Welcome to:
PhD thesis- Half-time review seminar

Familial Cerebrovascular Diseases

Friday, March 22, 2019
Conference room EA-block, level 4 at 12:30

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Background:

Stroke is in part genetically determined. Exact genetic mechanisms related to stroke risk are often unknown. Genetic factors may be of special interest in younger stroke patients. But even though new methods for genetic analyses are rapidly evolving, there is currently a knowledge gap in how to appropriately detect monogenic stroke.

Research questions/Methods:

I (published) The hypothesis that monogenic alterations are sometimes related to stroke is analyzed by investigating clustering of stroke in families of patients younger than 56 years from Lund Stroke Register under a 10 year period. Classical vascular risk factors, heredity for stroke and stroke subtypes are also considered.

II (published) A panel containing a comprehensive list of known relevant stroke-related genes including evaluation of potential pathogenicity is needed to interpret whole exome sequencing (WES) results in stroke patients. To build such a panel, genes were identified by systematic search on OMIM and specific criteria of pathogenicity were used based on available publications (PubMed).

III (not published) How well can a stroke gene panel (SGP) diagnose monogenic stroke? WES data for 22 families with stroke is interpreted using the SGP followed by cosegregation analyses in the families.

IV (not published) A large family pedigree without identifiable genetic cause for stroke is investigated to better understand the disease’s characteristics. WES, clinical data, brain images, skin-biopsies of 8 family members are analyzed.

Preliminary results:

Aggregation of stroke in families of early-onset stroke patients is not uncommon. We compiled a SGP with 120 stroke-genes, 62 genes associated with stroke-causing monogenic diseases and 32 stroke-risk GWAS determined genes. Each genes’ relation to specific stroke subtypes was assessed. When analyzing the 22 stroke families, using the SGP, no known pathogenic mutation were identified. Our detailed analysis of the large pedigree describes a new stroke-related syndrome.

Significance:

New methods for genetic analyses may expand knowledge about stroke mechanisms. A detailed SGP does not yield a large added proportion of stroke patients with an identifiable genetic variant. A SGP is therefore not superior to existing genetic diagnostic methods, but may be used as a filtering method for WES. A new stroke-causing disease and its implications is described.
Published articles:
