DANSK EPILEPSI SELSKAB
Danish Epilepsy Society

"Epilepsy and Evidence"

Annual Meeting
& General Assembly
Danish Epilepsy Society

Thursday 4 November to Friday 5 November 2021

Hotel
Comwell Middelfart
Karensmindevej 3
5500 Middelfart

Organising committee

Noémi Becser Andersen, Rigshospitalet
Lars H. Pinborg, Rigshospitalet
Christina Høi-Hansen, Rigshospitalet

The meeting is supported by pharmaceutical and medico companies

Meeting programme

Thursday 4 November

09.45 - 10.20	**Registration & coffee**
10.20 - 10.30	**Welcome** *Jakob Christensen,* Chairman of the Danish Epilepsy Society
Chairperson:	**Jakob Christensen**
10.30 - 11.15	**Evidence of first line monotherapy with antiseizure medication by seizure and epilepsy subtype** *Jakob Christensen, University Hospital Aarhus*
11.15 - 11.45	**Lamotrigine and cardiac side effects - current evidence and implications for clinical practice** *Marius Kløvgaard Sørensen, Rigshospitalet*
11.45 - 12.30	**The role of ketogenic diet in the treatment of epilepsy** *Mette Schou Larsen, Danish Epilepsy Centre, Filadelfia, Dianalund*
12.30 - 13.30	**Lunch**
Chairperson:	**Noémi Becser Andersen**
13.30 - 14.00	**VNS: evidence-based patient selection** *Ioannis Tsiropoulos,* Rigshospitalet
14.00 - 14.30	**Rolandic epilepsy in children – whom to treat** *Maria Miranda, Paediatric Department, University Hospital Herlev*
14.30 - 15.00	**Anti-seizure medication and bone health - current evidence and implications for clinical practice** *Noémi Becser Andersen, Rigshospitalet*
15.00 - 15.30	***Coffee break***
15.30 - 17.00	**Lecture competition – for young researchers**
	The Scandinavian *STXBP1* database *Francesca Furia, Danish Epilepsy Center – Filadelfia*
	Traumatic brain injury and risk of epilepsy *Kasper Lolk, National Centre for Register-based Research, Aarhus*
	Annual absolute risk of epilepsy after stroke *Mads Qvist Ebbesen, Dept. of Clinical Medicine, Aarhus University*
	Epilepsy and depression: a bidirectional relationship *Eva Bølling-Ladegaard, Dept. of Clinical Medicine, Aarhus University*
17.00 - 18.00	**General assembly**
19.00 -	***Dinner***

Friday 5 November

08.30 - 09.00	***Coffee***
Chairperson:	**Lars Pinborg**
09.00 - 09.45	**Emergency anticonvulsant treatment of acute seizures** *Christina E. Høi-Hansen, Department of Paediatrics, Rigshospitalet*
09.45 - 10.15	**Status epilepticus** *Christoph Beier Odense University Hospital and Annette Sidaros, Rigshospitalet*
10.15 - 10.45	**Value of the Epilepsy Monitoring Unit** *Martin Fabricius, Rigshospitalet*
10.45 - 11.15	***Coffee break***
Chairperson:	**Christina Høi-Hansen**
11.15 - 11.45	**Medical treatment during pregnancy** *Anne Sabers, Rigshospitalet*
11.45 - 12.15	**Use of evidence-based guidelines from a nurse perspective** *Merete K. Tschamper, Oslo University Hospital, Sandvika, Norway*
12.15 - 12.45	**Patient reported outcome - Ambuflex** *Liv Marit Valen Schougaard, Occupational Medicine Clinic, Herning*
12.45 - 13.00	**Concluding remarks**
13.00	***Lunch***

Abstracts

The Scandinavian *STXBP1* database

Francesca Furia[1,2], Claudia Bonardi[3], Anne Forsingdal Højte Hansen[1], Anne Pernille Fredslund[4], Charlene Son Rigby[5], Rikke S Møller[1,2], Elena Gardella[1,2]

[1]Danish Epilepsy Centre, Dianalund, Denmark

[2]University of Southern Denmark, Odense, Denmark

[3]University of Padova, Padova, Italy

[4]Scandinavian *STXBP1* family association

[5]American *STXBP1* family association

AIM

STXBP1 developmental and epileptic encephalopathy (DEE) is a rare disease. Individually, each rare disease affects a small number of people, but cumulatively rare diseases affect about 1 in 10 people and have a consistent socio-economic impact.

International disease registries are the gold standard tools to acquire the data for rare diseases, permitting natural history studies important for planning any stage of targeted care development.

We are creating the first Scandinavian *STXBP1* database with the aim to better delineate *STXBP1* DEE, to obtain early diagnostic and prognostic factors and to define a genotype-phenotype correlation.

METHODS

We are collecting detailed electro-clinical and genetic data from the Scandinavian patients with *STXBP1* pathogenic variants, through structured face-to-face interviews and surveys. We asked for genetic variants, motor and cognitive milestones, epilepsy features, EEG pattern and drug response, autistic features, behavioral problems, and eventual development of pyramidal and extra-pyramidal signs over time.

RESULTS

We have been in contact with 50 families and already enrolled 19 patients (8 males / 11 females), in age ranging from 8 months to 29 years. The majority of them (84%) presented with epilepsy with onset ranging from birth to 2.9 years of age. The most represented seizure types were: generalized tonic-clonic, absences and tonic seizures. At latest follow up, one half of the patients was seizure-free, while the others had persistent seizures with a frequency ranging from multiple/day to monthly. In 62.5% the EEG showed multifocal epileptiform abnormalities. The 72% took anti-seizure medications (ASM) and 33% of them was on polytherapy. The most used ASM were Levetiracetam, followed by Valproic Acid and Clobazam. Intellectual disability was observed in the 94%, with regression in half of them. Language problems were present in all the probands, ranging from absent speech (61%) to severe speech delay (39%). The 89% had ataxia or gait instability, 28% being not able to walk, the 53% presented with hypotonia and 33% with hypertonia. Autistic features were observed in 26% and behavioral problems in 37% of the probands. Sleep disturbances were reported in 63%, including insomnia and somnolence. Brain MRI was normal in most of the patients (71%); when altered it showed delayed myelination and cerebral atrophy.

We identified 19 different *STXBP1* variants, with de novo inheritance in 17/19, showing a wide phenotypic spectrum. From the analysis of the variants it didn't appear a clear genotype-phenotype correlation.

CONCLUSION

We designed a target protocol for data collection and built up a Scandinavian *STXBP1* database. The preliminary results of data collection show that most of the *STXBP1* have DEE with severe motor and speech impairment and heterogeneous outcomes. The genotype-phenotype correlation looks complex, suggesting a multidimensional spectrum of phenotypic features in *STXBP1*-related disorders. The future purpose of this study is to identify demographic, genetic, environmental, and other variables (e.g. type and timing of medications) that correlate with the disease's outcomes.

The broad potential of this targeted registry will permit to run retrospective and prospective natural history studies, allowing better family counseling as well as future precision-medicine approaches.

ABSTRACT

Author: Kasper Lolk[1,2,4]
Co-authors: Julie W. Dreier[1,4], Yuelian Sun,[1,3,5] and Jakob Christensen[1,3]

1. National Centre for Register-based Research, Department of Economics and Business Economics, Aarhus BSS, Aarhus University, Denmark
2. Department of Clinical Medicine, Aarhus University, Aarhus, Denmark
3. Department of Neurology, Aarhus University Hospital, Aarhus, Denmark
4. Centre for Integrated Register-based Research, CIRRAU, Aarhus University, Aarhus, Denmark
5. Department of Clinical Epidemiology, Aarhus University, Denmark

Background: Traumatic brain injury (TBI) and adverse perinatal outcomes, such as low gestational age, low birth weight, low Apgar score and being born small for gestational age, are well-established risk factors for epilepsy. It is, however, unclear whether these risk factors act independently of each other or if such perinatal adversities modify the risk of epilepsy following TBI.
Methods: We performed a nationwide register-based cohort study of all children born in Denmark between 1 January 1982 and 31 December 2011 who were alive and residing in Denmark on their fifth birthday. Children were followed from this day until onset of epilepsy, death, emigration from Denmark or 31 December 2016, whichever came first. During follow-up, persons were characterized with a first TBI if they had a TBI-related hospital contact. This was treated this as a time-varying exposure. We categorized perinatal adversities as a composite measure (Yes/No) of either preterm delivery (< week 37), low birth weight (< 2500 g), low Apgar score (<7), or being born small for gestational age. Cox regression models were used to estimate hazard ratios (HR) of epilepsy after TBI according to this composite measure of any perinatal adversity and by severity of TBIs.
Results: The risk of epilepsy was sligtly higher for children with an adverse perinatal outcome compared to children without any perinatal adversity. The risk of epilepsy increased after TBI in accord with the severity of said TBI, and was not modified by perinatal adversities for either mild TBI ($p = 0.3382$), skull fracture ($p = 0.6562$), or severe TBI ($p = 0.5999$).
Conclusion: Persons with adverse perinatal outcomes do not face an increased risk of epilepsy after TBI compared with persons without such perinatal adversities.

Title:
Annual absolute risk of epilepsy after stroke. A nation-wide register-based cohort study

Presenting author: Mads Qvist Ebbesen, Department of Clinical Medicine, Neurology, Aarhus University
Co-authors:
Julie Werenberg Dreier, Department of Economics and Business Economics, Business and Social Science, The National Center for Register-based Research, Aarhus University, Aarhus, Denmark
Søren Paaske Johnsen, Department of Clinical Medicine, Danish Center for Clinical Health Services Research, Aalborg University, Denmark
Grethe Andersen, Department of Neurology, Danish Stroke Center, Aarhus University Hospital, Aarhus, Denmark
Jakob Christensen, Department of Clinical Medicine, Neurology, Aarhus University

Rationale:
Stroke is a common cause of epilepsy, which may include seizures with temporary loss of consciousness. We examined the yearly absolute risk of epilepsy and status epilepticus after stroke, according to stroke type (acute ischemic stroke (AIS), transient ischemic attack (TIA), intracerebral hematoma (ICH)) and stoke severity.
Methods:
We included all individuals aged ≥18 years who were residing in Denmark, had no prior epilepsy and had a first stroke between 1 April 2004 and 16 December 2016. In Denmark, all admissions with acute stroke are included in the Danish Stroke Registry, and information on stroke type, stroke severity and several stroke risk-factors are included. The primary outcome was the combined outcome of any diagnosis of epilepsy or status epilepticus (ICD-8: 345, ICD-10: G40-G41), as identified in the Danish National Patient Registry. Follow-up began 14 days after the stroke, as early seizures may be part of the acute stroke. Patients were followed from first stroke until the primary outcome, death, emigration or 31 December 2016. We estimated the cumulative incidence of the primary end-point during each of the first 4 years following stroke stratified by stroke type and severity.
Results:
In total, 88,119 stroke patients (53.4 % male) were included in the study. We identified 7,661 patients with ICH, 70,157 with AIS and 10,301 with TIA. In total, 3,483 patients were diagnosed with epilepsy within the first 4 years after stroke. The highest risk was observed in the first year after very severe ICH, where the risk of being diagnosed with epilepsy or status epilepticus was 9.8 % (95 % CI: 7.8-11.7). For comparison, the same number was 5.1 % (95 % CI: 4.3-5.9) for patients with mild ICH, 7.8 % (95 % CI: 6.8-8.7) for patients with very severe AIS and 1.3 % (95 % CI: 1.2-1.4) for patients with mild AIS. For all groups the, risk decreased in the following years after stroke.
Conclusion:
The absolute risk of epilepsy or status epilepticus was higher for ICH patients than for patients with AIS after stroke. The risk was associated with stroke severity. In all of the stroke subgroups, the risk decreased in the years following stroke. Further studies are needed to further stratify the risk according to sex and age.

Epilepsy and Depression: a Bidirectional Relationship

Presenting author: Eva Bølling-Ladegaard, PhD-student
Department of Clinical Medicine, Neurology, Aarhus University, Aarhus, Denmark
National Centre for Register-based Research, Fuglesangs Allé 26, Bygning R, 8210 Aarhus V

Co-authors: Julie W. Dreier, Lars V. Kessing, Esben Budtz-Jørgensen, Kasper Lolk, Jakob Christensen

Background: Epilepsy and depression are two serious brain disorders that often co-occur, and the relationship between them has been suggested to be bidirectional; however, studies have provided ambiguous results, and the nature of the association between these two disorders remains to be fully understood.
Methods: In a nation-wide register-based cohort study, we identified all individuals who received a first diagnosis of epilepsy or depression from 1 Jan 1980 to 31 Dec 2016. For each person with epilepsy and depression we matched 5 persons without epilepsy and depression on age and sex at time of first diagnosis in the index person. We used Cox-regression to estimate the risk of epilepsy after depression and the risk of depression after epilepsy, adjusting for Charlson Comorbidity Index, substance abuse, and calendar time.
Results: In a population of 8,741,955 individuals, we identified 139,264 persons with epilepsy (54% males) with a median age at diagnosis of 42 years (interquartile range 17-65 years), and 219,990 persons with depression (37% males) with a median age at diagnosis of 43 years (interquartile range 29-60 years). The adjusted HR of depression after an epilepsy diagnosis was 1.89 (95 % CI: 1.83-1.96) compared to persons without epilepsy, and the adjusted HR of epilepsy after a depression diagnosis was 2.37 (95 % CI: 2.27-2.46) compared to persons without depression.
Conclusion: The risk of epilepsy is increased in persons with depression and the risk of depression is increased in persons with epilepsy. The results suggest a bidirectional association between depression and epilepsy and warrant further studies.
This research projected was funded by the Lundbeck Foundation and the Novo Nordisk Foundation (NNF16OC0019126).

DESITIN

CENTOGENE
THE RARE DISEASE COMPANY

Eisai

SERB
SPECIALTY PHARMACEUTICALS

ucb
Inspired by patients.
Driven by science.

UNEEG™ medical

GW
pharmaceuticals

Danish Care Technology

UNIMEDIC®
PHARMA

ARVELLE
THERAPEUTICS
- a company of the Angelini Pharma Group

ANGELINI
PHARMA

go
north
MEDICAL