

Тезисы докладов российских участников 32-го Международного эпилептологического конгресса (32nd International Epilepsy Congress), Барселона, 2–5 сентября 2017 г.

Глубокоуважаемые читатели, дорогие коллеги!

Большая часть тезисов постерных докладов из России, представленных на 32-м Международном эпилептологическом конгрессе, не была опубликована в специализированном журнале «Epilepsia». Поэтому редакционная коллегия настоящего спецвыпуска считает своим долгом заполнить данный пробел.

Recruiting rhythm and clinically evident seizure pattern in benign infantile convulsions associated with mild gastroenteritis

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Purpose: Description of characteristic ictal EEG in benign infantile convulsions associated with mild gastroenteritis (CwG). **Method:** We present the case in which ictal EEG was recorded in patient with CwG. The patient was 26 months old child with cluster of 6 focal/evolving to bilateral seizures on 4th day of norovirus gastroenteritis with mild diarrhea and vomiting. Seizure semiology: afebrile generalized tonic-clonic, some of them preceded by head version to the left or right. Fever was seen on 1st day of the disease, not measured. MRI was unremarkable (pineal cyst). No metabolic changes in blood. Norovirus found in stool. **Results:** Preictal EEG showed prolonged subclinical regional fast activity in left temporal region (T3). The run of fast activity was seen under one electrode, mimicking an artifact. In 2 minutes fast waves was transformed into slower rhythmic sharpened slow waves. Immediately after this run the seizure occurred. Clinically evident seizure correlated with multiple spikes in left parietal region (P3) with rapid bilateral spreading and transformation into diffuse sharp waves and gradually slowing spike-waves. Seizure semiology: initially versive to the left, impaired consciousness, asymmetric fencing posture, then bilateral tonic-clonic. Postictal confusion and drowsiness were associated with diffuse high amplitude irregular slowing combined with left temporal fast activity similar to preictal fast rhythm. **Conclusion:** Our findings support previous descriptions of ictal EEG in CwG showing preictal recruiting rhythm and further ictal pattern are located in different brain regions. Parietal and temporal discharges are characteristic features of CwG. Clinical lateralization signs in this patient was inconsistent with EEG picture. This may reflect nonlocalized cerebral dysfunction related to viral infection.

Correlation between hypnagogic hypersynchrony variants and speech development delay in children

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Hypnagogic hypersynchrony is known as the physiological pattern registered in sleep EEG in children from 3 months to 13 years. The number of publications describes atypical variants of hypnagogic hypersynchrony. In some publications, there are indications of a correlation between hypnagogic hypersynchrony and speech underdevelopment. **Purpose:** To determine the correlation between the pattern of hypnagogic hypersynchrony and its abnormal variants in children and speech underdevelopment. **Method:** we've examined 56 children aged 3–13 with emotional-volitional and speech underdevelopment. All children was conducted neurological examination, speech therapist examination and long-term sleep EEG recording. According to the EEG results of all the children were divided into two groups: group I (29 children) with atypical

hypnagogic hypersynchrony (with sharp waves on it) and group II (27 children) with abnormal hypnagogic hypersynchrony and epileptiform activity. All children in group I and II received same antiepileptic therapy with carboanhydrase inhibitors and speech therapy. All children underwent neuroimaging (CT, MRI) without any disturbances. **Results:** All children in both groups was observed positive dynamics within 1 year of observation in the form of increased vocabulary and decrease the degree of speech disorders. **Conclusion:** Atypical or epileptic hypnagogic hypersynchrony is likely to be treated with antiepileptic drugs and should be considered as one of the correlates of developmental disorders associated with epileptic disorders in the EEG or disintegrative disorder.

Epilepsy treatment in patients with comorbid anxiety and depression: ethical, clinical and social aspects

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Purpose: Investigating physicians' motivation to apply bioethical principles, considering social factors and patients' lifestyles, and utilizing an interdisciplinary approach while considering, its implications in the treatment of the comorbid patients — one of vulnerable groups. **Method:** 25 years of experience of teaching Bioethics to medical students and physicians; participating in expert ethics committees; over 10 years of clinical experience providing direct care to the patients with anxiety and mood disorders; sociological surveys, interviews with 265 physicians, individual and group psychotherapy in inpatient and outpatient settings. **Results:** Adherence to ethical principles epilepsy treatment in patients with comorbid anxiety and depression has been gradually implemented in the clinical practice epileptologists. Physician's Index of motivation to apply bioethical principles is high: 0.8–0.95. However, while over 97% try to follow ethical principles in their medical practice, 29% cannot identify the type of model they use in their work. 70% admitted deficits in ethical knowledge and its application. When treating comorbid patients, many neurologists refer them to psychiatrists or anti-depressants. However, in Russia with its history of punitive psychiatry, the patients rarely follow such referrals out of stigmatization. Given the stigma and the fact that anti-depressants, if prescribed without considering the neuropathology, can contribute to epileptogenesis, nonpsychopharmacological approaches, specifically psychotherapy, become an effective alternative. **Conclusion:** There is a discrepancy between clinicians' high level of motivation to apply bioethics and their poor knowledge of the subject, which may lead to failed interventions or even to the practices that reinforce stigma. Bioethical education will not only promote the adherence to bioethical principles, but by bringing the doctor's attention to the whole person with a variety of his or her individual concerns, it will also encourage epileptologists to cooperate with other professions and explore interdisciplinary solutions to their patients' clinical and psychosocial needs.

Beneficial effect of add-on perampanel on GTCS in patients with Lafora disease

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Purpose: Lafora disease is a rare severe form of progressive myoclonus epilepsy. GTCS have a major impact on the quality of life in patients with Lafora disease. We analyzed the effect of Perampanel on two Lafora patients during 12 months of PER therapy in combination with other drugs. **Method:** The study was performed on two siblings, 16-year-old boy and 14-year-old girl who had been diagnosed with Lafora disease by means of genetic testing. The boy's onset occurred at the age of 15 starting with focal visual seizures, followed by the addition of GTCS and myoclonic seizures. He had received VA 2000 mg/day, LEV 4000 mg/day, CZP 2 mg/day. GTCS continued with a frequency of about once per month having the type of status epilepticus. PER had been administered at 6 mg/day. The girl had experienced GTCS approximately 2–4 times per month from the age of 12; she had received VA up to 1250 mg/day. Further VA were combined with LA at 250 mg/day and then with LEV at 2750 mg/day. The dose of VA was increased to 2000 mg/day. GTCS continued 1–2 times per month. LA was discontinued and PER was administered at 6 mg/day. **Results:** Perampanel at the dose of 6 mg/day had a dramatically beneficial effect on GTCS. Both patients have been GTCS-free for over 12 months. PER had no impact on the frequency of myoclonic seizures. **Conclusion:** The use of Perampanel allowed to achieve remission of GTCS in Lafora patients. Perampanel did not cause worsening of any other types of seizures.

Clinical experience of using perampanel in the pharmacotherapy of focal epilepsies

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Purpose: To analyze the efficacy and tolerability of the innovative drug Perampanel (PER) as add-on treatment of focal epilepsy in patients older than 12 years. **Method:** Forty-six patients with focal epilepsy, aged from 12 to 63 years, mean age 31.7 years, were studied. Perampanel was administered once daily, at an initial dose of 2 mg that was subsequently gradually increased (in steps of 2 mg once a week or once in two weeks) until a clinical effect was achieved. The duration of follow-up ranged from 6 months to 2.5 years. **Results:** A decrease in the frequency of all types of seizures by >50% was noted in 46,5% of patients. Stopping of all types of seizures was found in 25.6% of patients, i.e. in every fourth patient, stopping of secondary generalized seizures in 39.5%. Adverse effects (AE) were identified in 13 (28.2%) of patients, including aggressiveness – 6 (13.0%); other AE were less frequent (<10%): sleepiness (8.7%), dizziness (4.3%), postural instability (4.3%), irritability (4.3%). PER was withdrawn in 3 (6.5%) patients due to AE. Mean effective dose was 6 mg/day. Quality-of-life improved in the majority of patients (71.7%). **Conclusion:** Perampanel has shown high rates of efficacy and good tolerability in routine clinical practice, with most adverse events being mild and no severe adverse events reported to date. Individualized and slow-dose titration can minimize adverse events. Single dose administration at bedtime improves compliance.

Outcomes of perampanel therapy in patients with symptomatic epilepsy against a background of glial brain tumours

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Purpose: To evaluate the efficacy and tolerability of perampanel therapy in patients with symptomatic therapy developing against a background of glial brain tumours. **Method:** Seventeen patients aged 27 to 60 years (8 male and 9 female) were followed up for 6–18 months during postoperative periods and in the course of radiation therapy. Fifteen subjects had frontal, temporal, or frontotemporal tumours. The epilepsy treatment duration was 2 years on the average. **Results:** Perampanel was administered as a first-line monotherapy to 6 subjects and as part of a two-drug therapy regimen to 11 patients (in combination with VPA to 8 of them). None of the patients had adverse events. Out of 12 patients suffering from complex partial seizures, 8 proceeded to a remission, 3 had a 75% decrease in the frequency of seizures, and 1 patient had a 50% decrease. Out of 5 subjects with secondary generalized convulsive seizures, a 75% frequency reduction was observed in 3 cases and a 50% reduction in the other 2. A remission of epilepsy was achieved in 8 patients (47%), quality of life improved in 16 subjects (94%). **Conclusion:** The use of perampanel in patients with symptomatic therapy developing against a background of glial brain tumours demonstrates high efficacy and good tolerability.

Generalized convulsive status epilepticus in adults according to hospital intensive care units in Moscow for the year

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Purpose: To examine the frequency of generalized convulsive status epilepticus (GCSE) in adult patients according to intensive care units of Moscow in 2015. **Method:** A retrospective analysis of GCSE in patients older than 18 years who were hospitalized to intensive care units from the Department of Health care of Moscow in 2015. Data from Moscow private medical centers and infectious hospitals were not taken into account. **Results:** There were 1487 cases of status epilepticus registered. Among them acute symptomatic status was diagnosed in 1293 patients and as a complication of epilepsy in 194 patients. Acute symptomatic status was established 6 times more frequently than GCSE in epilepsy: 1293:194=12:2. According to data of N.V. Sklifosovsky Scientific Research Institute of First Aid the relation was inverse 68:80=8.5:10 (Karlov V.A., 1968), so status epilepticus as a complication of epilepsy was found more frequently than symptomatic status epilepticus. Among 1293 (100%) patients with acute symptomatic status epilepticus – n=623 (48.18%) cases were established as a result of exogenous intoxication, status epilepticus in cerebrovascular diseases – n=344 (26.6%); in acute phase of cranial trauma – n=204 (15.78%); in brain tumors – n=118 (9.13%); in acute infectious diseases – n=4 (0.31%). According to data of Federal State Statistics Service an adult population of Moscow in 2015 was 10 727 210 people. So prevalence of status epilepticus was 13.86 per 100 000. **Conclusion:** The frequency of GCSE in adults in Moscow was 13.86 per 100 000. These results coincide with data of last research in the USA (12.5 cases per 100 000 adults in a year (Dham B.S. et al., 2014)). Herewith during the last 50 years the structure of GCSE in Moscow has changed with 6-time preponderance of symptomatic form of status epilepticus comparing to status epilepticus in epilepsy. The results can reveal the improvement of epilepsy treatment.

Surgical treatment of drug-resistant epilepsies

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Purpose: To evaluate seizure outcomes in patients with drug-resistant epilepsy surgically treated in Moscow. **Materials and methods:** The study population included 117 patients with drug-resistant epilepsy. The patients underwent resective surgery between 01.01.2014 and 01.02.2017. Patients were followed up at 12 months after surgery. Surgical outcomes (Engel's classification), complication rate, MRI results, pathology findings were analyzed. Duration of epilepsy before surgery was notably long (17.59 years). Invasive EEG monitoring was made for 46 patients (39%). **Results:** Temporal lobe epilepsy was in 56 (48%) patients, generalized forms – 3 (3%), temporal plus – 57 (49%), parietal form in 1. 31 (26.5%) patients had bilateral lesions. 117 patients had 117 surgical procedures: 97 (83%) patients had AMTLE, 6 (5%) patients – AMTLE plus extra temporal resections, 3 (2.5%) patients had temporal tumor resections, one patient – amygdalohippocampectomy, one patient – DNET plus amygdalohippocampectomy resection, 4 (3.5%) patients – VNS and 3 (2.5%) patients – gamma-knife and 2 patients endoscopic transnasal tumor resection. 2 (1.7%) patients had repeat surgery procedure because of failed surgery. Right resections were made in 39 patients (35%), left – in 71 (65%). Forty five patients evaluated 12 months after surgery: 31 patients (67%) became seizure free: 21 patients (45%) – Engel Ia, 6 (13%) – Engel Ib, 4 patients (9%) – Engel Id. Twelve patients (26%) had – Engel II. The unsatisfactory results of treatment were noted at 4 patients (9%): one patient – Engel IIIa, and 3 patients (6%) – outcome Engel IVa. According to histological study the most common seizure-causing lesion was FCD (92%). In 40% of cases-combination of FCD with hippocampal sclerosis (FCD IIIa). Isolated HS was seen in three cases. **Conclusion:** 3 year results in the surgical treatment of drug-resistant epilepsy demonstrate its efficacy and safety. 67% patients become seizure free.

Outcome after corpus callosotomy in children with intractable epilepsy

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Method: A retrospective study was analyzed in 23 children with intractable epilepsy at the Russian Polenov Neurosurgical Institute during the period 1994 and 2011. The age of patients was 2 to 17 years. Minimum follow-up time was 5 years. **Results:** All of the patients had a multiple types of seizures without discrete foci and were not indicated for focus resection. The most disabling seizure type was drop attacks, followed by generalized tonic-clonic seizures. 19 patients underwent dissection of the anterior 2/3 corpus callosum, and total callosotomy as the second stage of the operation – in 3. Favorable results of callosotomy (seizure free status, or seizure reduction >75%) achieved with drop attacks in 82,6%. In generalized tonic seizures favorable results were obtained in 75% of patients with generalized tonic-clonic in 66,6%. For other types of seizures also had obtained favorable results – in isolated cases. When callosotomy was total section, drop attack seizure-free rate was 100%. The effect of corpus callosotomy for drop attacks proved to be very effective when 2/3 or total

section was applied. The best results were obtained in patients with total callosotomy performed in 2 stages. The most appropriate surgical strategy seems to be the resection of the anterior 2/3 of the corpus callosum, but posterior extension may be considered as a second step if the first fails.

Conclusion: Callosotomy is an effective treatment for drug-resistant generalized seizures that are not amenable to focal resection and can reduce the frequency, severity of epileptic seizures. Seizure free results or significant reduction of the most disabling type of seizures with frequent falls and injuries leads to improved quality of life.

Posttraumatic epilepsy in children

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Purpose: Study features of posttraumatic epilepsy. **Method:** Examined 33 patients with traumatic brain injury. **Results:** There are several clinical groups: children with brain concussion (BC), with brain injury (BI), mild, moderate and severe degrees of severity. The largest group consisted of patients with BC: 18 children (54.5%), the second – with mild BI – 7 patients (21.2%), followed by – children with severe BI: 5 (15.2%) and 3 children (9.1%) in the group with an average degree of BI. EEG examination: in 3 (9.1%) cases revealed diffuse β -activity, 8 (24.2%) – local periodic slowing of bioelectrical activity, in 24 (72.7%) cases was sharp waves, complexes «sharp-slow» wave, and in 5 (15,1%) patients – a normal variant. The survey showed that in patients with mild BI dominated local periodical slowing on the EEG, and in the rest of the children surveyed, regardless of the type of intracranial injury prevailed electroencephalographic changes in the form of a sharp wave complexes and «sharp-slow» wave. Epilepsy was diagnosed in 17 (51.5%) patients: 12 (70.5%) children with focal seizures, 2 patients (11.8%) with generalised seizures and 3 patients (17.7%) – a form of epilepsy requires observation for classification. In 8 (47.1%) cases, seizures occurred after the BC, one child received BC during the first convulsive seizure, in 4 (23.5%) – after the mild BI, in 1 (5.9%), child with epilepsy before traumatic brain injury. After moderate BI resumed earlier cropped seizures, 4 (23.5%) children seizures occurred after the severe BI. 7 (41.2%) examined patients epileptic seizures occurred during the trauma and during the first week after its receipt, and in 5 (29,4%) patients- over 12 months, in 4 (23,5%) surveyed for 4 years, and 1 (5,9%) patients epileptic seizures occurred after 6 years. **Conclusion:** Epilepsy often develops after BI of different severity than BC.

Juvenile myoclonic epilepsy subsyndromes

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We defined 2 aims for our study: first, we identified phenotypes of ascertained JME (Juvenile myoclonic epilepsy) patients; second, we examined the variability of occurrence of different types of seizures and their combinations. In this retrospective cohort study, we included 4-year follow-up of clinical cases of 78 patients with JME, who was treated at the Medical Center of Neurology and epilepsy «EpiCentr», Volgograd, and were initially diagnosed by a single epileptologist. **Results:** We studied 78 prospectively ascertained JME patients and encountered four groups: (I) classic JME (86%), (II) CAE (childhood absence epilepsy) evolving to JME (4%), (III) JME with adolescent absence (8%) and (IV) JME with astatic seizures (4%). We examined clinical course, determined the occurrence of different kind of seizures. Therefore, absence seizures were more common in patients of CAE evolving to JME than in those of classic JME families. JME with astatic seizures were spotted only in 3 cases. A grand mal is often (89%) in classic JME, but not the necessary. We determined that one subsyndrome could have several kind of combinations of

seizures. For example, there were 4 types in classic JME, and only one – in CAE evolving to JME. JME with adolescent absence and JME with astatic seizures had two groups of seizures. **Conclusion:** According to received data on the territory of Volgograd region, all four subsyndromes of JME were existed with advantage of the Classic JME (86%). There was determined that the clinic may also be different inside of subsyndrome; it was depended on the combinations of different types of seizures.

Problems of diagnostic and therapeutic management of juvenile myoclonic epilepsy

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Purpose: To identify and analyze problems of management and repeated diagnostic errors in juvenile myoclonic epilepsy (JME) diagnosis in patients of the Siberia Federal District, Russia. **Method:** We randomly selected 123 patients with JME, who underwent preliminary anamnestic and clinical selection using stratified randomization. We analyzed the age of original diagnosis, the time between onset of the disease and diagnosis of JME and mistakes in the appropriate management of JME. **Results:** Geographical distribution of JME patients was 50.4% of Krasnoyarsk-city, 38.2% of Krasnoyarsk Territory regions and 11.4% from the neighboring regions of the Siberian Federal District. Disease debut age varied drastically, from 2 to 29 years old. Similarly, age of original diagnosis varied between 7 and 54 years old, with average age of 22.5 years old. The time between onset of the disease and diagnosis of JME varied between 0 and 41 years of age. In 68 of 123 cases there were mistakes in the appropriate management of JME before enrolling to the NC UH. Across geographical regions these mistakes were in approximately 50% of cases. Upon review of medical errors, mistakes in the original diagnosis were identified in 40 out of 68 cases; inadequate therapy for the disease onset was prescribed in 45 out of 68 cases; incorrect dose of AEDs was prescribed in 14 out of 68 cases and irrational combination of drugs – in 14 out of 68 cases. **Conclusion:** According to our data, mistakes in management of JME are systemic, witnessed in over 50% of diagnosed cases, similar to studies from abroad. Repeated mistakes in diagnosis and treatment of JME must be at clinical and institutional level, via appropriate training of medical practitioners, health administrators and clinical pharmacologists. This study and participation at the «32nd International Epilepsy Congress» was supported by the Krasnoyarsk regional state autonomous foundation «Krasnoyarsk Region Science and Technology Support Fund».

Autistic epileptiform regression: clinical and encephalographic correlation

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Purpose: Study of the combination of States of the autistic spectrum, epileptiform changes on EEG, epileptic seizures in children. **Method:** We observed 32 children aged 3–7 year with a delay in mental and speech development, impaired communicative functions, behavioral disorders in combination with epileptiform changes on EEG. All patients underwent VideoEEG-monitoring, brain MRI and the clinical neurological testing and examination by a psychiatrist. **Results:** All patients in the waking state was observed epileptiform changes on EEG – benign childhood epileptic patterns. When conducting video-EEG night's sleep revealed partial epileptic seizures were detected in 11 children. Diagnosed partial epilepsy and is assigned to antiepileptic therapy. Landau-Kleffner syndrome (Acquired epileptic aphasia) was diagnosed in one patient. In 9 children there was observed the increase of index of epileptiform activity during sleep (80–90%), predominantly in the frontal and temporal leads, or multi-regional. Epileptic seizures are not registered (in one patient,

febrile seizures at 15 months) We have established the diagnosis autistic epileptiform regression. Constant continued epileptiform activity on the EEG, marked disorders of cognitive functions, behavior and communication was the indication for prescription of antiepileptic therapy. **Conclusion:** Impaired social interaction of children, communication (primarily speech), and epileptiform changes on EEG require testing for video EEG for diagnosis and possible correction AED. Autistic epileptiform regression the special form of autistic disorder, characterized by development of severe communicative disorders in children as a result of continuous prolonged epileptiform activity on EEG the diagnosis is established in 28% of children that have this problem.

Symptomatic epilepsy in patients with developmental venous anomalies

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Developmental venous anomalies (DVAs) represent congenital, anatomical variant of pathways in the normal venous drainage of the brain area. A positive correlation, however, between the location of DVAs and the electroencephalographic seizure focus is debated. **Purpose:** Study the association of DVAs with epileptic seizures. **Method:** The present study provides a complete analysis of clinical, EEG and MRI characteristics of symptomatic epilepsy associated with cerebral venous malformations (CVMs). There are a total of 5.856 patients with epilepsy of which there are 105 patients with congenital malformations of the brain, and 32 of them were found to have DVAs. **Results:** The age of patients was 4–71 years, median – 27.5 (17.5:41.5); 8 (25.0%) children and 24 (75.0%) adults. The epilepsy onset age was 0.4–67 years, median – 9.5. The distribution of epilepsy seizure types was: simple focal – 18.8%, complex focal – 3.1%, combined simple and complex focal seizures – 18.8%, secondary generalized tonic-clonic seizures (SGTCS) in 3.1%, combined simple focal seizures and SGTCS in 15.6%, both complex focal seizures and SGTCS in 21.3%, and simple and complex focal seizures with SGTCS in 25% of cases. The location of the epileptic changes was principally presented by frontal lobe (13 [40.6%]) and temporal lobe seizures (13 [40.6%]). The associated analysis of all CVM localization (by MRI) and location of the epileptic activity (by video EEG monitoring) showed a direct relationship in 12 (37.5%) cases, a partial relationship with one DVA in 6 (18.8%) cases, and no associations in 14 (43.8%) cases. Cavernous angiomas prevailed among venous anomalies (53.1%); DVAs were registered in 46.9% of cases. The associated analysis of DVA localization and the epileptic seizure types showed a direct relationship in 60.0% cases. **Conclusion:** DVAs as a cause of seizures are important to consider when examining patients with epileptic seizures.

Potentially pathological forms of alpha-activity in patients with refractory epilepsy

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Purpose: In the majority of cases of epilepsy epileptiform patterns are described in patients' electroencephalography (EEG). However, in patients with long-term epilepsy and various seizure frequency EEG shows persistent alpha-activity deprived of distinctive epileptiform patterns. This phenomenon might be accounted for drug-induced patho-

morphosis of the brain electrical activity (the deformation of typical epileptiform sharp waves, spikes, polyspikes, sharp-slow wave complexes affected by the antiepileptic therapy). **Method:** In our study we analysed EEG-changes during restful wakefulness in patients with medically intractable epilepsy, whose EEG did not show classical epileptiform patterns, but demonstrated stable background alpha-rhythm. **Results:** We distinguished 3 variants of alpha-activity in these patients. The first variant was associated with weakly modulated alpha-rhythm with correct spatial distribution and sporadic sharpened potentials localized predominantly in frontotemporal leads. The second variant was characterized by background deformed sharpened alpha-rhythm with sharpened potentials slightly exceeding background activity in amplitude, often bilaterally synchronous. In the third group of patients alongside with deformed alpha-rhythm, alpha-spindles interspersed with bursts of high-amplitude sharpened potentials (usually marked as nonspecific pathological activity) were registered. **Conclusion:** Although these observations do not permit us to declare typical epileptiform activity, nevertheless, considering manifesting drug-resistant seizures, these potentially pathological EEG patterns could be interpreted as an equivalent of epileptiform activity.

Single word production and semantic processing in temporal lobe epilepsy

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Purpose: Our previous findings (Yurchenko et al., 2016) showed impaired noun and verb production (object and action naming, correspondingly) in individuals with temporal lobe epilepsy. However, the question whether these difficulties are related to semantic impairments is still open. **Method:** We created two non-verbal tests (for objects and actions) to assess semantic associations. In each test, trials include a target object or action black-and-white picture and four same-category items (e.g., objects: apple (the target), pear, orange, pineapple, watermelon; actions: to brush teeth (the target), to wash one's face, to dry oneself, to perfume oneself, to put on make-up). The task is to choose the item that has the closest associative relationship with the target (pear and to wash one's face, correspondingly). The targets in the two tests were matched on a range of psycholinguistic parameters. We are currently collecting data on the designed semantic processing task, as well as on noun and verb production in Russian individuals with left and right temporal lobe epilepsy and in healthy controls. The results will provide additional information on the nature of single word production impairments in individuals with temporal lobe epilepsy.

Comparative efficacy of early use of perampanel as adjunctive therapy for epilepsy (practical clinical experience)

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Purpose: To compare efficacy of early and late use of perampanel as adjunctive therapy for epilepsy. **Method:** Forty-six patients (male – 31, female – 15) aged from 12 to 41 years with epilepsy were followed up for 6–18 months. All patients received perampanel as adjunctive therapy. **Results:** The patients were distributed into two groups depending on time of inclusion of perampanel as a part of treatment regimen. Group 1 included 19 patients (average age – 25 years; average disease duration – 7 years) who received perampanel not later than as a part of third-line therapy regimen. Group 2 included 27 patients (average age – 19 years; average disease duration – 15 years). Symptomatic epilepsy was observed in 57.9% patients in Group 1 and in 1 patient (5.2%) in Group 2. Adverse

events (AEs) were reported in 1 (5.2%) and 14 (51.8%) patients in Groups 1 and 2, respectively. Perampanel was discontinued in 8 (29.6%) patients in Group 2 due to AE development. Remission was achieved in 5 (26.3%) and 6 (22.2%) patients in Group 1 and 2, respectively. Response to treatment was observed in 79% and 70.4% and lack of treatment response was registered in 4 (21%) and 7 (25.9%) patients in Group 1 and 2, respectively; increased frequency of seizures was observed in 1 (3.7%) patient in Group 2. The quality of life improved in 11 (57.9%) and 16 (59.2%) patients, and remained unchanged in 8 (42.1%) and 4 (18.6%) patients in Group 1 and 2, respectively. In 6 (22.2%) patients in Group 2 quality of life deteriorated. **Conclusion:** Early use of perampanel as a part of combination therapy regimen is therefore reasonable.

Additional effects of perampanel

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Purpose: to evaluate additional impact of Perampanel. **Method:** 25 children and adult (age range 9–40 y.o.) with refractory epilepsy receiving 1–4 AEDs were included and treated with Perampanel. Baseline seizure frequency, type of AEDs, previous adverse events (AE) and everyday activity were determined during 3 month base-line period before addition of Perampanel. AE, everyday activity were controlled after 3 month. **Results:** There were 8 children with epileptic encephalopathy, refractory focal epilepsy with intellectual disabilities receiving 1–3 AEDs and 17 adult with refractory focal, generalized epilepsies receiving 2–4 AEDs. Positive effect to everyday activity, cognitive functions observed in 7 cases (5 children and 2 adult). Spasticity significant decreased in 1 case of cerebral palsy. There were 3 cases of AE included hostile behavior due to Perampanel and Levetiracetam interactions. Man 30 y.o. with Lennox-Gastaut syndrome without seizure remission since onset at 4 y.o. age had 100% seizures regress with hostile behavior. Similar hostile behavior he had due to add-on of Levetiracetam two years earlier with positive effects from antipsychotics. We used antipsychotic during 3 month up-titration of perampanel with positive result of seizure freedom without additional AE. At present time patient continues intake Perampanel and Levetiracetam without behavioral AE, antipsychotics and had seizure freedom. Woman in age 36 years with normal intellect discontinued up-titration of perampanel in dosages 4 mg. due to hostile behavior. Girl in age 9 year with polymicrogyria, epileptic encephalopathy, and intellectual disability discontinued up-titration of perampanel due to behavioral AE without AE management. Good tolerability with perampanel was estimated in all other cases with individualized approach to dosing, including slower up-titration and bedtime dosing. **Conclusion:** Perampanel had positive effect to everyday activity, cognitive functions. Adverse events management allowed to achieve seizure freedom in patients with refractory epilepsies. The reported study was funded by Russian humanitarian scientific fund, research project №15-06-10816

Epilepsy surgery in tuberous sclerosis: the Russian experience

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Purpose: We evaluated the seizure outcome in patients with epilepsy associated with tuberous sclerosis complex (TSC). We report the pre-surgical identification of the epileptogenic tuber and post-surgical outcome of patients with TSC in the Russian Federation. **Method:** Of 93 patients with TSC (age from 6 months to 26 years) in the past 7 years who underwent pre-surgical evaluation, including a detailed seizure history, interictal and ictal video EEG registrations, 3D FLAIR MRI scans and

neuropsychological testing, 29 patients (17 boys and 12 girls) has epilepsy surgery. Presurgical evaluation was supplemented by ictal/interictal single-photon emission tomography, positron emission tomography, magnetoencephalography and intracranial monitoring in many patients. Seizure outcomes, scored with the Engel classification, and the neuropsychological outcomes were assessed at fixed post-surgery intervals (6 months, 1 year, 2 years and longer). **Results:** At 1 year or longer after the initial operation, 17 (58.9%) patients were class I, 2 (6.8%) — class II, 4 (13.7%) — class III, and 6 (20.6%) patients were class IV. Improved development was perceived by the parents of 12 patients (41.4%). A higher neuropsychological outcomes were found in the surgical patients compared to the non-surgical candidates. **Conclusion:** Epilepsy surgery in patients with tuberous sclerosis is an effective treatment that allows be seizure-free and reduce the appearance of epileptic encephalopathy. Thus, the availability of neurodevelopmental delay may be an additional indication for earlier surgical treatment of epilepsy.

Front and middle callosotomy combined with cingulotomy for treatment epileptic encephalopathy in children

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Purpose: To determine of indications and outcome of surgical treatment performed in the volume of the front and middle callosotomy combined with cingulotomy in case of the treatment of epileptic encephalopathy with primary generalized seizures. **Method:** A clinical observation of the patient was being treated in A.L. Polenov Russian neurosurgical institute diagnosed with epileptic encephalopathy epilepsy with primary generalized seizures. The examination included diagnostic neurosurgical complex, surgery. **Results:** A 3-year-old right-handed girl with drug-resistant epilepsy was admitted to our neurosurgery department due to increased seizure frequency. Epilepsy onset began on the 10th day of life in the form of a rotation of the head and eyes to the left, increasing the tone in the extensor limbs, loss of consciousness; seizures recur with a frequency of 3–20 times per day, for up to 5 minutes. She has a developmental delay and aggressive behavioral Anticonvulsant therapy hadn't positive effect in this case of West syndrom. Surgery was performed in the anterior and middle callosotomy in combination with cingulotomy. Already in the early postoperative period was marked complete seizure relief, aggressive behavior decreased. **Conclusion:** In cases of anterior and middle callosotomy combined with cingulotomy achieved a positive result due to more radical destruction of epileptic system and improve the effectiveness of surgery in children with epileptic encephalopathy with primary generalized seizures. The reported study was funded by the Russian Foundation for Humanities research (RFHR) according to the research project № 15-06-10816.

Functional left-sided hemispherectomy in adult patients with refractory epilepsy and preserved speech: neuropsychological outcome

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Purpose: Reports on hemispherectomy in adult patients are rare. Here we present two successful cases (22 and 29 years) of left-sided functional hemispherectomy. **Method:** After comprehensive presurgical evaluation including vEEG-monitoring, MRI, neurological and neuropsychological assessment, 2 patients with intractable left-sided hemispheric epilepsy and hemiplegia underwent functional hemispherectomy in 2016. In both cases the etiology of seizures was perinatal ischemic stroke. **Results:** MRI showed large cystic-atrophic lesions in the left perisylvian region with relative frontal lobe anatomical integrity in one case and

occipital lobe — in another. On vEEG-monitoring interictal and an ictal activity in the left hemisphere was recorded. Neuropsychological evaluation showed profound deterioration of executive functions, attention, verbal memory and visuo-spatial functions in Case 1. In Case 2 deficits in executive functions and attention were also found. She also had poor performance of the visuo-spatial memory and perception. At the same time, we observed only mild deficit of verbal memory which we considered as a «crowding effect» due to the atypical language dominance. MRI confirmed complete disconnection of the affected hemisphere in both cases. No deterioration of verbal performance was observed at 4 months after surgery. The executive functions and attention improved. After one year follow-up Engel 1A outcome was achieved in one patient and in another — only nocturnal seizures were observed (Engel 2D). **Conclusion:** The left-sided functional hemispherectomy in adults leads to significant improvement in seizure control without deterioration of neuropsychological functions.

Surgical treatment of focal cortical dysplasia in children with intractable epilepsy

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Purpose: To present the results of surgical treatment of medically refractory epilepsy (MRE) in children with focal cortical dysplasia (FCD). **Method:** A retrospective analysis of surgical treatment of 68 children and adolescents with MRE, examined and treated in the Department of Pediatric Neurosurgery A.L. Polenov RNRI from 2000 to 2012. Patient's age ranged from 1 to 18 years. Follow-up was at least 18 months. **Results:** MRI data revealed characteristic features of cortical dysplasia in 86.7% of patients. Temporal lobectomy was performed in 31 (54.6%) patients, extratemporal resection — in 22 (32.3%), multifocal resection, including temporal and extratemporal — in 15 (22.1%). Resections of dysplastic lesions supplemented multiple subpial transections in eloquent areas of the brain in 18 (26.5%). Histological examination defined FCD type I in 33 (48.5%), FCD type II in 27 (39.7%), and FCD type III (a and b) in 8 (11.8%) patients. Good outcome after surgical treatment was achieved in 49 patients (72.1%), including 37 (54.4%) with complete seizure-free outcome (Engel class I) and 12 (17.7%) with occasional fits (Engel class II). The results of surgery were significantly better in FCD type II group. In cases of cortical dysplasia type II good results were observed in 22 (81.5%) of 27, in cases of FCD type I — 25 (63.6%) of 33. After complete resection of FCD 42 (84%) of 50 patients had a good results. **Conclusion:** Surgical treatment of MRE in children with FCD leads to good outcomes with the cessation of seizures in most cases. Completeness of resection significantly determines the outcome of surgery. The results of treatment are better at FCD type II.

Cytochrome P450 2D6*10 (100C>T, rs1065852) genotype in Russian patients with epilepsy

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Introduction: The gene CYP2D6 is of great interest also due to its highly polymorphic nature, and involvement in a high number of medication metabolisms. The presence of polymorphisms in the CYP2D6 gene may modulate enzyme level and activity, thereby affecting individual responses to pharmacological treatment. **Purpose:** The study of CYP2D6*10 polymorphism prevalence in patients with epilepsy in the North-Western and the Siberian region of the Russia. **Materials and meth-**

ods: Allele and genotype frequency distributions of *CYP2D6*10* (*100C>T*, *rs1065852*) genotypes and predicted phenotypes were analyzed in blood samples of 123 patients (53 patients from North-Western region and 69 patients from Siberian region) using polymerase chain reaction (PCR) in real time. **Results:** The *T/T*, *C/T*, and *C/C* genotype frequencies of the *CYP2D6*10* allele were significantly different ($p<0.01$) in two regional groups. The frequency of the wild homozygous variant *C/C* of *CYP2D6*10* allele (extensive metabolizers) in the Siberian region was the highest, while the Nord-West region had the lowest frequency ($p<0.001$), which are 82.6% and 64.2%, respectively. The frequency of the heterozygous variant *C/T* of the *CYP2D6*10* allele (intermediate metabolizers) was significantly a bit high in the Nord-West region, while the Siberian region had the lowest frequency ($p<0.001$), which are 35.8% and 17.4%, respectively. The homozygous variant *T/T* of the *CYP2D6*10* allele (poor metabolizers) was not identified. **Conclusion:** The *C100T* polymorphism of the *CYP2D6* gene associated with several drug-induced reactions in patients with epilepsy. The differences in the prevalence of intermediate metabolizers in the North-Western and the Siberian regions of the Russia may be due to genetic drift and accumulation of alleles typical for European and Asian populations.

Gender features of female epilepsy in mono- and polytherapy AEDs groups

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Purpose: To investigate gender features of female epilepsy in mono- and polytherapy antiepileptic drugs groups. **Method:** The work was a part of prospective observation research of the antiepileptic drugs (AEDs) reproductive side effects in 155 WVE aged of 16–45 y.o. parted into 3 AEDs therapy groups: 1 gr. — monotherapy, 2 gr. — polytherapy, 3 gr. — no used. Epilepsy onset, catamenial epilepsy, reproductive complications were investigated. **Results:** 1 gr. included 68 patients (44%), 2 gr. — 67 (43%), 3 gr. — 20 women (13%). Average age of the surveyed women made 25 years. Resistant epilepsy prevailed in 2 gr. with disability in 40% ($p<0.001$). Epilepsy onset before puberty — 1–9 y.o. were in 15%, in puberty — 10–18 y.o. — 59%, after puberty — older 18 y.o. — 26%. Differences were statistically significant above in puberty ($p<0.001$). Prevalence of epilepsy onset in the integrated age range of 12–16 years was statistically reliable ($p<0.001$). Disease onset was early in 2gr. without significant differences. The general indicator of catamenial epilepsy in cohort was 32% and above in 2 gr. (43%) in comparison with 1 (24%) and 3 (25%) groups ($p<0.001$). The frequency of reproductive endocrine complications was 53%. Reproductive disturbances due to AEDs made 40%. AEDs polytherapy enlarged the frequency of reproductive disturbances and made 60% in 2 gr. in comparison with 1 (30%) and 3 (10%) groups ($p<0.001$). **Conclusion:** Gender aspects of female epilepsy were caused by influence of sexual hormones in pathogenesis. The epilepsy onset often occurred in periods of oestradiol production beginning and its ovulatory peaks. Catamenial epilepsy has to be considered as biomarker of drug resistance. Reproductive complications were frequent side effect of antiepileptic therapy and prevailed in resistant epilepsy. The reported study was funded by Russian humanitarian scientific fund according to the research project №15-06-10816.

Differential diagnosis of visual aura in migraine and epilepsy

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Purpose: The objective of this work was comparative clinical analysis of the visual aura in patients with migraine with aura and occipital epilepsy. **Method:** The study is based on clinical observation of 2 groups of patients: 99 with migraine and 155 with epilepsy. We have used clinical-neurological method and interviewing. **Results:** It was detected the frequency of migraine with aura 17% and occipital epilepsy — 3.2%. All patients with migraine with aura was observed visual aura (in 100%). Purely visual aura was found in 41% of patients (7 of 17). Visual aura was accompanied by a sensitive aura in 59% (10 of 17). Positive visual disturbances such as flickering, «sequins», glowing «flies», «sunbeams», scintillating scotoma were found in 14 patients (82%) and the negative visual phenomena such as scotoma and hemianopsia were found in 11 patients (65%). Hemianopsia occurred in 7 patients with migraine. Only 3 patients (18%) had exclusively negative symptoms — hemianopsia. Focal forms of epilepsy were 64.5%. Occipital epilepsy was found in 5 (5% for focal epilepsy). Visual aura before epileptic seizures wasn't observed in one patient, it preceded the oculomotor symptoms in 80% of cases (4 of 5). Epileptic visual aura typically manifests simple visual hallucinations (vision of colored dots or discs, bright sparks, multicolored circular or spherical form elements, ribbons, bright red staining of surrounding objects) or less complex visual hallucinations (images of any persons, individual body parts, shapes). **Conclusion:** Differential diagnosis of occipital epilepsy from migraine with aura can be difficult especially when there is no tonic or clonic motor manifestations. However, visual aura of migraine was different from aura in focal occipital epilepsy by visual images, dynamics and distribution of visual phenomena in the field of view, duration of the aura and time of occurrence of the subsequent headache. The reported study was funded by the Russian Foundation for Humanities research (RFHR) according to the research project №15-06-10816.

The role of CYP2C9 gene genotyping before the start of therapy for prevention of serum valproic acid accumulation during the treatment of epilepsy

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Purpose: To evaluate the role of genotyping on SNPs of CYP2C9 gene rs1799853 and rs1057910 before the start of therapy for prevention of serum valproic acid (VPA) accumulation during the treatment of epilepsy. **Method:** 69 adult patients were divided into 2 groups by the time of genotyping. Group 1: 23 patients (genotyping was performed before the start of treatment; daily dose of VPA was initially reduced in carriers of CYP2C9*1/*2 or CYP2C9*1/*3 by 25%, and in CYP2C9*2/*3 by 50% compared to mean dose of CYP2C9*1/*1 according to our algorithm (2011)). Group 2: 46 patients (genotyping was done after the start of therapy, VPA dose was equal for all genotypes carriers). Genotyping was performed using TaqMan technology by quantitative RT-PCR. VPA concentration in blood serum was measured after 12 hours (therapeutic drug monitoring — TDM1) and 2 hours (TDM2) after the medicament receiving. **Results:** Group 1: average TDM2 and genotype frequency in CYP2C9*1/*1 carriers were 53.7 ± 6.5 mg/mL and 65.2%, respectively; in CYP2C9*1/*2 and CYP2C9*1/*3 (genotype frequencies were 4.3% and

26.1%) TDM2 constituted to 49.7 mg/mL and 58.0±10.6 mg/mL, respectively; in compounds (4.3%) TDM2 was 54.0 mg/mL. Group 2: average TDM2 and genotype frequency in CYP2C9*1/*1 carriers were 83.5±4.6 mg/mL and 76.1%, respectively; in CYP2C9*1/*2 (19.6%) and CYP2C9*1/*3 (2.2%) the averages were 89.2±19.2 mg/mL and 65.3 mg/mL, respectively, in compounds (2.2%) TDM2 was 86.0 mg/mL. Averages TDM2 in group 1 and group 2 were 54.6±4.8 mg/mL and 84.3±4.9 mg/mL ($p<0.01$). The effective dose for seizure prevention in group 1 was 800±74.8 mg and 13.3 mg/kg, in group 2 was 1184.7 mg, 16.2 mg/kg. **Conclusion:** Genotyping before initiating of VPA therapy has several advantages: in group 1 ADRs and VPA accumulation up to subtoxic and toxic levels were absent. In group 2 VPA accumulation were observed in 36.9% of patients.

Prevalence and characteristics of epileptic disorders in patients with supratentorial brain tumors

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Purpose: Estimation of prevalence and characteristics of epilepsy in patients with supratentorial brain tumors. **Method:** Observational study of 204 patients with supratentorial brain tumors treated in neurosurgical oncology department since 01/01/2016 to 31/12/2016. All patients were examined by epileptologist. Diagnosis of epilepsy disorder was based on clinical and neurophysiological data. **Results:** Epileptic disorders were diagnosed in 110 patients (54%). 19 (17%) patients had single seizure and 69 (83%) fulfilled criteria for symptomatic partial epilepsy. Simple partial seizures were observed in 65 patients (59%), complex partial seizures in 17 patients (15%) and secondary generalized convulsive seizures in 70 patients (64%). In 88 cases (80% of patients with epileptic disorders and 43% of investigated cohort) seizure developed before tumor diagnosis was estimated. In 69 patients (63% and 34% respectively) seizures were the first symptom of tumor. During follow up period seizures occurred in 22 patients (20%): 10 patients developed epilepsy in 2–3 weeks after surgery, 2 during radiation therapy, 6 during chemotherapy and in 4 patients epilepsy developed due to tumor spreading. Out of 22 patients with late development of epilepsy 15 patients received prophylactic antiepileptic drug therapy. Out of 88 patients with epileptic disorder before tumor diagnosis was estimated 50 (57%) were seizure free after surgery during all follow up period, 29 of these patients (33%) were drug-free. Among 110 patients total seizures control was achieved in 71 cases (65%), partial control in 26 cases (23%). Pharmacoresistance was observed in 13 cases (12%). **Conclusion:** Epileptic disorders often pose a serious problem in treatment of patients with supratentorial brain tumors. Almost half of patients show only simple partial seizures that need precise diagnostic and can be missed by the patient and his family. In most cases epilepsy appears in early stage of the disease. Delayed seizure development is suspicious for tumor spreading.

Threatment approaches in pharmacoresistant childhood epilepsies

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Purpose: Childhood epilepsies a heterogeneous group of disorders and syndromes with different severity, prognosis and treatment. The purpose of study was to recognise the possible reason of nonadequate answer on AED treatment and to find the ways for overcome it.

Methods: 33 patients with different forms of epilepsy seizures frequency, illness duration aged from 3 months to 16 years not the candidate for surgical treatment have been studied. The long duration EEG, high resolution MRI, biochemical, lactate level, genetic investigation were performed to these children. **Results:** In 11 children the respiratory chain disorders confirmed by mtDNA sequence were found. Metabolic diseases were discovered in 8 patients: two glutaric aciduria type1, one propionic aciduria, one methylmalonic aciduria, one Gaucher type 3, one glycogenosis type6, two ceroid lipofuscinosis. In four children mutation in genes SCN8A, GRIN2A, KCNMA1 and duplication 15q11.2q13.3 were revealed. Five patients had genetic polymorphisms in CYP2C9, CYP2D6 and aggravation or not reduction of seizures while using the valproic acid in treatment. In other cases with normal MRI the reason of pharmacoresistant seizures was not discover yet. In children with metabolic disorders and energy metabolism disorders we use the specific therapy (diet, Lcarnitine, vitamins, enzyme replacement therapy etc) in cases which it possible, avoid valproic acid in treatment, as well we use the phenytoin in patient with potassium channel mutation. These treatment management leads to reduction in seizures frequency in epileptic patients or even to seizure free in some cases. **Conclusion:** The recognition and diagnostic of underlying the etiologies of intractable seizures improve the treatment management in many cases. Using the etiologic therapy as possible and rational antiepileptic treatment leads to better results in pediatric patients with previously intractable epilepsies.

The phenomenology of major depression in epilepsy

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Interictal dysphoric disorder (IDD) was first described as a pleomorphic affective syndrome specific for people with epilepsy. Further studies showed that IDD also occurred in migraine, leading to a hypothesis that IDD might be an organic affective syndrome in patients with neurological disorders. This assumption cannot be confirmed as there is no information on occurrence of IDD in people with depression without neurological disorders. The aim of our study is to assess whether IDD is associated with depression in patients with epilepsy, or is a nonspecific syndrome in patients with depression without neurological disorders. Patients between 18 and 45 years of age with depression (DSM IV criteria confirmed with SCID-1) and epilepsy were compared to patients with depression only. Clinical characteristics were assessed using the BDI, BAI, MDQ, PHQ-9 and IDDI. Preliminary results show that IDD was found in 88% (40/45) of patients with depression and epilepsy and 90% (54/60) of patients with depression only. The two groups differed significantly by the severity of depression as assessed by the BDI ($p=0.027$) and PHQ-9 ($p=0.0009$). No difference was found between groups in regard to the total IDDI score and inventory subscores, as well as the BAI and MDQ scores. In the combined study population, patients with IDD had significantly higher depression scores (BDI I: $p=0.034$; PHQ-9: $p=0.034$) and anxiety BAI scores ($p<0.001$), compared to persons without IDD. In those with epilepsy and those with depression without neurological disorders, a correlation was found between IDDI scores and BAI anxiety scores ($r=0.61$, $p<0.001$ and $r=0.30$, $p=0.029$, respectively). These preliminary results suggest that IDD is not specific to organic neurologic disorders. In those with depression and no neurologic disorder, depression symptoms may be mixed with IDD and should be accounted for when studying this disorder.