Longitudinal study of hand grip strength in twins

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- on behalf of the iGEMS consortium
Hand grip strength predicts...

Previous studies have demonstrated an inverse relation between grip strength and

- Disability
- Length of hospital stay
- Mortality
Predictors of hand grip strength

- environmental factors
- Stature, BMI, birth weight
- Marital status, wealth, nationality
- Dementia, chronic diseases
- Occupation, physical activity (work & leisure)
- Alcohol, smoking
- Age and sex

Frederiksen et al, Annal.Epidemiol., 2006
Hand grip strength

- heritability

- Level: 50-70%
  - remarkably flat across age ranges

- Decline: ~0%
Hand grip strength

- APOEε4 vs APOEε3
  - higher grip strength level

- APOEε2 vs APOEε3
  - lower grip strength level
  - Less decline

- ACE, ACTN3, PPARA...
## Sample

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>Male (%)</th>
<th>Age range (median)</th>
<th>Repeated measures – max (median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SATSA</td>
<td>851</td>
<td>41%</td>
<td>39-88 (63)</td>
<td>7 (4)</td>
</tr>
<tr>
<td>OctoTwin</td>
<td>640</td>
<td>34%</td>
<td>79-99 (82)</td>
<td>5 (3)</td>
</tr>
<tr>
<td>VETSA</td>
<td>1,215</td>
<td>100%</td>
<td>51-60 (54)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>LSADT</td>
<td>2,873</td>
<td>45%</td>
<td>70-97 (75)</td>
<td>4 (3)</td>
</tr>
<tr>
<td>MADT</td>
<td>4,274</td>
<td>51%</td>
<td>45-77 (56)</td>
<td>2 (2)</td>
</tr>
<tr>
<td>MIDUS</td>
<td>379</td>
<td>41%</td>
<td>34-82 (53)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>9,853</td>
<td>48%</td>
<td>34-99 (72)</td>
<td>7 (2)</td>
</tr>
</tbody>
</table>
Age- and sex- trajectories

* Rescaled due to different measuring device
Fisher’s test
- heterogeneity

Monozygotic twin pairs only!

\[ d = \text{within twin pair difference} \]
\[ h = \frac{d^2}{2} - \frac{\pi}{\bar{d}^2} \]
\[ \text{s.e.} = \frac{d^2}{\sqrt{n}} \sqrt{2\pi - 6} \]

Significant test indicates a mixture of distributions
- which again might indicate presence of GxE interaction
Fisher’s test

<table>
<thead>
<tr>
<th>All studies</th>
<th></th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>$N$</td>
<td>$t$</td>
<td>$p$</td>
</tr>
<tr>
<td>MALES</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>915</td>
<td>8.84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Decline</td>
<td>915</td>
<td>19.50</td>
<td>&lt;0.001</td>
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<tr>
<td>FEMALES</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>701</td>
<td>5.89</td>
<td>&lt;0.001</td>
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<tr>
<td>Decline</td>
<td>701</td>
<td>16.65</td>
<td>&lt;0.001</td>
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</tbody>
</table>

Evidence of a GxE interaction for level and decline of grip strength in males and females
Within twin pair differences

- APOEε2

Less variability in APOEε2 carriers compared with non-carriers
Within twin pair differences
- APOEɛ4

Similar variability in APOEɛ4 carriers and non-carriers

Males

Intercept - age 70

Decline

Within twin pair difference

Age

Within twin pair difference

Age

- apoe4 non-carrier
- apoe4 carrier
### Variance ratio test

- **Males**

<table>
<thead>
<tr>
<th></th>
<th>APOEε2 carrier/non-carrier</th>
<th>p-value</th>
<th>APOEε4 carrier/non-carrier</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>N-</strong></td>
<td></td>
<td></td>
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<tr>
<td>Intercept</td>
<td>530</td>
<td>0.95</td>
<td>433</td>
<td>1.04</td>
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<tr>
<td>Decline</td>
<td>0.73</td>
<td>&lt;0.05</td>
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<tr>
<td><strong>&lt;70</strong></td>
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<tr>
<td>Intercept</td>
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<td>0.74</td>
<td>366</td>
<td>0.90</td>
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<tr>
<td>Decline</td>
<td>0.48</td>
<td>&lt;0.001</td>
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<tr>
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<td></td>
</tr>
<tr>
<td><strong>&gt;=70</strong></td>
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<td></td>
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</tr>
<tr>
<td>Intercept</td>
<td>71</td>
<td>0.95</td>
<td>67</td>
<td>1.18</td>
</tr>
<tr>
<td>Decline</td>
<td>0.66</td>
<td>0.26</td>
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</table>
## Variance ratio test
### - Females

<table>
<thead>
<tr>
<th></th>
<th>APOEɛ2</th>
<th></th>
<th>p-value</th>
<th>APOEɛ4</th>
<th></th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N-</td>
<td>N+</td>
<td>carrier/non-carrier</td>
<td></td>
<td>N-</td>
<td>N+</td>
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<tr>
<td>Intercept</td>
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<td>71</td>
<td>0.78</td>
<td>0.20</td>
<td>276</td>
<td>125</td>
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<tr>
<td>Decline</td>
<td></td>
<td></td>
<td>0.55</td>
<td>&lt;0.01</td>
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<tr>
<td>&lt;70</td>
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<tr>
<td>Intercept</td>
<td>205</td>
<td>45</td>
<td>0.70</td>
<td>0.16</td>
<td>174</td>
<td>76</td>
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<td>0.54</td>
<td>0.02</td>
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</tr>
<tr>
<td>&gt;=70</td>
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<tr>
<td>Intercept</td>
<td>123</td>
<td>26</td>
<td>0.91</td>
<td>0.81</td>
<td>100</td>
<td>49</td>
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<tr>
<td>Decline</td>
<td></td>
<td></td>
<td>0.79</td>
<td>0.50</td>
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</tbody>
</table>
Conclusion

- Evidence of GxE for level as well as decline of grip strength based on tests of MZ twin pair differences in grip strength
- APOEε2 decreases variability of the decline of grip strength in males and females (age < 70 years)
- APOEε4 increases variability of the decline of grip strength in females (age < 70 years)
Acknowledgements

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