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Age-Related Differences in Complexity During Handgrip Control Using Multiscale Entropy

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ABSTRACT Changes in motor behavior during aging might be induced by complexity fluctuations in the neuromuscular system. Most previous studies have been performed based on single-scale entropies. In this paper, multiscale fuzzy entropy (MSFuzzyEn) was applied to characterize the changes in the complexity of simulated electromyogram (EMG) signals with the increasing motor unit number and signal-to-noise ratio. Age-related differences in multiscale complexity during handgrip control were also investigated. Ten young and 10 older adults were instructed to produce constant forces at 25%, 50%, and 75% of their maximal grip force with their dominant hands. The grip force and EMG signals of four forearm muscles were recorded simultaneously and analyzed using MSFuzzyEn. The simulation tests revealed that, as the time scale increased, the interference of noise in the EMG signals decreased. At time scale 1, the complexities of the force and EMG signals exhibited opposite changes with aging. When the time scale increased, we observed a loss in complexity with aging in both the force and EMG signals. These results confirmed the merits of MSFuzzyEn in noise abatement, and implied that entropy at relatively larger time scales might better characterize EMG signals. Further studies should extend the application of multiscale entropy in pathologies.

INDEX TERMS Aging, complexity, EMG, force, multiscale entropy.

I. INTRODUCTION

Advancing age is always accompanied by a reduced ability to rapidly and accurately execute movements [1], [2]. Many previous studies have investigated the changes in motor behavior that occur with aging. Teeken *et al*. [1] observed slower movement times with greater age during upper limb aiming tasks. As Pohl *et al*. [3] proposed, age-related movement slowing could be associated with slower feedback processes, which might indicate a central processing deficit. Such deficits in human behavior due to aging have also been found in reaction times and movement smoothness for both the dominant arm and the non-dominant arm [4]. Bennett*et al*. suggested that older adults generated strategic changes in movement kinematics to maintain a balance between speed and accuracy [5]. A previous study also observed that older adults produce weaker muscle strength compared with young adults [6]. Additionally, an increase in force variability is observed during aging [2], [7], [8] and might be associated with the discharge properties of single motor units (MUs) [9], [10]. To the extent of our knowledge, kinematic and kinetic indices characterize external motor behavior, while EMG signals represent intrinsic muscle activity in the neuromuscular system and certainly determine the external motor behavior. Accordingly, Vaillancourt *et al*. [11] investigated the effects of age on force variability and EMG activity and found that aging has a great influence on both force variability and the relative powers of EMG signals in different frequency bands, which might indicate a reduced capacity for older adults to achieve optimal force control. Based on EMG analyses, different patterns of muscle activation have been observed in children, adults, and aged people [12].

Previous studies of age-related changes have found losses of complexity in the cardiovascular system [13], postural control [14], finger flexion and abduction [15], [16],

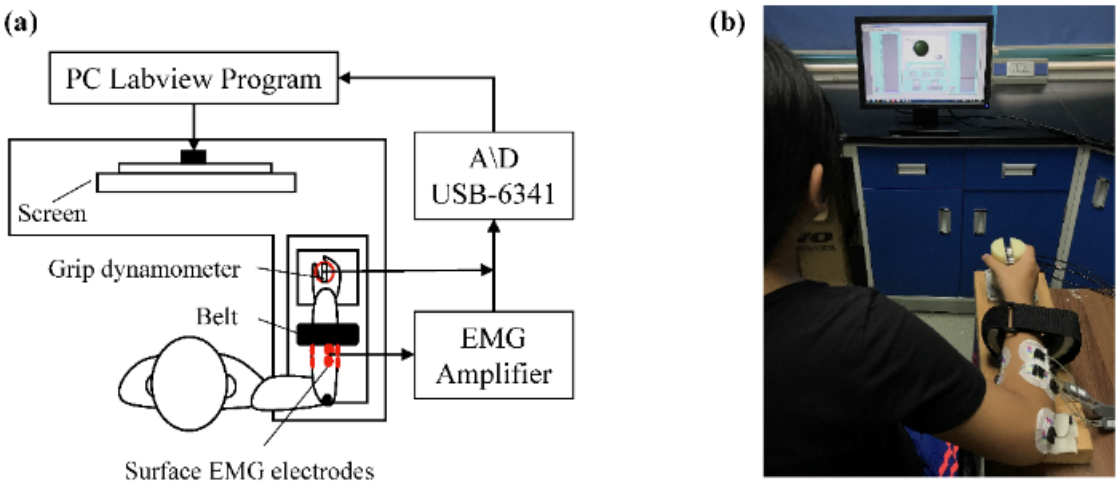

FIGURE 1. (a) Block diagram of the experimental setup; (b) a normal subject under test.

and muscle activity during treadmill walking [17]. Here, the entropy index was employed to quantify system complexity, which characterizes the irregular dynamics of physiological systems well. A loss in system complexity is associated with a greater regularity of related signals, which induces a decline in the entropy value [18]. Since the concept of entropy was first proposed by Shannon [19], different entropies have progressively been introduced and applied to the feature extraction from physiological signals [20]–[25]. Pincus introduced approximate entropy (ApEn) for short and noisy signals to generate reliable assessments of signal complexity [26]. Later, sample entropy (SampEn) was adapted from ApEn by eliminating self-matches, which improved the evaluation of signal complexity and resulted in the maintenance of better consistency under different parameter values [27]. Chen *et al*. [28] applied the fuzzy function that has a soft and continuous boundary instead of the Heaviside function that has a hard and sensitive boundary, to the measurement of the similarity of vectors, which contributed to the superiority of fuzzy entropy (FuzzyEn) in terms of robustness and validity with small parameters [29]. Besides, permutation entropy [30] and its variants (e.g. dispersion entropy [31]) were proposed to characterize the permutation patterns in a time series and computationally efficient, whereas its reliability of complexity measurement 'hasn't been widely recognized. Thus, FuzzyEn has potential for the characterization of the complexity changes in noisy and shorter signals from the neuromuscular system.

To the extent of our knowledge, based on previous entropy studies, higher entropy values might not result from increased system complexity, which is associated with the meaningful structural richness of the system [32], but rather from the interference of uncorrelated noises [33]. Additionally, previous entropies have been used to quantify the complexity changes at a single time scale, without considering the factor of time scale [2], [34], [35]. Multiscale entropy (MSE), adapted from SampEn, extracts more complete features of physiological signals across multiple time scales through the coarse-graining procedure [33], and shows that correlated random signals (e.g. colored noise) are more complex than uncorrelated random signals (e.g. white noise) [32]. Although MSE analyses of electroencephalogram (EEG) [36], heart rate dynamics [13], [37], gait dynamics [17], [38], muscle fatigue [39] etc. have proved their merits, few studies have reported age-related changes during handgrip control based on MSE analysis.

In our study, the effect of multiscale fuzzy entropy (MSFuzzyEn) on noise abatement was investigated in simulated EMG signals with different signal-to-noise ratios (SNRs) and real EMG signals of four forearm muscles. Moreover, MSFuzzyEn was utilized to detect the age-related changes in complexity across multiple time scales during sub-maximal grip force tasks with different force levels. We hypothesize that MSFuzzyEn has the property of noise abatement and can be utilized to quantify the complexity changes in force and muscle activities due to aging. This might contribute to a more comprehensive understanding of the effect of age on the neuromuscular system.

II. MATERIALS AND METHODS

A. SUBJECTS AND EXPERIMENTAL PROCEDURES

In our study, twenty healthy adults were recruited, and there were 10 young subjects (5 men, 5 women, mean age: 22±1.26 years) and 10 older subjects (5 men, 5 women; mean age: 51.7±6.24years). All subjects had written informed consent before participating in the experiment. Ethical approval of our study was granted by Sun Yat-sen Memorial Hospital.

The experimental setup is displayed in Figure 1. The subjects were instructed to be seated in a chair besides a table with their shoulder abducted at 15-20° and their elbow

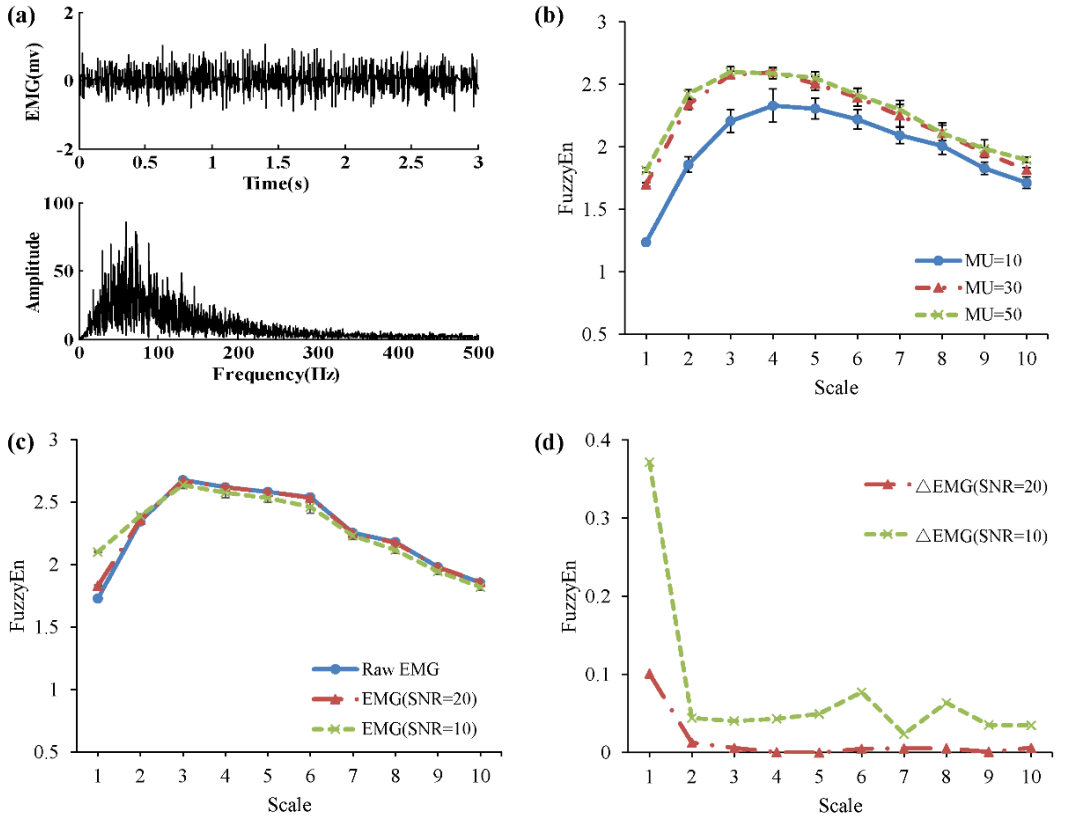

FIGURE 2. EMG simulation; (a) a 3000-sample simulated surface EMG signal in time domain and frequency domain (the MU number was 30); (b) the MSFuzzyEns of simulated EMG signals with three different MU numbers; (c) the MSFuzzyEns of raw simulated EMG signal (the MU number was 30) and simulated EMG signals with different SNRs; (d) the difference in MSFuzzyEn between the raw simulated EMG signal and the simulated EMG signals with different SNRs. In (b) and (c), the symbols represent the mean FuzzyEns at each scale for 10 simulated EMG signals, and the error bars represent standard deviation.

flexed at 90°. The forearm of each subject was constrained with a belt to prevent forearm motion. A tele-EMG system (MyoSystem2400T, Noraxon, USA) was used to capture and amplify EMG signals with two Ag-AgCl bipolar electrodes (Noraxon, USA) attached to the belly (center-to-center distance 2 cm) of each muscle (flexor carpi radialis, FCR; extensor carpi radialis, ECR; flexor digitorum superficialis, FDS;extensor digitorum communis, EDC) after the skin was shaved and cleaned with alcohol. The grip force was captured with a custom-made grip dynamometer at 1000 Hz and force transducers (LSZ-F03B, Suzhou Battelle Automation Equipment Company, Suzhou, China) mounted inside. Then a data converter (DAQ-6341, National Instruments, Austin, TX, USA) with a 16-bit resolution was used to sample the EMG signals and the grip force at 1000 Hz. In front of each subject, a LabVIEW program (LabVIEW 2012, National Instruments, Austin, TX, USA) from the computer screen provided real-time visual feedback. An indicator light reminded the subjects to start each trial.

After understanding the experimental protocol, the subjects were asked to generate 5-s maximal grip force (MGF) three times. The largest MGF was used to normalize the

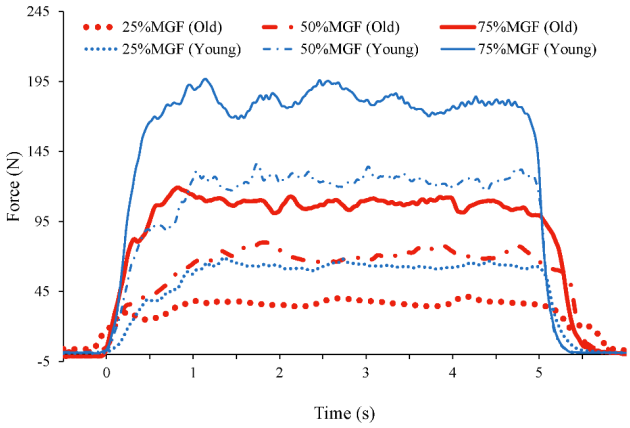

FIGURE 3. A sample of denoised force in three different levels (25%, 50%, and 75% of MGF) from a young subject and an older subject.

grip forces in the sub-maximal force task that included three different levels (25%, 50%, and 75% of MGF). Subjects were asked to achieve the target grip force and maintain that force for 5 s in each trial. Each subject completed the task three times at each level and was allowed a 30-s rest after each trial.

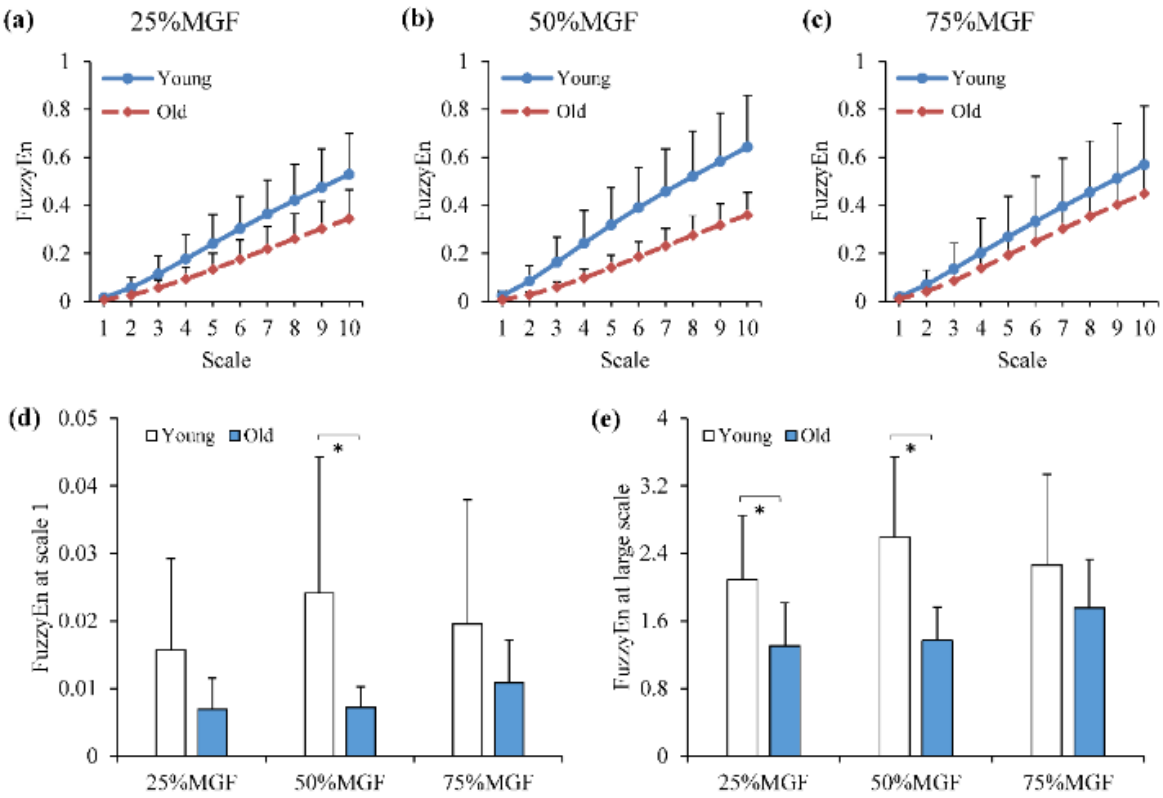

FIGURE 4. The MSFuzzyEn analyses of grip force in the young group and the old group; (a)-(c): the MSFuzzyEns in three different levels (25%, 50%, and 75% of MGF), respectively; (d)-(e): the FuzzyEns at scale 1 and large scale (τ = 6-10), respectively. The error bars represent standard deviation. $*$ Statistically significant difference ($p < 0.05$).

B. MULTISCALE FUZZY ENTROPY

The MSFuzzyEn, which combines multiscale entropy [28] with FuzzyEn [33], was applied to estimate the complexity of the physiological signals across multiple time scales. The algorithm consisted of two steps: (1) generating signals at different time scales through the coarse-graining procedure and (2) computing the FuzzyEn values of the signals at each time scale.

For a given sequence $\{u(i) : 1 \le i \le N\}$, a coarse-graining sequence $y_j^\tau = \frac{1}{\tau}\sum_{i=j\tau-\tau+1}^{j\tau} u_i (1 \le j \le \frac{N}{\tau})$at time scale τ can be derived. The coarse-graining sequence at time scale 1 is the given sequence. As τ increases, the coarse-graining sequence (N/τ) has a shorter length.

To compute the FuzzyEn of a given sequence $\{s(i) : 1 \le i \le N\}$, the sequence$X_i^m = \{s(i), s(i+1), \ldots, s(i-m+1)\} - s_0(i) (i = 1, 2, \ldots, N-m+1)$ could be formed, where $s_0(i) = \frac{1}{m}\sum_{j=0}^{m-1} s(i+j)$. The distance between X_i^m and $X_j^m (i, j = 1, 2, \ldots, N-m+1; i \ne j)$ can be calculated as follows:

$$d_{ij}^m = \max_{k\in(0,m-1)} |s(i+k) - s_0(j) - s(j+k) - s_0(i)| \quad (1)$$

The similarity between X_i^m and X_j^m was defined as $D_{ij}^m(n, r) = \exp(-\left(d_{ij}^m / r\right)^n)$, where r was the width of the exponential function and n determined the gradient of the boundary. Then, the similarity from any vector to another was averaged as$\varphi^m(n, r) = \frac{1}{N-m+1}\sum_{i=1}^{N-m+1} \ln(\frac{1}{N-m+1}\sum_{j=1, j\ne i}^{N-m+1} D_{ij}^m)$. The FuzzyEn of the given sequence can be estimated as follows:

$$FuzzyEn(m, n, r, N) = \ln\varphi^m(n, r) - \ln\varphi^{m+1}(n, r) \quad (2)$$

In this study, m = 2, n = 2, and r = 0.15$*$std (signal) was set referred to our previous work [40], and the maximum time scale τ_{max} of MSFuzzyEn was set as 10 for reliable statistics [41].

C. SIMULATION TEST

A simulated surface EMG signal during isometric contraction was generated by summing up all motor unit action potential trains (MUAPTs), which consisted of the MUAPs that differed in duration and amplitude [42]. The MUAP of a given MU was the summation of its all single fiber action potential (SFAP). A SFAP could be expressed as follows:

$$V_f(y_0, z_0, z) = K'K''\left\{\frac{\partial(e_i)}{\partial z}\cdot\frac{1}{r}\Big|_{s_1} + \int_{-\infty}^{+\infty}\frac{\partial^2(e_i)}{\partial z^2}\cdot\frac{1}{r}dz - \frac{\partial(e_i)}{\partial z}\cdot\frac{1}{r}\Big|_{s_2}\right\} \quad (3)$$

where the two coefficients $K' = 2/4\pi\delta_y$ and $K'' = \pi d^2\delta_i/4$; $r = \sqrt{(z-z_0)^2 + \delta_z/\delta_y(y-y_0)^2}$ was the distance between the observation point (y_0, z_0) and surface

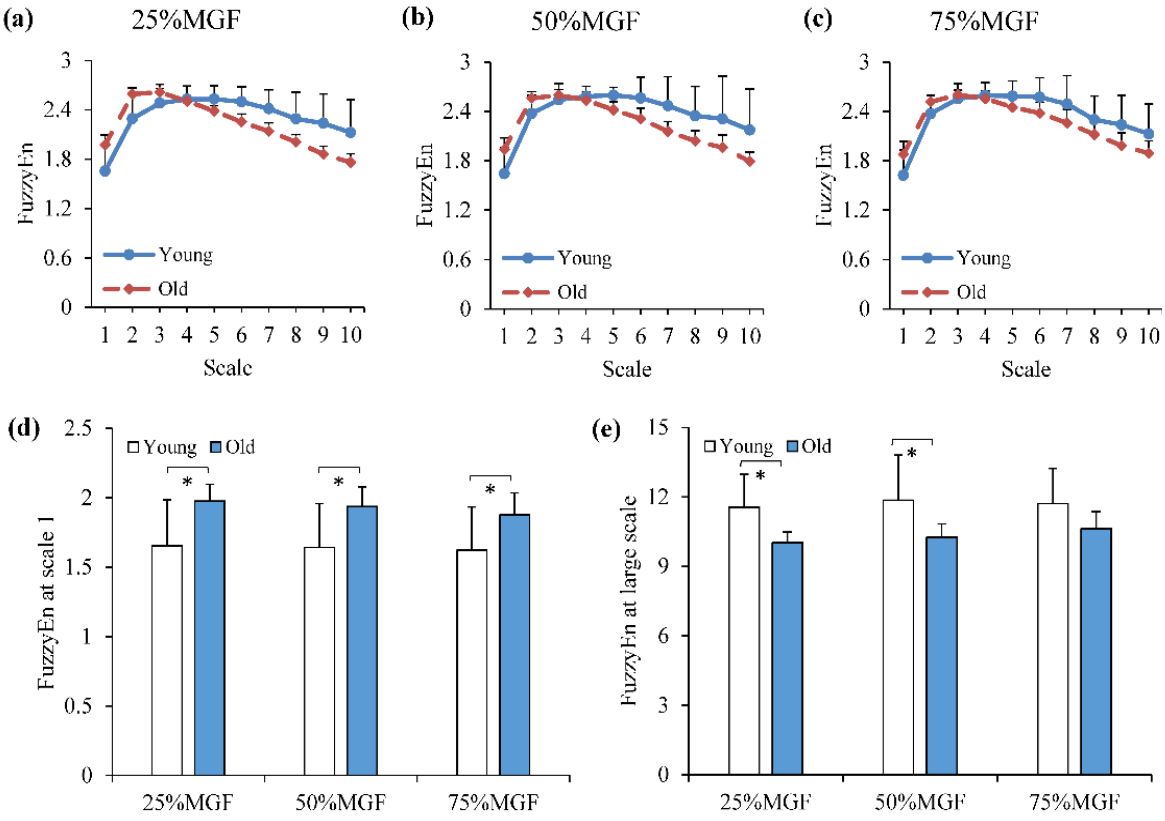

FIGURE 5. The MSFuzzyEn analyses of the FCR in the young group and the old group; (a)-(c): the MSFuzzyEns in three different levels (25%, 50%, and 75% of MGF), respectively; (d)-(e): the FuzzyEns at scale 1 and large scale (τ = 6-10), respectively. The error bars represent standard deviation. $*$ Statistically significant difference ($p < 0.05$).

element ds; z and y were the axial and radial direction; δ_z and δ_y were the muscle axial and radial conductivity, $e_i(z) = \left\{768\left(\alpha z^3\right)e^{-2\alpha z} - 90\right\}/\alpha^2$was the intracellular potential, with $\alpha = v_m/v_f$; and $s_1$and s_2 were the fiber sections at the fiber ends. The parameters in this EMG model can be found in previous studies [42]–[44].

The simulated EMG signals were set as 3 seconds (3000 samples). The MSFuzzyEns of three different kinds of simulated signals with different active MU number (10, 30, and 50) were calculated to estimate the influence of the active MU number. Meanwhile, simulated EMG signals mixed with different white noises were analyzed to detect the effect of random noise on signal complexity. The SNR was defined as follows:

$$SNR = 10 \cdot lg\left\{\sum_t y^2(t) / \sum_t x^2(t)\right\} \quad (4)$$

where y and x were the raw simulated EMG signal and the white noise, respectively. A total of 10 simulated signals were generated for each kind in order to get reliable statistics.

D. DATA PROCESSING AND STATISTICAL ANALYSIS

A 4th-order bandpass Butterworth filter (10-300 Hz) and a notch filter (50 Hz) were used to filter the real EMG signals. A low-pass Butterworth filter (20 Hz) was used to filter the grip force. The 5-s EMG signals and grip force were cut short with the first and last 1 second abandoned. The MSFuzzyEns for each group in the different levels at each time scale were the average of all subjects, and the FuzzyEns at the large time scale were the summation of scales 6 to 10 [41]. The effects of aging and force level on the complexity of the grip force and the EMG signals were assessed using two-factor analysis of variance (ANOVA, repeated measure). Statistical differences in the means of FuzzyEn between the young group and the old group at each force level were assessed using the independent-sample t test. SPSS21.0 (SPSS Inc., Chicago, IL, USA) was used to perform all statistical analyses.

III. RESULTS

A. MULTISCALE FUZZY ENTROPIES OF SIMULATED SIGNALS

As illustrated in Fig. 2a, the simulated surface EMG signal had a similar frequency range (20-150 Hz) to the real simulated EMG signal [45]. As illustrated in Fig. 2b and 2c, the FuzzyEns of the simulated EMG signals initially increased (τ = 1-4, 1-5) and later decreased (τ = 4-10, 5-10) when the time scale increased. As the MU number increased from 10 to 50, the simulated EMG signals exhibited larger FuzzyEn values at the scales 1 to 10. However, as the SNR decreased, the simulated EMG signals had larger FuzzyEn

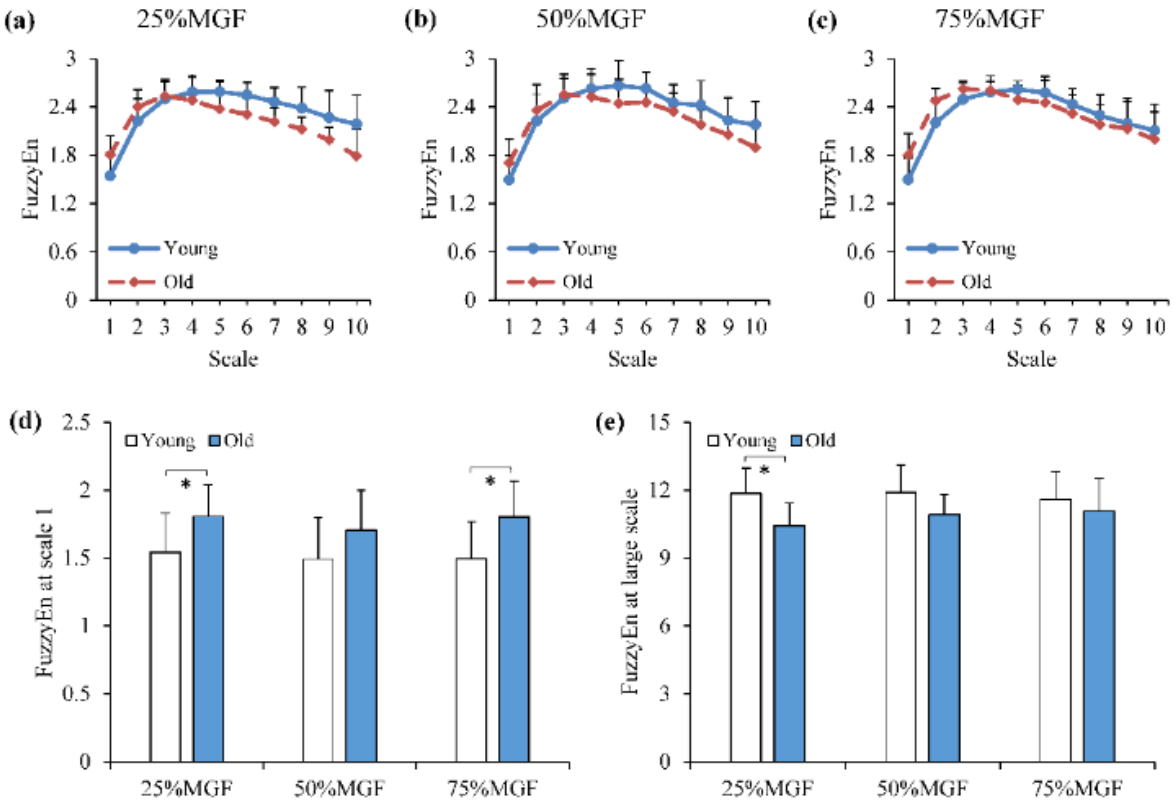

FIGURE 6. The MSFuzzyEn analyses of the FDS in the young group and the old group; (a)-(c): the MSFuzzyEns in three different levels (25%, 50%, and 75% of MGF), respectively; (d)-(e): the FuzzyEns at scale 1 and large scale (τ = 6-10), respectively. The error bars represent standard deviation. $*$ Statistically significant difference ($p < 0.05$).

values at scales 1 and 2 and had similar FuzzyEn values at the other scales.

B. MULTISCALE FUZZY ENTROPIES OF GRIP FORCE AND EMG SIGNALS

Fig. 3 displayed that the actual grip force of the young subject was larger than the older subject in each force level. As presented in Fig. 4a, 4b, and 4c, a rise in the FuzzyEn of the grip force was observed when the time scale increased from 1 to 10. However, as illustrates in Figs. 5, 6, 7, and 8, the FuzzyEn of the EMG signals (FCR, FDS, ECR, and EDC) initially rose (τ = 1-3, 1-4, 1-5) and later fell (τ = 3-10, 4-10, 5-10) when the time scale increased.

Statistical analysis revealed that the factor of the group significantly influenced the mean FuzzyEn of the grip force, FCR, and FDS at both of scale 1 ($p < 0.05$) and the large scales ($p < 0.05$), while it had no significant effect on the ECR (scale 1: $p = 0.123$, large scale: $p = 0.407$) or EDC (scale 1: $p = 0.192$, large scale: $p = 0.495$). The factor of the force level significantly affected the mean FuzzyEn of the FCR at scale 1 ($p = 0.004$) but did not significantly affect the mean FuzzyEns of the other signals at any scales.

In Fig. 4d and 4e, the FuzzyEns of grip force in the old group decreased compared with those in the young group at scale 1 (25% MGF: $p = 0.067$, 50% MGF: $p = 0.017$, 75% MGF: $p = 0.177$) and the large scales (25% MGF: $p = 0.014$, 50% MGF: $p = 0.001$, 75% MGF: $p = 0.205$). Regarding to the EMG signals, there was a rather different result based on the MSFuzzyEn analysis. Compared with the young group, the FuzzyEn of the FCR (Fig. 5) in the old group increased at scale 1 (all levels: $p < 0.05$) and decreased at the large scales (25% MGF: $p = 0.004$, 50% MGF: $p = 0.023$, 75% MGF: $p = 0.054$). Fig. 6d and 6e display similar results which indicated that compared with the young group, the FuzzyEns of the FDS in the old group rose at scale 1 (25% MGF: $p = 0.037$, 50% MGF: $p = 0.127$, 75% MGF: $p = 0.02$) and fell at the large scales (25% MGF: $p = 0.009$, 50% MGF: $p = 0.053$, 75% MGF: $p = 0.395$).

IV. DISCUSSION

This study sought to investigate the age-related complexity changes during sub-maximal force tasks at three different levels. The MSFuzzyEn was applied to detect the complexity of the grip force and the surface EMG signals across multiple time scales.

A. TIME SCALE AND COMPLEXITY

In our previous study, different kinds of physiological signals, i.e. force and EMG signals, generated rather different MSFuzzyEn values [46]. Compared with the grip

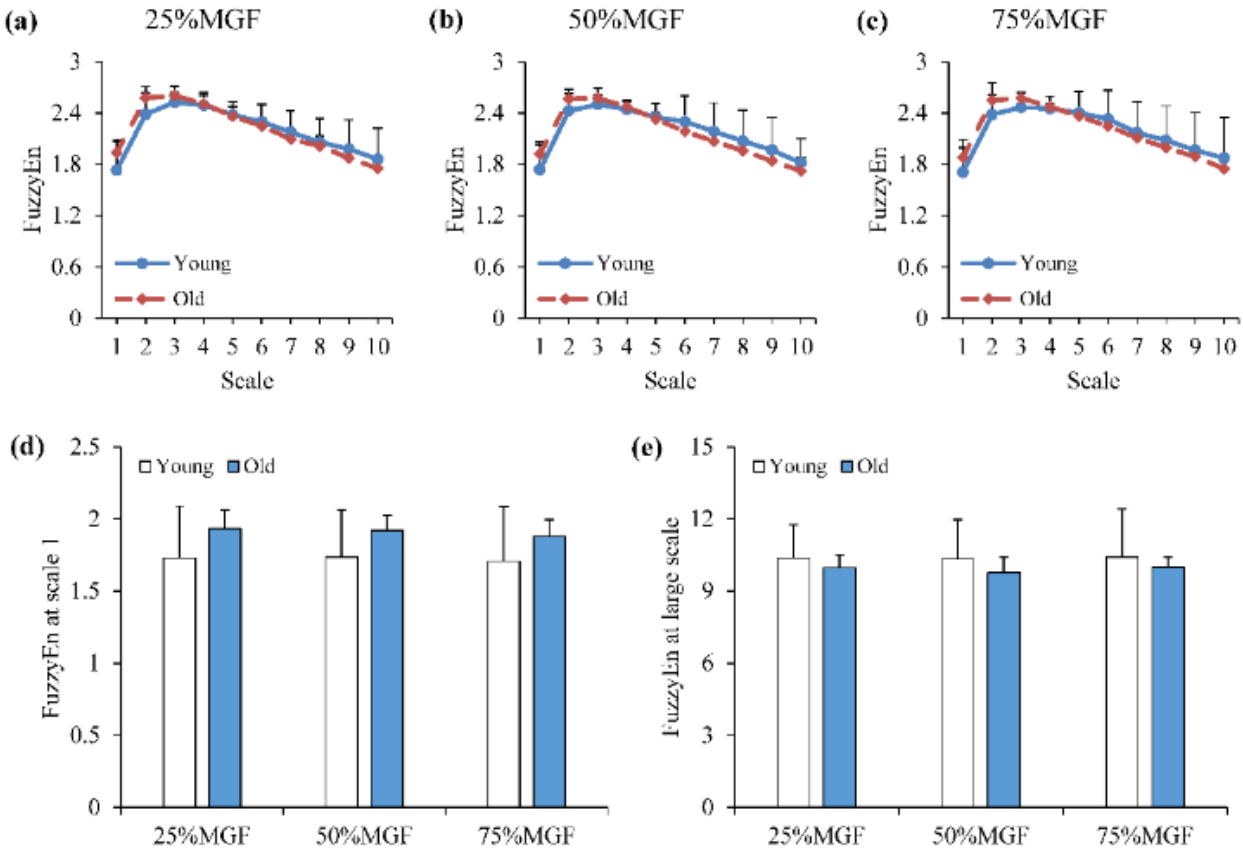

FIGURE 7. The MSFuzzyEn analyses of the ECR in the young group and the old group; (a)-(c): the MSFuzzyEns in three different levels (25%, 50%, and 75% of MGF), respectively; (d)-(e): the FuzzyEns at scale 1 and large scale (τ = 6-10), respectively. The error bars represent standard deviation. $*$ Statistically significant difference ($p < 0.05$).

force, the EMG signals were weaker, and useful information was easily confounded with uncorrelated noises [47]. Costa *et al*. [32] reported, both uncorrelated random noises and periodic information could be gradually filtered out of the original time series with a coarse-graining procedure. Thus, the decreased complexity of EMG signals with the increased time scale (τ = 6-10) might have been due to the noise abatement of the coarse-graining procedure. Similar downtrend of complexity towards increasing time scale have been observed in previous studies of EMG signals from leg muscles [17], spontaneous motor unit discharge patterns [48], human heartbeat signals [32], and gait dynamics [38]. The changes in FuzzyEn towards increasing time scales of the simulated EMG signals were also consistent with those of real EMG signals. Therefore, the coarse-graining signals at larger time scales (τ = 6-10) possessed higher SNR than those at smaller time scales (τ = 1-5), especially for the electrophysiology signals. As far as we know, 1/f noise with the property of long-range correlation generated stable entropy values across multiple time scales [32], [49], which was rather different from white noise with the property of uncorrelation. Thus, noises that could be depressed after coarse-graining were mainly due to its property of uncorrelation.

The increase in signal complexity as the time scale increased (EMG: τ = 1-5, Force: τ = 1-10) could be related to the decrease in data length. In our previous study, we confirmed the superiority of FuzzyEn over other entropies, whereas we found a minor increase in FuzzyEn with smaller data samples [40]. As far as we know, the decrease in data length was an inevitable consequence of successive coarse graining. Similar phenomena have been found in previous studies of heart rate signals from healthy adults [33] and EEG signals from rats [36].

B. AGING AND COMPLEXITY

The age-related decrease in the entropy of the grip force was associated with the inherent complexity in the human motor system. In a study of human heartbeat signals, a loss in multiscale complexity was observed among elderly people compared with young people [37]. Previous studies of postural sway suggested that aging tends to cause a decrease in the complexity of movement patterns, which, in turn, would lead to more regular movements [50], [51]. Sosnoff and Newell [15], and Sosnoff and Voudrie [16] proposed that the entropy of force output decreases due to aging, which characterizes the structural changes of force variability during index finger flexion and abduction . The changes in motor

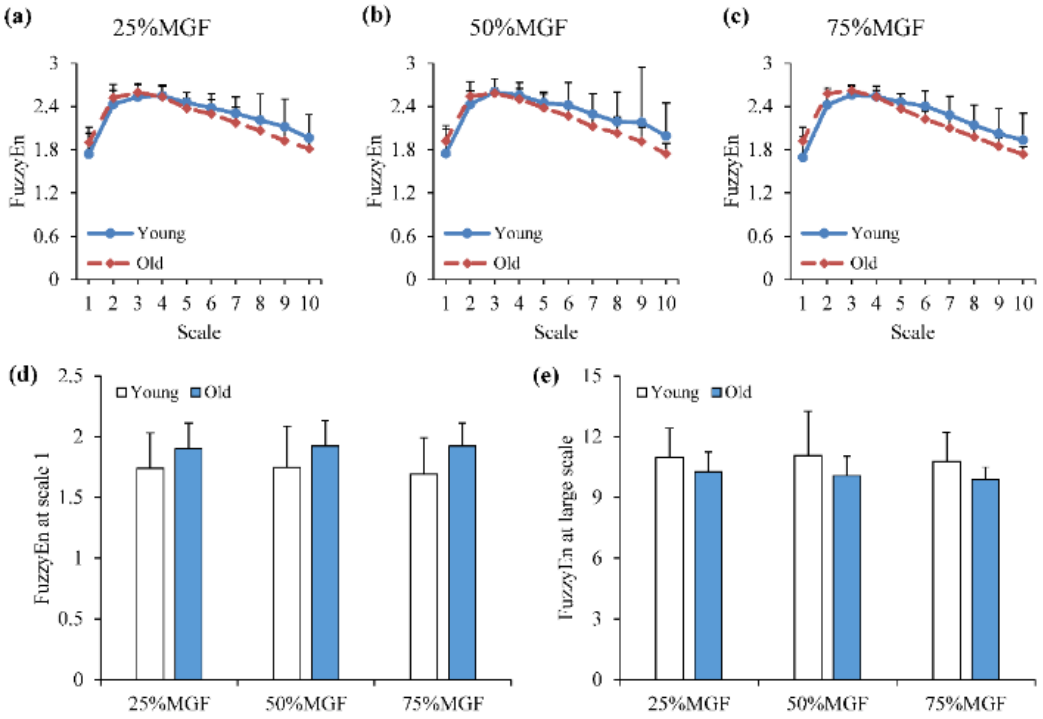

FIGURE 8. The MSFuzzyEn analyses of the EDC in the young group and the old group; (a)-(c): the MSFuzzyEns in three different levels (25%, 50%, and 75% of MGF), respectively; (d)-(e): the FuzzyEns at scale 1 and large scale (τ = 6-10), respectively. The error bars represent standard deviation. ∗ Statistically significant difference ($p < 0.05$).

unit synchrony, which refer to the simultaneous discharge of motor units, might be responsible for the evoked fluctuations in the structure of force variability [16]. Semmler *et al*. [52] demonstrated that elderly people perform worse in adapting motor unit synchrony to different contraction types, which could explain the changes in complexity during aging. Moreover, Pincus proposed that the decrease in signal complexity indicates a reduced coupling between components in the motor system [53]. Thus, the changes in the complexity of grip force might indicate a greater independence in single muscle firing patterns [54].

The multiscale entropy analysis extracted a thorough feature in the complexity of EMG signals. Similar to our study, Gu and Dingwell [17] found an increase in neuromuscular noise during the aging process, which might be the major factor in the entropy of smaller time scales (τ = 1-5). Previous studies demonstrated that the entropy of white noise degrades as the time scale increases [33]. Accordingly, our simulation tests confirmed that the entropy at smaller time scales (τ = 1-3) was influenced by random noises, while the entropy at larger time scales (τ = 4-10) was not. Thus, based on single-scale entropy analysis, it is difficult to distinguish the inherent complexity of the neuromuscular system from uncorrelated noises [33].

Depressing the domination of noise after coarse-graining, the entropy of EMG signals at large time scales (τ = 6-10) exhibited a loss in system complexity due to aging, and similar characteristics have been detected for leg muscles during treadmill walking [17]. Goldberger *et al*. [49] reported, the age-related loss in multiscale complexity might be associated with the breakdown in the correlation properties of signals, which indicated a reduction in the adaptive capacity of individuals. One possible explanation for the loss in complexity with aging in our study was sarcopenia and the related loss of motor units [48], [55]. As simulation test demonstrated, a reduced number of the active motor unit for the EMG signals evoked a decrease in multiscale entropy. Based on our previous study, another possible explanation for the loss of system complexity in the aging process is the decrease in the firing rate of the active motor unit [40]. The denervation of related peripheral neuromuscular system might cause the decrease in the number and firing rate of the active motor unit [56].

C. CLINICAL IMPLICATIONS

The features of intramuscular EMG signals have been extracted to detect neuromuscular changes due to aging [57], Parkinson's Syndrome [58], and other internal factors [59]. As far as we know, the surface EMG signals are simpler than intramuscular EMG signals, and can be obtained non-invasively. Previous studies have utilized the EMG amplitude to uncover the neurological changes that occur during the aging process [60], but the certainty of the measurements was highly susceptible to the location of the electrode, the EMG amplifier, the contact impedance between the skin surface and the electrode, as well as the uncorrelated noise. The MSFuzzyEn primarily characterized the internal irregular changes rather than the amplitude changes, which

contributed to its superiority [53]. Moreover, at large time scales, the FuzzyEn could depress the interference of uncorrelated noise. Additionally, the normalization for the EMG signals was contained in the MSFuzzyEn algorithm; thus, the experimental procedure and data processing can be simplified. Considering the above points, the MSFuzzyEns of surface EMG signals is quite promising in the clinical evaluation of age-related neurological changes. In future work, the MSFuzzyEns of surface EMG signals in pathological conditions deserves to be explored further in its clinical applications.

V. CONCLUSION

In the current study, the MSFuzzyEn method was applied to detect the complexity changes in simulated EMG signals with different MU numbers and SNRs. Age-related differences during sub-maximal force tasks with three different levels were also investigated using MSFuzzyEn. As the time scale increased, the complexity changes of the simulated EMG signals were consistent with those of real EMG signals, and the simulation tests confirmed the merits of MSFuzzyEn in noise abatement. Based on FuzzyEn at large time scales (τ = 6-10), age-related losses in complexity were observed in the grip force and EMG signals, which might result from the modifications of motor unit firing patterns during aging. Thus, multiscale entropy holds the potential to provide new insights into neuromuscular changes caused by aging or disease.

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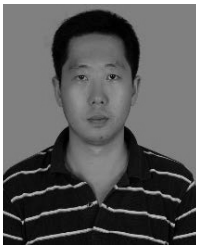

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