Published in final edited form as:

Neuroimage. 2014 August 1; 96: 81–87. doi:10.1016/j.neuroimage.2014.03.045.

Investigating Age-Related Changes in Fine Motor Control Across Different Effectors and the Impact of White Matter Integrity

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Abstract

Changes in fine motor control that eventually compromise dexterity accompany advanced age; however there is evidence that age-related decline in motor control may not be uniform across effectors. Particularly, the role of central mechanisms in effector-specific decline has not been examined but is relevant for placing age-related motor declines into the growing literature of age-related changes in brain function. We examined sub-maximal force control across three different effectors (fingers, lips, and tongue) in 18 young and 14 older adults. In parallel with the force variability measures we examined changes in white matter structural integrity in effector-specific pathways in the brain with diffusion tensor imaging (DTI). Motor pathways for each effector were identified by using an fMRI localizer task followed by tractography to identify the fiber tracts propagating to the midbrain. Increases in force control variability were found with age in all three effectors but the effectors showed different degrees of age-related variability. Motor control changes were accompanied by a decline in white matter structural integrity with age shown by measures of fractional anisotropy and radial diffusivity. The DTI metrics appear to mediate some of the age-related declines in motor control. Our findings indicate that the structural integrity of descending motor systems may play a significant role in age-related increases in motor performance variability, but that differential age-related declines in oral and manual effectors are not likely due to structural integrity of descending motor pathways in the brain.

Keywords

Aging; Diffusion Tensor Imaging; Motor Variability; Fiber Tracking

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Introduction

In advanced age, there is a decline in the accuracy and efficiency of movements that can compromise basic dexterity for skilled movements. Although this is often suggested to reveal systemic declines in movement control, there is evidence that age-related decline in motor function varies across effectors (Enoka et al., 2003). For instance, although upper limb dexterity declines with age, the rate of decline may not be uniform across the different effectors involved in motor control and could be force level dependent (Marmon et al., 2011; Shinohara, Latash, Zatsiorsky 2003; Sosnoff and Voudrie 2009). A demonstration of variation in effector control comes from work suggesting oral motor function is better preserved than manual function in advanced age (McHenry et al., 1999).

Although few studies have compared oral versus manual motor control in aging, there appears to be a general preservation of tongue and lip force control among healthy elderly individuals without a loss of strength reserve for daily movements (Nicosia et al., 2000; Youmans and Stierwalt 2006; Youmans, Youmans, Stierwalt 2009). However, these studies have not tested oral control at low and midrange force levels at which the disproportionate decrease in force control across manual effectors has been reported in elderly participants (Enoka et al., 2003). The decline of fine manual motor control with advanced age is characterized by an increase in the amount of force variability and a decrease in variation of its temporal structure (i.e. more predictable temporal signal) (Vaillancourt and Newell 2003). The use of the coefficient of variation (CV) and approximate entropy (ApEn) metrics enable quantification of isometric force variation and temporal complexity across both oral and manual effectors (Sosnoff and Newell 2008).

Age-related declines in motor control have traditionally been examined by studying effectors (limbs), muscle function, and peripheral nerves (Enoka et al., 2003). More recently there has been a shift in focus to understand how changes in the CNS are related to age-related motor declines. Functional, structural, and chemical changes within the CNS have been identified that are important for understanding age-related neurological and neuromotor declines (for a recent review see Seidler et al., 2010), however the possibility of CNS changes contributing to the differential decline of effectors remains unclear. Diffusion tensor imaging (DTI), a specialized MRI technique that examines restrictions to water diffusion in the brain, has provided a platform to detect structural changes *in vivo*. DTI has been verified in animal models to show that the diffusion properties in a neural fiber bundle give important information about the structural integrity of specific fiber pathways (Song et al., 2002; Sun et al., 2005; Wang et al., 2011).

Two DTI measures in particular, fractional anisotropy (FA) and radial diffusivity (RD), have been used to identify correlations between age-related cognitive decline and reductions in apparent myelination in humans (Bucur et al., 2008; Madden et al., 2004; Madden, Bennett, Song 2009; Metzler Baddeley et al., 2011). A third DTI metric, axial diffusivity (AD), has been shown to be less sensitive to age-related changes and to be better preserved in the presence of demyelination (Song et al., 2002). A commonly reported trend with age is a decrease in FA and an increase in RD, consistent with the myelodegeneration hypothesis (Davis et al., 2009). Previous studies have found pathways where DTI metrics correlate with

performance on several motor control tasks (Sullivan, Rohlfing, Pfefferbaum 2010; Zahr et al., 2009). These areas include the fornix, splenium, genu, and uncinate fasciculus. While these studies provide valuable insight into how motor control in the CNS changes with age, the age-related CNS changes that might occur in different effectors, such as between oral and manual effectors, have not been compared either behaviorally or with DTI methods.

In this study, white matter structural integrity within descending motor pathways (cortex to midbrain) was associated with fine force variability of oral and manual effectors in young and old adults to test whether age-related neural structural integrity changes in descending motor pathways differentiate and predict motor control changes in different effectors. Performing a low and mid-range force level control task with manual and oral effectors allowed for the assessment of differential declines in motor control at force levels that do not require maximal exertion. Specifically, oral effectors were predicted to show less prominent age-related increases in variability than manual effectors. These associated brain areas for these effectors are somatotopically organized in the motor cortex along with the descending motor pathways for these regions. We also predicted that changes in white matter structure would correlate with performance declines, with higher age-related differences in white matter structural integrity measures in manual versus oral effectors, in agreement with age-related behavioral declines. This would correspond to a medial-lateral axis of decline across the descending motor control pathways.

Methods

Older and younger adults were recruited for participation in this study. Participants underwent two experimental sessions, one for motor control measures and one for MRI measures. For the motor control session, participants performed resultant force production tasks at low force levels using the finger, lip, and tongue. For the MRI session, the participants underwent anatomical scans and functional MRI scans to localize the finger, lip, and tongue areas followed by a diffusion imaging scan to obtain white matter structural integrity measures.

Participants

Participants were recruited to the study in accordance with the Institutional Review Board at the University of Illinois at Urbana-Champaign. Thirty-two healthy, right handed, independently living subjects participated and were divided into two groups based on age: Fourteen older subjects (8 female) between the ages of 60–79 years old (mean 67 years, SD 4.5 years) and 18 young participants (12 female) between the ages of 20–30 years old (mean 22.6 years, SD 2.0 years).

Force Control Measures

Each participant was seated in front of a computer monitor that displayed a static target line and a dynamic cursor controlled by force output. The participant was required to align the resultant force produced by the index finger (dominant hand), lips, or tongue (indicated by a dynamic cursor) with a visually presented static target line and maintain that force level for 25 seconds (similar to the procedure in Ofori, Loucks, Sosnoff 2012). The task was

performed 3 times for each effector (finger/lip/tongue) at 2 target force levels, 10% maximal voluntary contraction (MVC) and 20% MVC, in separate conditions. It is essentially an isometric force control task but with oral effectors that have multiple contributing muscles, use of the term 'resultant force' is more accurate (following (Barlow and Muller 1991; McHenry et al., 1999). The resultant force data was acquired from custom-built transducers for the lip and tongue tip (Biocommunication Electronics, Madison, WI) and a load cell for the index finger (MSI Sensors, Hampton, VA) that were routed through an amplifier (Biocommunication Electronics, Madison, WI) and sampled at 100 Hz by a National Instrument A/D board. The sensitivity of each transducer was less than 0.01 Newton and visual display gain was ~256 pixels/N. The participant rested his/her forehead and chin with a head support throughout the study to minimize head motion. The lip transducer rested between the left and right angles between the upper and lower lips and essentially sampled 'inter-angle' span force or force generated by 'puckering' of the lips. The tongue transducer was controlled by upward force exerted by the tongue tip. Jaw motion during tongue contraction was further limited by forming a bite block between the upper and lower teeth with dental putty that also stabilized the tongue tip transducer. Index finger flexion force was measured by pressing down on a button transducer with the forearm stabilized on a table in front of the subject (see Ofori, Loucks, Sosnoff 2012). Custom routines written in Labview (National Instruments, Austin, TX) were used to control the experiment and acquire data. Maximal voluntary contraction was determined at the beginning of the experimental procedures.

The magnitude of variability in force output was indexed using coefficient of variation (CV) and the structure of force control variability was indexed with approximate entropy (ApEn), which were determined using customized Matlab routines (Mathworks, Natick, MA, Version 2007B). CV is a measure of relative variability and is calculated as the standard deviation of a time series divided by its mean. ApEn is a measure of a time series regularity or time-dependent structure (Pincus 1991). This measure obtains the repetition of vectors of length m and $m + 1$ that repeat in a tolerance range of r of the standard deviation of the time series. The parameters set for the calculation of ApEn values ($m = 2$ and $r = .2 * \text{standard deviation}$) were based on previous studies (Sosnoff and Newell 2008). Consequently, a predictable signal (i.e. structured) such as an ideal sine wave would have a value of 0 and a signal that is not predictable (non-structured) would have a value approaching 2. A less structured signal is interpreted to be more complex (Pincus 1991). To ensure that only continuous force production was analyzed, the first five seconds of the force signal were excluded from analysis.

Neuroimaging measures

MRI measurements were performed on a Siemens (Erlangen, Germany) Trio 3 T scanner. In order to localize the finger, lip and tongue areas for determining relevant fiber tracks, participants first performed an fMRI experiment where they were instructed to activate each effector according to a visual and auditory cue. Participants were shown a picture of a finger, lips, or tongue while an auditory tone sounded at 2 Hz. Participants were instructed to tap the effector in time with the tone. Each effector was shown in four blocks and the task consisted of 10 s tapping, 14 s rest, with randomized order of effectors. The fMRI

acquisition was an EPI sequence with thirty-four 3 mm thick slices with a TE of 25 ms, TR of 2 s, FOV of 220 mm, and a matrix size of 96×96. To aid in registration of the functional results, a T2 overlay with the same slice prescription was acquired. Additionally a high-resolution (0.9 mm isotropic) 3D T1-weighted structural scan was acquired (MPRAGE) for normalization of the participant's brain to an MNI template (Fonov et al., 2009). fMRI data processing was performed in using FSL FEAT. Prior to fMRI data processing the fMRI data was corrected for motion and a 5 mm smoothing kernel was applied. A general linear model regression was performed on the timing vectors for the three task conditions. Temporal derivatives were included in the model. Gaussian random field thresholding was performed with a z-score of 2.0 and cluster threshold of $p=0.05$ to correct for multiple comparisons. Activation maps were then masked with motor cortex from the MNI atlas in FSL to restrict activations only to primary motor cortex. The subject-space motor cortex mask was determined by applying the inverse of the participant's normalization transform to a mask of the primary motor cortex in MNI space. The pixel with the maximum z-score was then chosen to be the center of the seed region for tracking, as described below.

The diffusion imaging acquisition used a b-value of 1000 s/mm² with a single-shot EPI acquisition with 72 slices, 2 mm thick, TE of 98 ms, parallel imaging factor of 2 with GRAPPA reconstruction (Griswold et al., 2002) and a TR of 10 s. The EPI diffusion acquisition had a spatial resolution of 1.88×1.88×2 mm³ and included 30 diffusion encoding directions along with 2 images with no diffusion encoding. A diffusion tensor was fit to the data using DTIFit in FSL 4.1 (<http://www.fmrib.ox.ac.uk/fsl/>) (Behrens et al., 2003b). Registration of the functional and diffusion images, along with the normalization of the MPRAGE, was done using FSL's linear registration tool (FLIRT) (Jenkinson et al., 2002), with the skull removed prior to registration (Smith 2002).

Probabilistic fiber tractography was used for identification of effector specific fiber tracts connecting the motor cortex to the brainstem. Tractography was performed using the Bayesian Estimation of Diffusion Parameters Obtained using Sampling Techniques (BEDPOSTX) and probabilistic tractography (PROBTRACKX) from FSL 4.1 (Behrens et al., 2003a). Default parameters were used with BEDPOSTX which uses a two fiber model for each voxel. PROBTRACTX was run with a curvature threshold of 0.1, a step length of 1.0 mm, 2000 steps, and 5000 samples modelled per voxel to track between a seed region and a target region of interest (ROI). Seed regions were defined by taking the point of maximal activation after clustering using a z-score of 2.0 in the motor cortex for each effector from the fMRI localization task and then placing a 2 cm diameter sphere at the highest activation point. Using the maximum point of activation with a fixed seed size allows for a reasonable comparison between subjects and effectors as the seed region size does not depend on the level and extent of signal change, only on the location of maximum signal changes between effectors. This resulted in one seed ROI for each effector on each side of the brain within the motor cortex for each participant. The target region mask of the brainstem was identified by the use of Harvard/Oxford atlas (cma.mgh.harvard.edu/) on the MNI space brain and transformed to the subject-space DTI. Additionally, the internal capsule was used as a waypoint mask to limit the tracking to only pathways that pass through the internal capsule. The Internal capsule mask came from the JHU white-matter atlas (<http://www.mrm.med.jhmi.edu/>) and was transformed into the subject-space

DTI. Furthermore, an exclusion mask for the contralateral hemisphere was used to prevent tracks from crossing between the hemispheres.

Based on the resulting tracts, measures of FA were made by taking the average FA value for each voxel on the tract, weighted by the probability of a fiber tract passing through that voxel. This is essentially a probability weighted FA value (Hua et al., 2008), but performed on an individual basis. This produced measures of FA for the fiber pathway for each effector in each hemisphere of the brain. The measures from the left and right pathways of the brain were then averaged to produce a single value of FA for each effector. This same technique was also applied to achieve values for the diffusion metrics of RD and AD.

Statistical Analysis

To investigate differences between age groups, effectors, and force levels, a three-way mixed model ANOVA with age group (young adults and older adults) as the between subject factor and effector (finger, lip, and tongue) and force level (10% MVC and 20% MVC) as within subject factors was used to investigate differences in force control measures. Additionally, a two-way mixed model ANOVA with age group as the between subject factor and effector as the within subject factor was used to look at differences in DTI measures.

In order to look further at the influence of neural measures on force control, a mediation analysis (Baron and Kenny 1986; Sobel 1982) was adopted. The mediation analysis assesses the significance of DTI measures in mediating age-related changes in force control. In order for the DTI measures to function as a mediator of age effects in force control performance, there must be a significant relationship between age and the DTI measures and between DTI measures and force control. The mediation effect can then be determined by looking at changes in how well age explains motor control performance after controlling for DTI measures. As an additional measure of the ability of DTI measures to explain age-related motor declines, a hierarchical regression analysis (Rosenberger et al., 2008; Salthouse 1996) was used to measure the amount of variance in the age-related motor control measures that is explained by the DTI metrics. To determine this dependency, first, age-related variance in a behavioral measure is calculated. This is followed by calculating the residual age-related variance after regressing out an additional explanatory variable, such as the FA measure from DTI. The proportion of the age-related variance that was explained by the DTI metric is determined from the residual age-related variance in the behavioral metric.

RESULTS

Motor control measures

The mean value for each force control measure, age group, and effector are given in Table. Significant differences ($p < 0.001$) in the force control metrics were found across age groups and between effectors using the measures of CV and ApEn using ANOVA (see Table II). An additional main effect of force level (10% vs 20% MVC) was found in CV ($p < 0.05$), but not ApEn. Due to the lack of significant differences between force levels for measures of ApEn, further analysis of ApEn was collapsed across force level. A significant interaction

between age group and effector was found in measures of both CV and ApEn. The only other significant interaction ($p < 0.05$) was between age group and force level in measures of CV.

The statistical differences between young and old adult groups related to different effectors and force levels were examined further with two-tailed t-tests (see Table III). Overall, older adults showed significantly more variable force output as indexed by higher CV values compared to young adults. The time series of the force signals of the older adults were also found to be more structured as indicated by lower ApEn values than the young adults although the difference in the tongue was not significant. A comparison of MVC between the age groups did not identify age-related differences in contraction force or apparent strength of the effectors which is discussed more in a separate work (Bronson-Lowe et al., 2013).

The ANOVA demonstrated a significant age x effector interaction. Descriptively from Table III, the change in mean CV with age is larger for the oral effectors than the fingers; however the ApEn measure shows a larger age-group decline for the finger. Additionally, CV showed a larger age-group related increase in variability for the lower force level. In terms of effector differences, only CV yielded consistent age-related effects for each effector. In contrast, ApEn showed age-related effects in the finger and lip, but not for the tongue.

Neuroimaging Measures

The fMRI task elicited significant activation within the motor cortex, as expected. Importantly, the clusters of activity were somatotopically organized according to effector within the motor cortex, as illustrated for in Figure 1. The seed regions for tractography are shown with the spheres centered at the point of maximum activation in the fMRI task. Figure 1 also shows examples of fiber pathways that were tracked from the cortical seed regions to the brainstem. DTI metrics were then measured on these fiber pathways, weighting the measures by the probability of tracking a fiber through a particular voxel, resulting in tract specific measures for each effector.

The mean value for each DTI measure for each age group and effector are given in Table IV. Based on ANOVA, significant differences ($p < 0.01$) in DTI metrics were found across age group and across different effectors using FA and across age group for RD, but not AD (Table II). Table III shows the magnitude of the age-related changes in the DTI measures for each effector. However, the ANOVA demonstrated no significant interaction between age-group and effector, so no statistical significant interpretation of the size of the changes across different effectors can be performed.

Contribution of DTI measures on Age-related Motor Performance

Our first approach to characterizing potential relationships between white matter structural integrity and force control was mediation analysis. This approach can identify if the DTI measures significantly mediated the age-group differences in motor control (see Table V). In order for DTI measures to mediate age-related motor control differences, age must be correlated with DTI measures and the DTI measures must be correlated with motor control measures. A significant main effect of age was observed for DTI measures in the ANOVA

analysis. However, not all motor control measures showed a significant relationship with DTI measures. After adjusting for multiple comparisons using a rough false discovery rate corrected p-value adjusted to 0.026 (Benjamini and Yekutieli 2001), and excluding relationships that did not meet criteria for performing a mediation analysis, the only mediator relationship that existed was in RD mediating the age related changes in CV at 10 and 20%.

Our second approach to characterize the relationship between white matter and force control was hierarchical regression. We performed hierarchical regression of the DTI measures on the motor control measures to determine how much of the age-group differences in motor control could be explained by the DTI measures (see Table V). DTI measures were found to explain 28% and 26% of the age-related variance in the ApEn measure for the finger for FA and RD respectively, and 12% and 16% for ApEn in the lip. Additionally, DTI measures accounted for 28–37% of the age-related variance in measures of CV at 10% MVC and 14–21% of the age-related variance at 20% MVC. DTI measures explained more of the age-group related variance in the ApEn measure of the finger than for lip.

Discussion

The primary hypothesis of this work was that oral effectors would exhibit differential age-related decline in behavioral performance and in structural integrity in neuronal pathways compared to a manual effector. The second related hypothesis was that effector-specific changes in performance could be predicted by the DTI metrics. Although we found a significant interaction between age and effector with the motor control measures, a similar interaction was not seen for the DTI measures. Overall, this suggests that DTI metrics on descending motor pathways provide information about global declines in the motor system, but do not explain differential performance declines between effectors. Specific findings of the study that support this summary are discussed below.

Motor control measures

In agreement with previous literature and in line with our predictions, both measures of force control variation, coefficient of variation (CV) and approximate entropy (ApEn), showed significant differences between the young adults and older adults. Additionally, interactions between age group, effectors, and force levels for the motor control data were identified. Our results indicate that age-related declines of both manual and oral force control are observable in aging populations (i.e. 60–79 years old), even in the absence of significant strength decrements.

The interaction between effectors and age group for both force metrics indicate that the fine force control of the effectors changed by different amounts. The Age by Effector interaction for ApEn matched our prediction of effector-specific increases in variability, with the larger variability increment in the fingers. However, the CV interaction showed the alternative pattern, with oral effectors showing a larger increase in variability. These age-by-effector differences between the force control measures are challenging to interpret but could signal the utility of the measures for future studies. In general, the oral effectors have not shown the same sophistication in temporal structure as manual effectors (Bronson-Lowe et al.,

2013; Ofori, Loucks, Sosnoff 2012). Oral muscles are generally involved in activities that require flexibility and speed, such as talking and chewing, rather than holding fixed postures or weight bearing. The fingers, in contrast, regularly are called upon for dexterity, speed, weight-bearing and fixed postures and these demands change unpredictably. In these cases, the simpler measure of variability magnitude (CV) may be a more appropriate index of oral variability, while the ApEn measure which samples temporal structure might be a better indicator of how finger performance changes with age. In previous publications, we have also discussed other effector specific differences, such as muscle fiber composition and their skeletal attachments, which are relevant to explaining effector differences (Bronson-Lowe et al., 2013; Loucks et al., 2010; Ofori, Loucks, Sosnoff 2012). While these age-by-effector differences between the two metrics highlight the importance of studying oral and manual effector differences (Gentil and Tournier 1998), our primary observation of age related increases in variability is highly relevant to knowledge of motor control.

The additional interaction of age group and force level in CV measures revealed a greater age-related loss in performance at the lower force level. Since lower force levels are involved in many daily manual manipulation tasks, this could have important consequences in the aging population. Also of importance is that there was no interaction between force level and effector, indicating the force levels used were reasonable to compare across the three effector systems considered.

Neuroimaging Measures

The DTI tractography approach was able to track fiber pathways from the functionally identified regions in the primary motor cortex down to the brainstem. The trackings indicated separate pathways for the manual and oral motor systems from the cortex through the internal capsule to cerebral peduncle. As shown in Figure 2, the manual fibers are in lateral aspects of the cerebral peduncle while the oral fibers are more medial. This organization and structure of the motor control fiber pathways agree with previous work with DTI and fMRI, showing a preservation of somatotopic organization in the motor control system from the motor cortex to the cerebral peduncle (Guye et al., 2003; Hong, Son, Jang 2010; Kamada et al., 2005; Kwon et al., 2011; Park et al., 2008; Park et al., 2008; Virta, Barnett, Pierpaoli 1999).

Following our prediction, age-related declines in fractional anisotropy (FA) and increases in radial diffusivity (RD) were identified, consistent with recent literature in both motor (Sullivan, Rohlfing, Pfefferbaum 2010; Zahr et al., 2009) and cognitive studies (Bucur et al., 2008; Madden, Bennett, Song 2009; Metzler Baddeley et al., 2011). A trend was observed suggesting somatotopic differentiation in decline in FA, with the highest declines for finger, intermediate in lip, and lowest for tongue. However, from the ANOVA analysis the descriptive trend is not significant in this age cohort as there is no interaction between effector and age group. This trend should be explored further with an additional older cohort of adults along with larger sample sizes. Instead, the current results demonstrate a more global change in white matter structural integrity. Without a significant relationship between age group and effector, the DTI metrics were unable to predict tract-specific motor performance declines in this study.

Contribution of DTI measures on Age-related Motor Performance

Along with standard ANOVA analyses, we tested whether the DTI metrics potentially act as mediating variables that explain some of the changes in motor variability across the age groups. This alternative approach showed statistical support for attributing some of the influence of central neural structural integrity changes to distinct effectors; however, more statistical power is needed to determine if the significant mediation by CNS pathways exist for each effector. The significant mediation of DTI metrics suggests a contribution from a central source to age-related motor performance declines. We cannot posit a causative role by the central fiber pathways in the behavioral declines based solely on the mediation results, but it provides evidence to motivate further research while supporting the hypothesis by Seidler and colleagues (Seidler et al., 2010) that age-related changes in central pathways may drive age-related changes in motor performance.

Of all effectors, the tongue was most variable and perhaps contributed to reduced power of the analyses. Further investigations could include tongue force tasks with lower lingual variability.

The DTI measures in the identified pathways do not unambiguously account for the differential amounts of variability increases across effectors. Investigations of other pathways may also prove to be important in looking for CNS-contributions to age-related differences in motor control performance. Possible pathways to target include those related to sensory feedback or sensorimotor integration as performance on motor tasks with auditory vs. visual feedback has been shown to be related to the type of sensory feedback (Ofori, Loucks, Sosnoff 2012) and differences in sensory motor activation have been found with age (Malandraki et al., 2011). The ability to measure effector-specific pathways may also prove to be useful in studying changes in motor control due to training, as older adults have shown improvements in motor control performance with training. DTI measures may provide a means to see if these training changes are related to neuroplasticity and if they are specific to trained effectors.

Our current approach averaged DTI metrics over the fiber pathways from cortical surface superiorly to the brain stem inferiorly. This method does not enable information about a superior-to-inferior axis of white matter changes that may exist as suggested by Seidler and colleagues (Seidler et al., 2010). We chose the particular axis in this study to focus on the corticomotor anatomy that is anatomically conceived as the pathway for voluntary control of these effectors. Progress in these studies could involve fractionating measures along cortex to midbrain axis to test uniformity along the pathway. We did determine there are also increasing levels of overlap in the tracked fiber bundles towards the midbrain, due to spatial resolution constraints in the DTI acquisition. This results in difficulty to finely parse distinct fiber pathways as they approach the midbrain and pons. The tracking results indicate the lip and tongue tracts show a higher degree of overlap compared to the manual tract as they proceed inferiorly. Continued refinements in diffusion imaging spatial resolution that allow for separation of these oral fiber tracts will enable sensitive measures of effector-specific pathways (Holtrop, Van, Sutton 2012).

Changes in functional motor cerebral activity, such as dedifferentiation (Bernard and Seidler 2012; Carp et al., 2011), and sensorimotor integration could also cause changes in motor performance that would not be reflected in our structural measures. The fMRI task used in this study did not control the magnitude of the force production while in the MRI scanner, making it difficult to draw any conclusions about different patterns of activity that accompany force level, age, and effector. Future work should take advantage of fMRI's ability to be sensitive to different patterns of activity during motor tasks (Coombes, Corcos, Vaillancourt 2011; Coombes et al., 2010) in an attempt to better understand the CNS changes in fine motor control.

Conclusion

In this study we compared fine manual and oral motor systems to determine if there are effector-specific decreases in motor performance in aging and to assess the contributions of white matter changes to this decline. We found that both oral and manual motor effectors showed significant age-related increases in variability in motor control and increases in predictability of the force output during isometric force tasks at low force levels. Additionally, all effectors showed significant age-related declines in neural fiber pathway structural integrity as assessed by fractional anisotropy and radial diffusivity. DTI measures were shown to mediate the age-related declines in the finger and lips as assessed by ApEn. But across effectors, DTI measures did not predict differential age related declines in motor performance.

Acknowledgments

This research was conducted while Brad Sutton, Jacob Sosnoff, and Torrey Loucks were AFAR Research Grant recipients from the American Federation for Aging Research. The project described was supported, in part, by Award Numbers R21EB010095 and R21EB009768 from the National Institute of Biomedical Imaging And Bioengineering. This project was also partly funded by a pilot grant from the Center for Health, Ageing, and Disability at the University of Illinois at Urbana-Champaign. The content is solely the responsibility of the authors and does not necessarily represent the official views of the American Federation for Aging Research, National Institute Of Biomedical Imaging And Bioengineering, the National Institutes of Health, or the Center for Health, Aging, and Disability.

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Highlights

- Motor control measurements were made that enable performance comparisons between oral and manual effectors
- Neural structural integrity measures were obtained that are specific to the control of oral and manual effectors
- Effector-specific age related declines in motor control were observed.
- Age-related declines in motor control were correlated to changes in white-matter structural integrity.
- White matter integrity did not specifically predict differential decline in behavior among the pathways

Figure 1. Example of fiber tracking with red indicating finger, blue indicating lip, green indicating tongue, and the brainstem in yellow. (*left*) Functional areas within the motor cortex. (*middle*) 3D view showing somatotopic organization of the different fiber tracts. (*right*) shows the ROIs used for tracking and the resulting fiber tracts.

Table I

Mean motor control values for finger lip and tongue at 10% and 20% MVC. Standard deviations are given in parentheses.

		Finger	Lip	Tongue
CV (10% MVC)	Old	0.0415 (0.0244)	0.0139 (0.1230)	0.240 (0.0928)
	Young	0.0205 (0.0064)	0.0386 (0.0179)	0.157 (0.0440)
CV (20% MVC)	Old	0.0290 (0.0124)	0.0765 (0.0501)	0.213 (0.0856)
	Young	0.0202 (0.0078)	0.0431 (0.0287)	0.159 (0.0496)
ApEn (10% MVC)	Old	0.330 (0.1265)	0.268 (0.1600)	0.289 (0.0861)
	Young	0.453 (0.0959)	0.367 (0.1516)	0.294 (0.1418)
ApEn (20% MVC)	Old	0.281 (0.1125)	0.289 (0.1024)	0.229 (0.0804)
	Young	0.428 (0.1272)	0.357 (0.1550)	0.257 (0.1031)

Table II

Results from an ANOVA analysis of the motor control and diffusion tensor imaging measures. Main effects of age group, effector, and force level are examined, along with their interactions.

	Main Effects			Interactions			
	Age	Effector	Force Level	Age x Effector	Age x Force Level	Effector x Force Level	Age x Effector x Force Level
CV	F =	39.24	150.26	3.99	5.05	0.71	1.03
	P =	<0.001	<0.001	0.047	0.026	0.491	0.358
	Partial η^2 =	0.179	0.625	0.022	0.027	0.008	0.011
ApEn	F =	18.82	11.4	2.26	0.02	0.82	0.27
	P =	<0.001	<0.001	0.135	0.898	0.443	0.767
	Partial η^2 =	0.095	0.112	0.012	<0.001	0.009	0.003
FA	F =	32.15	10.50	-	0.46		
	P =	<0.001	0.001	-	0.632		
	Partial η^2 =	0.263	0.189	-	0.010		
RD	F =	26.19	2.46	-	0.22		
	P =	<0.001	0.091	-	0.804		
	Partial η^2 =	0.225	0.052	-	0.005		
AD	F =	0.09	2.70	-	0.06		
	P =	0.764	0.072	-	0.943		
	Partial η^2 =	0.001	0.057	-	< 0.001		

Table III

Group differences between young adults and older adults on motor control measures and diffusion tensor imaging data.

	FINGER	LIP	TONGUE
CV (10% MVC)	0.021** (0.001)	0.100** (0.001)	0.083** (0.002)
CV (20% MVC)	0.009* (0.020)	0.034 * (0.024)	0.054* (0.033)
Apen	-0.135** (<0.001)	-0.083* (0.024)	-0.017 (0.540)
FA	-0.026** (<0.001)	-0.017* (0.015)	-0.021** (0.005)
RD ($\mu\text{m}^2/\text{ms}$)	0.042** (<0.001)	0.036* (0.010)	0.031* (0.029)

All values are Old - Young. Age group difference measures (bold) with the p-value of older adults versus young adults in parentheses. Measures that are $p < 0.05$ are denoted by a * and measures that are $p < 0.01$ are denoted by **. The p-value is from a two tailed t-test of older adults versus young adults. Values are: **subtraction of old-young**/(p-value of difference).

Table IV

Mean diffusion imaging parameters from different effectors. Standard deviations are given in parentheses.

		Finger	Lip	Tongue
FA	Old	0.563 (0.013)	0.552 (0.020)	0.545 (0.013)
	Young	0.589 (0.019)	0.569 (0.018)	0.565 (0.029)
RD (mm ² /s)	Old	534 (29)	542 (46)	547 (33)
	Young	491 (27)	506 (30)	517 (41)
AD (mm ² /s)	Old	1,342 (48)	1,325 (59)	1,315 (57)
	Young	1,344 (35)	1,324 (32)	1,322 (36)

Table V

Contributions of variance in motor control measures. The measures of RD in the lip were found to be significant mediators ($p < 0.05$) in age related variance in CV at 10% and 20%.

		Finger	Lip	Tongue
CV (10% MVC)	Variance explained by age group	29%	28%	27%
	Age-related Variance explained by FA	30%	29%	28%
	Age-related variance explained by RD	29%	*37%	28%
CV (20% MVC)	Variance explained by age group	17%	16%	14%
	Age-related variance explained by FA	17%	17%	14%
	Age-related variance explained by RD	18%	*21%	14%
ApEn	Variance explained by age group	26%	8%	< 1%
	Age-related variance explained by FA	28%	12%	-
	Age-related variance explained by RD	26%	16%	-