pattern during exploration and REM sleep. In humans most investigators either failed to find hippocampal theta (Uchida, 2001; Bódizs, 2001a) or reported theta with features differing from those characterizing animals (Cantero et al., 2003; Ekstrom et al., 2005). Here we report navigation-related mesiotemporal delta activity which increased progressively across resting, non-learning, recall and acquisition. Like in animals this activity was present bilaterally and tonically. We suggest that in conjunction with our previous findings on REM sleep (Bódizs et al., 2001a; Clemens et al., 2009) the present data provide additional evidence that it is delta rather than theta that should be regarded as the human analogue of the animal hippocampal RSA. As argued earlier (Blumberg et al., 1989; Bódizs et al., 2001a; Clemens et al., 2009) decreased frequency of RSA as compared to rodents may be due to larger brains or lower metabolic rates (Deboer, 2002) characterizing humans.

Abbreviations

EEG, electroencephalogram; FO, foramen ovale; REM, rapid eye movement; RSA, rhythmic slow activity.

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Figure legends

Fig.1.

Sample views of the virtual environment. During the acquisition phase (A) patients were instructed to explore the town and memorize locations. During the recall sessions (B) patients had to navigate to a hallmark location appearing in the right-bottom corner of the screen. In the non-learning route-following condition (C) patients were instructed to follow red arrows placed on the ground without learning the track.

Fig. 2.

X-ray views (A: coronal view, B: lateral view) and high resolution MRI scans (C: coronal section, D: axial section) of the scull showing the location of FO electrodes (arrows)

Fig. 3.

Examples of FO EEG traces (low-pass filtered at 30 Hz) in four patients during resting (with eyes opened) and acquisition. Y-axis represents values in μV. Note increased low-frequency activity during acquisition compared to resting. Traces are scaled similarly within the same patient.

Fig. 4.

Simultaneous FO and scalp electrode traces (low-pass filtered at 30 Hz) during acquisition, resting with eyes opened and resting with eyes closed in a representative patient. Contacts FO1-4 correspond to the right and FO5-8 correspond to the left side, FO4 and FO8 contacts are located most anteriorly. Note that during acquisition increased low-frequency activity is present in FO electrodes but not in scalp electrodes (In Fp1 and Fp2 electrodes eye movements are superimposed on scalp EEG activity.) Alpha activity during the resting states is present throughout all electrodes. During resting with eyes closed alpha activity becomes predominating. All electrodes are referenced against a vertex electrode and are scaled similarly in each conditions.

Fig. 5.

Power spectra with 0.25 Hz resolution during resting (with eyes opened) and the three navigation conditions in a representative patient. Note gradual increase of the 1.75 Hz activity across resting (with eyes opened), non-learning, recall and acquisition. Alpha activity peaking at 7.75 Hz decreased during all three navigation conditions.

Fig. 6.

Group-level averages and SD (n=47) of the log(10)-transformed and normalized power spectral values for each frequency bin and condition. Asterisks indicate significant differences

for pairwise comparisons (***p<0.001, **p<0.01, *p<0.05). Activity in the 1 Hz, 2 Hz, 3 Hz and 4 Hz frequency bins increased gradually across resting (with eyes opened), non-learning, recall and acquisition. Activity in the 7 Hz, 8 Hz, 9 Hz and 10 Hz bins show a U-shaped relationship across the same conditions. No significant differences were found in the 5 Hz and 6 Hz frequency bins.

Fig. 7.

A: Group-level averages (n=47) and SD of the log(10)-transformed mesiotemporal power spectral values during resting with eyes opened and closed. Asterisks indicate significant differences (***p<0.000001, **p<0.001, *p<0.05). B: Power spectral values in the right FO and O2 electrode of a representative patient. From front to back: acquisition, resting with eyes opened, resting with eyes closed in the FO electrode and resting with eyes closed in the O2 electrode. Note the similar shape of the alpha peak in the 6-9 Hz range progressively increasing in amplitude across acquisition, resting with eyes opened and resting with eyes closed. Alpha activity in the O2 electrode peaked at a higher frequency (~7.5-9 Hz).

Fig.1

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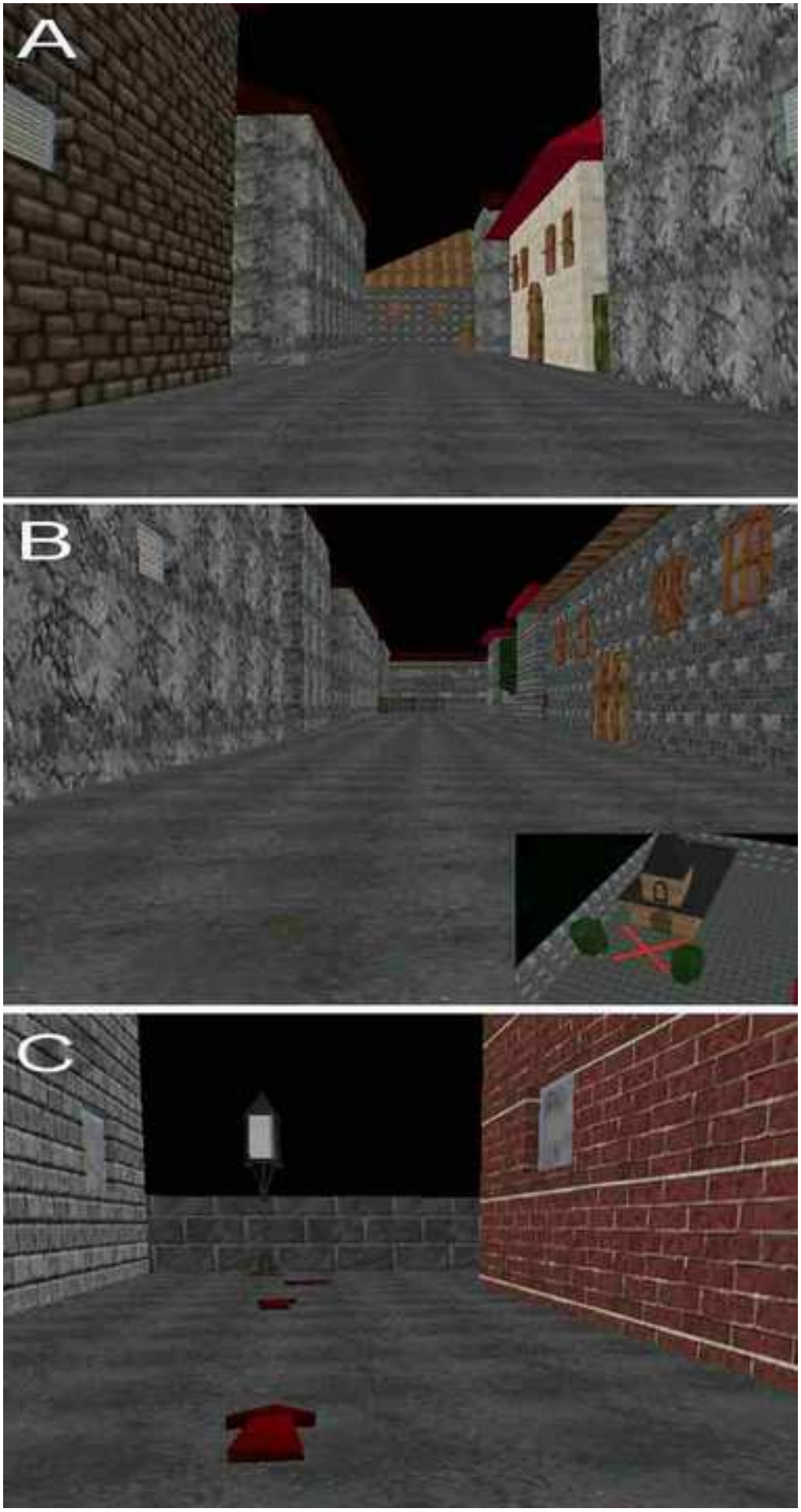

Fig.2

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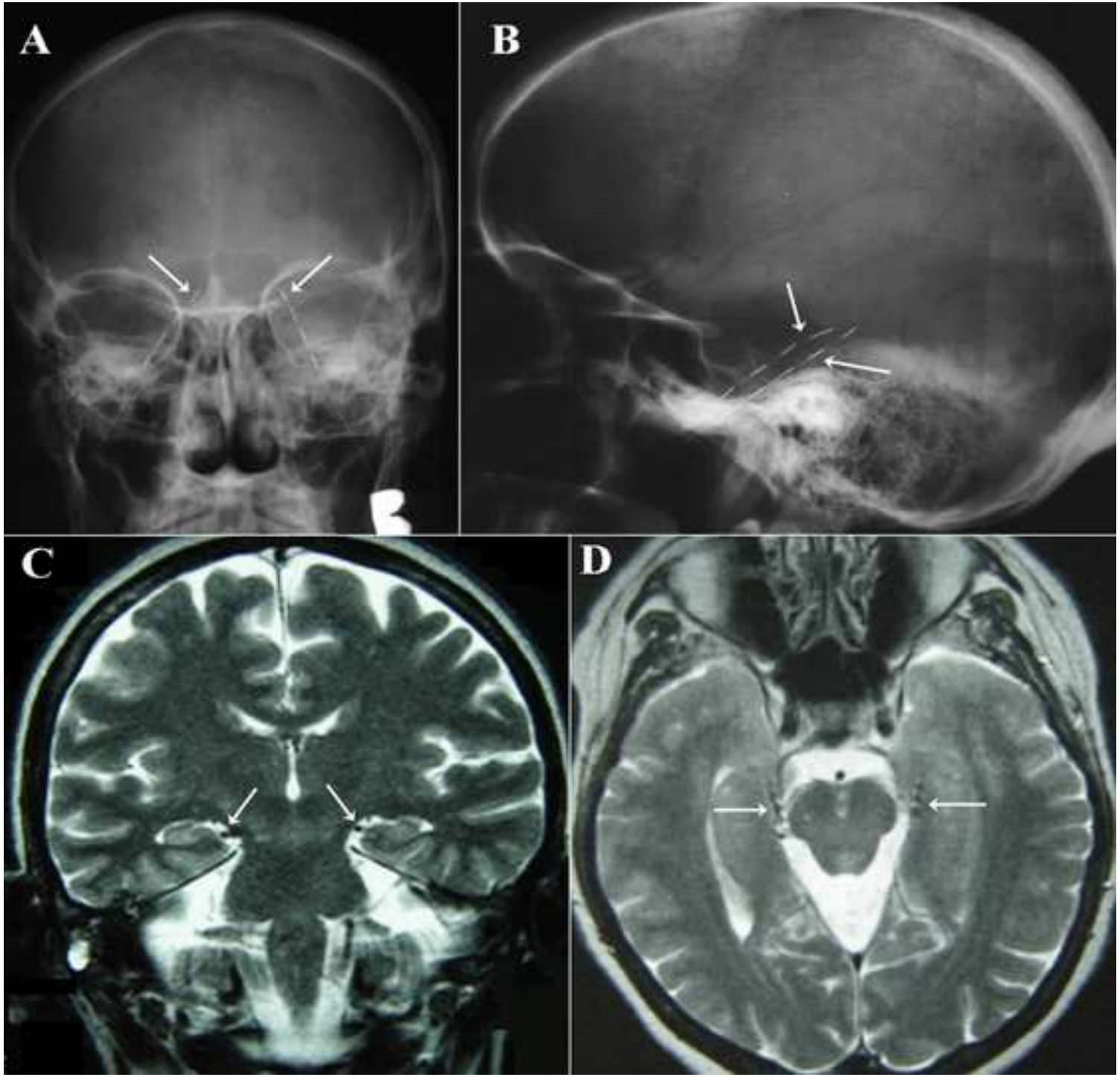

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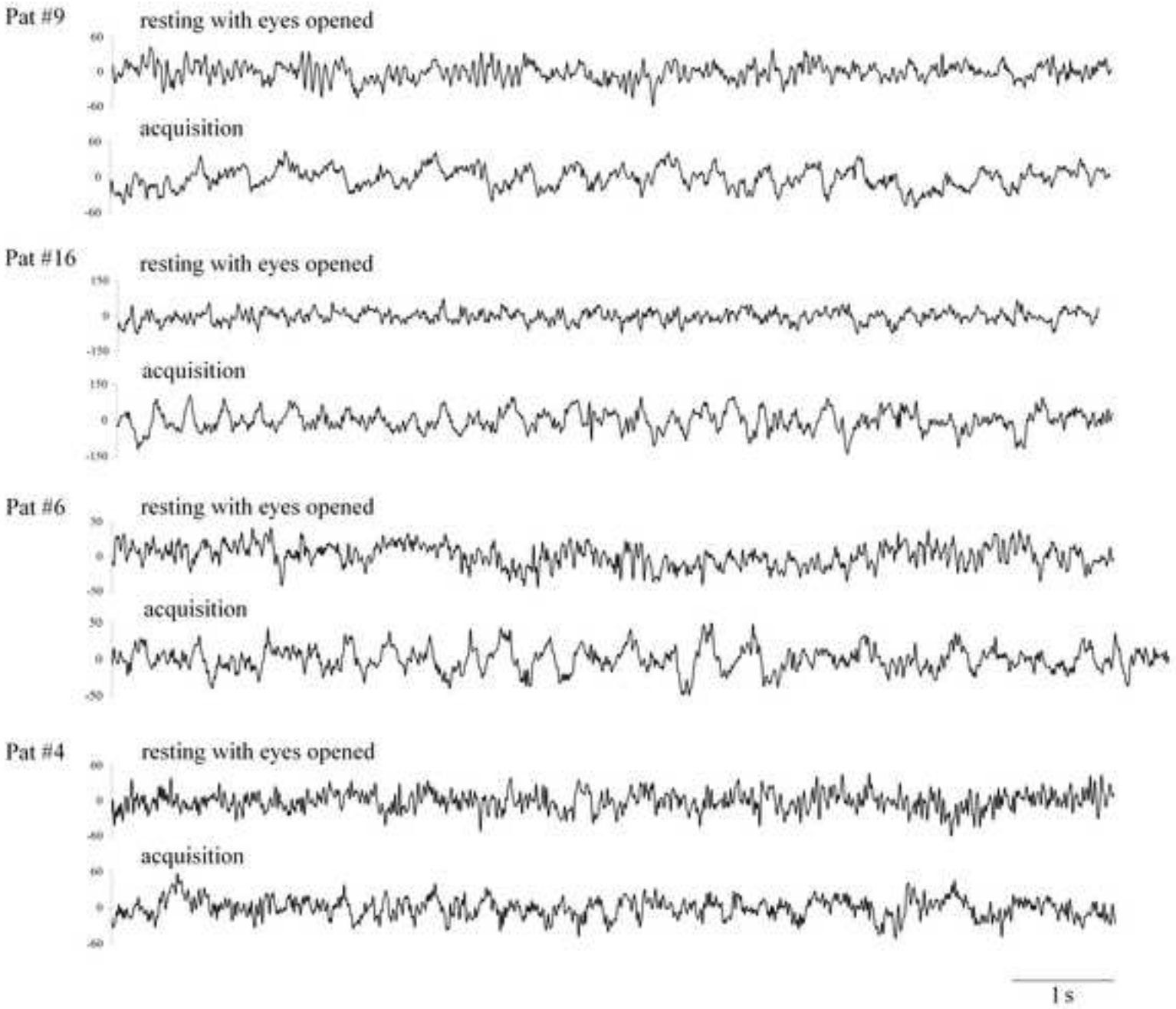

Fig.4

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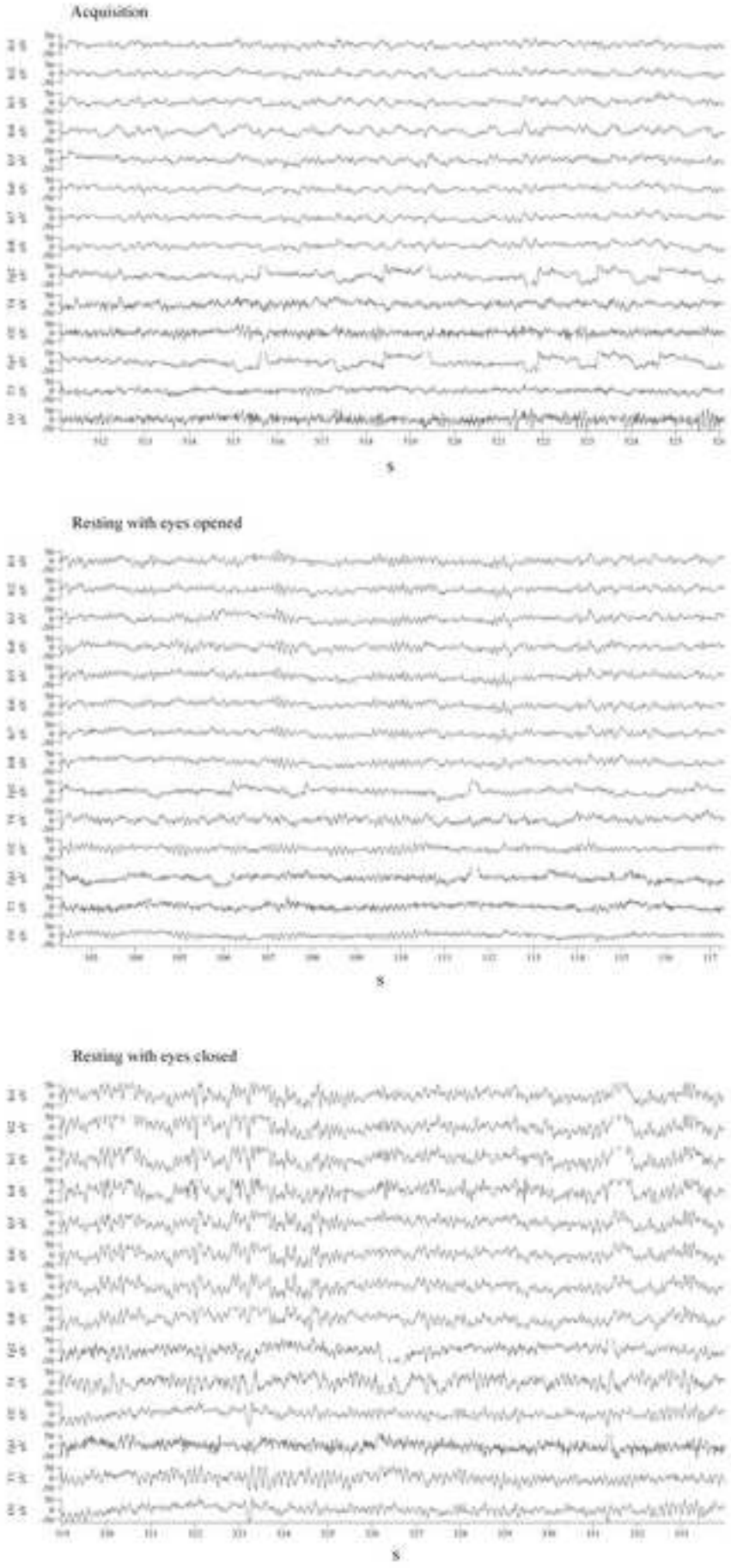

Fig.5

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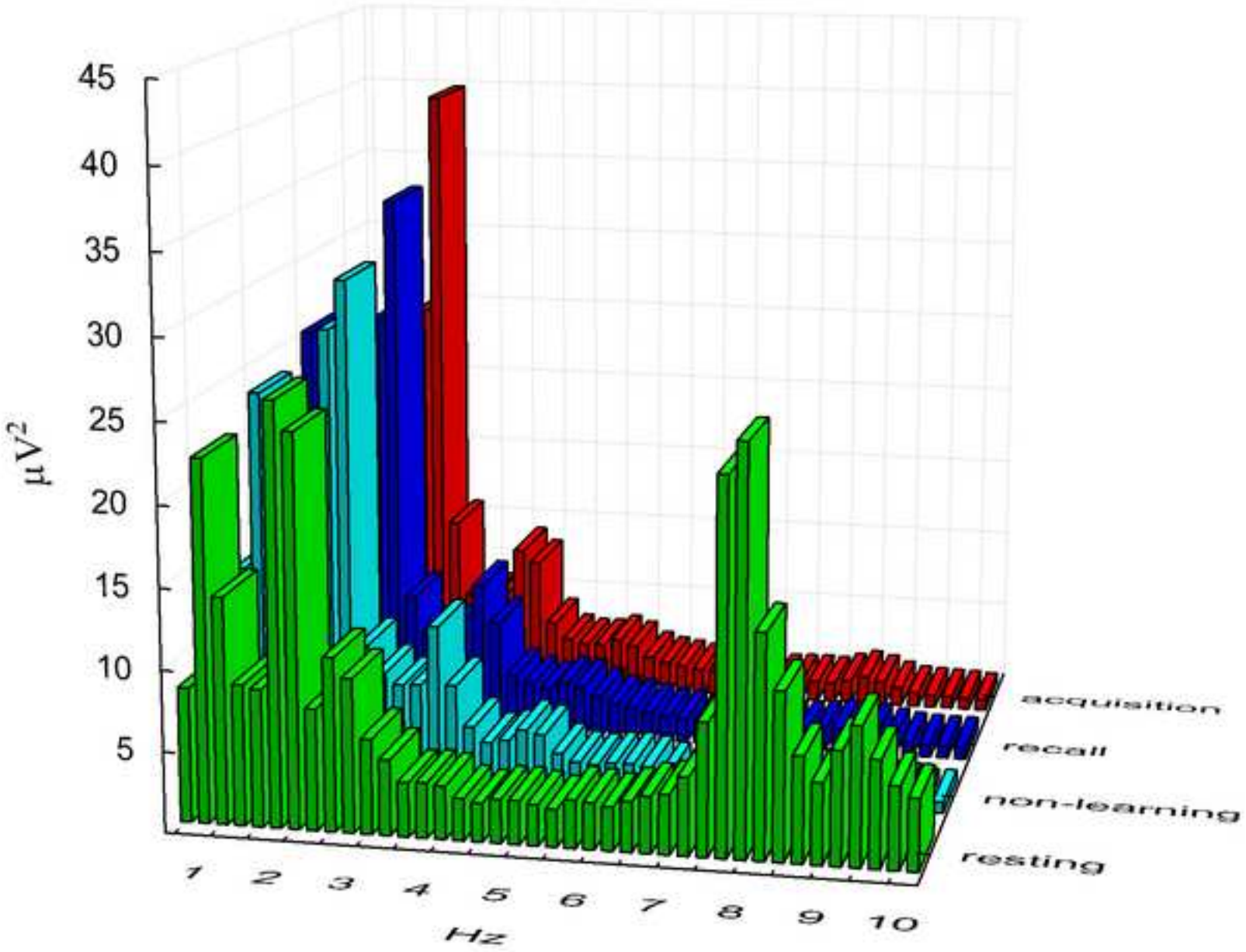

Fig.6

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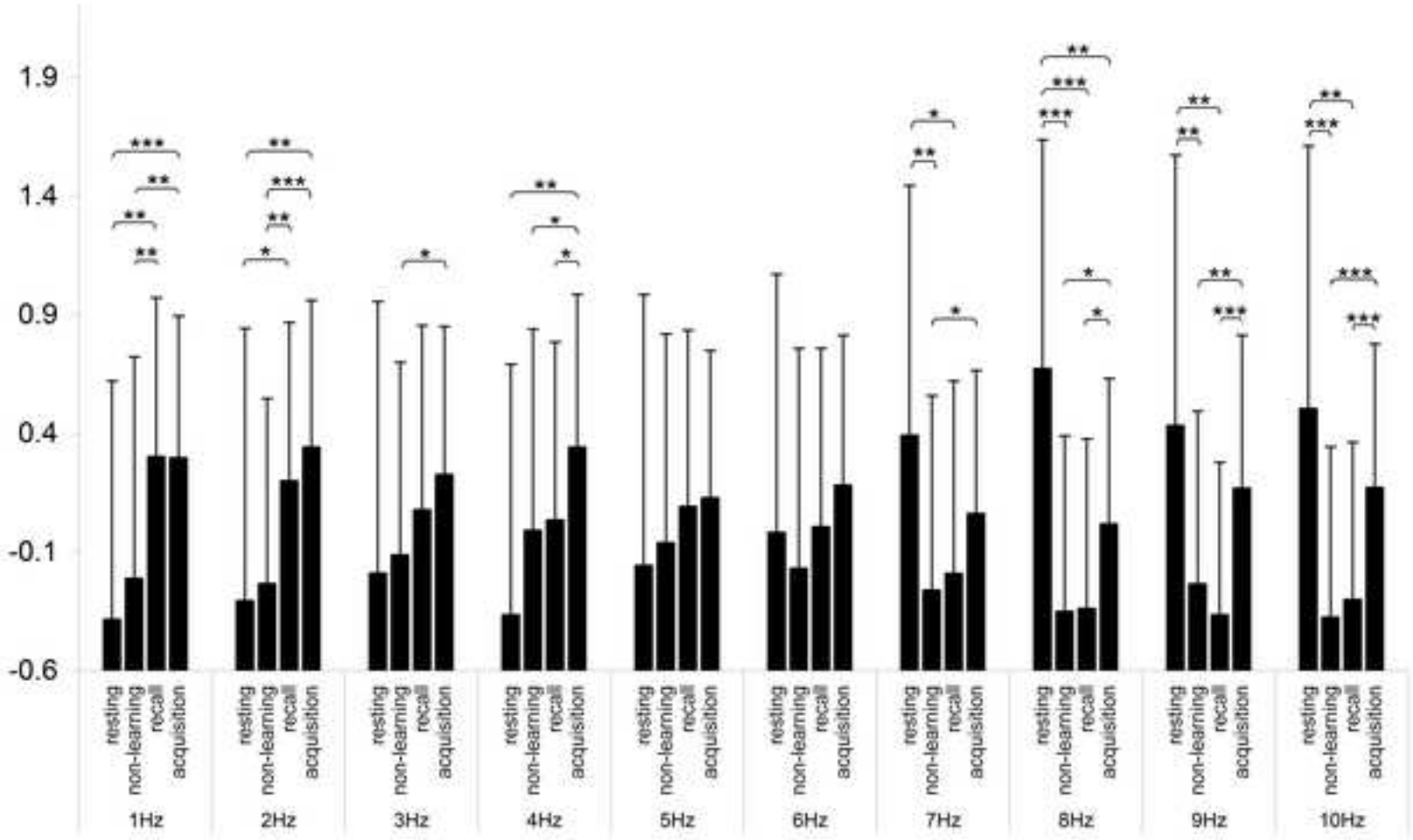

Fig.7

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