Summary

Epilepsy represents the most common neurological disease, its prevalence reaching up to 1%, and around 30% of patients become refractory to treatment. In these patients, epilepsy surgery is often their only chance for disease-free life.

Aetiology of epilepsy is heterogenous; we recognize genetic, structural-metabolic epilepsy and epilepsy with unknown aetiology. Patients with focal pharmacoresistant epilepsy may become candidates for epilepsy surgery; the same does not apply to patients with metabolic or neurodegenerative disease. Multiple factors influence decision about epilepsy surgery, the most important ones being (i) the type of known or presumed structural lesion and (ii) the possibility to precisely delineate the epileptogenic zone (the area of seizure generation). Another factor that needs to be accounted for is the proximity of epileptogenic zone to the eloquent cortical areas (the areas with important neurological functions, e.g. motor or speech functions).

Epilepsy surgery principally aims for complete removal the epileptogenic zone, and subsequently for complete freedom from seizures. Hypothesis on the localization of the epileptogenic zone arises from the combined information gained from various diagnostic, mostly neuroimaging, methods.

Cognitive profile examination includes assessment of core cognitive domains, using standardized techniques with high-quality psychometric features, and their evaluation is a result of a comparison with up-to-date normalized data. In paediatric population, it is of absolute importance to use age- and mental level - appropriate techniques, in addition to sensitive consideration of developmental characteristics of a given tested function.

Epilepsy surgery represents a standard method with unequivocally documented effectiveness; we consider epilepsy surgery successful when patients reach freedom from seizures and from anti-epileptic medication. However, cognitive abilities are of no less importance; in children and their families it is often the main parameter that influences their quality of life.

The majority of epilepsy surgery patients show stable profile of cognitive functionsin longitudinal follow-up studies, the majority of them focused on memory functions in adult population. In children, however, changes in cognitive profile occur as well, mostly in their developmental dynamics. The original developmental trajectory may either (i) remain unchanged, or (ii) progress, or (iii) stagnate. Favourable cognitive outcomes significantly associate with freedom from seizures and to a lesser extent with reduction in antiepileptic medication.

In our study, we aimed to evaluate the dynamics of cognitive changes in paediatric population undergoing epilepsy surgery related to the epilepsy characteristics. In paediatric neuropsychology, cognitive profile is deeply related to the intellectual potential of the examined patient. In the main study of the thesis, we decided to focus on the central topic of paediatric

neuropsychology ï the intellectual level. At the same time we studied the features of cognitive profile in selected groups of patients; the conclusions are included in the additional studies.

In the main study we hypothesise that the intellectual/developmental level of children with pharmacoresistant epilepsy significantly depends on the character and clinical course of their epilepsy. At the same time we presume that a successful epilepsy surgery, rendering the patient seizure-free, plays an important role in the subsequent intellectual/developmental maturation.
The four main research questions we pose are the following. (1) Does focal pharmacoresistant epilepsy pose a risk for the developmental/intellectual performance of the patient? (2) Is there a relationship between the developmental/intellectual level of the patient and his/her epilepsy-related characteristics? (3) Does epilepsy surgery in childhood introduce change in the developmental/intellectual maturation of the patient? (4) Is there a relationship between post-operative intellectual performance and epilepsy-related characteristics?

We performed a retrospective analysis in a group of 197 children (up to 19 years of age) who underwent epilepsy surgery in our centre since year 2000 until 1.11.2016.

We included patients who (a) suffered from focal epilepsy, (b) had their first epilepsy surgery (resection or hemispherotomy), (c) underwent full pre-operative diagnostic work-up, (d) had all data available from the full diagnostic evaluationone year after surgery.
Data used for our analysis comprised patientôs medical history, results of pre-operative diagnostic examinations, information on the course of epilepsy surgery (including complications and histopathological diagnosis), and epilepsy surgery outcome.

We conclude that focal pharmacoresistant epilepsy indicated for epilepsy surgery poses a significant risk for developmental/intellectual performance.

We have confirmed the hypothesis that epilepsy-related characteristics and developmental/intellectual level are indeed related. Early seizure onset, frequent generalized seizures, acquired motor deficits and in particular a specific epileptic syndrome represent a significant risk for future cognitive development.

We provide evidence that curative epilepsy surgery has significant effect on trajectory of cognitive development in patients with focal phramacoresistant epilepsy.

Post-operative development of cognitive performance is associated with epilepsy-related features. Epilepsy surgery enables the patient to continue in his/her developmental trajectory. Any changes in patientôs developmental trajectory depend on the age of seizure onset and the age at surgery. Epileptic syndrome also influences epilepsy surgery outcome.

Further research studies performed by our team also provide evidence for the relationship between the epilepsy-related characteristics and cognitive performance.

Our findings show that atypical functional cortical organization, particularly atypical cortical representation of speech functions, represents a risk factor for optimal cognitive development in patients with focal pharmacoresistant epilepsy.

In addition, so-called electro-clinical features of focal pharmacoresistant epilepsy may influence cognitive development; this applies specifically to the presence of interictal epileptiform discharges in sleep with their negative impact on cognitive development.

According to another study by our team, specific features of pharmacoresistant epilepsy in children with tuberous sclerosis complex are associated with negative cognitive outcome, including the development of autism spectrum disorder.

In summary, the conclusions of our study are as follows.

The group of focal pharmacoresistant epilepsies can be divided into multiple sub-groups based on the specific domains with weaker performance in neuropsychological profile, and this should be reflected in the choice of optimal therapy.

Resective epilepsy surgery often represents the only therapeutic option that may lead to stabilization or even reversal of cognitive decline caused by incessant seizure activity.

Neuropsychological examination represents a vital part of pre- and post-surgical diagnostic process. We fully support the recommendations of the algorithm for pre- and post-surgical follow-up that was presented by the work group for neuropsychological diagnostics named by the ILAE Neuropsychology Task Force, Diagnostic Method Commision.