RESEARCH ARTICLE

Heritability of proprioceptive senses

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1Ersoyphysiology Research Laboratory, Department of Sport Medicine and Biology of Physical Activity, National and Kapodistrian University of Athens, Athens, Greece; 2School of Medicine, National and Kapodistrian University of Athens, Athens, Greece; 3School of Medicine, University of Crete, Heraklion, Greece; and 4Human Motor Control and Neuroplasticity Laboratory, Department of Neurology, University of Leipzig, Leipzig, Germany

Submitted 12 June 2017; accepted in final form 5 March 2018

Missitzi J, Geladas N, Misitzi A, Misitzis L, Classen J, Klissouras V. Heritability of proprioceptive senses. J Appl Physiol 125: 972–982, 2018. First published March 8, 2018; doi:10.1152/japplphysiol.00544.2017.—Heritability studies using the twin model have provided the basis to disentangle genetic and environmental factors that contribute to several complex human traits. However, the relative importance of these factors to individual differences in proprioception is largely unknown despite the fact that proprioceptive senses are of great importance, allowing us to respond to stimuli stemming from the space around us and react to altering circumstances. Hence, a total of 44 healthy male twins (11 MZ and 11 DZ pairs), 19–28 yr old, were examined for movement, position, and force sense at the elbow joint, and their heritability estimates were computed. Results showed that genetic factors explained 72 and 76% of the total variance of movement sense at the start and the end of the movement, respectively, 2) 60 to 77% of the total variance of position sense, depending on the angle of elbow flexion and whether forearm positioning was active or passive, and 3) 73 and 70% of the total variance of the force sense at 90 and 60° of elbow flexion, respectively. It is concluded that proprioception assessed by these conscious sensations is to a substantial degree genetically dependent, with heritability indexes ranging from 0.60 to 0.77, depending on the task.

NEW & NOTEWORTHY Proprioceptive acuity varies among people, but it is not known how much of this variability is due to differences in their genes. This study is the first to report that proprioception, expressed as movement sense, position sense, and force sense, is substantially heritable, and it is conceivable that this may have implications for motor learning and control, neural development, and neurorehabilitation.

INTRODUCTION

The information collected through proprioceptors is of great importance. It leads to the creation of an internal representation of the external world, of the body’s state, and of motor activity, which is used for acquisition and execution of motor skills (39). The central nervous system (CNS) is thus given the opportunity to control motor activity by programming, adjusting, and confirming the quality of movement in terms of accuracy and economy.

Recent studies in animals have provided evidence that individual differences in some proteins in peripheral receptors may explain the individual differences observed in tests of proprioception (25, 70, 81), but genetic polymorphisms are not established for the genes coding the proprioception-related channels, and most likely there are many more relevant genes.

In humans, several studies on proprioceptive acuity have shown notable interindividual variability after intraindividual variability was taken into account (12, 31, 62). However, and despite the fact that proprioception is crucial for neuromuscular control and human performance (60), its heritability is largely unknown. Without assuming which genes are involved, a twin study design allows us to decipher the relative share of environmental and genetic factors in the variation observed in any phenotype, thus enhancing progress in the field (63). Previous twin studies of other neuromuscular phenotypes, such as muscle fiber distribution (42), neuromuscular coordination (51), intracortical inhibition and facilitation (59), plasticity of motor cortex (52), and motor control and learning (53), have shown a significant genetic influence.

A wealth of evidence exists pointing out that aging, cryotherapy, and exercise-induced fatigue have deleterious effects on joint proprioception, whereas moderate exercise or warmup exercise enhances proprioceptive acuity. Additionally, it seems that regular physical activity plays an undeniable role in the preservation of proprioceptive function (64), whereas in the fields of rehabilitation, proprioception training is considered a key source of feedback for promoting neural plasticity (18, 44). Furthermore, enhanced proprioceptive senses have been identified in athletes (4, 30, 47, 54), and tuned sensorimotor function has been reported in dancers (10), but it remains unknown whether intraindividual differences in these traits are the result of genetic differences or intensive training.

Therefore, the aim of this study was to assess the relative contribution of genetic and environmental factors to the variation observed in proprioception, where little is known yet on its molecular basis, by selecting a homogeneous sample of monozygotic (MZ) and dizygotic (DZ) twins and comparing the intrapair differences between the two types of twins. We have restricted our study to the conscious sensation of the limb position and movement and the sense of force. Studying the heritability of these senses may reveal the relative importance of endowment and may have implications for the enhancement.
of proprioceptive acuity in various forms of physical performance as well as in neurorehabilitation.

METHODS

A total of 44 healthy male twins (11 MZ and 11 DZ pairs), 19–28 yr old (23.5 ± 3.5 and 24.4 ± 2.6 yr, respectively; means ± SD), participated in the experiments, which were approved by the Ethics Review Board at the Department of Sport Medicine and Biology of Physical Activity, National and Kapodistrian University of Athens. The sample was derived from the metropolitan area of Athens, Greece. Because environmental comparability is a fundamental assumption made in the twin model, special attention was given to a large variety of potential confounding factors to ensure that environmental influences were comparable in both types of twins. For this purpose, a detailed questionnaire was administered regarding physical activity during work hours, sports participation, some other lifetime occupational and leisure time physical activities, loading of the upper extremity, and health condition, with five response options, ranging from “almost never” to “exercise very much” (5). This of course does not mean that physical activity and lifestyle were constant but varied approximately in the same direction and to the same degree for all twins. All volunteers were right-handed, except for two twin pairs, who were left-handed according to the Oldfield handedness inventory (55). Exclusion criteria included a history of upper extremity orthopedic injury or pathology, cardiovascular or coronary disease, current medication affecting neuromuscular coordination, or disease affecting the sensory motor, vestibular, and ocular system. Twins were fully informed about the protocol before giving their written consent, and the protocol complied with the Declaration of Helsinki.

Zygosity was assessed through direct observation of relevant morphological characteristics and physical similarities, as well as the testimony of the obstetrical archives, and confirmed by serological examination of genetic markers (specifically ABO, MN, CDE, P, Rh, Kell, Duffy, Kidd, Lewis, and Lutheran) in all twins. Discordance for a single antiserum was regarded as sufficient evidence of dizygosity (52).

Testing procedures. Measurements were performed in a quiet room at 22–23°C. Testing was conducted at the same time of day under similar environmental conditions to reduce the effect of diurnal variations. None of the twins performed any vigorous activity or consumed alcohol or caffeine during the 24 h before the tests, and all were informed of the importance of having the same adequate sleep during the night preceding the tests. Before the actual experiments, all twins were familiarized with understanding the experimental procedures.

Test/retest reliability for the test protocols was acceptable, since intraclass coefficients of 0.85, 0.78, and 0.81 were obtained for the thresholds to detect passive movement, joint position test, and force reproduction, respectively. Furthermore, the optimal number of trials needed to obtain stable results for each test was established. Significant differences in the mean values between three and six trials were found only in the passive movement threshold.

Movement sense. The threshold for the perception of the start and the end of the movement was used to assess movement sense (1, 57). Subjects were made to sit on the chair of the dynamometer Biodex System 3 (Biodex Medical Systems, New York, NY), with their dominant upper extremity placed in the arm of the testing apparatus. Trunk and pelvic stabilization secured participants to the chair to decrease extraneous movement from the scapula and trunk during the experimental procedures. The center of rotation of the elbow was carefully positioned to coincide with the center of rotation of the dynamometer arm. The forearm was strapped securely to the dynamometer arm, the speed and direction of which was controlled by the dynamometers’ software. Hand placement was on the hand grip connected to the lever arm of the Biodex system 3. To minimize cutaneous sensation, the extremity to be tested was covered by an air splint from the distal forearm to the hand with an internal pressure of 4 kPa (30 mmHg; VainoAeroCath, System 30AG Diapharm). Consequently, this resulted in the equal distribution of the cutaneous input to the limb for both brothers in a pair. Subjects were blindfolded, and headphones were applied to eliminate visual and auditory cues, respectively. Each test started with the shoulder fixed at 40° of flexion and the elbow at 70° of flexion. To avoid a small vibration that occurs with the starting operation of the machine, the test began randomly 5–20 s after the dynamometer’s start. The passive movement began after the subject was informed (by tapping on the upper leg) that the test was about to begin, with a velocity of 0.25°/s. At the perception of the movement, notified by the subjects with a word signal (“now”), a button was pressed by the examiner.

The thresholds for the perception of the start of the movement (TPSM) and the end of the movement were determined in degrees of elbow flexion, as previously described (57), by using the formula: TPSM (°) = t(s) × v (°/s), where, t(s) is the time elapsed from the start of the movement to the examiner’s pressing the button for TPSM and from the end of the movement to the examiner’s pressing the button for the threshold for the end of movement, where v (°/s) is the actual angular velocity for both. Each test, perception of the start and end of the movement, consisted of six trials, and values obtained in these six trials were averaged. Before the actual experiments, subjects were familiarized with the procedure.

Position sense. Position sense was examined by the active reproduction of passive positioning as well as an active reproduction of active positioning. Twins were positioned, as previously described for the movement sense tests, to the Biodex system 3. During the active reproduction of passive positioning, the twins attempted to reproduce actively the static angle at which they had passively placed their elbow joint of the same limb (11, 45, 71, 72). The internal electrogoniometer of the isokinetic dynamometer was used to define the anatomical zero of the elbow joint, and 10° of flexion was determined as the beginning reference angle. After three practice attempts, subjects kept their upper extremities relaxed and the attached lever of the isokinetic dynamometer passively bent the elbow joint in one of the three preset angles of 30, 60, and 90°, with a constant angular velocity of 5°/s (9). During the test, subjects were instructed to relax, with their elbow passively rotated to the test angle. Subjects were given 10 s to concentrate on the test angle before their elbow was passively returned to the reference angle. At this point, the participants, after 5 s of rest, were instructed actively to reproduce the test angle. To control for the possible use of time and displacement from the starting position, elbow joint returned to different angles between 10 and 15°. Three trials were made, with 30-s intervals between each trial and 1 min for each angle for both passive and active positioning tests. Data of the position matching errors obtained from the target deviation, as absolute errors, were averaged across the three trials for each angle separately for all MZ and DZ twin pairs. Counterbalancing of the three testing angles was used to eliminate any ordering effect but was always the same for each member of a given twin pair. A headset and blindfold were fitted to eliminate visual and auditory cues. Active reproduction of active positioning was evaluated similarly, but twins actively placed their limb to the test angle.

Force sense. The maximal voluntary contraction was measured for each subject. Subjects were seated on the chair of the dynamometer Biodex System 3 (Biodex Medical Systems), with their dominant upper extremities placed in the arm of the testing apparatus and their elbows at 90° of flexion. Once subjects’ forearms were secured they were asked to produce a maximum contraction of the elbow flexors without using back or shoulder muscles (76). Three maximal voluntary contractions (MVCs) of 5-s duration were carried out at 1-min intervals. The best of the three trials was included in the statistical analysis. The maximal voluntary contraction was used to calculate 30% MVC, which was displayed on the dynamometer screen as a line visible to the subject. The twins were then asked to generate an isometric torque with their dominant hand sufficient to reach the target.
on the screen. In this case, under visual control, data recording showed that the arm always reliably generated the target torque. Once subjects reached the target and maintained it for 2 s, they relaxed for 5 s before they tried to repeat the reference torque without vision. They were asked to maintain the matching torque for 3 s. This procedure was performed three times and at two different angles of 90° and 60°, giving a total of 12 trials (6 with visual control, 6 without). The inaccuracy was determined as the absolute difference between the force that was produced with visual feedback and the reproductive force with visual occlusion. Torque values were averaged over the last second of each match. Before commencing the experiment, subjects became familiar with the procedure, having visual feedback for 10 trials for both testing angles.

**Heritability estimates.** Heritability (h²) is defined as the proportion of phenotypical variance attributable to observed individual differences and was estimated on the basis of the intrapair difference between MZ and DZ twins. MZ twins have identical heredity, whereas DZ twins, like ordinary siblings, share half of their segregating genes. In this way, it is possible to separate the relative contribution of genotype and environment for the observed differences in proprioceptive senses, namely movement, position, and force sense. Data obtained were analyzed using the single-factor analysis of variance (ANOVA) for each variable to determine the significance of the differences between the mean monozygotic and dizygotic intrapair variance, taking into consideration genetic type and pair factor. The variance ratio (F), F = MwDZ/MwMZ with the respective df, nMZ = number of MZ pairs and nDZ = number of DZ pairs, derived from the single-factor ANOVA, determined whether further analysis was necessary. The following Clark equation based on intrapair variance was used to estimate heritability: h² = (s² DZ - s² MZ)/s² DZ) × 100, where s² DZ is the variance of intrapair differences in DZ twins and s² MZ is the variance of intrapair differences in MZ twins. The computation of h² was carried out, provided that the difference in genetic variance between the twin types was significant and the difference between means and total variance of both types of twins was nonsignificant (15). Therefore, it is assured that the parameters assessed are independent of the twin type. Statistical analyses were performed using SPSS (12.0 for Windows; SPSS, Chicago, IL) and statistical functions built in Excel 2002 (Microsoft). Since our total sample size was n = 44, with type I error probability at 0.05 and the smallest expected difference between MZ and DZ set at h² = 0.50, a power level of ≥95% is secured in this analysis (19).

**RESULTS**

**Characteristics of the subjects.** No significant differences in age, weight, or height were seen between MZ and DZ twins (23.5 ± 3.5 and 24.4 ± 2.6 yr, 76.7 ± 11.1 and 75.7 ± 8.2 kg, and 177.5 ± 7.1 and 179.8 ± 5.2 cm for MZ and DZ, respectively). Intrapair differences in weight (2.9 ± 2.5 kg) and

![Fig. 1. Intrapair differences (means ± SD) for detection of the start and end of passive movement in monozygotic (MZ) and dizygotic (DZ) twins, with movement velocity of 0.25°/s (paired t-test; **P < 0.01).](image-url)

height (0.7 ± 0.6 cm) for MZ twins were insignificant, as also evidenced by the correlation coefficient (r = 0.99 and 0.96 for height and weight, respectively). On the contrary, there were larger intrapair differences in DZ twins in both weight and height (6.2 ± 3.9 kg and 3.2 ± 2.7 cm), and correlation coefficients were r = 0.66 and 0.72, respectively. Physical activity was similar between zygosity groups, as seen by mean values and standard deviation in MZ (8.5 ± 2.1) and DZ (8.3 ± 2.9), and intrapair differences were insignificant (1.2 ± 1.7 and 2.9 ± 4.0). Two pairs were eventually excluded from the sample, the first because of injuries suffered by one of the two brothers in the upper extremity and the second because of unequal environmental influences since only one of the two trained for motor cross. The number of subjects included was 44 twins throughout the study (11 DZ and 11 MZ pairs of twins pairs). This number of subjects is depicted in all figures and presented in recorded parameters. However, in some figures the number of dots appear to correspond to fewer than 22 pairs due to the fact that one set of values of a pair of twins coincides with another or two other sets of values representing other twins.

![Fig. 2. Individual values of deviation of the successful detection of movement in monozygotic (MZ) and dizygotic (DZ) twin pairs: start of movement (top) and end of movement (bottom).](image-url)
Heritability of movement sense. The mean detection thresholds for the start and the end of the movement were 1.06 ± 0.29 and 1.08 ± 0.30, respectively, in MZ twins, and 1.05 ± 0.28 and 1.06 ± 0.27 in DZ twins. The intrapair difference for MZ twins for the detection of the start of the movement was 0.13 ± 0.06 and 0.28 ± 0.08 for DZ twins (paired t-test; P < 0.01; Fig. 1). The intrapair correlation was significant for monozygotic (r = 0.88, P = 0.0004) and not significant for dizygotic twins (r = 0.47, P = 0.14). Likewise, intrapair differences for the perception of the end of the movement were 0.12 ± 0.07 in MZ and 0.28 ± 0.07 in DZ (Fig. 1). There was a high and significant intrapair correlation (r = 0.89, P = 0.0002) in MZ twins and a no significant intrapair correlation (r = 0.40, P = 0.22) in DZ twins. The difference for the latter case is shown in Fig. 2, where the values for MZ twins are closer to the identity line (Fig. 2, middle line in both graphs), whereas for DZ twins are more scattered. The area between the top and bottom diagonal lines in both graphs of Fig. 2 represents the limits of the deviation of the successful reproduction for the MZ twins. Statistical analysis of the data revealed that the differences between means and total variance of both types of twins were not significant, whereas the genetic variance between the twin types was significant (F = 3.7 and 4.2, P = 0.008 and = 0.009; Table 1). Therefore, heritability (h²) estimates were carried out and revealed that genetic factors explained 72 and 76% of the total variance of movement sense for the start and the end of the movement, respectively.

Heritability of position sense. Forearm position sense was examined both by active reproduction of passive positioning along with an active reproduction of active positioning with the

Table 1. Testing statistical hypotheses for the derivation of h² in movement sense

<table>
<thead>
<tr>
<th>Hypotheses</th>
<th>Start</th>
<th>End</th>
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<tbody>
<tr>
<td>t'-Test</td>
<td>0.03 (0.6, t &lt; t₀)</td>
<td>0.07 (0.6, t &lt; t₀)</td>
</tr>
<tr>
<td>F'-test</td>
<td>1.09 (11.3 and 16.2, F' &lt; f₀)</td>
<td>1.23 (12.3 and 17.8, F' &lt; f₀)</td>
</tr>
<tr>
<td>F-test</td>
<td>3.7 (P = 0.008)</td>
<td>4.2 (P = 0.009)</td>
</tr>
<tr>
<td>h²</td>
<td>0.72</td>
<td>0.76</td>
</tr>
</tbody>
</table>

h², Heritability. t'-Test signifies the difference between the means of the twin pairs, F'-test the difference in total variance of both types of twins, and F-test the difference in genetic variance between the twin types; ln t₀ and f₀, the subscript denotes the critical value.

Fig. 3. Intrapair differences (means ± SD) for deviation of the successful active reproduction of passive positioning at 30, 60, and 90° of flexion in monozygotic (MZ) and dizygotic (DZ) twin pairs (paired t-test; **P < 0.01, ***P < 0.001).

Fig. 4. Individual values of deviation of the successful active reproduction of passive positioning at 30 (A), 60 (B) and 90° (C) of flexion. Individual values in A are identical for 2 different dizygotic (DZ) pairs (4.3/2.7) as well as for 1 monozygotic (MZ) and 1 DZ pair (5.7/4.0). Individual values in C were identical for 2 different DZ pairs (4.0/2.7) as well as for 2 cases of 1 MZ and 1 DZ pair (1.3/2.3 and 5.3/3.3).
The computation of heritability ($h^2$) was carried out, and it was significant between the twin types (Table 2). Consequently, statistical analysis of the data showed that the differences in the pair values for MZ and DZ twins are more scattered. After testing the statistical hypotheses for matching accuracy of the entire sample of 44 twins at 30, 60, and 90° of elbow flexion were 0.87 ± 0.55, 0.69 ± 0.40, and 0.75 ± 0.54 in MZ twins and 1.58 ± 0.40, 1.53 ± 0.71, and 1.49 ± 0.38 in DZ twins, for 30, 60, and 90°, respectively (Fig. 3). The similarity in MZ twins is also apparent from the respective intrapair correlations, which were higher and significant for monozygotic and not significant for dizygotic twins ($r = 0.74$, $P = 0.009$ and $r = 0.32$, $P = 0.34$ for 30°, $r = 0.31$, $P = 0.35$ for 60°, $r = 0.80$, $P = 0.003$, and $r = 0.36$, $P = 0.28$ for 90°). The difference in the pair values for MZ and DZ twins is shown in a plot of the X-Y coordinates system (Fig. 4). Statistical analysis of the data showed that the differences between means and total variance of both types of twins were not significant, whereas the genetic variance between the twin types was significant (Table 2). Consequently, computation of heritability ($h^2$) was carried out, and it was found that genetic factors explained 62, 77, and 67% of the total variance for the active reproduction of passive positioning at 30, 60, and 90° of flexion.

**Active reproduction of passive positioning.** The means and standard deviation for matching accuracy for the entire sample of 44 twins at 30, 60, and 90° of elbow flexion were 3.45 ± 1.28, 3.16 ± 1.32, and 3.05 ± 1.28, respectively. Analysis of variance did not show any statistical difference in the matching accuracy between the tree angles. Average intrapair differences were $0.87 \pm 0.55$, $0.69 \pm 0.40$, and $0.75 \pm 0.54$ in MZ twins and $1.58 \pm 0.40$, $1.53 \pm 0.71$, and $1.49 \pm 0.38$ in DZ twins, for 30, 60, and 90°, respectively (Fig. 3). The similarity in MZ twins is also apparent from the respective intrapair correlations, which were higher and significant for monozygotic and not significant for dizygotic twins ($r = 0.74$, $P = 0.009$ and $r = 0.32$, $P = 0.34$ for 30°, $r = 0.31$, $P = 0.35$ for 60°, $r = 0.80$, $P = 0.003$, and $r = 0.36$, $P = 0.28$ for 90°). The difference in the pair values for MZ and DZ twins is shown in a plot of the X-Y coordinates system (Fig. 4). Statistical analysis of the data showed that the differences between means and total variance of both types of twins were not significant, whereas the genetic variance between the twin types was significant (Table 2). Consequently, computation of heritability ($h^2$) was carried out, and it was found that genetic factors explained 62, 77, and 67% of the total variance for the active reproduction of passive positioning at 30, 60, and 90° of flexion.

**Active reproduction of active positioning.** Means and standard deviation for matching accuracy for the entire sample of 44 twins at 30, 60, and 90° of elbow flexor were 3.06 ± 0.94, 2.95 ± 1.14, and 2.76 ± 1.05, respectively. Analysis of variance did not show any statistical difference in the matching accuracy between the tree angles. Average intrapair differences were $0.70 \pm 0.31$, $0.69 \pm 0.40$, and $0.75 \pm 0.54$ in MZ twins and $1.13 \pm 0.46$, $1.36 \pm 0.44$, and $1.33 \pm 0.30$ in DZ twins for 30, 60, and 90°, respectively (Fig. 5). Respective intrapair correlations were higher and significant for monozygotic and not significant for dizygotic twins ($r = 0.81$, $P = 0.002$ and $r = 0.28$, $P = 0.40$ for 30°; $r = 0.80$, $P = 0.003$ and $r = 0.28$, $P = 0.40$ for 60°; $r = 0.73$, $P = 0.01$ and $r = 0.31$, $P = 0.35$ for 90°). These differences are shown in Fig. 6, where the intrapair values for monozygotic are closer and for dizygotic twins are more scattered. After testing the statistical hypotheses of genetic variance (Table 3), we computed heritability ($h^2$) estimates for the three different elbow positions of 30, 60, and 90° of flexion, and it was found that genetic factors explained 60, 71, and 77% of the total variance, respectively.

**Comparison between passive and active positioning.** Deviation for matching accuracy of the entire sample of 44 twins at the predetermined positions of 30, 60, and 90° of elbow flexion at active reproduction of active positioning was smaller than the one that appeared at active reproduction of passive positioning, whereas the total deviation for all three positions between active and passive positioning presented a statistically significant difference ($2.89 \pm 1.04$ and $3.23 \pm 1.29$, $P = 0.05$). The bigger deviation was presented at 30° and the smaller at 90° in both active and passive positioning, but without a statistically significant difference.

**Heritability of force sense.** Reference torques were generated without any difficulty, when it was done under visual control. Imprecision was determined as the absolute difference between the tension produced by visual feedback and the level of tension developed without visual aid. The average inaccuracy for the three efforts performed in the reproduction of the tension for the entire sample at 90° and 60° was $2.22 \pm 1.28$ and $2.41 \pm 1.31$, respectively. The average reproduction tension was better at 90°, but without a statistically significant difference. Subjects varied in their ability to reproduce the tension without visual feedback, but they presented consistency on the error’s extent and direction. Average intrapair differences between the two types of twins were almost double. For MZ twins, intrapair difference was found to be $0.78 \pm 0.66$ and $0.68 \pm 0.52$, and for DZ twins intrapair difference was $1.55 \pm 0.97$ and $1.73 \pm 0.93$, for 90 and 60° of elbow flexion, respectively (Fig. 7). The respective intrapair correlation, which was significant for MZ and not significant for DZ twins, was $r = 0.72$, $P = 0.01$ and $r = 0.31$, $P = 0.35$ for 90°, and $r = 0.76$, $P = 0.007$ and $r = 0.30$, $P = 0.37$ for 60°. The difference in the pair values for MZ and DZ twins is shown in Fig. 8, where the values for monozygotic are closer to the line of identity, and for dizygotic twins they are more dispersed. Statistical analysis of the data showed that the differences between means and total variance of both types of twins were

<table>
<thead>
<tr>
<th>Hypotheses</th>
<th>30</th>
<th>60</th>
<th>90</th>
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<tbody>
<tr>
<td>$t^r$-Test</td>
<td>0.30 (115 $r &lt; t_c$)</td>
<td>0.10 (127 $r &lt; t_c$)</td>
<td>0.19 (128, $t &lt; t_c$)</td>
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<tr>
<td>$F$-test</td>
<td>1.18 (14 and 19.5 $F^r &lt; f_c$)</td>
<td>1.25 (123 and 19.1, $F^r &lt; f_c$)</td>
<td>1.24 (13.15 and 17.8, $F^r &lt; f_c$)</td>
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<tr>
<td>$F$-test</td>
<td>2.63 ($P = 0.026$)</td>
<td>4.52 ($P = 0.002$)</td>
<td>3.02 ($P = 0.017$)</td>
</tr>
<tr>
<td>$h^2$</td>
<td>0.62</td>
<td>0.77</td>
<td>0.67</td>
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$h^2$, Heritability. $t^r$-Test signifies the difference between the mean of the twin pairs, $F$-test the difference in total variance of both types of twins, and $F$-test the difference in genetic variance between the twin types. In $t_c$ and $f_c$, the subscript denotes the critical value.

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**Table 2. Testing statistical hypotheses for the derivation of $h^2$ in position sense**

<table>
<thead>
<tr>
<th></th>
<th>Passive Reproduction of Active Positioning, °</th>
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<tr>
<td>30</td>
<td>0.30 (115 $r &lt; t_c$)</td>
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<tr>
<td>60</td>
<td>2.63 ($P = 0.026$)</td>
</tr>
<tr>
<td>90</td>
<td>3.02 ($P = 0.017$)</td>
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**Fig. 5. Intrapair differences (means ± SD) for deviation of the successful active reproduction of active positioning at 30, 60, and 90° of elbow flexion in monozygotic (MZ) and dizygotic (DZ) twin pairs (paired $t$-test; *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$).**
not significant, but the genetic variance between the twin types was significant \( P < 0.05 \) (Table 4). Therefore, heritability estimates revealed that genetic factors explained 73 and 70% of the total variance in the reproduction of the tension for 90 and 60°, respectively, of elbow flexion.

**DISCUSSION**

Our study appears to be the first to investigate the extent to which individual variation in proprioception is influenced by genetic factors. The comparison between MZ and DZ twins demonstrated that proprioception assessed by position, movement, and force sense is to a substantial degree genetically dependent, with heritability indexes ranging from 0.60 to 0.77, depending on the task. It should be noted, however, that a highly heritable attribute does not mean that it is predetermined and that the environment has no effect or influence; it simply indicates that observed individual differences in these attributes are due to genetic differences and are highly predictable. In other words, what is really meant is that after individuals have reached their upper limits on their proprioceptive acuity, with appropriate training, there will still be a wide interindividual variability, which is genetic in origin.

Notwithstanding that the sample size was relatively small, it allowed inferential statistical analysis, and a power level of \( 95\% \) was secured (19). Furthermore, the computation of \( h^2 \) was carried out, provided that there was a significant difference in genetic variance between the twin types as well as a homogeneity of the sample (15). Furthermore, a better control of environmental influences for all twins under study was warranted, considering that this is the most fundamental assumption of the twin model, which is poorly adhered to in many twin studies with a large sample size.

Considerable progress has been made on the identification of genes regulating the formation of neuromuscular synapses and muscle spindles as well as genes required for normal mechanoreceptor functioning and proprioceptive control (3, 6, 16, 22, 35, 36, 56, 58, 79, 83). Epithelial sodium channels proteins are expressed in rat muscle spindles (70). Mechanically activated nonselective cation channel Piezo2 is expressed in sensory endings of proprioceptors innervating muscle spindles and Golgi tendon organs in mice (81). Because the loss of this channel results in uncoordination of body movements and limb positions, Piezo2 may emerge as the major mechanotransducer of proprioceptors. This conclusion is supported by findings showing that deficits in balance and coordination were caused by the selective deletion of the channel in a unique population of purely proprioceptive neurons in the brainstem, which fully depended on Piezo 2 (25). Although these new studies give valuable insight into how proprioception in mammals may be found in individual proteins, it should be noted that these genes and their polymorphisms are only one example of genetic susceptibility. Polymorphisms of other genes whose product is involved in proprioception are of similar or even greater relevance (35, 46). Hence, because proprioception presents a high heritability, more studies are needed to determine which gene polymorphisms or a combination thereof may underline the difference found between MZ and DZ twins in this study.

The role of twin studies in understanding the difference between responders and nonresponders to standardized behavioral interventions is very important and a noted contribution to

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**Fig. 6.** Individual values of deviation of the successful active reproduction of active positioning at 30 (A), 60 (B), and 90° (C) of flexion. Individual values in A were identical for 1 monozygotic (MZ) and 1 dizygotic (DZ) pair (3.3/2.3). Individual values in B were identical for 2 different MZ pairs (3.0/2.7) as well as for 1 MZ and 1 DZ pair (4.0/3.0). Individual values in C were identical for 2 different MZ pairs (3.0/2.7).
elbow flexion in monozygotic (MZ) and dizygotic (DZ) twin pairs (paired Fig. 7). Intrapair differences (means for the performance of functional tasks, are all substantially well as the motor responses (53) resulting in muscle activation of the motor cortex (52) that may alter movement strategies, as centers, the central command generators (51), and the plasticity system and signals related to motor commands (current study), its transmission via afferent pathways to the central nervous (37, 73).

Accordingly, it can be argued that individual differences in the sensorimotor system, which involves a loop of the acquisition of a sensory stimulus, its conversion to a neural signal, its transmission via afferent pathways to the central nervous system and signals related to motor commands (current study), the processing and integration of the signal by the various centers, the central command generators (51), and the plasticity of the motor cortex (52) that may alter movement strategies, as well as the motor responses (53) resulting in muscle activation for the performance of functional tasks, are all substantially under genetic influence.

Heritability of movement sense. The threshold for the perception of the start of the passive movement is a useful method to access proprioception (61, 65, 66). A common finding of these studies is that the subject’s ability to detect movement without optico-acoustic feedback differs significantly (62). The magnitude of our reported thresholds is well in line with available threshold data obtained at the elbow and other joints (1, 57, 72). However, Khabie et al. (41) has applied fourfold velocity and showed surprisingly significant higher movement threshold in comparison to the aforementioned studies.

It is largely agreed that muscle spindle primary endings are the major contributors to movement sense (28). Studies have shown that muscle spindles have preferred sensory directions, and weighing individual responses based on each spindle’s preferred direction results in a population code that accurately represents a limb’s movement direction (8, 38, 67). On the other hand, studies have also implicated a role of joint receptors (23, 49) and cutaneous receptors (17, 20) for the detection of passive movement. Furthermore, previous studies suggest that movements with a velocity of 1°/s trigger mainly joint mechanoreceptors and less participation of muscle spindles (29). Based on these observations, we could postulate that in the present study the heritability found for movement sense, using the detection of passive movement in elbow joint with a velocity of 0.25°/s and the absence of skin information, more likely reflects the contribution of joint and muscle spindle primary endings receptors, although the ratio of their participation and their interaction remains unknown. Therefore, the heritability index for movement sense may concern mainly the accumulative influence of these factors.

Table 3. Testing statistical hypotheses for the derivation of $h^2$ in position sense

<table>
<thead>
<tr>
<th>Hypotheses</th>
<th>30</th>
<th>60</th>
<th>90</th>
</tr>
</thead>
<tbody>
<tr>
<td>$t'$-Test</td>
<td>0.11 (10.4 $t' &lt; t_c$)</td>
<td>0.13 (9.3 $t' &lt; t_c$)</td>
<td>0.06 (5.9 $t' &lt; t_c$)</td>
</tr>
<tr>
<td>$F$-test</td>
<td>1.08 (14.04 and 20.3 $F' &lt; f_c$)</td>
<td>1.02 (13.5 and 19.7, $F' &lt; f_c$)</td>
<td>1.8 (13.2 and 18.4, $F' &lt; f_c$)</td>
</tr>
<tr>
<td>$F$-test</td>
<td>2.51 ($P = 0.029$)</td>
<td>3.55 ($P = 0.006$)</td>
<td>4.47 ($P = 0.002$)</td>
</tr>
<tr>
<td>$h^2$</td>
<td>0.60</td>
<td>0.71</td>
<td>0.77</td>
</tr>
</tbody>
</table>

$h^2$, Heritability. $t'$-Test signifies the difference between the means of the twin pairs, $F$-test the difference in total variance of both types of twins, and $F$-test the difference in genetic variance between the twin types. In $t_c$ and $f_c$, the subscript denotes the critical value.

Fig. 7. Intrapair differences (means ± SD) for deviation of the successful reproduction of 30% of maximal isometric contraction at 90° and 60° of elbow flexion in monozygotic (MZ) and dizygotic (DZ) twin pairs (paired $t$-test; **$P < 0.01$).

Fig. 8. Individual values of deviation of the successful reproduction of 30% of maximal isometric contraction at 90° of elbow flexion.
Heritability of position sense. Evaluating joint position sense involves active reproduction of a previously passive or active presented position. Passive movement is used to diminish the influence of the γ-motor system on muscle spindles, whereas active movements are more representative of human movements. Active and passive tests of joint position sense have not shown significant differences in the absolute errors of matching accuracy (11, 68). Earlier studies using similar methods report a mean deviation for matching the accuracy of 2.0 to 5.0 (2, 7, 11, 73). Deviations from the target in each of the three measured positions were found to be lower for the active reproduction rather than for the passive, without statistical significance. However, the comparison of the total testing angles (30, 60, and 90°) showed statistically significant lower deviation for the active reproduction. This could be explained by the fact that fusimotor neurons are coactivated during voluntary contractions, providing more accurate information. Furthermore, the smaller deviation at 90° of elbow flexion both in active and passive position reproduction could be attributed to the relatively greater contribution of joint receptors that fire mainly in extreme position.

Position reproduction was performed with a velocity of 5°/s for maximal muscle spindle activation and minimal joint afferent participation (43). The prevailing view is that in the absence of visual information, both the primary and secondary spindle afferents discharge for the position sense. Additional information could be gained from cutaneous and joint receptors (29, 78). Some spindles generate background activity at all muscle lengths, no matter how short the muscle; others fall silent at short lengths (32). Researchers also argue that muscle spindles discharge mainly until the limb reaches the target, whereas for the maintenance of the position, the demanding effort to keep the position against the gravity is of great importance, involves collylary discharges, and gives additional information concerning position sense (29, 48, 73, 75, 78, 80, 82). Thus, more accurate placement in active positioning may be achieved through combined information mainly from muscle spindles and from signals related to the sense of effort (29, 78). Although there is possibly different afferent participation in passive and active position tests, heritabilities were found to be quite similar in each test, showing a high heritability in each afferent component of proprioceptive information.

Heritability of force sense. The traditional view of the neural basis for the sense of muscle force is that it is generated at least in part within the brain (70, 73). However, recently, it has been proposed that force sensations do not arise entirely centrally and that there is a contribution from peripheral receptors within the contracting muscle (13, 69). Therefore, in this study, along with centrally generated motor command signals, afferent information is likely to play a major role.

Accuracy in torque reproduction without vision was diminished on an average of 3.5% when forces were expressed on the basis of maximal isometric contraction. Other studies are in agreement with our findings, regardless of the muscular group that performs the testing when the force reduction is expressed by the relative change in muscle length (27, 37). The ability to reproduce 30% of maximal isometric contraction in this study is possibly due in part on the discharge of the Ib afferents of tendon organs. During isometric contractions, tendon organ responses increase, whereas the sensitivity of spindle primaries diminishes (21). However, because Ib afferents are characterized by a gradual increase and decrease of the discharge rate, during mild increases and reductions of muscle force, reflecting the gradual recruitment of motor units, this raises the question of whether the tendon organs can themselves provide information on muscle strength. Several studies support the importance of cutaneous afferents. The absence of skin information has led to an overestimation of force amount (24, 37). The importance of afferent cutaneous information in the sense of force, potential genetic differences in this kind of information may explain in part the significant genetic effect found in this task. Therefore, in this study, the ability to reproduce a specific amount of force is more likely to occur due to the contribution of the accumulative information from tendon organs as well as from cutaneous and joint afferents, at least regarding the peripheral component of force sense.

Conclusions and Implications. Proprioceptive senses, namely movement, position, and force sense, are in substantial part genetically determined. Our findings, along with those demonstrating a major influence of genes on the plasticity of motor cortex (52), underline the importance of genetic contribution to physiological factors relevant to sensorimotor behavior.

Because the proprioceptive acuity is significantly associated with the performance level achieved by elite athletes, it was hypothesized that the amount of improvement in proprioceptive acuity associated with sport-specific training may be constrained by biologically determined factors (33). Our results strengthen this view, namely that athletes with superior performance may be born with enhanced proprioceptive abilities, which allows for better afferent information and thus programming of more accurate motor responses. This may have implications in both talent identification and coaching for attainment of elite sport performance (34, 74). Additionally, previous studies on use-dependent plasticity have demonstrated that proprioceptive feedback plays a critical role in the reorganization process and subsequent recovery of the neuromotor system. In the physical therapy and rehabilitation fields, much attention is focused on sensory feedback acuity, in particular proprioceptive acuity, in both the clinical practice and laboratory (18). The sense of proprioception is considered a key source of feedback for promoting neural plasticity. Our findings may be relevant to understanding why functional deficiencies and recovery outcomes differ widely between patients with identical peripheral injuries (40), possibly as a result of different expressions on both central motor plasticity (52), as well as differences in sensitivity of proprioceptive senses. The fact that heredity accounts for a substantial

### Table 4. Testing statistical hypotheses for the derivation of $h^2$ in force sense

<table>
<thead>
<tr>
<th>Hypotheses</th>
<th>Reproduction of 30% of Maximal Isometric Contraction, °</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>90</td>
</tr>
<tr>
<td></td>
<td>60</td>
</tr>
<tr>
<td>t'-Test</td>
<td>0.40 (11.5 $t' &lt; t_c$)</td>
</tr>
<tr>
<td></td>
<td>0.31 (13.6 $t' &lt; t_c$)</td>
</tr>
<tr>
<td>F'-test</td>
<td>2.03 (17.1 and 14.3 $F' &lt; f_c$)</td>
</tr>
<tr>
<td></td>
<td>1.54 (19.1 and 10 $F' &lt; f_c$)</td>
</tr>
<tr>
<td>F-test</td>
<td>3.8 ($P = 0.007$)</td>
</tr>
<tr>
<td></td>
<td>3.4 ($P = 0.026$)</td>
</tr>
<tr>
<td>$h^2$</td>
<td>0.73</td>
</tr>
<tr>
<td></td>
<td>0.70</td>
</tr>
</tbody>
</table>

$t'$-Test signifies the difference between the means of the twin pairs, $F'$-test the difference in total variance of both types of twins, and $F$-test the difference in genetic variance between the twin types. In $t_c$ and $f_c$, the subscript denotes the critical value.
Genetic Variation of Proprioception

part of the existing differences in proprioception as well as in plasticity of human motor cortex, in conjunction with the implication that movement strategies, which are organized in the CNS, are strongly genetically dependent (51), may support the argument that this influence is a factor in the neural development and recovery from neurological injuries.

On the basis of the aforementioned studies and based on our findings, we consider it likely that the differences in rehabilitation after an injury as well as in any type of motor skill acquisition in sports or in professional, artistic, and recreational activities may be explained by genetic differences. Finally, it seems that our results could contribute to the idea of designing more individualized therapy regimes for individuals who manifest disorders in this function, including the injured and the elderly.

Acknowledgments

We thank George Vagenas for advice in statistical analysis, Irene Kamberidou for assistance with editing the manuscript, and the twins for enthusiastic participation in the study.

Grants

This study was supported by the Hellenic General Secretariat for Research and Technology as well as the Ministry of Education via the Heraclitus Program.

Disclosures

No conflicts of interest, financial or otherwise, are declared by the authors.

Author Contributions


References


GENETIC VARIATION OF PROPRIOCEPTION


