

Letter to the Editor

Resilience Versus Robustness in Aging

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In a highly interesting and timely article by Whitson and colleagues (2016), the authors suggested “a working definition of physical resilience at the whole person level: A characteristic which determines one’s ability to resist or recover from functional decline following health stressor(s).” We believe that in the much-needed attempts to define “physical resilience” and its relevance to aging and health, it is important to distinguish between the ability to *resist* deviation from the original state (we will call it “robustness”) from the ability to *recover* after such deviation (resilience per se). There are several reasons to do so.

Generally, response to a stressor includes two key steps: (i) deviation from the original (baseline) state, if any and (ii) return to the original state (recovery). Respectively, stress resistance can be characterized by the two different components: (i) ability to resist the deviation from the baseline (robustness) and (ii) ability to quickly and fully recover after such deviation (resilience). Measures of robustness may include *magnitude of deviation* from the original state and *time to a peak* value; whereas measures of resilience may include *time to recovery* and *completeness* of the recovery.

The robustness and resilience may both change with aging of an individual; however, their change may potentially *differentially* influence health decline and longevity. Although declines in both robustness and resilience may contribute to disease risk and associated mortality, the decline in resilience but not necessarily in robustness is likely to be a *universal* factor responsible for the increase in vulnerability to death in healthy oldest old people.

Indeed, as people age, they inevitably decline in resilience, for instance, in the ability to quickly and fully recover after acute damage, such as caused by hip fracture, pneumonia, internal bleeding, and wound, meaning that the same damage would affect their recovery and survival chances less if they were younger. Robustness may also decline with age, which can be seen by increases in risks of some major disorders (eg, Alzheimer’s disease and stroke) and related mortality toward the oldest old age. However, the age decline in

robustness is *not* universal, people do not always decline in robustness with age and may even improve it at older ages in some health domains.

For instance, risks of some major diseases (eg, cancer, asthma, diabetes) decline in advanced years of life. For cancer, this decline is also confirmed in experimental animals (1,2). Earlier, we discussed causes of such decline in several articles and proposed that certain components of the aging process (such as the slowdown in metabolic, growth/proliferation, and information processing responses) may not only promote but also *oppose* development of some major chronic diseases, in other words, improve individual robustness to occurrence of these diseases in advanced years of life (1–3). For example, for cancer, one potential mechanism of declining its risk at oldest old ages may involve a typically slower development of latent tumors in an older body, so that the older person will have lower chances of clinical manifestation of respective cancer, that is, will be more robust in this regard (1,2). Paradoxically, the same aging component (the slowdown) that may reduce risks of some major chronic diseases also makes worse the senescence-related conditions, such as poorly healed fractures and wounds due to slow regeneration, heart failure due to muscle atrophy, renal failure due to slow metabolism, complications of chronic obstructive pulmonary disease, and flu and pneumonia due to slow immune response. The slower responses make recovery from such conditions longer and less complete. Such decline in resilience in turn contributes to an increase in vulnerability to death. That is, even when robustness improves in some health domains (risks of cancer, asthma, diabetes, and hypertension all decline at oldest old ages), resilience continues to deteriorate, which results in greatly reduced overall survival chances following an adverse event in the very old. This kind of a “trade-off” between robustness and resilience may in part explain why the all-cause mortality risk continues to increase toward extreme ages, while the risks of many chronic diseases decline at the same ages (1–3).

Older people may also have a better robustness to certain infections compared with younger individuals. For example, during 2009 pandemic of H1N1 influenza, few cases occurred in people older than 65 years compared with young adults and children. A study conducted by the Centers for Disease Control and Prevention indicated that children had no existing cross-reactive antibody to the 2009 H1N1 flu virus, whereas about one third of adults older than 60 years had such antibody, potentially due to immunity developed through past exposure to infection or vaccination (4). However, if the older person does not have such past immunity and becomes ill, such person will have overall lower chances of recovery and higher chances of dying following this infection than s/he would have earlier in life, that is, this person will be on average less resilient than s/he was at a younger age.

Also, of note, a so called “male–female health-survival paradox” (5) (better health but worse survival in men compared with women) might in part be related to a “trade-off” between robustness and resilience in men and women, meaning that women may be less robust than men in relation to acquiring some health disorders but more resilient when it comes to recovery and survival after an adverse life event.

In sum, the differential effects of robustness and resilience on all-cause mortality are possible. Some components of physiological aging (eg, the slowdown) may universally contribute to the decline in resilience, but not necessarily in robustness. Decline in resilience could primarily be responsible for the continuing decline in recovery and survival chances at oldest old ages, despite decreasing risks of many chronic conditions at these same ages, and so it could be a major factor determining one’s potential to achieve extreme longevity.

We therefore suggest that in addition to combining the different components of stress resistance in one composite phenotype, such as “ability to resist or recover from functional decline following health stressor,” it may also be reasonable to explore these components separately, as follows:

(1) **Robustness**—Ability to resist deviation from the original (baseline) state. In biomarker studies, robustness may be character-

ized by the magnitude of deviation of a biomarker from its baseline level after a stress, as well as by the time to a peak value. For example, a degree of the increase in blood pressure after a cold stress applied to the arm would characterize individual robustness. On the level of health outcomes, factors characterizing robustness are those influencing disease risk, but not necessary recovery and survival following the diagnosis.

(2) **Resilience**—Ability to quickly and completely recover after a deviation from the original state. For example, the speed of returning of the blood pressure to its baseline values after withdrawal of the cold stress, as well as the excess of the blood pressure over its original baseline value after a specified timespan, would characterize individual resilience.

In this framework, complex physiological and health indicators, such as glucose tolerance test, could potentially be decomposed into several phenotypes reflecting mostly robustness (magnitude of glucose increase after loading and time to peak) or mostly resilience (time to returning of the blood glucose to its baseline level and the excess of the glucose level over the baseline, if any).

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