Genetic Association Analysis of Essential Tremor

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July 19, 2012
Overview

• Background information in genetics
• Pedigree structure
• Essential Tremor Disorder
• Project Methodology
• Results and Conclusion
• Further information
Cells are one of the most basic structures of life.
Each cell contains a full set of chromosomes.
Karyotypes show all the chromosomes of an individual.
Normal individual has of 22 chromosomes and a sex chromosome.
• Deoxyribonucleic acid.
• Consists of two long chains of subunits twisted around one another to form a double-strand helix.
• Contains four chemical components called bases:
  • Adenine (A) Thymine (T) Guanine (G) & Cytosine (C)
DNA Replication

- Helix separates and serves as a temple for replication.
- Results in two strands of DNA each containing one of the original strands.

Sexual Reproduction

- Combination of Sperm and Egg each of which contain 23 chromosomes.
- Form Zygote with 23 chromosomal pairs.
- Offspring Characteristics
  - Phenotype: Physical Characteristics
  - Genotype: Genetic Characteristics
Genetic Markers

- A strand of polymorphic DNA.
- Alleles are particular forms of genetic markers.
- Single Nucleotide Polymorphism are makers that only differ at a single nucleotide.
- Each has two alleles, one from the maternal and the other from the paternal chromosome.
- The two alleles are called an individual's genotype.
- Homozygous
  - Two alleles are the same
- Heterozygous
  - Two alleles are not the same

http://www.abpischools.org.uk
MENDELIAN GENETICS

• In gamete formation, allele separate in such a way that each gamete is equally likely to contain any allele.

• Leads to easy straightforward predictions of offspring's characteristics.

PRACTICAL GENETICS

• Many alleles and traits are linked so they do not segregate independently.

• Not all alleles are dominant or recessive

• Interactions between genes.

• Makes it more difficult to predict and trace traits.
Pedigree Structure

- Pictorially shows a trait in a group of related individuals.
- Can show genotypes and/or phenotypes.
Essential Tremor

• Neuromuscular disorder that causes shaking of the hands, head, and voice.
• Usually a dominant trait.
• Most common in people older than 65.*
• Affects 4% to 5% of people age 40 to 60.*
• Affects 6.3% to 9%. Of people 60 and older. *
• Exact cause is unknown.
• Believed to have both neurological and genetic component.

*Statistics from National Center for Biotechnology Information
**Methodology**

**Purpose:** To identify possible single nucleotide polymorphisms linked to Essential Tremor through genotype analysis.
Data Acquisition

Genotype Data

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<th>probeset_id</th>
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<th>7</th>
<th>8</th>
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Map File

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## Genotype Comparison Tables

<table>
<thead>
<tr>
<th>Genotype</th>
<th>AA</th>
<th>AB</th>
<th>BB</th>
<th>Total</th>
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</thead>
<tbody>
<tr>
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<td>5</td>
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<tr>
<td>Affected Individuals</td>
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<tr>
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<td>13</td>
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</tbody>
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### Pearson Chi-Square Statistics Test

- Tests for independence between the row and the column
- If no interaction the same proportion should be in each column
- Follows Chi-Square distribution with 2 degrees of freedom

\[
\text{Test Statistic} = \sum_{6 \text{ cells}} \frac{(\text{Observed} - \text{Expected})^2}{\text{Expected}}
\]
Manhattan Plot for Study of Essential Tremor

• Plot of P-value vs SNP location
Results and Conclusion

• No p-values are significant at genome wide significance level ($1 \times 10^{-8}$).
• Some suggestive locations.

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Gene name</th>
<th>Function</th>
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<tbody>
<tr>
<td>5</td>
<td>DEP1B</td>
<td>Regulation of GTPase activity</td>
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<tr>
<td>14</td>
<td>RAD51 homolog B</td>
<td>DNA repair protein</td>
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<td>6</td>
<td>GPR6</td>
<td>Nerve growth and myelin</td>
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• More study need on this disorder in genetics and neurobiology.
Further Information

International Essential Tremor Foundation

National Center for Biotechnology Information