SHORT REPORT

Polymorphism of the IGF2 gene, birth weight and grip strength in adult men


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Abstract

Background: grip strength is a simple measure of skeletal muscle function but a powerful predictor of disability, morbidity and mortality. Recent evidence has shown that prenatal and infant growth influence grip strength in later life; this may reflect genetic influences on muscle size and function, although strong candidate genes have not been identified. IGF II has proliferative effects in adult muscle and is one of the major determinants of fetal growth; polymorphism in the IGF2 gene could therefore link early growth to adult grip strength.

Objectives: to determine whether polymorphism of the IGF2 gene influences adult grip strength and mediates the association between size at birth and grip strength in later life.

Methods: polymorphism of the ApaI marker in the IGF2 gene was determined for 693 Hertfordshire men and women born between 1920 and 1930 who had taken part in a study linking early growth to ageing. Grip strength was measured using isometric dynamometry. Genotyping assay development was undertaken in Southampton Genetic Epidemiology Laboratories (http://www.sgel.humgen.soton.ac.uk).

Results: in univariate analyses, IGF2 genotype and birth weight were both significant predictors of adult grip strength in the men after adjustment for age and current height. Significant associations were not seen in the women. When IGF2 genotype and birth weight in men were studied simultaneously, both contributed significantly to grip strength after adjustment for age and adult height.

Conclusions: these results show that polymorphism of the IGF2 gene and birth weight have independent effects on adult grip strength in men and suggest that IGF2 polymorphism does not explain the association between size at birth and grip in later life. This study provides preliminary evidence for independent genetic and early environmental programming of adult muscle strength.

Keywords: grip strength, IGF2 gene, growth, birth weight

Introduction

Grip strength is a simple measure of skeletal muscle function but a powerful predictor of disability, morbidity and mortality [1–3]. Wide variation in grip strength exists between individuals of the same age, and well-documented influences include gender, size and physical activity [4]. Recent work has shown that prenatal and infant growth are related to adult grip strength independently of adult size [5]. The mechanism is not known but may involve genetic factors.

Insulin-like growth factors (IGFs) are peptides that regulate the growth, differentiation and regeneration of cells [6]. Insulin-like growth factor II (IGF II) has a proliferative action in adult muscle [7] and it has been suggested that age-associated loss in muscle fibres may be related to the decline in the local production of growth factors. IGF II is also one of the major determinants of fetal and postnatal growth [8, 9]. We therefore investigated whether polymorphism in the IGF2 gene explains the link between early size and grip strength in adult life.
IGF2 gene, growth and grip strength

Table 1. Univariate relationship between grip strength and IGF2 genotype and birth weight

<table>
<thead>
<tr>
<th>Birthweight (tertiles, oz)</th>
<th>IGF2, GG Mean (sd)</th>
<th>IGF2, GA Mean (sd)</th>
<th>IGF2, AA Mean (sd)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 112</td>
<td>34.9 (8.1)</td>
<td>38.1 (5.9)</td>
<td>38.4 (4.9)</td>
</tr>
<tr>
<td>n = 68</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-128</td>
<td>38.6 (6.9)</td>
<td>39.5 (7.0)</td>
<td>36.3 (4.3)</td>
</tr>
<tr>
<td>n = 80</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;128</td>
<td>39.1 (6.1)</td>
<td>39.8 (7.6)</td>
<td>40.9 (7.1)</td>
</tr>
<tr>
<td>n = 54</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 112</td>
<td>22.3 (5.1)</td>
<td>22.2 (5.0)</td>
<td>20.2 (3.2)</td>
</tr>
<tr>
<td>n = 69</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-128</td>
<td>21.7 (5.7)</td>
<td>22.8 (5.9)</td>
<td>24.4 (5.7)</td>
</tr>
<tr>
<td>n = 62</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;128</td>
<td>23.2 (5.8)</td>
<td>25.1 (4.3)</td>
<td>22.7 (2.1)</td>
</tr>
<tr>
<td>n = 37</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Methods

We studied a group of 717 Hertfordshire men and women aged 64–74 who had historical records of birth weight. This cohort has been described before [5]. Grip strength, height, weight and self-reported walking speed were recorded. Blood samples were obtained from 693 of the study subjects for DNA extraction and IGF2 ApaI Amplification Refractory Mutation System (ARMS) PCR and genotyping were carried out. The alleles were coded G or A giving rise to three genotypes – GG, GA, AA. The population studied was in Hardy-Weinberg equilibrium. IGFII levels were measured in a subgroup of 99 people. Ethical approval for this study was obtained from the East and North Hertfordshire Health Authority Local Research Ethical Committee. All statistical analyses were carried out using STATA, release 6 and the relationship between IGF2 genotype, birth weight and grip strength was explored using multiple linear regression.

Results

We studied 397 men and 296 women with an average age of 67.5 years. Average grip strength was 38.2 kg and 22.5 kg in the men and women, respectively. Univariate analysis showed that grip strength was significantly (P<0.05) associated with gender, age, height, weight and self-reported walking speed. The strongest correlates of adult grip strength were age (r = -0.18, p = 0.003) in men, r = -0.19, p = 0.007 in women) and current size, of which height was a stronger predictor than weight in the men (r = 0.29, p < 0.0001) and women (r = 0.20, p = 0.0007). Birth weight was significantly associated with adult height and weight in the men but only correlated significantly with adult weight in the women.

IGF2 genotype was not significantly associated with adult height or weight although there was a non-significant trend for men of the GG genotype to be heavier and taller than those of the AA genotype. These results are consistent with previous findings [10]. The patterns were reversed in the women. Birth weight was highest for the GG genotype in the men and women but the differences were not statistically significant (data not shown). The GG genotype was associated with lower IGFII levels (391.2 ng/ml) than the AA genotype (403.9 ng/ml). The difference was not statistically significant but was consistent with previous work [10]. IGFII levels were not associated with adult grip strength in the men or women.

In univariate analyses adult grip strength in the men was significantly associated with both IGF2 genotype (p = 0.05) and birth weight (p = 0.04) after adjustment for age and current height. Significant relationships were not seen in the women for univariate analysis (Table 1) or multivariate analysis (Table 2). When IGF2 genotype and birth weight were studied simultaneously in men, both contributed significantly to grip strength after allowing for age and adult height (Table 2) and these relationships remained after including walking speed in the model. The proportion of variance in grip strength attributable to the IGF2 genotype was 1% in comparison to 6% accounted for by height.
**Discussion**

Grip strength is strongly associated with health in later life. Its determinants are of considerable interest. In an exploratory analysis, we have shown that birth weight and IGF2 genotype exert independent additive effects on adult grip strength in men such that those who weighed least at birth and had the GG genotype, had 6 kg lower grip strength than those who weighed most at birth and had the AA genotype. This is a clinically relevant reduction in grip strength. A previous study found that a 5 kg decrease in grip strength was associated with a 1.52 odds ratio of difficulty performing three or more activities of daily living [11].

There were clear sex differences. Grip strength was significantly lower in the women as has been reported previously [4] and, in contrast to the men, did not appear to be determined by birth weight or IGF2 genotype. The reasons for the gender specific effect are unclear but differences between the sexes in response to environmental factors operating in early life have been demonstrated before [12]. We postulate that adult environmental factors may be more important in women. However the findings from this study need to be interpreted with caution. The number of subjects was small, particularly for measurement of IGFII levels and may have lacked power to detect significant associations. Multiple comparisons increase the risk of associations arising by chance alone. The differences demonstrated between men and women may reflect these limitations of the study or represent true biological variation.

Our findings provide preliminary evidence for independent genetic and early environmental programming of adult grip strength. Replication studies are needed to look at the contribution of IGFII levels and early growth to adult grip strength in different cohorts. Improved prediction of adult muscle function may help identify individuals most in need of preventive strategies to conserve muscle strength in later life.

**Key points**

- In this study polymorphism of the IGF2 gene and birth weight had independent effects on grip strength in men suggesting that IGF2 polymorphism does not explain the observed association between early growth and grip.
- These results provide preliminary evidence for independent genetic and early environmental programming of adult grip strength.

**References**


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