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Can genetic testing predict talent? A case study of five elite athletes

Abstract

Purpose: The genetic influence on the attainment of elite athlete status is well-established, with a number of polymorphisms found to be more common in elite athletes than in the general population. As such, there is considerable interest in understanding whether this information can be utilised to identify future elite athletes. Accordingly, the aim of this study was to compare the total genotype scores of five elite athletes to those of non-athletic controls, to subsequently determine whether genetic information could discriminate between these groups, and, finally, to suggest how these findings may inform debates relating to the potential for genotyping to be used as a talent identification tool. **Methods:** We compared the total genotype scores for both endurance (68 genetic variants) and speed-power (48 genetic variants) elite athlete status of five elite track and field athletes, including an Olympic Champion, to those of 503 Caucasian non-athletic controls. **Results:** Using the speed-power total genotype score, the elite speed-power athletes scored more highly than the elite endurance athletes. However, using this speed-power score, 68 non-athletic controls registered higher scores than the elite power athletes. Surprisingly, using the endurance total genotype score, the elite speed-power athletes again scored more highly than the elite endurance athletes. **Conclusions:** These results suggest that genetic information is not capable of accurately discriminating between elite athletes and non-athletic controls, illustrating that the use of such information as a talent identification tool is currently unwarranted and ineffective.

Key words:

Genetic testing; elite athlete; talent; talent identification; Olympic

99 **Introduction**

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Over the last thirty years, our appreciation of how genetics influences elite sports performance has grown exponentially, with previous estimates of the heritability of elite athlete status within a population reported to be approximately 66%.¹ Similarly, our understanding of how specific genetic variants, such as *ACTN3*,² may predispose towards elite performance has developed. Such advances have led to speculation that genetic testing may be a viable tool to identify individuals with an increased likelihood of achieving elite athlete status in the future, with some direct-to-consumer genetic testing companies already offering this service.³

However, at present, the scientific consensus suggests that such approaches are ineffective at identifying future talented performers.³ Previously, Williams & Folland⁴ incorporated 23 genetic variants associated with elite endurance performance in a data simulation, with subsequent results suggesting that there was only a 0.0005% chance of any single person in the world having the optimal form of all 23 performance-associated variants. A further issue is that, within this simulation, there was considerable similarity in polygenic profiles between individuals, with the clustered distribution of genotype scores limiting the emergence of genetic outliers, who we might reasonably predict are more likely to be elite athletes. Similar findings, relating to muscular strength and power characteristics, have also been demonstrated.⁵ Such issues have also been explored experimentally, most commonly via the use of Total Genotype Scores (TGS). Here, a score is assigned for each genotype of interest, and then summed into a final score for that athlete. For example, Ruiz and colleagues⁶ collected data on elite Spanish endurance athletes and controls. Whilst, on average, the athletes within that cohort had a greater TGS for a panel of seven endurance-related polymorphisms than non-athletic controls, there was considerable overlap in score between the populations, thereby illustrating that the predictive capability of this particular TGS was low. Indeed, whilst individuals with a TGS above 74.71 were over five times more likely to be elite athletes, only 43.5% of elite athletes attained such a score. Similar results were reported for elite power athletes;⁷ again, the athletes had a higher average power TGS than both controls and endurance athletes, but with a large crossover of standard deviations between the groups, indicating limited sensitivity and specificity.

Such evidence suggests that utilising a relatively low number of polymorphisms to identify elite athletes is unlikely to provide meaningful insights. However, many more polymorphisms than the 23 or fewer utilised in the studies to date have been associated with elite performance. A recent literature review,⁸ for example, reported that at least 155 genetic markers have been associated with elite athlete status, with further associations emerging since that article's publication.⁹ Additionally, in a recent survey in the UK, 67% of athletes and 48% of support staff stated that genetic testing would form a valuable addition to talent identification processes within their sport,¹⁰ suggesting that there is an appetite for such information within the sports performance world.

Despite this apparent enthusiasm, however, further research in this area is clearly required. Currently, it remains unclear whether genetic information can accurately discriminate between elite performers and members of the general public. In addressing this lack of evidence-led insight, within this investigation we used an expanded TGS, incorporating an increased number of genetic variants, to determine whether such a panel can reliably distinguish between a sub-population of five elite athletes and a control population of European Caucasians. To the best of our knowledge, such a large scale TGS has not

149 previously been utilised to identify talented athletes, demonstrating the novelty of such a case
150 study.

151

152 **Methods**

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154 **Participants**

155 The participants were five former or current high-level athletes. All participants gave written,
156 informed consent for their genotype results and identity to be shared here. All participants
157 read the final version of this manuscript prior to submission, and consented to its publication,
158 and their naming within this publication. The study protocol was approved by the University
159 of Central Lancashire Ethics Committee, in accordance with the Declaration of Helsinki
160 (Ethics Board number BAHSS 575)

161

162 Participant A (Andrew Steele) is a former 400m runner. He competed at one Olympic
163 Games, winning a medal in the 4x400m relay. His personal best time is 44.94s, and he was a
164 high-level athlete for approximately 11 years.

165

166 Participant B (Greg Rutherford) is a former long jumper. He has competed at three
167 Olympic Games, winning a Gold and a Bronze medal. His personal best distance is 8.51m,
168 and he was a high-level athlete for approximately 13 years.

169

170 Participant C (Craig Pickering) is a former sprinter. He competed at one Olympic
171 Games, and has a World Championships Bronze medal in the 4x100m relay. His personal
172 best 100m time is 10.14s, and he was a high-level athlete for approximately 7 years.

173

174 Participant D (Tom Lancashire) is a middle-distance runner, competing primarily over
175 1500m, the distance at which he was selected for an Olympic Games. His personal best
176 1500m time is 3:33:96, and he was a high-level athlete for approximately 13 years.

177

178 Participant E (Andrew Lemoncello) is a long-distance runner, with a Marathon
179 personal best time of 2:13:40. He competed at two World Championships, and one Olympic
180 Games, and was a high-level athlete for approximately 12 years.

181

182 All participants are of primarily European Caucasian ethnicity, although Participant
183 D's mother is Mauritian.

184

185 **Genetic Testing**

186 Each participant volunteered a saliva sample, which was collected through sterile and
187 self-administered buccal swabs. The samples were sent to AKESOgen, Inc (Peachtree
188 Corners, GA, USA), where DNA was extracted from the saliva samples using Qiagen
189 chemistry on an automated Kingfisher FLEX instrument (Thermo Fisher Scientific,
190 Waltham, MA, US), following the manufacturer's recommended protocols and standard
191 operating procedures. PicoGreen and Nanodrop measurements were taken to measure the
192 quality and quantity of the DNA. Input to the custom testing array occurred at 200ng in
193 20µL. Amplification, fragmentation, and resuspension was performed using Biomek FXP
194 following Affymetrix's high throughput protocol for Axiom 2.0. Hybridization was
195 performed for 24 hours at 48°C in a Binder oven, and staining and scanning of the arrays was
196 performed using GeneTitan instrumentation (Thermo Fisher Scientific, Waltham, MA, US),
197 all following the same Affymetrix high throughput Axiom 2.0 protocol. Data analysis was

198 then performed using a raw CEL file data input into the Affymetrix Axiom Analysis Suite
199 (Affymetrix, Santa Clara, CA, US).

200

201 **Creation of Total Genotype Scores**

202 In order to best examine the potential use of genetic information in identifying elite
203 athletes, polymorphisms previously linked to elite speed-power and elite endurance athlete
204 status were collated through a structured literature search.

205

206 *Speed-Power Athlete Status:* A total of 48 genetic variants associated with power
207 athlete status were identified from two review articles.^{8,11} Of these 48, one marker (*ILIRN*)
208 could not be genotyped due to lack of coverage on the AKESOgen chip array. A further SNP,
209 rs2854464 in *ACVR1B*, was added to the panel based on subsequent research.¹² Three
210 additional SNPs in the carnosine genes *CNDP1* and *CNDP2*, associated with elite power
211 athlete status⁹ were also not present on the chip array, and so were not assessed.
212 Mitochondrial DNA (mtDNA) was not assessed. The effect allele of one SNP, rs11091046 in
213 *AGTR2*, was reversed given the findings of a recent meta-analysis.¹³ Accordingly, 48 genetic
214 variants were utilised in the power TGS within this study.

215

216 *Endurance Athlete Status:* A total of 68 genetic variants associated with endurance
217 athlete status were identified from two review articles.^{8,11} Of these, the genotype of 5
218 (*ADARA2A* 6.7/6,3kb, *BDKRB2* +9/-9, *COL5A1* rs71746744, *NOS3* 4A/4B, *PPP3R1* 5I/5D)
219 could not be determined due to insufficient coverage. We also added rs10497520 *TTN* to the
220 TGS.¹⁴ mtDNA was not assessed. Accordingly, 64 genetic variants were utilised in the
221 endurance TGS within this study.

222

223 **Scoring**

224 For each genetic variant, a score of 0, 1 or 2 was given depending on the genotype of
225 the athlete. A score of 2 represents the possession of two alleles associated with elite athlete
226 status (e.g. CC for *ACTN3* rs1815739 within the power TGS); a score of 1 represents carriage
227 of one such allele (e.g. CT for *ACTN3* rs1815739 within the power TGS); and a score of 0
228 represents the possession of no elite athlete-associated alleles for that genetic variant (e.g. TT
229 for *ACTN3* rs1815739 within the power TGS). For each trait, the scores were then summated,
230 divided by the total possible score, and multiplied by 100 to get a percentage. This method is
231 identical to that utilised in previously published research utilising a TGS to explore elite
232 athlete status.⁴⁻⁷ The analysis was carried out in Excel 16.13.1 (Microsoft, Redmond, WA,
233 USA).

234

235 **Control Population**

236 In order to develop an adequate control population, genotype scores for 503 European
237 Caucasians were downloaded from e!GRCh37 (<http://grch37.ensembl.org/index.html>) into a
238 spreadsheet for analysis. For each genetic variant, a score of 0, 1, or 2 was given as per the
239 speed-power and endurance TGS detailed previously. The sum of scores for each variant was
240 then calculated, and converted into the TGS% as per the previously detailed method.
241 Additionally, the mean and standard deviation score for this reference population were
242 calculated.

243

244 **Results**

245

246 **TGS Scores**

247 Table 1 shows the results of all five participants' speed-power TGS, as well as the
248 mean score expected in European Caucasians. The three speed-power athletes had the highest
249 TGS, whilst the two endurance athletes had the lowest. This trend held up in comparison to
250 the mean score for European Caucasians, with the speed-power athletes having a higher score
251 than the mean, and the endurance athletes a lower score than the mean. Table 1 also
252 demonstrates the results of the endurance TGS. Here, the two endurance athletes still have
253 the lowest TGS – lower than the elite speed-power athletes and the mean for European
254 Caucasians.

255
256 **Insert Table 1 around here**

257 **Comparison to previously published TGS**

258 The next stage of our analysis was to calculate the TGS from previously published
259 research by Ruiz and colleagues.^{6,7} The results for both the speed-power and endurance TGS
260 developed by Ruiz are shown in table 2.
261

262
263 **Insert Table 2 around here**

264 **Non-athlete Control Results**

265 We then calculated the frequency distributions for 503 non-athletic Caucasian
266 controls for both the power (figure 1) and endurance (figure 2) TGS. In general, the results of
267 the controls are fairly tightly distributed around the mean. Within the power TGS, no
268 participants fell below a score of 26%, or above a score of 53%. Similarly, within the
269 endurance TGS, no participant had a score below 34% or above 55%.
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274 **Insert Fig 1 around here**

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276 **Insert Fig 2 around here**

277 **Discussion**

278 Using a 48 SNP TGS of speed-power associated SNPs, we found a general trend for
279 the elite speed-power athletes to score more highly (range 42.7-44.8%) than the elite
280 endurance athletes (37.5%) in our cohort. The mean score for our control population of
281 European Caucasians was 39.4%; lower than the scores achieved by the speed-power
282 athletes, but higher than the elite endurance athletes. These outcomes may appear to
283 provisionally support the use of genetic information to identify talented performers; however,
284 both endurance athletes and two of the three power athletes were within one standard
285 deviation of the non-athletes mean score. Indeed, in the 503 European reference samples
286 utilised, 68 individuals had higher speed-power TGSs than athlete A, the highest scoring
287 athlete in our cohort. The highest score in the control population was a TGS of 50%, just over
288 2SDs greater than the mean.
289

290 The results for the 64 SNP endurance TGS further demonstrated the lack of utility of
291 genetic testing for talent identification. Here, all three speed-power athletes (range – 43.8-
292 47.7%) out-scored the endurance athletes (39.8 – 42.2%), who in turn scored lower than the
293

297 mean for European Caucasians (43.8%). The SD for scores in the 503 European reference
298 samples was 3.8%, with 82 control participants having an endurance score >1SD outside of
299 the mean. The highest score was 54.6%.

300

301 The comparison to the previously published TGS utilised by Ruiz and colleagues^{6,7}
302 provides some interesting results. In our cohort, the elite endurance athletes scored more
303 highly on Ruiz and colleagues'⁶ endurance TGS (64 and 71%) than our speed-power athletes.
304 This is the opposite result to that seen when utilising the larger scale TGS developed for our
305 study. This potentially suggests that the utilisation of fewer genetic variants within a TGS
306 may enhance the predictive ability of such a model, potentially because the selected variants
307 have a greater effect size, or that the reported effects in the literature are correct, and not
308 spurious. Larger sample sizes are required to further test this. Regarding the power TGS, the
309 athletes in our cohort all scored lower than the mean power score in the Ruiz and colleagues'⁷
310 cohort; two just outscored the mean for European Caucasians, whilst participant C—a
311 European medalist over the 60m sprint—scored below the mean for European Caucasians,
312 and was outscored by participant E, the long-distance runner. Again, this is in contrast to our
313 results, where the speed-power athletes all outscored the endurance athletes, suggesting that
314 the larger scale TGS is potentially more sensitive in determining speed-power athlete status.

315

316 The two genetic variants most well-associated with elite athlete status are *ACE* and
317 *ACTN3*.^{2,15,16} Regarding *ACTN3*, the C allele of rs1815739 is consistently associated with
318 elite speed-power athlete status, with two recent meta-analyses^{17,18} finding that individuals
319 with the TT genotype were significantly less likely to achieve elite speed-power athlete status
320 compared to those with at least one C allele. The three speed-power athletes within our
321 cohort exhibit the full range of *ACTN3* genotypes (data not shown). Participant B, the highest
322 achieving of our cohort, possesses the CC genotype. Participant C, the short sprinter,
323 possesses the CT genotype, whilst Participant A, the Olympic 400m relay medallist, is a TT
324 genotype. This latter result is somewhat surprising given that this genotype is considered
325 unfavourable for elite speed performance, a result which has also been demonstrated in 400m
326 runners.¹⁶ Furthermore, the endurance athletes in this cohort possessed the CT and CC
327 genotype respectively, both of which might be considered slightly unfavourable for elite
328 endurance performance.¹⁷ This relationship, however, appears complex and poorly
329 understood; whilst some studies suggest an association between the *ACTN3* T allele and elite
330 endurance status², others do not.¹⁹

331

332 The genotype results for *ACE* were similarly heterogenous (data not shown). For this
333 genetic variant, the D allele is considered favourable for elite speed-power athlete status,^{17,18}
334 with the I allele favourable for elite endurance athlete status.¹⁷ Within our speed-power
335 cohort, two athletes had the ID genotype, and one the II genotype; neither is considered
336 optimal for elite speed performance. Conversely, both endurance athletes had the favourable
337 II genotype.

338

339 Non-athletic controls exhibited extensive similarities in polygenic profiles, with a
340 minimal spread of results across individuals. This similarity in polygenic profiles in non-
341 athletes has previously been reported with a lower number of generic variants for both
342 endurance⁴ and strength/power⁵ phenotypes. Within this case study, none of the elite athletes
343 were significant outliers in terms of TGS%, demonstrating that, for the polymorphisms
344 tested, genetic information is not sufficient to discriminate between elite athletes and non-
345 athletic controls.

346

347 **Would genetic testing have helped identify these athletes at a young age?**

348 Based on these results, it seems unlikely that genetic testing of these athletes during
349 their teenage years would have correctly identified them as potential future elite athletes
350 relative to a group of non-athletes. In fact, it's unlikely that this information would have
351 proved more useful than traditional talent identification methods. Participant A, for example,
352 was English Schools 400m Champion at age 16. Participant B is the British under-20 Long
353 Jump record holder and former European under-20 Champion. Participant C won multiple
354 national age group titles at under-15 and under-17, and the European under-20
355 Championships. Participant D won multiple junior national titles, and Participant E also won
356 national age-group championships. Consequently, given the failure of genetic information to
357 provide insights over and above that provided by inspecting results and observing
358 performances, the practical utility of such tests for the specific purpose of talent identification
359 is not supported by these case study results. In addition, the utilisation of genetic testing in
360 under-18s is ethically troubling, with a number of key researchers recommending against
361 such practice.^{3,20,21}

362

363 **Limitations**

364 There are some limitations to the present study that must be considered when
365 interpreting the results. Firstly, we were unable to collect data on mitochondrial DNA
366 (mtDNA). Mitochondrial haplotypes have been associated with elite athlete status, with
367 different variations conferring an advantage or disadvantage in achieving elite athlete status
368 for both speed-power and endurance athletes.^{8,22-24} Furthermore, we were unable to collect
369 genotype data for a small number of polymorphisms, due to a lack of coverage on the testing
370 array. There is the potential that the athletes in this study may have held favorable versions of
371 these variants, which would have increased their scores. Nevertheless, even given these
372 limitations, the genotype panel created for use in this study represents the most
373 comprehensive gene score to appear in the published literature with regards to elite athlete
374 status. Furthermore, we utilised an unweighted TGS, with each variant having a score of 0, 1,
375 or 2 depending on genotype. A weighted TGS, with genetic variants with demonstrably larger
376 effect sizes getting a greater score, may have proved more accurate. However, at present,
377 very few genetic variants associated with elite athlete status have been adequately replicated,
378 making the development of such a weighted, multi-variant TGS difficult to achieve.

379

380 In addition, the comparison population utilised within this study was an anonymous
381 group of 503 European Caucasians. One issue with using such a group is that the identities of
382 the participants is unknown; there is the possibility that this group was comprised of a large
383 number of elite athletes, which would have skewed the results, although this is very unlikely.
384 Finally, the sample sized utilised within this study is extremely limited, with further research
385 with larger numbers of athletes required.

386

387 **Practical Applications**

388

389 It seems clear that, at present, genetic testing cannot adequately discriminate between
390 elite athletes and non-athletes. In the current study, the TGS scores of five elite athletes did
391 not deviate substantially from average population scores, nor did they reach the thresholds
392 typically seen in elite athletes from other published TGS-elite athlete status associations,^{6,7}
393 although the number of genetic variants used within these earlier studies was very small.
394 Indeed, within this present cohort, and utilising a larger-scale TGS, all three of the elite
395 power athletes had a higher endurance score than both the middle-distance and long-distance

396 runners. As a result, it appears that current commercially available genetic tests purporting to
397 assist in the talent identification process have minimal utility,²¹ and should not be used.³
398

399 Athletic success is predicated on a wide variety of capacities. In the future, as a
400 greater number of genetic variants associated with elite athlete status are identified, especially
401 in areas involved in the psychological,^{25,26} anatomical,²⁷ and skill acquisition²⁸ aspects
402 associated with elite athlete status, it is feasible that the predictive ability of future TGSs may
403 improve. Such improvements could be further facilitated by the use of weighted algorithms,
404 where genetic variants with relatively larger effect sizes achieve a higher relative score
405 compared to variants with a smaller effect size. However, at present, and as clearly illustrated
406 by this case study involving highly elite athletes, the similarity of polygenic profiles within
407 populations limits the capacity of genetic information to adequately discriminate between the
408 general population and high performing athletes. For further insights into the limitations of
409 genetic testing for talent identification, interested readers are directed to reviews by Webborn
410 and colleagues³ and Pickering et al.²¹
411

412 **Conclusion**

413

414 The results of this study suggest that, at present, the ability to utilise genetic
415 information to identify talented performers holds limited predictive utility. The reasons for
416 this are potentially varied, but include a limited understanding of the genetic variants that
417 predispose to elite performance, the importance of non-genetic factors in the talent
418 development process, and a similarity of polygenic profiles amongst athletes and controls.
419

420 **Footnotes**

421

422 **Supplementary files:** S1 – List of SNPs included within the TGS utilised within this study.
423
424

425 **Funding:** Genetic testing for this case study was provided free of charge by DNAFit Life
426 Sciences, a genetic testing company.
427

428 **Competing interests:** CP is a former employee of DNAFit Life Sciences, a genetic testing
429 company. He received no payment for carrying out this work, which was undertaken as part
430 of his doctoral studies. JK has no competing interests relevant to the content of this article to
431 declare. The results of the current study do not constitute endorsement of the product by the
432 authors or the journal.
433

434 **Data availability:** Athlete genotype data, other than that reported here, cannot be shared due
435 to the terms of the ethics approval. Genotypes of the non-athletic controls are publicly
436 available.
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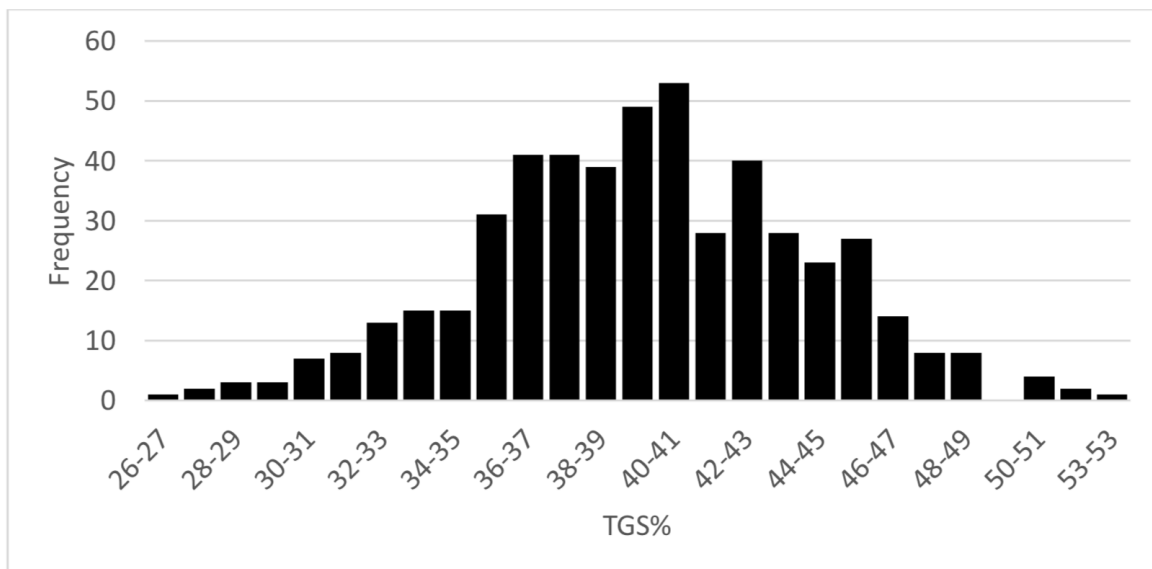
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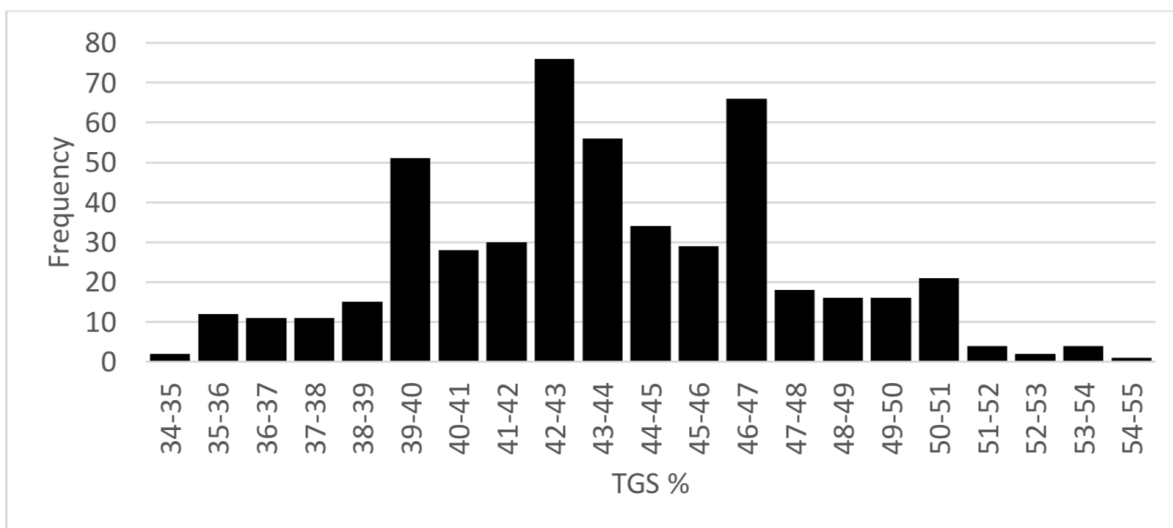
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545 **Figure Captions**
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549 **Fig. 1** Frequency distribution of power TGS% for non-athletic controls
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553 **Fig. 2** Frequency distribution of endurance TGS% for non-athletic controls

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Participant	A	B	C	D	E	European Average
Speed TGS	44.8	43.8	42.7	37.5	37.5	39.4
Endurance TGS	46.9	47.7	43.8	42.2	39.8	43.8

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567 Table 1 – Comparison of athletes’ scores in both the speed and endurance TGS utilised
568 within this study, against the European Average score.
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Participant	A	B	C	D	E	European Average	Ruiz Endurance	Ruiz Power
Ruiz Power TGS⁷	66.7	66.7	50	50	58.3	62.5	60	70
Ruiz Endurance TGS⁶	57.1	42.9	57.1	64.3	71.4	60.7	70.2	

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Table 2 – Overview of the athletes’ scores on previously published research by Ruiz and colleagues^{6,7}.