Effects of normal aging on visuo-motor plasticity

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Abstract

Normal aging is associated with declines in neurologic function. Uncompensated visual and vestibular problems may have dire consequences including dangerous falls. Visuomotor plasticity is a form of behavioral neural plasticity which is important in the process of adapting to visual or vestibular alteration, including those changes due to pathology, pharmacotherapy, surgery or even entry into a microgravity or underwater environment. In order to determine the effects of aging on visuomotor plasticity, we chose the simple and easily measured paradigm of visual-motor re-arrangement created by using visual displacement prisms while throwing small balls at a target. Subjects threw balls before, during and after wearing a set of prisms which displace the visual scene by twenty degrees to the right. Data obtained during adaptation were modeled using multilevel analyses for 73 subjects aged 20 to 80 years. We found no statistically significant difference in measures of visuomotor plasticity with advancing age. Further studies are underway examining variable practice training as a potential mechanism for enhancing this form of behavioral neural plasticity.

Keywords: aging; neural plasticity; sensorimotor adaptation; visuo -motor plasticity; multilevel analysis; prisms

1. Introduction

Decrements in visual, vestibular and somatosensory function occur due to disease and as a consequence of normal aging. Deterioration with advancing age has been demonstrated in measures of optokinetic nystagmus response, visual following and vestibulo-ocular reflex (VOR) function [5,8,12,23]. Normal elderly people are also subject to increased postural sway when confronted with a dynamic visual environment [1] or other "conditions which result in sensory conflict, especially conflicting visual and somatosensory conditions" [19]. Uncompensated, these changes can lead to dangerous falls, which are reported to occur at least yearly in 20% of neurologically normal individuals and in two-thirds of patients with disequilibrium [13].

Adjustment in the coordination of visual and motor systems in the presence of vestibular alterations- whether pathologic, pharmacologic, iatrogenic or environmental- is crucial to an individual's ability to continue to function in the physical world. Demer has emphasized that individuals must utilize synergistic mechanisms available to supplement their failing vestibular systems in order to adapt [6]. For example, visual cues attain increased importance to patients with vestibular dysfunction as well as to astronauts experiencing weightlessness [29,32].

Plasticity is a neural property that allows sensorimotor systems to adapt to novel situations and maintain that adaptive change, thus allowing behavior to match the prevailing environment. Studies have shown that adaptation to novel environments leads to measurable changes in central nervous system structure, including increases in cortical thickness, size of synaptic contacts, number of dendritic spines, and dendritic branching [25]. Developed motor skills and the associated increase in synapse number have been found to persist even in the absence of further training [4,14].

Plasticity persists in animals throughout their lifespan, however some studies indicate a general decline in the degree of plasticity with age [7,9,20]. Significant differences in the degree of plasticity have been demonstrated in young versus older individuals in such diverse tasks as acquisition of second languages and adaptation of vestibulo-ocular reflex [10,22]. Conversely, on a molecular level, it has been shown that although neuron survival in culture decreases with age, dendritic regenerative capacity is maintained [2]. This finding suggests that the biologic process underlying neural plasticity remains intact despite aging.

Sensorimotor (visuo-motor) change may be induced in the laboratory by the use of goggles containing visual displacement prisms. This paradigm has been extensively utilized as a mechanism to alter parameters of the vestibulo-ocular reflex and motor coordination and as a means to study sensorimotor plasticity [31]. Martin et al (1996) utilized 30 diopter base-right visual displacement prisms to demonstrate that individuals can adapt performance of a throwing task within 10 to 30 throws, but that the presence of an olivocerebellar lesion impairs the ability to adapt to these prisms [17,18].

Using this type of prism-containing goggle as a model for alteration of visual-motor interaction, we recorded performance on a simple motor task (throwing balls at a target). The individual adaptation curves generated were then mathematically modeled in order to study the effects of advancing age on the visuo-motor plasticity of individuals. This information will be useful in the development of age-appropriate rehabilitation strategies for patients who have suffered specific sensory or motor losses or are affected by disequilibrium of aging.

2. Methods

2.1. Subjects

Seventy-three volunteers aged 20 to 80 years (mean 45.0 years, standard deviation 17.9) were recruited from faculty, staff and students at this institution. Forty-one subjects were female, thirty-two were male. Subjects were screened for conditions that might affect visual, vestibular or motor performance with exclusion criteria including (but not limited to) prior traumatic or surgical cervical or brain injury, history of cerebrovascular accident, seizures, stapedectomy or other surgery involving the labyrinth or adjacent structures, radiation to the head or neck, Meniere's disease, recent dizziness or vertigo, use of meclizine, anti-seizure medications, anti-psychotic medication or beta-blockers.

2.2. Basic experimental protocol: ball-throwing while wearing prisms

Subjects stood 2 meters from a target at eye level and threw small balls before, during and after wearing prism-containing goggles (see Figure 1). The target consisted of a Velcro sheet measuring 1 m by 1 m, with a 2 cm by 2 cm "bull's eye" at the center. The target hung on a wall in a quiet room with overhead fluorescent lighting.

Subjects threw Velcro-covered wiffle balls the size of golf balls at the circle on the target sheet. Thirty balls were placed in a basket and held in the subject's non-dominant hand, and the subject would reach into the basket for successive balls at a pace comfortable for the subject. Thirty throws constituted a set. Each subject performed two sets of throws initially as a warm-up. After the warm-up period, each subject performed a set of 30 throws while wearing a pair of goggles containing 20-degree rightward displacement prisms. Use of corrective lenses was permitted and encouraged, and the goggles fit easily over eyeglasses. Next, the goggles were removed and subjects performed one final set of 30 throws.

Throws were performed overhand with each subject's dominant throwing hand (writing hand was used in the absence of a throwing preference). Each throw was recorded on videotape, and the ball removed from the target prior to the next throw. The videotape was reviewed later, and the location of impact of each throw recorded in Cartesian (X=horizontal displacement, Y=vertical displacement) coordinates based on a grid imprinted on the target.

In order to minimize vestibular input, subjects were asked to keep their heads still while wearing the prisms. Subjects were informed of the potential for visual alteration by prisms, but not of the nature or direction of the alteration. The test administrator was necessarily aware of the nature of the lenses that each subject wore. Testing of each subject was performed in a single session lasting one half-hour. This study was approved by the Institutional Review Board for Human Subjects Research at this institution. Subjects gave informed consent prior to participation in the study.

2.3. Statisical methods

Multilevel models (also termed random coefficient models or hierarchical linear models) were used to describe performance and assess the effects of explanatory variables. Multilevel modeling is an emerging analytic technique that has been used in biostatistics [16], behavioral sciences [3,26,27] and education [11,15]. These techniques permit appropriate statistical modeling of situations involving repeated measurements because they can account for the correlations within groups and between repeated measurements on subjects.

Multilevel models were used to describe changes over the 30 throws (adaptation) in the performance of the throwing task and to evaluate the effects of age on rate of adaptation. The multilevel model involved two levels: at level 1, the horizontal displacement over the 30 throws were characterized by intercept and slope terms for each individual. The estimated regression coefficients for each individual were treated as a multivariate summary of that individual's adaptation with successive throws. At level 2, the coefficients from the subjects were related to the effects of age. The fit of each model was evaluated by graphical analyses of the level 1 and level 2 residuals. Judgements about the significance of variables were made by examining the improvement (deviance) in the –2ln(likelihood) statistic after each variable or group of variables was added to the model and by examining the estimated regression coefficients and their standard errors.

Log-transformed and linear terms for throw best described the changes in X-displacement during the task. A log-transform of throw number described the initial sharp downslope in the adaptation curve, corresponding to the active period of adaptation to the prisms. The addition of a linear term described the leveling-out of the adaptation curve in subsequent throws. An additional term for age was added in separately, to determine its influence on the model.

3. Results

Performance on the ball-throwing task was evaluated mathematically for 1) overall adaptive performance, 2) rate of adaptation, and 3) degree of adaptation. The final five throws were eliminated from each subject's dataset due to a general fatigue factor noted across all subjects. Prior to the decision to eliminate these data, it was determined that the effect was indeed present without bias of age. Removal of these five throws did allow for more accurate statistical modelling of the remaining data.

3.1. Overall adaptive perfomance

Figure 2 shows the raw data plotted as horizontal displacement (X) versus throw number for all subjects. This overall performance curve reveals the typical pattern of performance on the throwing task while wearing the 20 degree rightward displacement prisms. The first throw typically shows significant lateral displacement (positive displacement is to the right), and subsequent throws are incrementally closer to the center of the target (X=0 cm). By the fifth throw, the steep portion of the adaptation curve begins to level out and performance becomes more linear.

Figure 3 [A] demonstrates the predicted performance by subject and Figure 3 [B] the overall predicted performance with 95% confidence interval envelope after modeling by the equation:

$$\mathbf{X_{ij} = \beta_0 + \beta_1 \log(throw)_{ij} + \beta_2\, throw_{ij} + \gamma_{0j} + \gamma_{1j} \log(throw)_{ij} + \beta_3(age)_j + \varepsilon_{ij}}$$

where X = horizontal displacement from target center, i = throw number, j = subject, β's are fixed coefficients, γ's are random coefficients and ε is the random error term.

The linear and log terms in throw number were fixed effects (common to all individuals). The random effects (coefficients varied among individuals) were the intercept and logarithmic term for throw. Therefore the factors that were significant predictors of overall performance were the logarithm of throw number ($p<0.000001$) and the linear term for throw ($p<0.000001$). Age was not a statistically significant predictor of overall performance in adapting to this novel visuo-motor situation ($p=0.114$).

3.2. Rate of adaptation

Most of the adaptive process in this task takes place within the first few throws, as is clearly visible in Figures 2 and 3. We therefore modelled the first ten throws separately to achieve a description of the active adaptation. The logarithm of the throw number was again found to be predictive of performance ($p<0.00001$). Age is not predictive of the rate of adaptation to a novel visuo-motor situation ($p=0.20$).

3.3. Degree of adaptation

Once the steeply logarithmic portion of the adaptation curve is complete (after throw number 10), the predicted performance becomes asymptotic in keeping with the linear throw term described in the overall performance model. This linear portion of the curve represents the level of accuracy achieved by a subject once he or she has adapted to the lenses, but before fatigue becomes significant. We used the mean of throws 21 through 25 and called it the degree of adaptation. For this situation, we used Kruskal-Wallis test to compare the degree of adaptation for subjects in each decade. While there was a trend toward a slight increase in the mean displacement from target center for subjects over the age of seventy (see figure 4), this trend was not statistically significant ($\chi^2 = 3.49$, $p = 0.63$, degrees of freedom = 5).

4. Discussion

This study determined the effects of normal aging on visuo-motor plasticity. We had hypothesized that visuo-motor plasticity would deteriorate as a result of normal aging. This hypothesis was based on the age-related declines in many neurologic functions. Our data reveal no deterioration in visuo-motor plasticity with normal aging.

Declines have been reported in VOR and other measures of visuo-vestibular interaction, as well as in plasticity of VOR response to 2.0X magnifying lenses. In a study of 36 subjects aged 18 to 89 years, individual VOR response to magnifying lenses was found to differ somewhat between young and elderly subject groups, with a small decrement in phase response but no alteration with respect to gain [22]. This finding contrasts, however, with the age-related deterioration of gain reported by others [24,30].

Frequently, studies of aging compare subjects in artificially determined groups, defining selected age ranges as young or elderly, and, at times, including a middle age category. While this practice simplifies the process of statistical analysis, it disregards the gradual, spectral nature of aging. Data are modeled on an individual level, but the output is lumped together into artificial categories. Multilevel analysis is a powerful tool for modeling complex data without the need for divisions into artificial groups. In this study performance was modeled first by subject and then, on the next level, contribution of variables was analyzed. The use of multilevel analyses allowed for description of variations in performance trends throughout the entire spectrum of ages tested.

After rigorous statistical analyses of descriptors of the adaptation process (including rate of adaptation, degree of adaptation and overall performance), we found no significant difference in visuo-motor plasticity with age. This finding does not mirror the losses described in individual neurologic functions (e.g. VOR and smooth pursuit). It does reflect, however, the preservation of cerebellar pathways involved in this type of sensorimotor adaptation. One neurologic pathway corresponding to adaptation to lateral displacement of vision has been localized to the olivocerebellum [17]. Using lateral displacement prisms, adaptive performance of groups of subjects with known cerebellar infarctions was compared. Patients with infarctions in the distribution of the posterior inferior cerebellar artery had impaired or absent adaptation in the absence of ataxia. This finding implicates climbing fibers from the inferior olive, mossy fibers from the pontocerebellar nuclei, and cerebellar cortex within the distribution of the posterior inferior cerebellar artery as necessary for adaptation to this visuo-motor re-arrangement. In the absence of a lesion in these areas, the framework for an adaptive response is intact. Our data indicate that this adaptive response remains robust with age.

Additionally, preservation of visuo-motor adaptability with age parallels the preservation of the neuron's ability to generate dendrites despite aging [2]. The re-organization between synapses is part of the physiologic basis of learning. Therefore we might have expected visuo-motor plasticity, which is a form of learning, to reflect this process rather than the state of end organs.

The finding that visuo-motor plasticity remains intact despite normal aging, at least until the age of 80, may explain in part the ability of patients suffering from disequilibrium to continue to function. These patients often suffer from deficits in many neurologic areas, and these may be dynamic, evolving over time. Visuo-motor plasticity may allow individuals to integrate their remaining visual and motor function to help compensate for various and varying types of disequilibrium. Further studies are underway in an attempt to use variable practice in order to maximize utilization of visuo-motor plasticity as a tool for balance rehabilitation.

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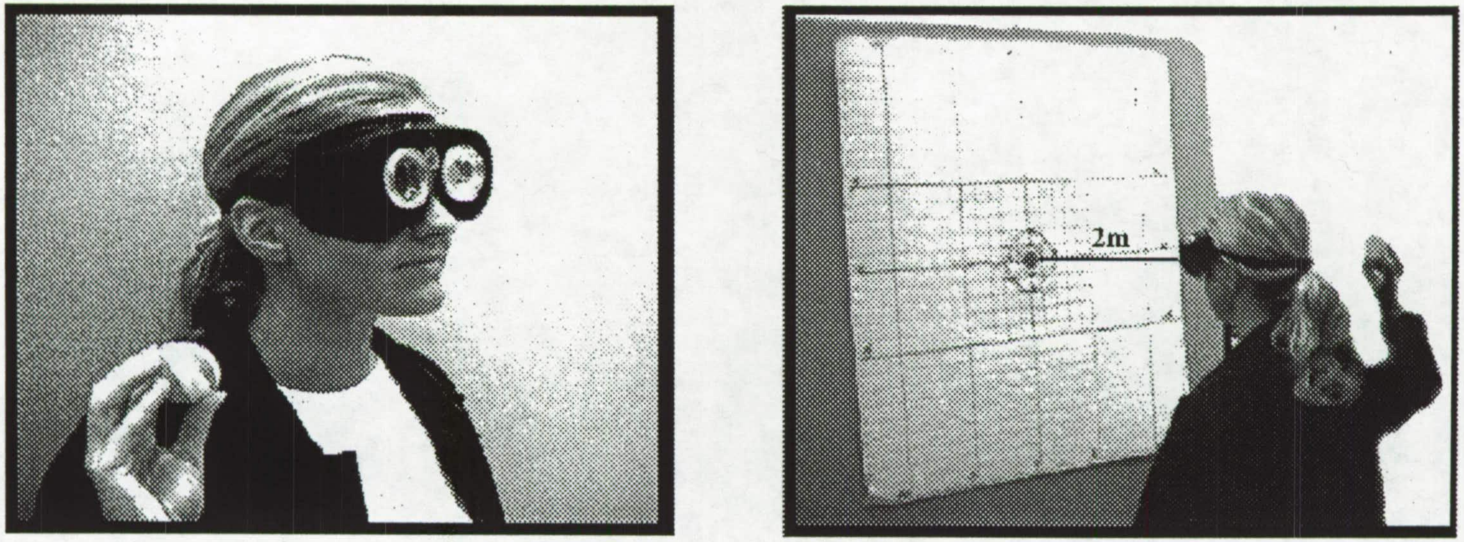

[A] **[B]**

Figure 1. Experimental set-up. Subject wearing prism-containing goggles [A] stands 2 m from target, which is at eye level [B].

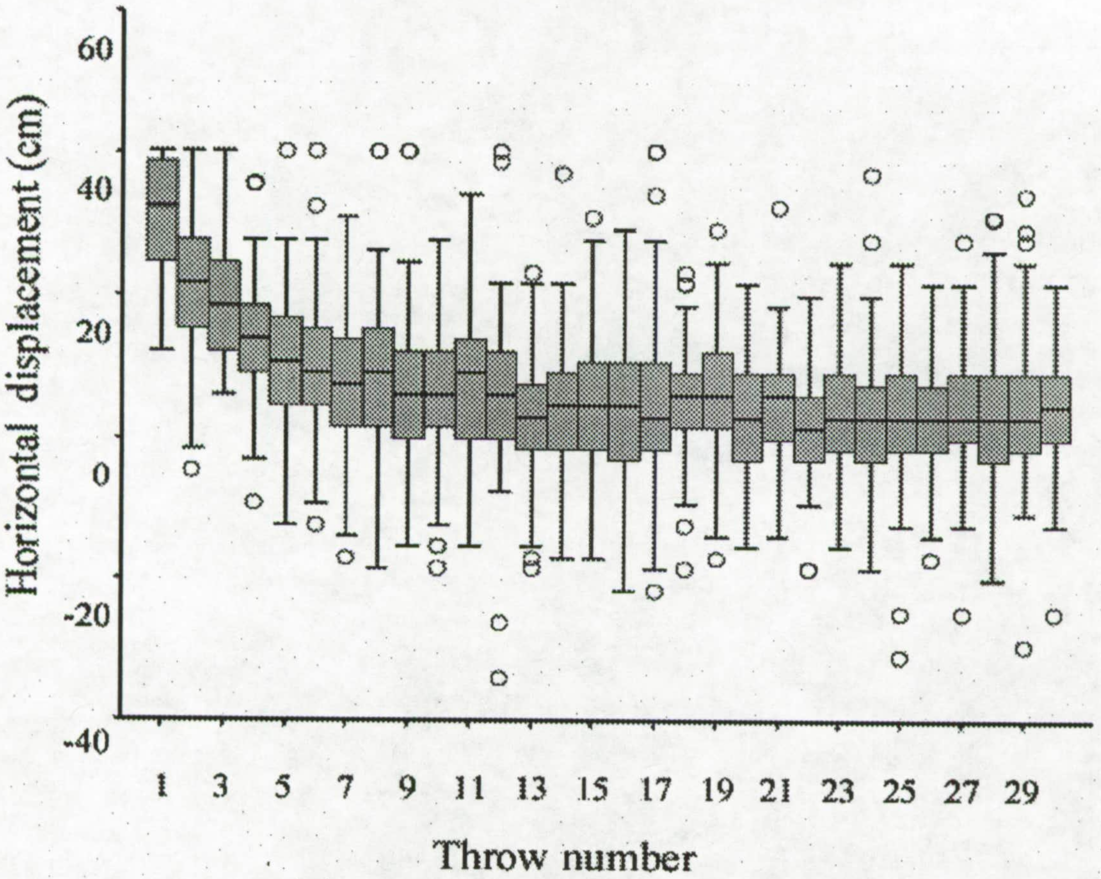

Figure 2. Raw data for all subjects: Horizontal displacement plotted by throw number. Boxes represent interquartile range containing 50% of values with median demarcated as a line through the center. Whiskers delimit highest and lowest values, excluding outliers which are indicated by "o".

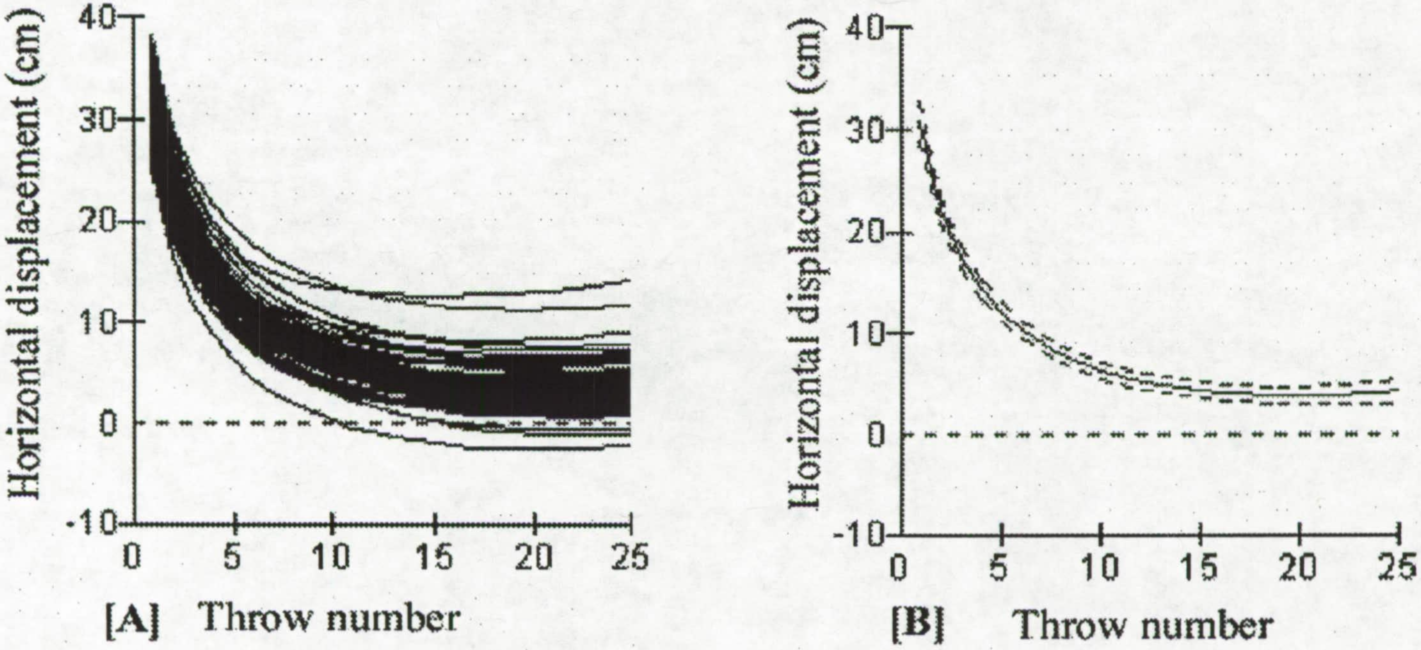

Figure 3. Horizontal displacement vs. throw number modeled by log-linear equation. [A] Predicted performance by subject. [B] Overall predicted performance with 95% confidence interval envelope.

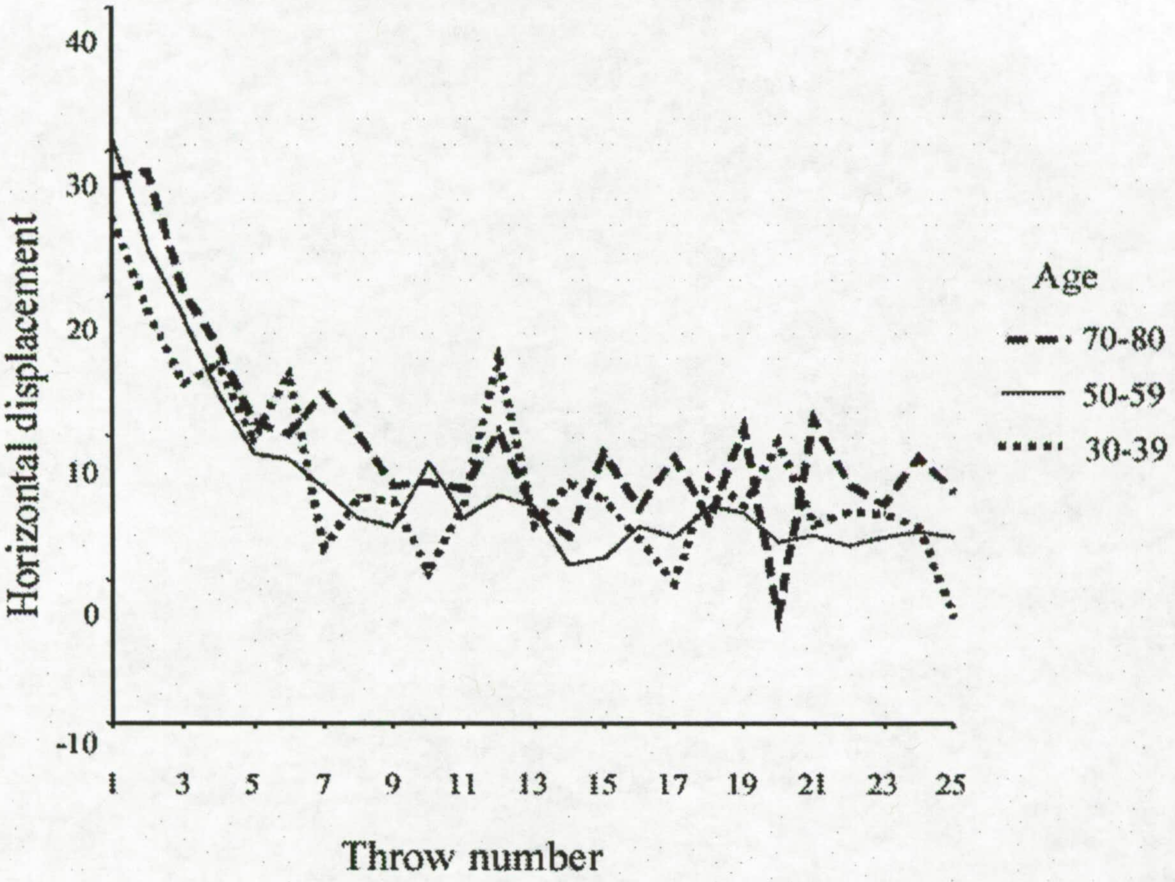

Figure 4. Raw data averaged over each throw and shown for representative decades. The curves are similar across the age range.

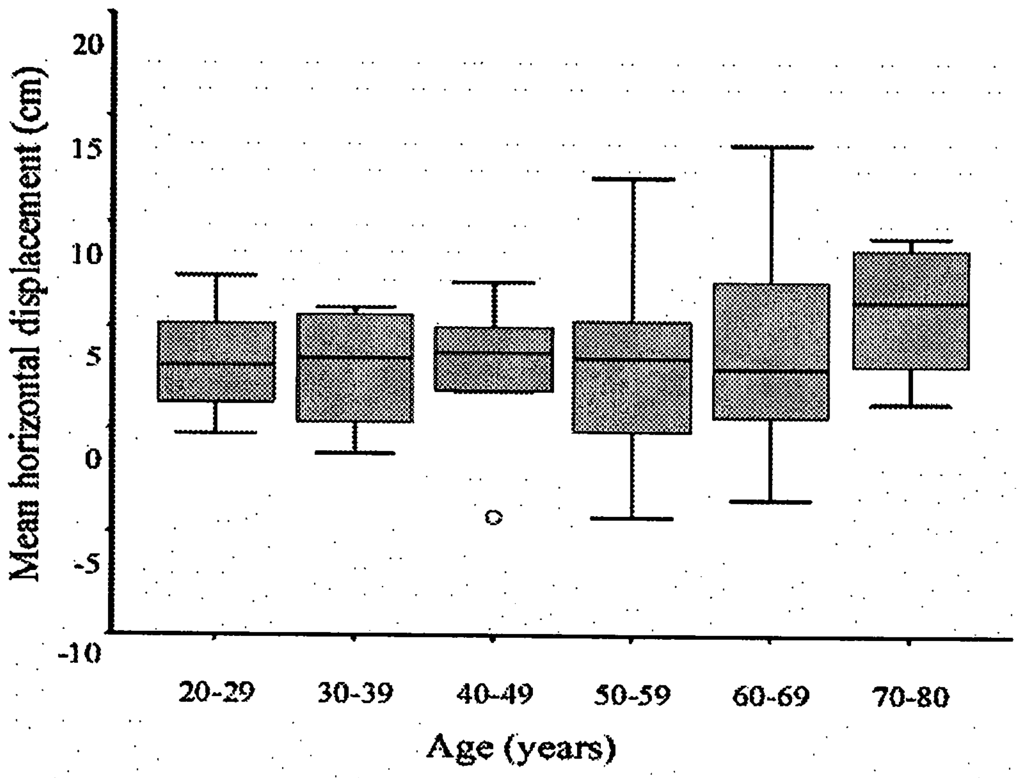

Figure 5. Mean horizontal displacement for throws 21 through 25 displayed by decade. Boxes represent interquartile range containing 50% of values with median demarcated as a line through the center. Whiskers delimit highest and lowest values, excluding outliers (indicated by "o").