

NEUROIMAGING AND COGNITIVE CHANGES DURING DÉJÀ VU

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Supplementary data attached to the manuscript!

Abstract

Purpose: The cause or the physiological role of déjà vu (DV) in healthy people is unknown. The pathophysiology of DV-type epileptic aura is also unresolved. Here we present a 22-year-old woman treated by deep brain stimulation (DBS) of the left internal globus pallidus due to hemidystonia. On a certain stimulations settings, DBS elicited reproducible DVs.

Methods: Neuropsychological tests and SPECT were performed during DBS-evoked DV and during normal DBS stimulation without DV experiences.

Results: SPECT during DBS-evoked DV revealed hyperperfusions in the right side (contralateral to the electrode) hippocampus and other limbic structures. Neuropsychological examinations performed during several evoked DV experiences revealed disturbances in the non-verbal memory.

Conclusion: Our results confirm the role of mesiotemporal structures in the pathogenesis of DV. We hypothesize that the individual neuroanatomy, disturbance in gamma oscillations or in dopaminerg system can play a role in DBS-elicited DV experiences in our patient.

Keywords: déjà vu, deep brain stimulation, pallidum, SPECT, SISCOM, adverse reaction, epilepsy, dystonia, MRI, aura

Introduction

Déjà vu (DV) is “any subjectively inappropriate impression of familiarity of present experience with an undefined past” [1]. Although 60-80% of the healthy population has experienced déjà vu [2], DV aura is one of the leading symptoms of temporal lobe epilepsy [3] occurring in 10% of all epileptic auras [4]. DV aura is the most characteristic symptom of familial mesial temporal lobe epilepsy reported in about one-third of these patients [5, 6]. DV experiences occurring in other brain disorders (e.g. depression [7] and schizophrenia [8]) were also analyzed in more details.

Studying DV is difficult because of its rarity, unpredictable appearance and heterogeneity. Contrary to spontaneous DV experiences, the induced DV can be examined objectively during presurgical evaluation of epilepsy [3]. The stimulation of the temporal structures [9] or the rhinal cortex [10] often, but not always [11] could elicit DV in temporal lobe epilepsy (TLE) patients. Most studies found that DV was confined to the non-dominant temporal lobe and accompanied by hallucinations or illusions [3, 4, 9, 11]. Furthermore, DV experience could also be provoked by electrical stimulation of brain structures contralateral to the epileptic focus suggesting that DV can also be elicited in normal brain tissue [12].

Despite numerous investigations, the pathomechanism of DV experiences in healthy people is still unknown. The “**small seizure**” theory is based on the clinical findings that DV is an aura type in TLE. It is hypothesized that in non-epileptic population a “small temporal lobe seizure” may elicit déjà vu episodes without producing clinical seizures [13, 14]. However, there are several counter-arguments about this theory: the DV is much more common than TLE [15, 16] and only a portion of TLE patients have DV auras [17].

‘**Tape-recorder**’ theory [18] is one of the most known DV theories applying the dual-processing approach. It assumes that two different memory-related processes that normally synchronously work become asynchronous or one process becomes activated in the absence of the other. Under normal condition, the memory encoding (“recording head”) and the retrieval (“playing head”) work with appropriate timing and synchronization. According this speculation if the new sensory information is simultaneously encoded and retrieved, the sensory input is accompanied by familiarity resulting in déjà vu feeling. Based on the clinical evaluation of

electrically evoked déjà vu experiences of 16 TLE patients underwent presurgical depth electrode implantation, Bancaud and colleagues [9] postulated the neuroanatomical bases for the 'tape-recorder' theory. Because association cortical and limbic areas encode the holistic memory of an event, and perceptual information is encoded by the temporal neocortex and stored in the hippocampus, the inappropriate activation of centers can lead to the experience of déjà vu. Similar electrophysiological results [19] expanded Bancaud's theory by the complementary assumption of parallel neuronal networks underlying encoding and retrieval [20].

Interestingly, a recent case-study described a "drug-induced" DV, where a patient experienced recurrent DV after receiving a combination of amantadine and phenylpropanolamine [21]. Because both drugs can facilitate dopaminergic neurotransmission and recent animal studies proved that hippocampal dopaminergic systems are involved in the spatial memory processes [22], this case suggests that an increased dopaminergic activity probably might play a crucial role in the development of DV [21].

In a very recent case report, hypothalamic deep brain stimulation (DBS) was found to evoke detailed autobiographic memories, but not déjà vu [23].

These data inspired us to systematically analyze the pathophysiology of DV by applying functional neuroimaging (SPECT) and neuropsychological batteries in a case where the DBS of left internal globus pallidum (GPi) elicited DV. As far as the authors are aware, this is the first study utilizing direct, reproducible and integrative neuropsychological and neuroimaging investigations during DV.

Methods

The patient

The 22-year-old female university student was born with a right-sided spastic hemiparesis due to a perinatal injury. Although the strength of the right limbs normalized, the abnormal posture of the right upper limb was noticed at the age of 2 months, developing to a drug-refractory and painful secondary hemidystonia. The locomotive and intellectual development was otherwise normal.

Brain MRI revealed a 4x15x18mm lesion in the left GP. At age 22, she underwent a microelectrode-guided Medtronic quadripolar 3389 DBS electrode implantation into the left posteroventral GPi without perioperative complications. The patient has given written informed consent to the whole surgical procedure, pre- and postsurgical examinations and publication of the present case report, whereas the study was also approved by the Local Ethical Committee.

Stimulation settings

On the first postoperative day, contact 1 was activated in a monopolar mode (C+1-, 120 μ s, 130Hz, 3.2V) without any adverse reactions. The patient was admitted to the Neurological ward on the 3rd postoperative week to learn the use of patient controller. During the testing of electrodes, we noticed that the monopolar stimulation of contact 0 with the amplitude exceeding 2.7V could elicit several DV episodes. As the turning on or off the stimulation had an immediate effect on this experience, we assumed it to be a stimulation-related adverse reaction. The impedance of contact 0 (C+0-, 3.2V, 120 μ s, 130Hz) was 562 Ohms.

SPECT

The current safety regulations do not permit using functional MRI during DBS [24]. Therefore, we performed 99mTc-hexamethylpropyleneamineoxime SPECT to study the pathophysiology of DV because 99mTc HMPAO has faster binding (2-10 minutes) compared to PET tracers [25].

The SPECT acquisition was performed 1 month postoperatively. To exclude the long-term duration effect of DBS, the '**baseline**' SPECT was obtained during the **normal stimulation** of contact 1 (C+1-, 3.2V, 120 μ s, 130Hz). For studying the pathophysiology behind DV, three days later we stimulated simultaneously both contact 0 and 1 (C+0-1-, 120 μ s, 130Hz, 3.2V referred to as **DV-inducing stimulation**). Analogously to epilepsy studies we defined this setting as '**ictal**' SPECT.

As the 99m-TcHMPAO tracer (750MBq) was administered immediately after starting the DV-inducing stimulation and the patient experienced numerous DV experiences during the first 5 minutes of stimulation, we assumed that the tracer binding in the 'ictal' SPECT represented the

combination of acute DV induction and normal pallidal stimulation. Therefore, the subtraction of baseline from the 'ictal' SPECT images theoretically corresponded only to the areas activated during DV experience. The comparison of baseline and 'ictal' SPECT was performed by the subtraction ictal SPECT co-registered to MRI (SISCOM) method, which is also applied in the presurgical evaluation of epilepsy [26].

Neuropsychological tests

The subject underwent neuropsychological examinations three times: 9 months preoperatively, 2 months postoperatively with and without DV eliciting stimulation. There was 1 day difference between the postoperative examinations, where Rey and Medical College of Georgia Complex Figure, Rey 8/64, Benton Visual Retention, Boston Naming and Rey Auditory Verbal Learning Tests were obtained [27, 28]. **(Supplementary data).**

Results

The appearance of DV

Preoperatively the patient had never experienced any DVs. Immediately after turning on the DV-inducing stimulation; an unusual and obscure feeling appeared. Besides discomfort and slight disturbance, the subject had intact reality sense; she was able to observe what is going on around her and maintain verbal and behavioral responsiveness. We defined this experience as '**standby-state for DV (SSDV)**'. The SSDV persisted until the stimulation of contact 0 was turned off or the amplitude of stimulation was lowered below 2.7 Volts.

During SSDV, sudden, impulse **DV experiences** appeared lasting 4-5 seconds. At these occasions she felt that the situation seemed familiar. No visual, auditory illusions or hallucinations accompanied the DV. Besides, the patient felt neither the ability to predict the future nor unreality about the current circumstances.

DV appeared more frequent immediately after turning the stimulation on (approximately 2-5 DV during the first 5-10 minutes) and became rarer as the time went by (approximately another 3-5 DV in the first hour and 2-3 in the second hour). Interestingly, DV appeared only if her eyes were

open and questions were addressed directly to the patient (e.g. “What is the name of your physiotherapist?”). However, not all of the direct questioning of the patient elicited DV. Standard digital EEG recording showed physiologic activity and there were no clinical signs of epilepsy either.

MRI

Preoperative speech-activated functional MRI demonstrated right-sided language dominance (**Supplementary data**) based on the technique described previously [29]. The postoperative MRI demonstrated that the stimulating electrode passed through the GPi, which was confirmed by the fact that the normal stimulation improved the severity of dystonia. Visual inspection and the application of electronic version of stereotactic atlas [30] verified that this contact was situated between the GPi and the underlying white matter (**Figure 1**). The electrode did not reach either the fornix or the hippocampus or any other mesial temporal structures. The exact position of the lowest contact, whose stimulation could elicit DV, was the following: 22 mm lateral from the midline, 13 mm anterior to the posterior commissure, 12 mm below the intercommissural line (the distance between the anterior and posterior commissure was 24.9 mm).

SPECT

The results of SISCOM analysis are demonstrated on **Figure 2** and the list of hyperperfusion and hypoperfusion clusters are presented in the **Supplementary data**. Compared to the baseline, SPECT during DV showed ***right-sided hyperperfusion*** of hippocampus, parahippocampal gyrus, fusiform gyrus, cerebellum and temporal superior pole. ***Left-sided hyperperfusion*** appeared in the cerebellum, operculum, insula, lingual gyrus, precuneus and middle temporal gyrus. Hypoperfusion appeared bilaterally in the precentral and postcentral gyri, as well as, in the frontal (especially supplementary motor cortex) and parietal areas.

Neuropsychological tests

The results of neuropsychological batteries are summarized in the **Table 1**. Preoperatively the Hungarian Standardized version of WAIS revealed an IQ of 119 [31].

During *normal stimulation* there was better performance in verbal fluency, copy score of Complex Figure, delayed memory of Benton test and Trail Making A and B version compared to the preoperative state. However, the recall memory of Complex figure became worsened during the normal stimulation.

During *DV-eliciting stimulation* there was some deterioration in verbal fluency and Boston Naming tests. Furthermore, severe non-verbal memory impairment could be demonstrated by Complex Figure Test, and Rey 8/64 visual learning test compared to either the normal stimulation or the preoperative state.

Discussion

In our patient the electrically evoked déjà vu phenomenon could be easily studied because of several reasons: (1) it could be repeated without any restraints; (2) déjà vu could be elicited several times; (3) no other neurological phenomenon disturbed the evaluation (e.g. altered consciousness during an epileptic seizure); (4) the anatomical site of electrical stimulation could be determined by a high-resolution MRI-examination; (5) the functional changes in the brain during DV could be identified by functional neuroimaging and (6) the examinations did not bother or harm the patient.

The main findings of our study:

(1) This case report demonstrates that pallidal DBS may evoke déjà vu as an adverse reaction, which can be resolved by changing to a more proximal contact or reducing the stimulation amplitude.

(2) The elicited déjà vu can be characterized as the 'non-pathological' form [15].

(3) Contrary to the unreliable results of electrical stimulation in epileptic patients [12], in our case the setting of certain stimulation parameters reliably and reproducibly elicited déjà vu.

(4) Neuropsychological examinations indicate prominent alterations of visual learning and retrieval during déjà vu. During *normal stimulation* the performance of most neuropsychological tests improved compared to the preoperative state, which might be associated with dystonic pain-assuaging effect of normal stimulation. Conversely, *déjà vu-eliciting stimulation* slightly worsened the verbal and severely impaired the non-verbal memory performance.

(5) This is the first study in which functional neuroimaging was performed during DV.

(6) The SPECT analysis revealed hyperperfusion of mesiotemporal structures contralateral to the stimulating electrode during déjà vu.

Clinical manifestation

Standby-state for déjà vu (SSDV)

A surprising finding was that the pallidal DBS elicited two distinct types of symptoms: SSDV and DV. Immediately after turning on the DV-eliciting stimulation, the patient experienced a feeling of slight discomfort. This state was coined as 'standby-state for déjà vu (SSDV)' and appeared as a not habituating adverse reaction, which could be resolved by either changing to a more proximal contact or reducing the stimulating amplitude. We tested several times the turning on or off the stimulation of contact 0 and decreasing or increasing the stimulation voltage across the threshold-level; but the patient always adequately indicated the presence or absence of SSDV without exception.

While the *normal stimulation* improved the overall neuropsychological functions compared to the preoperative state, the *DV-eliciting stimulation* worsened cognitive (mainly memory) functions. Because the dystonic pain had been eased equally by the time of the postoperative neuropsychological tests, the neuropsychological differences between the normal and the DV-eliciting stimulation were probably due to the different stimulation settings and they were unrelated to the impact of pain on the attention. Interestingly, these disturbances during the SSDV did not interfere considerably with the everyday functioning; the subject had intact reality sense and maintained verbal and behavioral responsiveness.

Déjà vu

The actual DV phenomena appeared suddenly without prodrome and lasted for 3-5 seconds during which the patient could talk. The fact that **open eyes** and **direct questioning** were required to elicit DV indicated that certain level of arousal and/or visual stimuli were needed for DV.

The occurrence of DV seemed to have a **habituating** feature, i.e. in the first 5 minutes starting the stimulation of contact 0 produced more frequent DV appearance (2-5 during the first 5 minutes), which became rarer with time.

Because DV is a transitory experience lasting for a few seconds, obviously we could not apply neuropsychological tests targeting directly it. However, on the 'ictal' SPECT scan we could identify the brain structures involved in DV, since the patient experienced several DVs during the interval of tracer binding. Therefore, the subtraction of ictal and baseline images presumably corresponds to only those areas responsible for both DV.

Neuroanatomical considerations

Based on the position of the stimulation electrode, we might speculate the anatomical target responsible for DV. The postoperative MRI scans demonstrated that contact 0 was situated in the border of GPi and the underlying white matter. The spreading of electrical current is roughly spherical around the activated contact and in no case extends underneath the electrode [32]. We can also presume that the electricity can diffuse approximately up to 4 millimeters in a low impedance tissue from the surface of the contact [33]. Because mesial temporal structures (e.g. hippocampus and fornix) are situated below the lowest contact, the direct stimulation of these mesiotemporal structures was unlikely.

We performed subtraction SPECT analysis comparing 'ictal' and baseline SPECT images. The subtracted picture revealed hyperperfusion in the right mesial structures contralateral to the stimulation. There was also hyperperfusion of ipsilateral (left) operculum, insula, precuneus and lingual gyrus. This finding is in harmony with TLE studies [9] demonstrating that the elicitation of DV involves mainly mesiotemporal structures.

Proposed theories on pathophysiology on DV

We cannot explain the pathophysiology of DBS-evoked DV. However, we can provide some possible theories concluding from our results.

As far as the authors are aware, there is not even a single case published describing the occurrence of déjà vu after pallidotomies, despite several ten thousands were performed worldwide

[34, 35]. Because ablative procedures could not evoke DVs and certain stimulation settings were required to produce DV, we may presume the importance of high-frequency stimulation in the background.

(1) We can hypothesize that **several independent constellations** together led to DV: (i) the altered memory functions of the SSDV and a certain combination of (ii) visual and (iii) direct verbal stimuli requiring memory matching processes. This hypothesis is based on the fact that the DV-inducing stimulation itself was unable to produce DV in the lack of simultaneous visual and verbal stimuli; it elicited “only” the SSDV with non-verbal memory disturbances. Clinically, DV appeared only when the patient was addressed with questions and her eyes were open. The type of visual stimuli seemed to be irrelevant in the elicitation, because DV appeared in both dim and bright rooms, either with or without persons in the visual field. On the contrary, only direct questioning of the patient was able to elicit DV, other auditory stimuli (e.g. environmental noises, conversation between other persons not involving the patient) never did so. However, not all questioning elicited DV. One potential explanation for this phenomenon might be that direct questioning requires high-level attention, interpretation and memory processing.

(2) Probably not only the left GPi stimulation itself, but also the **individual (atypical) neuroanatomy** might play a role in the development of DV. The atypical language dominance suggests that due to the perinatal brain injury our patient developed an atypical brain anatomy [36-39]. Because the reorganization of the injured brain is not always complete, similar modalities might be present bilaterally and the division of labor between dominant and non-dominant hemisphere functions might not be completed. Normally, language-dominant hemisphere is more strongly engaged in memory processing of verbal material [40]. However, in our case the individual neuroanatomy might have produced that non-verbal functions are confined to both hemispheres. If this speculation is true, the disturbing effect of left GPi DBS might have greater impact on one hemisphere and less on the other one producing DV in a similar way described in the dual-processing theories. The elicitation of DV seemed to be a habituating phenomenon. An explanation for this habituation may be that the memory processing system(s) noticed the DVs as errors. Possibly, this error recognition enabled the system to adapt to the SSDV resulting in less DV experiences over time.

(3) **Dopaminerg system** might also take part in the elicitation of DV. Previously a case study demonstrated that the concomitant use of amantadine and phenylpropanolamine could produce recurring DVs [21]. Based on PET studies carried out on Parkinson's disease patients, the pallidal DBS might interfere with endogenous dopamine release and/or dopamine-receptor functions [41]. Recent study investigating drug effects on schizophrenic patients found that the dosage of antipsychotic (anti-dopaminerg) drugs positively correlated with the frequency of DV experiences [42], which contradicts that DV is a result of an elevated dopaminerg activity, but underline the role of dopaminerg system in the pathophysiology of DV. Therefore, we cannot rule out the possibility that not the stimulation itself, but the disturbances in the dopaminerg system were responsible for DV. However, one could expect that considerably more time would be needed to alter the dopaminergic system.

(4) Another hypothesis might be that DV is caused by **separation of two main memory systems: familiarity and recollection**. Recent neuropsychological data suggest that recognition memory applies of two different mechanisms: recollection and familiarity discrimination [43, 44]. Therefore, in certain situations it is possible to recognize that a person or a subject is familiar even without the ability to recollect any particulars about it. Electrophysiological studies in monkeys demonstrated that the neurons in the rhinal cortex responded differently on the basis of the relative familiarity or novelty of presentation of the stimuli, which occurred much rarely in the hippocampus [45]. Therefore, possibly two separate memory compartments may co-exist: one, including the hippocampus, enables recall and conscious recollection of contextual elements, while the other system, including the structures of the parahippocampal gyrus, is important for familiarity judgments [46, 47]. In our case the DV-eliciting stimulation altered the non-verbal memory processes, including recollection as demonstrated by neuropsychological tests. Thus, during déjà vu both recollection and familiarity discrimination was affected, which contradicts that déjà vu is a result of a separation of these two memory systems. We might presume that the elicitation of DV might be the result of the altered dual-processing due to atypical functional localization of recollection and familiarity systems. Possibly, the heavy memory-related load induced by the visual and auditory stimuli produced a delay in memory processing between the hemispheres resulting in false familiarity recognition.

(5) The **non-dominant localization of the GPi stimulating electrode** might have also had an impact on DV-elicitation. Previous electrophysiological studies confined the DV to the non-dominant hemisphere. However, these studies were limited to the TLE [9, 19].

(6) Furthermore, experimental studies demonstrated a **functional relationship between the hippocampus and the contralateral basal ganglia** [48]. In rats, the electrical stimulation of GP altered the **contralateral hippocampal** theta field activity presumably via a septohippocampal pathway. This relationship between the GPi and hippocampal formation has not been verified in humans yet. However, there are some indirect data suggesting this hypothesis, for example the transitory unilateral ictal dystonia in TLE could be associated with hyperperfusion of the basal ganglia ipsilateral to the seizure focus [49]. Alternatively, GPi stimulation could be accompanied by hypoperfusion of the mesiotemporal structures [50].

(7) Analogously we can assume that ***high-frequency deep brain stimulation can interfere with high-frequency (gamma) oscillations of the contralateral mesiotemporal structures***, which in turn play a crucial role in memory functions. Phase synchronization of gamma oscillations of around 40-50 Hz is a general mechanism underlying transient functional coupling between different neuroanatomical structures playing an important role in every aspect of memory functions [51, 52]. Thus, one may expect that high-frequency DBS can interfere with the gamma oscillation in the brain independent of the stimulating site. Moreover, novel studies hypothesize that déjà vu may be related to the alteration of gamma-oscillations of mesiotemporal structures [51].

(8) Since the major output from GPi is to thalamus and from there to cortex, its role also should also be considered for the development of déjà vu. However, several thousands of GPi DBS had been implanted worldwide either for Parkinson's disease or dystonia, and not even a single case report mentioned déjà vu as a stimulation-related side-effect. Therefore, the sole alteration of pallido-thalamico-cortical pathways is unlikely to produce DV experiences.

In a recent case report, hypothalamic DBS could evoke detailed autobiographic memories [23]. The stimulation increased recollection, but not familiarity-based recognition, nor déjà vu. EEG source localization suggested an activity in the mesiotemporal structures [23]. Summing up, our case with Hamani's case, we may assume that in the case of certain constellations (e.g. during specific electrode localizations, stimulation parameters and individual neuroanatomy), the deep

brain stimulation can interfere with some memory-related processes. However, these types of memory alterations due to deep brain stimulation are rather rare.

Open questions and limitations

Several questions remain unanswered in our case. We only compared the functional neuroimages between the DV-eliciting and the “normal” pallidal stimulation. Because during the interval of tracer binding four déjà vu episodes occurred, the difference of these scans probably identifies the anatomical structures responsible for DV. However, we should have obtained a third SPECT scan during SSDV without DV during tracer binding to compare the different activations between the DV and SSDV and between the SSDV and the normal stimulation. This way, we could have identified those structures, which are directly responsible for the DV experience but does not contribute to the SSDV. Moreover, the SPECT scan methodology (SISCOM) was adapted from epilepsy studies, which is usually useful for seizures lasting more than 20-30 seconds. The single observation in this patient of a DV lasting less than 10 seconds is of uncertain significance. To test reproducibility, we planned wanted to repeat the baseline (normal stimulation) and ictal (DV-eliciting stimulation) SPECT images, but respecting the request of our patient, we have forborne from these acquisitions.

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Disclosure of conflicts of interests

None of the authors has conflict of interest to disclosure.

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Figure legends

Figure 1 The localisation of the stimulating electrode (A coronal MP-RAGE, B coronal FLAIR and C sagittal MP-RAGE). Visual inspection and the application of electronic version of the Schaltenbrand stereotactic atlas verified that the contact responsible for DV was situated between the GPi and the underlying white matter. The electrode did not hit the mesial temporal structures.

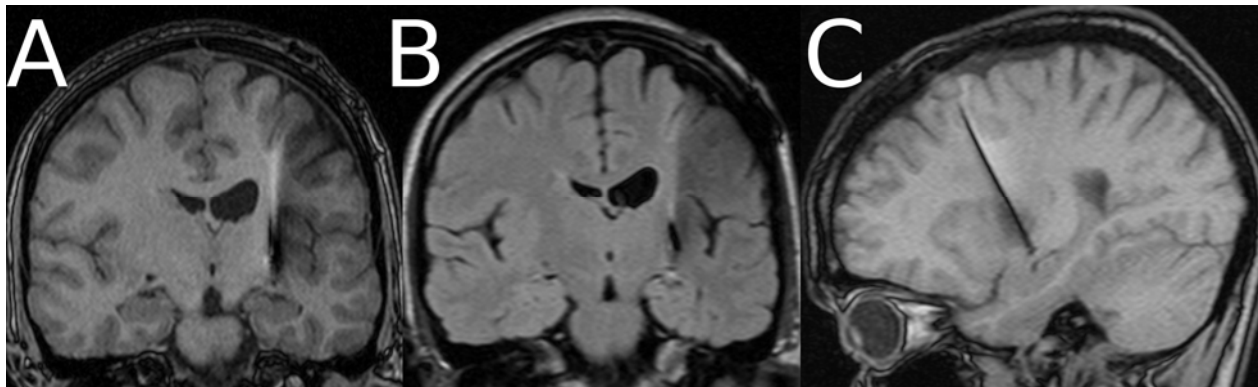
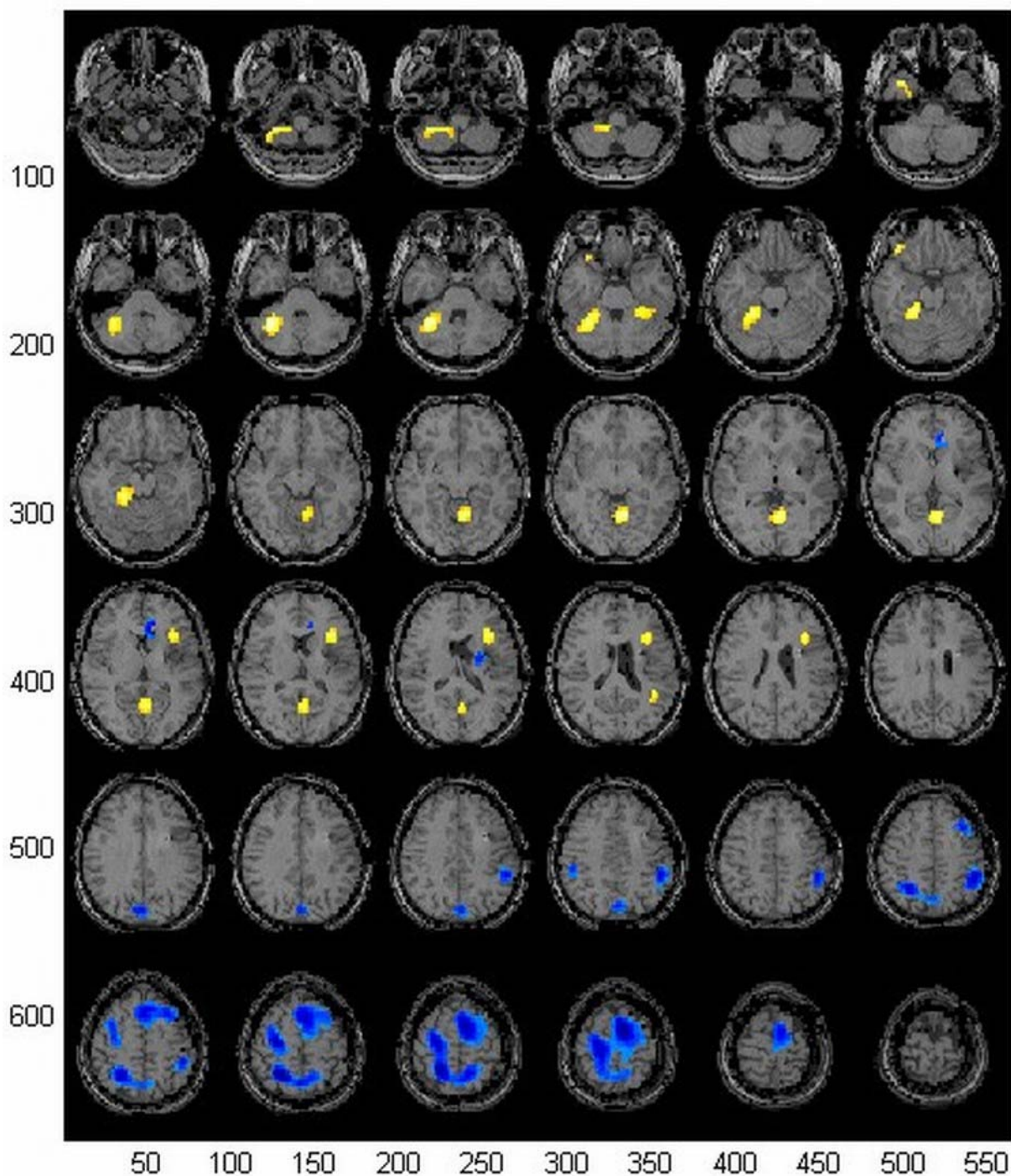


Figure 2. SISCOM analysis comparing déjà vu-eliciting stimulation (ictal) the normal (interictal) SPECT superimposed on axial MRI scans. (yellow: hyperperfusion, blue: hypoperfusion). Compared to the baseline, SPECT during DV showed **right-sided hyperperfusion** of hippocampus, parahippocampal gyrus, fusiform gyrus, cerebellum and temporal superior pole **left-sided hyperperfusion** appeared in the cerebellum, operculum, insula, lingual gyrus, precuneus and middle temporal gyrus. Hypoperfusion appeared bilaterally in the precentral and postcentral gyri, as well as, in the frontal (especially supplementary motor cortex) and parietal areas.



Table

Table 1. Neuropsychological test results preoperatively and postoperatively with standard stimulation (C+1-, 120 μ s, 130Hz, 3.2V) and déjà vu-eliciting stimulation settings (C+0-1-, 120 μ s, 130Hz, 3.2V).

	Preoperative	“Standard stimulation”	“Déjà vu stimulation”
Digit span forward	5	4	5
Corsi	4	4	4
Trail making (A/B)	35 / 71 sec	24/44	27/48
Verbal fluency	F:12, A:8, S:9, category:26	P:17, E: 16, M: 13, category: 17	F:9, A:9, S:7, category: 20
Boston naming test	Not obtained	60	57 [†]
	Learning phase: 47 recalled words	Learning phase: 49 recalled words	Learning phase: 54 recalled words
AVLT language learning	New information:7, Interferency:10 Delayed Recall: 10 Recognition: 100%	New information:4 Interferency:9 Delayed Recall: 11 Recognition: 100%	New information: 3 [†] Interferency:12 Delayed Recall: 14 Recognition: 100%
Rey and Medical College of Georgia Complex Figure (copy/recall)	30/26	35/18	36/12
Benton Visual retention test:	C-figure memory: 6/10 D-figure copy: 10/10	E-figure delayed recall: 8/10	C-figure: 7/10 D-figure delayed recall: 6/10 [†]
Rey 8/64 visual learning test	Not obtained	Learnt by the 6 th trial	No learning

[†]While the subject was performing these tests, she experienced a sudden déjà vu feeling lasting for several seconds.

SUPPLEMENTARY DATA

Applied neuropsychological tests [27, 28]

Visual memory and Learning

1. **Complex Figure Tests: Rey Complex Figure test** was assessed by subject before surgery. After copying the Rey Complex Figure, the patient has to draw it by memory in immediate recall. Postoperatively (during both normal and déjà vu-inducing stimulation) two figures of **Medical College of Georgia Complex Figure** test were applied in repeated visual memory testing. In every Complex Figure Test standard scoring system was administered with the maximum of 36 points. Each figure was divided into 18 different blocks. When subject drawn properly placed, correct blocks, she got 2 points. In case of properly paced and distorted or poorly placed and correct blocks 1 point was given. Distorted, poorly placed blocks were scored with half point. Absent or not recognizable blocks gave no points.
2. **Rey 8/64 test** is the visual pair of Rey Auditory Verbal Learning Test. During testing period the neuropsychologist touch 8 squares one after the other in 8x8 square grids. Subject must touch same squares in this grid. Ten trials were used to measure the visual learning during testing. The result shows the trials when the visual learning was correct.
3. **Benton Visual Retention Test** is a widely applied method to measure the visual perception, memory and construction abilities. Test consists of three forms: each C, D, and E forms have 10 figure series. D form was used in perceptual session, where the subject had to copy the given figure. In preoperatively C form the patient saw each figures in 5 seconds, after presentation she draw the figure immediately by memory. C form was applied in the copying session of postoperative déjà vu elicitation trial. Figures of D forms were used in 5 seconds delayed recall after 5 seconds presentation in postoperative session with déjà vu elicitation. Figures of the E form were solely used during normal

stimulation period with above mentioned delayed recall trial. Each drawing was worth 1 point when the figures were drawn in correct mode. If drawing had error it did not get point.

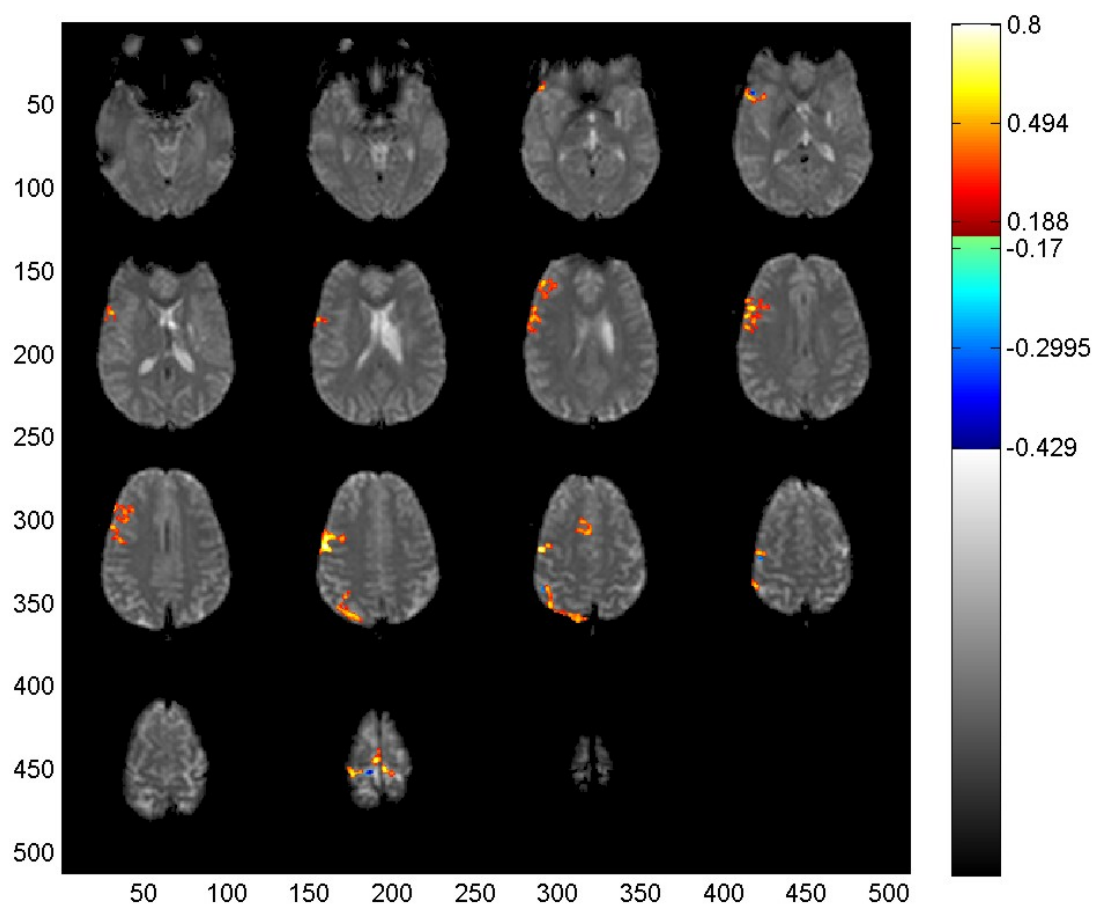
Verbal Learning and Skills Tests:

1. **Boston Naming Test** consists of 60 line-drawing from high familiar to low familiar items. Stimulus cues (e.g. this is a sea animal) and phonetic cues (e.g. first syllable) are presented if items were unnamed.
2. **Rey Auditory Verbal Learning Test** measures verbal series learning ability using 15 common nouns (A and B list). Five presentation of A list was given. After each presentation the subject had to recall the words from list. Learning over five trials was evaluated. After fifth trial a B list was read and subject had to remember this new list. In 7th trial the subject recalled the A list without auditory presentation. 8th trial presented the delayed recall after 20 minutes.

Intelligence quotient:

The Hungarian version of WAIS was obtained [31].

Figure of supplementary data



Preoperative fMRI demonstrated right hemispherical language dominance during word generation task.

Table of supplementary data

Hyperperfusion and hypoperfusion clusters and their size revealed by the SISCOM method.

	Anatomical localization	Number of voxels
Hyperperfusion Cluster: 1		168
	Vermis_R	
	Cerebellum_R	
Hyperperfusion Cluster: 2		20
	Frontal_Inf_Orb_R	
Hyperperfusion Cluster: 3		12
	Temporal_Pole_Sup_R	
Hyperperfusion Cluster: 4		36
	Fusiform_R	
	Temporal_Inf_R	
Hyperperfusion Cluster: 5		648
	Fusiform_R	
	Hippocampal_R	
	ParaHippocampal_R	
	Cerebellum_R	
Hyperperfusion Cluster: 6		60
	Cerebellum_L	
Hyperperfusion Cluster: 7		196
	Frontal_Inf_Oper_L	
	Insula_L	
Hyperperfusion Cluster: 8		436
	Calcarine_L	
	Lingual_L	
	Precuneus_L	
	Cerebellum_L	
	Vermis_L	
Hyperperfusion Cluster: 9		28
	Temporal_Mid_L	

Hypoperfusion Cluster 1		104
	Cingulum_Ant_L	
	Caudate_L	
Hypoperfusion Cluster: 2		44
	Insula_L	
	Putamen_L	
Hypoperfusion Cluster: 3		208
	Cuneus_L	
	Precuneus_L	
Hypoperfusion Cluster: 4		3056
	Precentral_L	
	Precentral_R	
	Frontal_Sup_L	
	Frontal_Sup_R	
	Frontal_Mid_L	
	Frontal_Mid_R	
	Supp_Motor_Area_L	
	Supp_Motor_Area_R	
	Frontal_Sup_Medial_L	
	Occipital_Sup_R	
	Postcentral_L	
	Postcentral_R	
	Parietal_Sup_L	
	Parietal_Sup_R	
	Parietal_Inf_R	
	Angular_R	
	Precuneus_L	
	Precuneus_R	
	Paracentral_Lobule_L	
	Paracentral_Lobule_R	
Hypoperfusion Cluster: 5		44
	Postcentral_R	
	SupraMarginal_R	
Hypoperfusion Cluster: 6		380
	Postcentral_L	
	Parietal_Inf_L	
	SupraMarginal_L	
