EEG characteristics of déjà vu phenomenon

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SUMMARY

Introduction. Déjà vu (DV, from French “already seen”) is an aberration of psychic activity associated with transitory erroneous perception of novel circumstances, objects, or people as already known.

Aim. Investigation of clinical and diagnostic significance of derealization episodes in epilepsy.

Materials and methods. The study involved 166 individuals (mean age 25.2 ± 9.2 yrs; 63.2% women). DV episodes were characterized and compared in groups of healthy volunteers (n = 139) and epilepsy patients (n = 27). The subjects participated in a survey concerning déjà vu characteristics and in a long-time ambulatory EEG monitoring (12–16 h).

Results. In epilepsy patients, DV episodes were equally frequent in cryptogenic and symptomatic focal epilepsy, occurred in combination with nearly all types of seizures, and could occur both as an aura and as an individual seizure. The major clinical features distinguishing DV in healthy subjects from DV in epilepsy patients were the frequency and emotional perception of DV episodes, and preceding fear. A critical diagnostic marker is the dynamics of DV characteristics: an increase in frequency and duration, negative emotional background. In EEG, DV episodes in patients began with polyspike activity in the right temporal lobe and, in some cases, ended with slow-wave theta-delta activity in the right hemisphere.

Conclusion. Our combined clinical and electrophysiological investigation identified two separate DV types: epileptic Déjà Vu characteristic of epilepsy patients and equivalent to an epileptic seizure, and non-epileptic Déjà Vu occurring in healthy individuals, which is basically a psychological phenomenon.

Key words: déjà vu • epilepsy • ambulatory EEG monitoring

INTRODUCTION

Déjà vu (DV, from French déjà vu – already seen) is the term describing an aberration of psychic activity associated with transitory erroneous perception of novel circumstances, objects, or people as already known. This phenomenon belongs to the group of derealization disorders, which includes also such states as DÉjà vÉcu (already experienced), DÉjà entendu (already heard), Jamais vu (never seen). According to another classification DV is a memory-based illusion (Illman et al., 2012). The term was coined by the French psychologist Emile Boirac (1851–1917) in his monograph L’Avenir des sciences psychiques (The Future of Psychology, 1918).

The DV phenomenon attracts special interest because, on the one hand, it occurs in most healthy individuals (up to 97% of the general population), spontaneously or in association with sleeping disorders or anxiety. On the other hand, it can be a sign of certain psychoneurological diseases, such as Charles Bonnet syndrome, temporal lobe epilepsy (TLE), depression, or schizophrenia, and can be an early symptom of a mass
lesion of the brain (Karlov, 1999; Brown, 2003; Warren-Gash and Zeman, 2003; Dobrokhotova et al., 2006). Thus, DV is observed both in healthy people and in patients with organic brain damage. Under these circumstances, it seems reasonable to identify differential diagnostic criteria to discriminate whether DV represents a normal phenomenon or a sign of a disease.

A number of recent publications concern the mechanisms underlying DV, its characteristics, and prevalence (Bancaud et al., 1994; Adachi et al., 1999; Spatt, 2002; Warren-Gash and Zeman, 2003; Brown, 2003). We also described major clinical differential diagnostic characteristics of DV in healthy individuals (Vlasov and Chervyakov, 2009), in patients with mass lesions of the brain (Vlasov et al., 2011), and in patients with epilepsy (Vlasov and Chervyakov, 2012).

DV is particularly interesting as a sign of epilepsy. A DV aura occurs in 10% of patients with TLE (Palmi

ni and Gloor, 1992); however, DV as a sign is present in 1/3 of patients with familial mesial temporal lobe epilepsy (Striano et al., 2008). Autosomal dominant temporal lobe epilepsy (ADLTE) is characterized with focal seizures with auditory symptoms or aphasia. More than 50% of ADLTE patients have an LGI1 mutation. Recently, ADLTE cases with psychic presentations (DV and fear) but lacking classic aphasia and auditory symptoms have been described. These patients had a previously unknown LGI1 mutation, Arg407Cys, which, in contrast to the mutations described earlier, did not prevent protein secretion in vitro (Striano et al., 2011). To identify the brain regions involved in DV, TLE patients with and without DV episodes were investigated using voxel-based analysis of 18FDG-PET brain scans. TLE patients with DV episodes exhibited unilateral EEG focus hypometabolism in the superior temporal gyrus and the parahippocampal region, in the vicinity of the perirhinal and entorhinal cortex (Guedj et al., 2010).

Gloor et al. (1990) implanted electrodes to 35 TLE patients with pharmaco-resistant seizures and found that most DV episodes were associated with stimulation of the right hemisphere. Ide et al. (2000) performed a SPECT investigation of a patient with frequent DV auras and detected hyperperfusion in right temporal and frontal lobes. Following pharmacotherapy, the frequency of seizures and DV episodes decreased, and the perfusion characteristics returned to normal.

The main unanswered clinical question is whether DV can be considered a sign of epilepsy. Neppe (1983) found that DV occurred more frequently in TLE patients (86%) than in control individuals (68%), but was unable to determine the clinical significance of this difference. Other authors argue that DV can occur as a simple partial seizure, as a part of a complex partial seizure, or as an aura of a secondarily generalized tonic-clonic seizure (van Paesschen et al., 2001).

Apparantly, the problem cannot be solved without describing the specific ictal EEG pattern of DV, which has not been done so far. It is also necessary to identify the clinical differential diagnostic characteristics of DV differing between healthy subjects and TLE patients.

AIM

The aim of the present study was to investigate the clinical and the electroencephalographic characteristics of the DV phenomenon in patients with epilepsy and in healthy subjects.

MATERIALS AND METHODS

Patients

This study investigated 166 individuals (mean age, 25.2 ± 9.2 yrs; 63.2% females). DV characteristics were analyzed in two groups, the first one comprising of healthy volunteers (n = 139; 23.17 ± 11.51 years; 56.8% females), and the other one comprised patients with epilepsy (n = 27; 27.19 ± 6.86; years; 69.6% females). The groups were matched by age and sex. Healthy volunteers were enrolled in the study based on the lifelong absence of paroxysmal conditions of different genesis, such as syncopal attacks, autonomic paroxysms, psychogenic seizures, epileptic seizures, febrile seizures, etc. One third of control subjects were randomly selected for a standard EEG investigation to exclude any epileptiform activity. The patients with epilepsy were diagnosed based on the results of clinical, neuroimaging, and neurophysiological investigation.

Analysis of DV prevalence in epilepsy patients showed that it was not typically observed as an isolated symptom, but occurred in combination with secondarily generalized tonic-clonic seizures, simple and complex partial seizures. Importantly, DV never was the first sign of epilepsy, and only in four patients (17.4%) it appeared simultaneously with other types of seizures. DV was observed in different forms of epilepsy (Table 1). The majority of patients with DV were diagnosed with cryptogenic and symptomatic focal epilepsy (CI method, P < 0.95). However, DV was also observed in idiopathic generalized epilepsy. In 14.3% of
EEG of déjà vu cases, it was difficult to make the syndrome diagnosis. These observations were classified as undifferentiated epilepsy cases.

DV occurred in combination with other seizures as an individual simple partial seizure, as an aura of a complex partial or a secondarily generalized seizure, or in a combination of different seizure types in the same patient. A DV aura was observed in 13.0 ± 4.1% of patients. Significantly more frequently DV was registered as a simple partial seizure (56.5 ± 8.9%) (CI method, P < 0.05).

Methods
1. One-time survey (n = 166). All subjects completed an original questionnaire (Table 2) to characterize their DV experiences. The questionnaire was developed based on the available published data and aimed at characterizing the presence of DV experiences, their frequency, duration, accompanying emotions, and fear preceding other derealization episodes.
2. Hospital Anxiety and Depression scale; Cambridge depersonalization scale.
3. Prospective annual DV investigation in healthy indi-

<table>
<thead>
<tr>
<th>Table 1. Epilepsy types in patients with DV</th>
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<tr>
<td><strong>Epilepsy type</strong></td>
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</tr>
<tr>
<td>Idiopathic generalized epilepsy</td>
</tr>
<tr>
<td>Cryptogenic focal epilepsy</td>
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<tr>
<td>Symptomatic focal epilepsy</td>
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<tr>
<td>Epilepsy, undifferentiated*</td>
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* both the signs of focal and idiopathic generalized epilepsy were observed

**Table 2. Original questionnaire**

Dear respondent!

Déjà vu – the feeling that the situation in which you are now, have occurred previously. Feeling “that all this has happened”. Please try to answer as accurately as possible to the questions below by selecting one option from each item. Thank you in advance!

1. Your gender:
   A Male
   B Female

2. Your age: ______

3. State your guiding hand:
   A Right, I’m right handed
   B Right, I’m left-handed
   C It is equally good at both hands (ambidexterity)

4. Have you ever felt déjà vu in your life?
   A Yes, it have felt it
   B No, I haven’t felt it

5. At what age did you first feel the déjà vu? ______

6. How often do you feel déjà vu?
   A A few times a day
   B 1–2 times a week
   C 1–2 times a month
   D Several times a year
   E After 1–2 times in my life
   F Never felt

7. How long do you feel déjà vu when it happens?
   A 1–2 seconds
   B 5–10 seconds
   C 20–30 seconds

8. What is the situation most often you associate appearance at déjà vu?
   A Appears spontaneously
   B Appears during extreme fatigue
   C Appears during long time without sleep
   D From alcohol
   E Other _________________________________

9. Please write, 2–3 emotions that accompany you déjà vu:
    ________________________________________________
    ________________________________________________

10. What emotions do you accompany a sense of déjà vu?
    A Positive (euphoria, interest, relaxation)
    B Negative (fear, anger, nausea, disorientation)
    C It does not cause any emotions

11. Are you afraid of the onset of déjà vu?
    A Yes, I’m afraid
    B No, I’m afraid
    C Do not know

12. Do you suffer from a chronic disease of the below (underline epilepsy, schizophrenia, alcoholism, drug addiction and other _________________________________
    _________________________________________________
    _________________________________________________

Date ____________________
individuals (n = 20). To evaluate the true frequency of DV episodes, their duration, and accompanying emotions, 20 healthy volunteers kept during a one year period a specially developed "Déjà vu diary", where they noted and described each DV they experienced. The DV characteristics noted included episode duration, accompanying emotional and physical sensations, as well as the presence of fear prior to each DV. For women, the day of the menstrual cycle when a DV occurred was also registered.

4. Long-time ambulatory EEG monitoring (Holter EEG, n = 47). This investigation implies autonomous registration of EEG on a memory card of the recording device, without phono- or photostimulation, while the patient is free in his movement and activities, and independent of the computer. This investigation was performed in all epilepsy patients and in 20 healthy volunteers. It provides a possibility to detect the pattern of rare seizures (including DV) during a subject’s normal wakefulness. We used 10/20 electrode placement arrangement.

5. Clinical investigation techniques: magnetic resonance tomography, computer tomography, and standard EEG were used to verify the diagnosis and specify the localization of the disease focus (brain mass lesion, epileptic focus).

6. Statistical analysis. The data obtained were analyzed using Statistica 7.0 (StatSoft Inc. for Windows) and involved two major steps:

A) Analysis of trait distributions was performed using the Shapiro-Wilk test: the null hypothesis assumed that the trait distribution was normal; the alternative hypothesis was that the trait distribution was different from normal. For P > 0.05, the null hypothesis was not rejected; i.e., the trait distribution was considered as normal. Otherwise (P < 0.05), the trait distribution was considered as different from normal.

B) Depending on the distribution type, the method of data analysis was chosen. We use methods of parametric (for normally distributed traits) and non-parametric statistics (Mann-Whitney and Wilcoxon tests, Pearson’s correlation, χ² test, analysis of variance, and the method of confidence intervals (CI), P ≤ 0.05).

Normally distributed data were described using means (M) and standard deviations (s) as M ± s; the data with non-normal distributions were described using medians (Me) and quartiles (Q1; Q2) as Me (Q1; Q2); qualitative traits were described using relative trait frequencies (%) and confidence intervals (CI) as % ± CI.

The study was approved by the local Ethics Committee of Research Center of Neurology Russian Academy of Medical Science.

RESULTS

There were no significant differences between healthy respondents and patients with epilepsy with regards to the Hospital Anxiety and Depression Scale and the Cambridge Depersonalization Scale. Therefore, for subsequent analysis we used our own questionnaire.

Routine EEG and ambulatory EEG monitoring during 12–18 hours were undertaken as in patients with epilepsy and DV.

The analysis of routine interictal EEG (Table 3) revealed that an epileptiform pattern occurred as frequently as the no focal slow wave activity and this made a differential diagnose hard. Significantly fewer patients with no change in the EEG slow-wave activity (22.22% and 14.81%) were observed in comparison to patients with epileptiform discharges or with non-specific changes.

Ambulatory EEG monitoring was performed with simultaneous recording of experiences and the patient’s condition to clarify the pattern of electrophysiological changes in DV. The maximum record was 18 hours.

Table 3. Intercital routine EEG patterns in epilepsy DV

<table>
<thead>
<tr>
<th>EEG pattern</th>
<th>%</th>
<th>n</th>
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<tbody>
<tr>
<td>The absence of abnormal (epileptiform and slow wave) activity</td>
<td>22.22</td>
<td>6</td>
</tr>
<tr>
<td>Focal slow-wave activity</td>
<td>14.81</td>
<td>4</td>
</tr>
<tr>
<td>Epileptiform discharges - generalized and partial (spike-slow waves, polyspike, sharp wave-slow wave)</td>
<td>44.44</td>
<td>12</td>
</tr>
<tr>
<td>Nonspecific changes (diffuse changes of bioelectrical activity)</td>
<td>55.56</td>
<td>15</td>
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Note: In some patients there was a combination of EEG changes.

Electroencephalography of DV Episodes in Healthy Volunteers and in Epilepsy Patients

Employing the possibility of long-time ambulatory EEG registration, we performed EEG monitoring in
five healthy volunteers with frequent DVs and in 23 epilepsy patients. In the course of ambulatory EEG monitoring, DV episodes was registered in one healthy volunteer and in three epilepsy patients. We were unable to find any description of EEG patterns of DV in the available literature.

**Observation examples**

*Subject S., 20 yrs, female.* For a long time (since the age of 15) the subject had been complaining of moderate tension headaches with a predisposition to meteo-sensitivity. At approximately the same age, she began to experience DV episodes, which had been occurring more frequent.

At examination, the patient complained of headaches. DV episodes occurred several times per day, lasted up to 10 sec, and were accompanied with positive emotions (surprise, interest) and no fear. Neurological examination showed signs of vegetative parasympathetic dysfunction, in particular, acrohyperhidrosis. Brain MRI did not show any pathology. Doppler ultrasound of main head arteries was according to the patient’s age. A routine EEG showed moderate diffuse changes of bioelectric brain activity, without epileptiform signs. A 24-hour ambulatory EEG monitoring registered a DV episode.

At 00.42, the patient was in the kitchen, when she experienced a feeling of unreality and expected a DV. Subject S. pressed the marker button. She felt interest and pleasant emotions, and became attentive to her condition. Subject S. had a feeling that everything had happened before and knew what was going to happen next (anticipation). The episode lasted about 10 to 15 sec (Fig. 1).

As visible in the EEG fragment, there were no epileptiform changes during a DV episode in a subject without epilepsy. The observation showed rhythm desynchronization. The data suggest that DV in healthy subjects is basically a non-epileptic phenomenon.

*Patient D., 29 yrs, male.* The childhood history was normal. Since the age of 15, patient D. was experiencing rare DV episodes, such as perceiving things as already seen in the same circumstances, for up to 5 sec in duration. At the age of 24, he suffered a closed craniocerebral injury and cerebral concussion as a result of a traffic accident. Six to seven months after the injury, the patient began to suffer from generalized tonic-clonic seizures with tongue bites, recurring about five
Figure 2. Patient D, 29 yrs. The beginning of a DV episode. The red line is the patient’s label (10 µV; 30 mm/sec).

Figure 3. Patient D, 29 yrs. A DV episode, continuation (10 µV; 30 mm/sec).
times per year. DV episodes became more frequent and more vivid. In April 2011, patient D. was seen at the Research Center of Neurology. At that time seizure frequency had increased to once per month. DV episodes occurred once or twice per week, lasted up to 30 sec and were accompanied with fear and unpleasant feelings; however, the patient was willing to relive the experience. A neuroimaging study did not detect any pathology. A routine EEG showed rhythm disorganization with moderately decreased amplitude; paroxysmal activity, predominantly frontal and central, more on the left; enhanced by hyperventilation.

During a 12-hour EEG monitoring, at 23.30 the patient experienced derealization and anxiety, followed by a DV accompanied with an unpleasant feeling of anguish. The episode lasted up to 32 sec. The episode was accompanied by the following changes in EEG (Fig. 2, 3). Several fractions of second before patient’s pressing the button (the beginning the seizure), a galvanic skin response was registered. Dominant alpha rhythm changes to a polymorph epileptiform activity with slow waves of theta-band and sharp waves (Fig. 2). Amplitude of the slow and sharp waves gradually increased up to 200 µV by the attack. Epileptiform activity predominated in the right temporal lobe. The recruitment phenomenon was registered (Fig. 3). Figure 4 shows a perspective view of a patient seizure. The total duration of the seizure is a 32 seconds. The pathological activity lasted for 32 sec and was subsequently replaced by background activity.

A dipole localization procedure using the BrainLock program localized the focus of both the initial activity and the subsequent slow-wave activity as occurring in the medial temporal lobe and the medial frontal lobe of the right hemisphere (Fig. 4). In two other ambulatory EEG records of DV episodes, the polyspike activity lasted for 8 sec and also showed distinct right hemisphere lateralization, predominantly in the temporal lobe.
DISCUSSION
The major questions addressed in DV investigations are its clinical significance (e.g. whether it is a basically pathological phenomenon) and, accordingly, the necessity of treatment, and the mechanisms of its generation.

Naturally, particular attention is drawn to DV episodes in healthy individuals. Most authors believe that DV is a neurologic analogue of a seizure involving psychoactive zones, rather than a psychopathological phenomenon (Brown, 2003).

An original hypothesis of DV generation was proposed by Spatt (2002). It assumes that the functions of the hippocampus and the prefrontal cortex involve recognition of new information and relating it to the previous experience. The parahippocampal system coordinates the comparison, and aberrations of its functioning cause novel information to seem familiar, i.e., produce a DV. It was concluded that DVs occur as a result of an impaired contact between the neocortex and the medial temporal lobe structures, when the cortical influence weakened (sleep, fatigue).

DV states described in our study were heterogeneous in origin. EEG results together with clinical, psychological, and neuroimaging data suggest that two DV types exist: pathologic and non-pathologic.

In most healthy individuals, DV is non-pathologic, non-epileptic, as it does not show an epileptiform EEG pattern, has low frequency and low duration, and occurs mostly as an induced phenomenon. However, it cannot be ruled out completely that such non-pathologic DVs might be associated with aberrations of neuron functioning and spontaneous neuron discharging. However, the activity is probably restricted to such a small area (within the parahippocampal zone) that it does not produce any distinctive EEG pattern. On the other hand, pathologic epileptic DVs occurring in epilepsy are characterized with a specific pattern of EEG activity and typical clinical features, such as increased frequency and duration, and negative emotional perception. That is, a pathologic DV occurs as a result of excessive mass neuron discharges and is, in fact, a simple partial a simple partial psychic seizure.

Other authors also proposed a similar division in two DV types, although they did not provide any electrophysiological evidence to support the notion (Adachi, 2010).

The EEG data suggest that DV generation largely involves the right hemisphere. However, two EEG records of DV episodes showed polyspike activity in the right hemisphere, lasting for 8 sec, while in a longer episode polyspike activity was followed by slow-wave activity. It is possible that DV is not generated in any single hemisphere, but results from impairment in their interaction. Importantly, PET and SPECT studies detected hypometabolism areas in temporal lobe structures (entorhinal and perirhinal cortex) (Engel, 1999; Bartolomei et al., 2004; Takeda et al., 2011). The slow-wave activity detected in an epilepsy patient during a DV episode can be an electrophysiological reflection of the previously described hypoperfusion.

CONCLUSION
In patients with epilepsy, DV is equally frequent in cryptogenic and symptomatic focal epilepsy; it can accompany nearly all seizure types, occur as a simple seizure, or as a part of a partial or a secondary generalized seizure. Major clinical features distinguishing DV in epilepsy patients from that in healthy individuals are its frequency, the fear preceding a DV, and the emotional perception. A very important criterion is DV dynamics, such as increasing frequency and duration, or appearance of negative emotions. In EEG, DV began with a polymorphic spike and slow wave activity in the right temporal lobe. Our combined clinical and electrophysiological investigation identified two separate DV types: epileptic Déjà Vu characteristic of epilepsy patients and equivalent to an epileptic seizure, and non-epileptic Déjà Vu occurring in healthy individuals, which is basically a psychological phenomenon.

CONFLICT OF INTEREST DISCLOSURE
Authors have no conflicts of interest to declare.

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