J Appl Physiol 97: 454–455, 2004;
10.1152/japplphysiol.00244.2004.

The following is the abstract of the article discussed in the subsequent letter:

Vaillancourt David E., and Karl M. Newell Aging and the time and frequency structure of force output variability. *J Appl Physiol* 94: 903–912, 2003; 10.1152/japplphysiol.00166.2002.—The present study examined the time and frequency structure of force output in adult humans to determine whether the changes in complexity with age are dependent on external task demands. Healthy young (20–24 yr), old (60–69 yr), and older-old (75–90 yr) humans produced isometric force contractions to constant and sine wave targets that also varied in force level. First, force variability on each force task increased with advancing age. Second, both time and frequency analysis showed that the structure of the force output in the old and older-old adults was less complex in the constant-force level task and more complex in the sine wave force task. Third, the alterations in force output with aging were primarily due to low-frequency bands <4 Hz. These results support the postulation that the observed increase or decrease in physiological complexity with aging is influenced by the relatively fast time scale of external task demands (Vaillancourt DE and Newell KM. *Neurobiol Aging* 23: 1–11, 2002).

Age-related changes in complexity depend on task dynamics

To the Editor: The changes in complexity most frequently cited in both aging and diseased systems have physiological output consistent with a loss of complexity (3). However, across the cardiovascular, nervous, and endocrine systems, both increases and decreases in complexity with aging and disease occur, collectively termed the bidirectional complexity hypothesis (7). Our recent study tested the bidirectional complexity hypothesis in young (21–35 yr), old (60–75 yr), and older-old (75–90 yr) participants during constant and sinusoidal isometric force production tasks (6). The findings were consistent across all dynamical metrics in showing bidirectional changes in complexity with age that were dependent on the intrinsic dynamics of the experimental task.

The bidirectional complexity hypothesis has been criticized for relying on entropy-based metrics that ignore sequential properties across multiple time scales, thereby misinterpreting the changes of reduced complexity with aging and disease (1, 2). The critique is based on the notion that greater entropy values are not always associated with an increase in physiological complexity. For instance, a white Gaussian noise time series returns a high entropy value even though there is no underlying dynamical structure in the time series. An aggregate analysis method, multiscale entropy analysis (MSE), has been suggested to overcome the limitations of single-scale entropy measures by calculating entropy over different variations of the same data set following a moving average window that varies in length or scale (1).

The purpose of this commentary is to reexamine our previous findings (6) using the MSE method to determine whether the finding of age-related bidirectional changes in complexity was due to biological variation or because of the use of dynamical measures that do not account for scales other than the shortest one. Figure 1 depicts the results from the MSE analysis, in which sample entropy (SampEn) (5) was calculated over different time scales during constant (Fig. 1*A*) and sinewave (Fig. 1*B*) force production tasks. ANOVA statistics were used to examine the SampEn ($m = 2$; $r = 0.2$) changes across age (3-between subject factor), task (2-repeated factor), and time scale (20-repeated factor) with a Type I α-level set to 0.05. In both constant and sinewave force production tasks, the SampEn values increase from between 0.25 and 0.50 at the shortest time scale, to greater than 1.25 at the highest MSE time scale (time scale effect, $P < 0.05$). Although the directionality of age differences in SampEn values was maintained across all time scales, there was a bidirectional change in SampEn with age, depending on the force production task (age by task interaction, $P < 0.05$). We further explored the age-by-task interaction by conducting two separate two-way ANOVAs for age and time scale. The constant force task (see Fig. 1*A*) supports the loss of complexity viewpoint, that is, that SampEn was reduced with aging at each time scale (age effect, $P < 0.05$). In contrast, Fig. 1*B* demonstrates the opposite finding during the sinewave task, in which the older-old adults had greater SampEn values compared with the young subjects (age effect, $P < 0.05$).

Thus the MSE analysis produced a consistent pattern at short time scales as in our previous work (6), and the findings also demonstrated a similar pattern of age-related changes in complexity at long time scales. The findings demonstrate that the bidirectional change in complexity with advanced age is not an

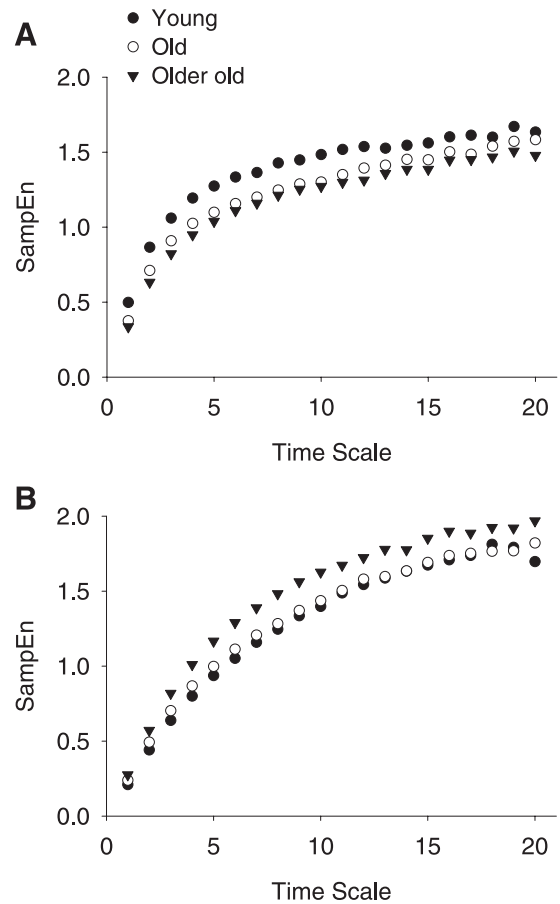

Fig. 1. Multiscale entropy analysis (MSE) across time scales. The dependent variable, sample entropy (SampEn), was calculated on the force output data set across each time scale. We report sample entropy instead of approximate entropy because sample entropy is robust across a different number of time series data points. However, approximate entropy (4) did produce similar findings as sample entropy (5). Each data point represents the average across sample entropy values for 10 subjects at each time scale in the young (21–35 yr; ●), old (60–75 yr; ○), and older-old (75–90 yr; ▼) groups. The task required participants to abduct their index finger against the compressive force load cell, matching the visually determined constant (*A*) and 1-Hz sinewave (*B*) force targets.

artifact of the dynamical measures used (2). In conclusion, the age-by-task interaction supports the primary thesis of the bidirectional complexity hypothesis that aging physiological systems are deficit in their ability to adapt to environmental stressors and directional changes in complexity depend on the nature of the task and dynamics of the specific physiological system (7).

ACKNOWLEDGMENTS

We thank Dr. Randall Moorman and Dr. Douglas Lake for supplying the algorithm to calculate sample entropy.

GRANTS

This work was supported by grants from the National Institutes of Health (F32-NS-44727, T32-AG-00048, and R01-HD-46918).

REFERENCES

1. **Costa M, Goldberger AL, and Peng CK.** Multiscale entropy analysis of complex physiologic time series. *Physiol Rev Lett* 89: 068102, 2002.
2. **Kyriazis M.** Practical applications of chaos theory to the modulation of human ageing: nature prefers chaos to regularity. *Biogerontology* 4: 75–90, 2003.
3. **Lipsitz LA and Goldberger AL.** Loss of "complexity" and aging. Potential applications of fractals and chaos theory to senescence. *JAMA* 267: 1806–1809, 1992.
4. **Pincus SM.** Approximate entropy as a measure of system complexity. *Proc Natl Acad Sci USA* 88: 2297–2301, 1991.
5. **Richman JS and Moorman JR.** Physiological time-series analysis using approximate entropy and sample entropy. *Am J Physiol Heart Circ Physiol* 278: H2039–H2049, 2000.
6. **Vaillancourt DE and Newell KM.** Aging and the time and frequency structure of force output variability. *J Appl Physiol* 94: 903–912, 2003.
7. **Vaillancourt DE and Newell KM.** Changing complexity in human behavior and physiology through aging and disease. *Neurobiol Aging* 23: 1–11, 2002.

David E. Vaillancourt
Department of Movement Sciences and Center for Magnetic Resonance Research
University of Illinois at Chicago
Chicago, Illinois 60612
court1@uic.edu

Jacob J. Sosnoff[1,2] and Karl M. Newell[1,3]
Departments of [1]Kinesiology and [3]Biobehavioral Health, and [2]Gerontology Center
The Pennsylvania State University
University Park, Pennsylvania 16802