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Physical Resilience: Not Simply the Opposite of Frailty

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Physical resilience, which we define as one's ability to withstand or recover from functional decline following acute and/or chronic health stressors[1], is a construct that resonates with older patients and caregivers. Indeed, successful aging often depends on a person's response to the inevitability of late-life stressors. Physical resilience is distinct from the well-studied, and also important, construct of psychological resilience[1,2]. Whereas psychological resilience refers to a person's ability to adapt well in the face of adversity, trauma, tragedy, threats or significant sources of stress[3–5], physical resilience focuses on the maintenance or recovery of function after biomedical or pathological challenges[6]. Physical resilience is presumed to reflect adaptive physiological responses at the level of organs, cells, and molecules (e.g., musculoskeletal, neurological, immunological processes) that support homeostasis under changing conditions[6]. Physical resilience has been a topic of interest at the National Institute of Aging[6,7], and it is the theme of Duke's Claude D. Pepper Older Americans Independence Center, where we have focused on recovery of physical and cognitive function after health stressors.

As our Center has worked to refine and test hypotheses about physical resilience, we have engaged in many dialogues - amongst ourselves and with colleagues, collaborators, and reviewers from around the world - about the construct itself. One question has recurred frequently: Is physical resilience simply the opposite of frailty? We have come to the conclusion that, while there are clearly points of conceptual overlap, physical resilience is not simply the opposite of frailty (at least as frailty is most typically defined at present). Here, we outline our thinking on the common and distinguishing features of these two constructs.

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Although different methods have been proposed to operationalize a definition of frailty[8–10], most aging researchers agree that frailty is a state of physiological vulnerability to stressors, which results from age-related decline in biological systems and manifests clinically as an increased risk of adverse outcomes[11]. A reasonable expectation is that frailty and resilience are correlated, such that frail individuals have low resilience. Additionally, both constructs speak to the important role of stressors (e.g., infection, surgery, cancer, widowhood) in influencing health outcomes in late life. Both constructs acknowledge that the pace of physiological decline at the cellular and molecular level is heterogeneous in an aging population, rendering some older adults more vulnerable than others when catastrophe strikes. Two people of the same chronological age may respond to the same stressor quite differently; the ability to identify frailty or predict resilience should provide clues about how to optimize health for both individuals.

One way that our notion of resilience differs from frailty is that we conceptualize resilience as a continuous spectrum that applies across the lifespan; in theory, any person's level of resilience could be quantified at every point in his or her lifetime. In contrast, frailty often evolves near the end of life and represents an extreme stage in the healthspan. As other investigators have noted, frailty typically refers to age-related decline in tissue and organism function and manifests in only a small proportion of older individuals, whereas young individuals exhibit different degrees of resilience[12]. If this were the only difference between frailty and resilience, one could argue that frailty merely represents the lowest end of the resilience spectrum. Even so, it would be impractical to quantify resilience with current measures of phenotypic frailty, as frailty measures rely on features associated with evident decline, such as slowness and wasting[13], and thus would have an unacceptable ceiling as resilience measures.

A second difference in our conceptual models of frailty and resilience is that confirmation of a resilient response entails the observation of one or more time points after the stressor. If an older adult who undergoes a stressor (e.g., surgery) has a high risk of complications (e.g., surgical site infection) and functional decline, we may accurately label this person's pre-existing vulnerability to the stressor as frailty. However, if the same person recovers rapidly from the infection and ultimately rebounds to a functional level near or as high as his pre-surgical level, this individual would be aptly labeled as having demonstrated resilience. Our working definition of physical resilience emphasizes the trajectory of functional response after the stressor. Thus, as measures to predict physical resilience are developed, it will be important to validate them against outcomes collected at multiple time points after the stressor.

Third, we propose that one's likelihood to suffer physical decline associated with frailty and one's likelihood to counteract or recover from functional loss during and after stressors (physical resilience) may depend on different mechanisms. Here, we turn to the concept of physiological reserve. We have defined physiological reserve as the "potential capacity of a cell, tissue, or organ system to function beyond its basal level in response to alterations in physiologic demands[1]." Our notion of physiological reserve is in line with the related concept of "intrinsic capacity," which has been introduced by the World Health Organization[14]. To our thinking, frailty can be understood as a state of low physiological reserve across multiple biological systems, such that the organism has limited capacity to deal with perturbation. Likewise, we have postulated that one's physical resilience (i.e., capacity for physical recovery) at any given moment is constrained by one's level of physiological reserve in various tissues and biological systems that may be subjected to stress. However, factors including environment, social support, and psychological health may also influence the degree of functional recovery that is achieved and are thus also contributors to one's physical resilience. If the spectrum from robustness to frailty reflects the amount of physiological potential one has to react to stressors, physical resilience refers to the actualization of that potential.

While low reserve in any biological system may render a person more frail (i.e. vulnerable to stress), an intriguing possibility is that certain biological processes are particularly key to resilience. For example, research in model organisms, such as the tardigrade water bear or hibernating mammals, may offer clues about why these animals exhibit striking physical resilience when exposed to extreme environmental conditions. This line of research has suggested that nimble maintenance and recovery of homeostasis under stressful conditions may rely on factors such as metabolomics, mechanisms that protect and repair DNA and proteins, and precise regulation of stem cells[15–18]. Perhaps one of the most compelling reasons to distinguish the constructs of physical resilience and frailty is that they may involve different molecular targets for pharmacological intervention.

As we have teased out distinctions between the concepts of frailty and physical resilience, we have made use of a metaphor, which we call "the castle under siege." Imagine a castle that is being attacked by an enemy army (the stressor). The age of the castle likely plays a part in whether or not it will crumble under the assault, as even a well-built castle will suffer some structural weakening over the years, especially if its maintenance has been neglected. Even before the army attacked, one might have observed cracks in the castle's foundation or missing stones – these would be evident phenotypic features of the castle's frailty. Whether or not the castle will fall depends both on the magnitude of the attack/stressor as well as on how much reserve the castle possesses, both in its structural integrity and in its defensive mechanisms. Aspects that would be associated with higher reserve, rendering the castle less frail and less vulnerable to falling down, include smart architectural design (e.g., reinforced doorways, sophisticated engineering) and sturdy building materials. Even if the walls hold, the castle and its occupants will likely suffer some degree of damage from each assault. The speed, magnitude, and efficiency with which the castle can mobilize defensive resources (e.g., deploy archers), and then be restored (e.g., repair damage) contributes to the castle's ultimate resilience. We expect an older, cracked-wall, poorly designed (i.e., frail) castle to suffer more damage during the assault. However, there may be hidden resources that are especially important during the repair process – for example, stonemasons to shore up damaged walls and stores of oil and food to outlast a siege. Thus, understanding which types of reserve resources and processes are most critical to successfully withstanding and recovering from the assault are very different from understanding why the castle became cracked and weakened over time.

Understanding patterns and mechanisms of physical resilience is an exciting frontier for aging research. Semantic discussions like the one here are important, to a point, inasmuch as they help establish the common language and conceptual model necessary to develop measurement tools, experiments, and ultimately interventions. But we caution the field not to become stymied by semantics. Rather, we encourage investigators to acknowledge that the vocabulary is still evolving and to provide a precise definition of terms as they are being used. Some terms - such as reserve, frailty, and resilience - are still subject to ambiguity and misinterpretation. Whether or not others agree with our assertion that resilience and frailty are not simply mirror-image opposites of each other, research into these complementary constructs has great potential to improve older adults' capacity to respond to stress and preserve health. We welcome further discussion.

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