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Psychological and social resources relate to biomarkers of allostasis in newly admitted nursing home residents

Suzanne Meeks[a]*, Kimberly Van Haitsma[b], Benjamin T. Mast[a], Steven Arnold[c], Joel E. Streim[c], Sandra Sephton[a], Patrick J. Smith[a], Morton Kleban[d] and Michael Rovine[e]

[a]*Department of Psychological & Brain Sciences, University of Louisville, Louisville, KY, USA;* [b]*College of Nursing, Pennsylvania State University, 201 Health and Human Development East, University Park, PA, USA;* [c]*Geriatric Psychiatry Section, Department of Psychiatry, University of Pennsylvania, Philadelphia, PA, USA;* [d]*Polisher Research Institute, Abramson Center for Jewish Life, North Wales, PA, USA;* [e]*Department of Human Development and Family Studies, College of Health and Human Development, Pennsylvania State University, University Park, PA, USA*

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Objectives: This paper presents preliminary baseline data from a prospective study of nursing home adaptation that attempts to capture the complexity of residents' adaptive resources by examining psychological, social, and biological variables from a longitudinal conceptual framework. Our emphasis was on validating an index of allostasis.
Method: In a sample of 26 long-term care patients, we measured 6 hormone and protein biomarkers to capture the concept of allostasis as an index of physiological resilience, related to other baseline resources, including frailty, hope and optimism, social support, and mental health history, collected via interview with the resident and collaterals. We also examined the performance of self-report measures reflecting psychosocial and well-being constructs, given the prevalence of cognitive impairment in nursing homes.
Results: Our results supported both the psychometric stability of our self-report measures, and the preliminary validity of our index of allostasis. Each biomarker was associated with at least one other resilience resource, suggesting that our choice of biomarkers was appropriate. As a group, the biomarkers showed good correspondence with the majority of other resource variables, and our standardized summation score was also associated with physical, social, and psychological resilience resources, including those reflecting physical and mental health vulnerability as well as positive resources of social support, optimism, and hope.
Conclusion: Although these results are based on a small sample, the effect sizes were large enough to confer some confidence in the value of pursuing further research relating biomarkers of allostasis to psychological and physical resources and well-being.

Keywords: nursing homes; allostasis; biomarkers; well-being; resilience

Introduction

Approximately, 45% of Americans over the age of 65 use a nursing home, and about 24% of these individuals will stay for a year or more (Congressional Budget Office, 2004). Nursing homes serve individuals with high likelihood of physical disability (U.S. Census Bureau, 2014), who carry risks of comorbid physical, cognitive, and mental disorders that diminish quality of life at the end of life (e.g., National Center for Health Statistics, 2008; Wulsin, Valliant, & Wells, 1999). Admission to a nursing home for long-term care is a crisis point that carries high risk for mental illness and further decline, but also affords an opportunity for positive mental health outcomes.

We know little about the characteristics of nursing home residents and their experiences post-admission that are related to optimal well-being. Capturing the complexity of patient adjustment following nursing home admission requires an integrated consideration of both biological and psychosocial characteristics. Recent reviews of successful or resilient aging have highlighted the importance of behavioral and biological processes as predictors of outcomes (e.g., Aldwin & Igarashi, in press; Depp, Vahia, & Jeste, 2010; Friedman & Ryff, 2012a). The work of Friedman and his colleagues has demonstrated how inflammatory processes are intertwined with affective and social processes in community samples of middle-aged and older adults (e.g., Friedman & Ryff, 2012b); however, psychological studies of adaptation to nursing homes have not included measures of such stress-related biological processes. In the current paper, we present preliminary baseline data from a prospective study of nursing home adaptation that attempts to capture the complexity of nursing home residents' adaptive resources by examining psychological, social, and biological characteristics.

The longitudinal framework that informs our larger study is shown in Figure 1. This framework depicts a set of psychological, social, and physical health "resilience resources" that form the foundation of an individuals' adaptive capacity, leading to psychological, social, or biological processes that in turn may enhance well-being. The term "resilience" has variously been used to characterize response to or recovery from specific stressors or challenges (Ryff, Singer, Love, & Essex, 1998; Zautra, Arewasikporn, & Davis, 2010), to define personality traits that allow a

*Corresponding author. Email: smeeks@louisville.edu

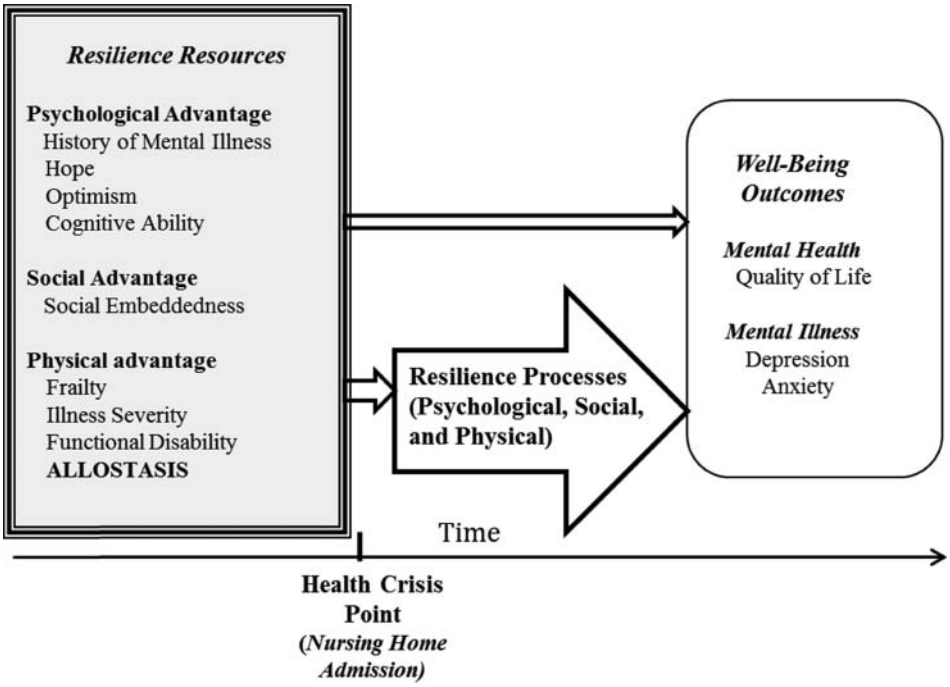

Figure 1. The longitudinal framework for studying resilience processes as mediators of baseline resilience resources and well-being outcomes over one year following nursing home admission. The focus of the present paper is on the cross-sectional relationships among biological, psychological, and social resources depicted in the left-hand box.

person to recover or thrive following adversity (Haight et al., 2002), or to describe the process of reaching positive outcomes (e.g., Greve & Staudinger, 2006; Ryff & Singer, 2003). We view resilience as the overall process of preparation for and responding to stressful circumstances, consistent with the ecological model of resilience posited by 2012; Aldwin and Igarashi (2015). Thus, in Figure 1 we show resilience *resources* that prepare or hinder a person's ability to adapt to duress, and resilience *processes* that unfold during stressful encounters. For our outcome measures, we use the term high well-being (Meeks, Van Haitsma, Kostiwa, & Murrell, 2012; Kolanowski, Van Haitsma, Meeks, & Litaker, 2014) to denote the positive outcome of a "resilience trajectory" (Ryff et al., 1998, p. 74) that begins when an individual is admitted to a nursing home. Our use of the term high well-being corresponds to what Zautra and colleagues (2010) called "resilient outcomes," and is consistent with the notion that it is possible to have high well-being despite the presence of chronic disease (Aldwin & Igarashi, 2015; Friedman & Ryff, 2012a; 2012b; Pruchno, Wilson-Genderson, & Cartwright, 2010), provided there are sufficient resources and the presence of adaptive processes to respond to the stress that results from disease.

In the current paper, we examine characteristics that may reflect patients' biopsychosocial capacity for resilience at or just prior to admission, i.e., the resilience resources shown in the left-hand box in Figure 1, measured via blood draws and participant interview taken within 30 days of their transition to long-term care. We focus on the concept of *allostasis* as an index of physiological resilience, reflecting contemporary resilience models that show important inter-relationships among physiological, psychological, and contextual resources and processes related to successful adaptation; to our knowledge, no one has examined the allostasis construct in this population. Whereas there are studies of individual markers that are thought to reflect the biological capacity to respond to stress, the degree to which these markers can collectively describe the abstract construct of allostasis as a physiological resource, and thus be used to predict successful adjustment to nursing home placement, has not been studied. Our primary purpose is to validate the allostasis concept in this vulnerable population, in relation to other baseline resources and indicators of high well-being.

Allostasis in nursing home residents

Allostasis, meaning "stability through change," describes the ability to maintain stability in a changing environment through physiological or behavioral change (McEwen & Seeman, 1999; Sterling & Eyer, 1988). From a physiological perspective, resilient outcomes might be measured by the body's ability to respond to environmental change with appropriate activation of stress responses (i.e., autonomic, hypothalamic pituitary adrenal axis – HPA), followed by a return to basal functioning (McEwen & Seeman, 1999). The flexibility of these physiological responses is reduced with aging or chronic stress (McEwen & Seeman, 1999). Autonomic and HPA responses are important regulators of cardiovascular, metabolic, immune, and circadian function. "Allostatic load" (AL) describes the effects of cumulative wear and tear on these body systems related to frequent and/or repeated stress-response activation. AL is marked by dysregulation of endocrine responses and alteration of downstream

physiological pathways including cardiovascular, metabolic, and inflammatory parameters. Thus, poor allostasis may be indicated by biomarkers of dysregulated stress responses (e.g., measures of HPA integrity, proinflammatory cytokines; Seeman, Epel, Gruenewald, Karlamangla, & McEwen, 2010), as well as traditional risk factors for progressive illness such as body mass index, blood pressure, glycosylated hemoglobin, cholesterol, C-reactive protein (CRP), and albumin (Seeman, Singer, Rowe, Horwitz, & McEwen, 1997). In general, parameters of AL appear to increase rapidly during the second to fifth and into the sixth decade of life. However, after age 60, when nursing home admission is most likely to occur, AL indices stabilize, most likely because those individuals with the greatest continuing increases in AL have lower survival rates (Crimmins, Johnston, Hayward, & Seeman, 2003). In support, a growing body of evidence demonstrates that AL is an important predictor of mortality (Juster et al., 2010; Karlamangla et al., 2006). The capacity for allostasis is an important physiological resource that should support resilience processes and outcomes (O'Hara et al., 2010).

Several allostatic biomarkers have been associated with resilience processes and response to depression treatment (Arai et al., 2008; Charney, 2004; Haglund et al., 2007), as well as physical frailty and poor clinical outcomes (Ceda et al., 2005; Fried et al., 2009; Leng et al., 2004). We, therefore, measured a selective group of biomarkers as candidate descriptors of allostatic capacity. Many stress biomarkers, such as glucocorticoids, vary over short periods of time, in association with circadian rhythms or other changes in the individual's internal and external environment; interpreting associations of such measures with more stable indicators of resilience process is complicated. In this work, we focused on six relatively stable hormonal and protein biomarkers that are potential baseline indicators of resilience capacity at the time of admission to long-term care. Our choices reflect the status of the individual over longer periods of time: dehydroepiandrosterone sulfate (DHEA-S), insulin-like growth factor-1 (IGF-1), CRP, interleukin-6 (IL-6), interleukin-10 (IL-10), and myeloperoxidase (MPO). Our reasoning for these choices follows.

Dehydroepiandrosterone (DHEA) is a stress-responsive steroid hormone that has been shown to be related to stronger resilience (Cicchetti & Rogosch, 2007; Ozbay. Fitterling, Charney, & Southwick, 2008; Southwick, Vythilingam, & Charney, 2005). It has anti-glucocorticoid properties. The unconjugated form fluctuates over the course of 24 hours; we, therefore, measured DHEA-S, which exists in higher levels in peripheral blood and shows greater stability than the unconjugated form due to slower metabolic clearance. Thus, DHEA-S provides a time-integrated marker of adaptive stress responses (Kroboth, Salek, Pittenger, Fabian, & Frye, 1999). IGF-1 is a potent anabolic hormone with a molecular structure similar to that of insulin. It supports cell growth and proliferation, and inhibits programmed cell death. IGF-1 mediates many of the effects of growth hormone (GH) and has been shown to decline with age. IGF-1 may be associated with sarcopenia (an important measure of physical frailty), probably due to decreased GH secretion (Singleton & Feldman, 2001). Glucocorticoids and other stress-related hormones also inhibit the GH system, so higher levels of IGF-1 may indicate lower levels of stress. We measured three additional biomarkers that are established measures of AL and/or regulators of inflammatory processes: CRP, Il-6, and IL-10. CRP (Brambilla & Maggioni 1998) and IL-6 (Alesci et al., 2005; Chrousos, 2000; Kiecolt-Glaser et al., 2003; Maes et al., 1997; Nicklas et al., 2008) are well-established biomarkers of inflammation associated with stress, frailty, and poor health outcomes in older adults. Elevated IL-6 has also been associated with increased depression (Alessi et al., 2005). Although CRP is an acute phase reactant that increases transiently during acute illnesses, baseline elevations of CRP are predictive of coronary disease risk, and elevations have been shown to be sustained in depressed patients even during medication-free periods of remission (Kling et al., 2007), suggesting its potential utility as a biomarker of risk. Elevations of both IL-6 and CRP occur with chronic medical conditions. Interestingly, self-reported purpose in life, positive relations with others, and positive affect seem to buffer the association between chronic illness and inflammation (Friedman & Ryff, 2012b). While these inflammatory cytokines are well-known as predictors of morbidity, stress-induced secretion of proinflammatory cytokines may also be involved in mental health outcomes (Maes et al., 1999).

The cytokine IL-6 regulates immune responses and inflammation in multiple ways. One set of pathways requires the interaction of IL-6 with a soluble receptor (sIL-6R). Cytokine receptors occur in soluble and membrane-bound forms, and agonize or antagonize the actions of their specific ligand. sIL-6R is an agonist to IL-6 function. Recent work suggests binding of IL-6 to sIL-6R is a necessary factor of disease progression (Jones et al., 2005). In this study, we measured sIL-6R. Elevated levels of IL-6 and sIL-6R have been noted among patients with chronic inflammatory and autoimmune diseases as well as cancer. Thus, it is reasonable to posit that levels of circulating Il-6 and sIL-6R may both be predictive of morbidity as well as poor mental and emotional well-being.

The cytokine IL-10 inhibits the synthesis of some pro-inflammatory cytokines by macrophages and certain T-cells. It is known to down regulate hyperactive immune responses in certain autoimmune diseases and allergic reactions. Animal studies show that chronic stress reduces IL-10 secretion. Further, IL-10 protects against cardiovascular dysfunction associated with aging (Voorhies et al., 2013). Thus, IL-10 is an important anti-inflammatory cytokine for which a significant interaction between stress and aging has been demonstrated (Glaser et al., 2001).

Finally, MPO is an inflammatory enzyme produced by activated leukocytes that reflects oxidative stress. When neutrophils are activated, MPO is released into plasma. MPO has been found to be elevated in depression (Vaccarino, et al., 2008) and predicts the risk of coronary heart disease and mortality (Wang, et al., 2010). Levels of MPO are correlated with successful coronary term capacity for response to disease states.

Measurement of psychological and social resources in nursing home residents

The study of resilience in nursing home populations occurs in the context of considerable cognitive impairment, ranging from 48% to 55% (e.g., Magaziner et al., 2000; Bernstein & Remsburg, 2007); measurement choices must be made with this context in mind. Although we have incorporated traditional measures of mental health functioning as rated by clinicians, we also draw upon the person-centered literature that suggests that to understand positive outcomes, one must consider the perspective of the resident (Kitwood, 1997; Maslow, 2013; Mast, 2012). Despite the challenges cognitive impairment poses for self-report measurement in some domains (e.g., self-reported memory functioning), a growing body of research has demonstrated good to excellent psychometric properties of a variety of self-report measures in demented individuals particularly for constructs that reflect quality of life and other indicators of well-being (see Mast, Shouse, & Camp, 2015). In this study, we piloted several measures that can be used as indicators of psychological and social resources and well-being in this population. These measures were selected based on hypothesized resilience models that incorporate both personality attributes such as optimism and hope, and social resources. Whereas measures of social network characteristics, religious activity, and quality of life have been used previously with nursing home residents, others, including hope and optimism, have not. Thus, alongside our goal of validating an index of allostasis, we wished to examine the reliability of the baseline self-report measurement of social and psychological resources and well-being.

The primary aims of this paper, in sum, were to examine the psychometric performance of our proposed allostasis index as a cohesive index, and to test the assumption that biomarkers of allostasis reflect the capacity for resilience among nursing home residents by demonstrating cross-sectional relationships between our index of allostasis and indicators of physical (frailty, illness severity, disability), and psychological (prior psychiatric history, hope and optimism, cognitive ability) advantage, as well as baseline well-being indicators (quality of life, depression, and anxiety).

Method

Recruitment procedures

Inclusion criteria were being age 55 or older, and having been admitted for a long-term stay or transferred from acute rehabilitation to a long-term stay within the previous 30 days. Residents were excluded if their English proficiency, hearing, or verbal response capabilities were too limited for an in-person interview, if they were unable to answer study questionnaires due to severe cognitive impairment, or if they had unstable or terminal medical conditions. All procedures, protocols, and forms were reviewed and approved by the Institutional Review Board of the University of Louisville. Residents were referred for recruitment by the social service departments at the facilities. Eligible residents were approached by research staff and asked to participate. After being tested for ability to give consent, residents consented, declined, or assented to having their responsible party provide consent by proxy when they were deemed too impaired to provide their own consent. The baseline assessment began within one week of consent.

Participants

Thirteen facilities in the Louisville metropolitan area were recruited to participate. We enrolled 26 individuals out of a possible 76 referrals from these facilities. Of those not enrolled, 28 refused participation and 22 were found to be ineligible. Twenty-five consented to blood draws, but we were unable to collect blood from 3, resulting in 22 usable samples of plasma for the current analyses; we used the full sample of 26 to conduct analyses that were based solely on the self-report questionnaires.

Participants ranged in age from 58 to 91, mean age 76.68 (SD = 10.23); 10 were men (38.5%) and 16 were women (61.5%). Three were African-American and 23 (88.5%) were non-Hispanic whites. The majority (53.8%) was admitted to long-term care (LTC) following a Medicare-eligible, post-acute rehabilitation stay at the same facility, one was transferred from a post-acute stay at another facility, and the others were admitted from home (19.2%) or from an acute hospital stay (23.1%). The mean number of Medicare days prior to LTC for those admitted from post-acute beds was 33.27 (SD = 16.15). The 22 participants for whom we had plasma data had a similar demographic profile. All reported annual incomes below $30,000 a year, although nine participants declined to report (or did not know) their annual income.

Measures

Demographics and measures of physical resources

Demographic and physical health data came from nursing home medical records, primarily the Minimum Data-set 3 (MDS-3) (Saliba & Buchanan, 2008), the standardized assessment used in all federally regulated nursing homes beginning in October 2010. Demographic information taken from the MDS-3 included age, sex, ethnicity, former occupation, marital status, and source of payment.

Functional disability was assessed using the Activities of Daily Living self-performance (ADL) scale from the MDS-3, which consists of 12 items completed by nurse raters to indicate the highest level of functional impairment in the last five-day period. In the MDS-3 field trials, the average gold standard to facility nurse kappa for this scale was .956 (Saliba & Buchanan, 2008). Scores on the ADL scale can range from 0 to 84, with lower scores indicating better functioning; we pro-rated scale scoring when there were items coded as not performed.

The Cumulative Illness Rating Scale for Geriatrics (CIRS-G; Miller & Towers, 1991) is a widely used clinician-rated scale of health status among frail older adults. The CIRS has been shown to correlate with medication use and disability, and to predict mortality, hospitalization, and disability (e.g., Borson, Scanlan, Lessig,

& DeMers, 2010; Parmelee, Thuras, Katz, & Lawton, 1995). In our study, the CIRS-G was completed by a licensed registered nurse with training and supervision from one of the study physicians (JS). We excluded the psychiatric item in our analyses to reduce redundancy with our mental health measures. We used a severity score calculated by dividing the total score by the number of categories scored greater than 0.

Physical frailty is a construct that predicts disability and mortality among older adults (Bandeen-Roche et al., 2006; Boyd, Xue, Simpson, Guralnik, & Fried, 2005; Fried et al., 1998). Frailty is defined as the presence of three or more risk factors that include poor grip strength, unintentional weight loss, sarcopenia (loss of muscle mass), low activity and fatigue, and slow walking. We measured grip strength using a hand dynamometer during the initial interviews; however, the grip strength scores obtained all were below the cut scores for frailty on this index; given that there was no variability in this index, we did not include it in our further analyses. We assessed unintentional weight loss of 10 or more pounds in the past year and via resident or informant self-report. Weight loss was recorded as "yes" or "no," with "yes" taken as one indicator of frailty. Inactivity was assessed with a modified version of the measure used in the Women's Health and Aging and Cardiovascular Health Studies (Bandee-Roche et al., 2006), including 13 items such as walking, jogging, gardening, or biking, performed in the month prior to admission. It was scored as days *x* minutes, with a range of 0−4200. Frailty was considered anything less than or equal to 195 (pro-rated from cutting score cited by Bandeen-Roche et al., 2006). Serum albumin and serum creatinine levels were available on nursing home charts and are associated with sarcopenia (Katz et al., 1993). We used cut scores from prior research of less than 1.4 for creatinine, and less than 3.5 for albumin (Katz et al., 1993). We followed the practice established by Fried and her colleagues (Boyd et al. 2005) of creating a dichotomous index (Bandeen-Roche et al., 2006) based on whether scores of 3 or more of the indicators listed above are in the frailty range.

Allostasis. As described above, we derived the following biomarkers, assayed with Enzyme Linked Immunosorbent Assay (ELISA), from plasma samples, for our index: Dehydroepiandrosterone sulfate (DHEA-S), (IGF-1), CRP, soluble interleukin-6 receptor (sIL-6r), Interleukin 10 (IL-10), and Myelopoxidase (MPO). Blood was drawn into 10.0 mL tubes on-site at facilities and stored upright in an ice-packed cooler during transit. Tubes were centrifuged for 10 minutes at 1800 RCF using a Scilogex DM 0412 Clinical Centrifuge. Centrifugation occurred within one hour of collection. Three of the 22 samples were centrifuged a second time due to incomplete separation. Plasma was then aliquoted into 0.5 mL cryovials and frozen at −30 °C until shipped in batch for biomarker measurement.

All ELISAs were performed in plasma with commercial kits according to manufacturer's instructions. These included: (a) DHEA-S, IBL International (Toronto, ON, Cat#RE52181); (b) IGF-1, RayBiotech (Norcross, GA, Cat#ELH-IGF1-001); (c) CRP, R&D Systems (Minneapolis, MN, Cat#DCRPOO); (d) sIL-6R, Invitrogen (Grand Island, NY, Cat#KHR0061); (e) IL-10, Invitrogen (Cat#KHC0104); and (f) MPO, Calbiochem/EMD Millipore (Billerica, MA, Cat#475919).

Measures of psychological resources

We derived the history of depression and anxiety disorders, psychosis, and substance abuse from the structured clinical interview for DSM-IV (SCID) screening items and mood and anxiety disorders sections (First, Gibbon, Spitzer, & Williams, 2001), administered at baseline. In the present analyses, we included the following variables derived from the SCID interviews: presence or absence of any mental health history (any diagnosis in the past), coded 0 or 1, number of past mental health diagnoses on the SCID, presence or absence of any current mental health diagnosis (coded 0 or 1), and number of current diagnoses on the SCID.

We used the Adult Hope Scale (Snyder, 2002; Snyder et al., 1991) to measure dispositional hope, a positive mental health attribute associated with goal-directed coping behaviors. Snyder (2002) has defined hope as "the perceived capability to derive pathways to desired goals, and motivate oneself via agency thinking to use those pathways" (p. 249). The scale consists of eight self-rated items falling on two empirically validated subscales, Agency Thinking and Pathway Thinking (4 items each, score 1-4 each), with internal consistency ranging from .63 to .86; full-scale alphas ranged from .74 to .88 (Snyder, 2002).

We used the Life Orientation Test − Revised (Scheier, Carver, & Bridges, 1994) to measure dispositional optimism, another well-studied positive mental health attribute associated with well-being (Rasmussen, Wrosch, Scheier, & Carver, 2006). The LOT-R consists of six items rated on a 5-point scale. It can be coded as an overall optimism scale, or scored in two subscales, optimism and pessimism, which is how we treated it in this study. Each scale range was 3−15. The LOT-R has been used extensively in social psychology and health psychology research, and correlates with a host of positive and negative mental health indicators, even controlling for neuroticism, trait anxiety, self-mastery and self-esteem (Scheier et al., 1994).

The Mattis Dementia Rating Scale -2 is a broad measure of cognitive functioning for use among demented patients. The MDRS has good clinical utility for detecting cognitive impairment in frail geriatric patients (Mast, MacNeill & Lichtenberg, 2000; Shay, Duke, Conboy, & Harrell, 1991; Vitaliano et al 1984). Higher scores indicate better overall cognitive functioning.

The symptoms of dementia screener (SDS) is an 11-item questionnaire designed to detect dementia-related symptoms and behaviors. We obtained SDS ratings from key informants regarding participants' cognitive functioning prior to admission to the nursing home. The total score reflects the number of items endorsed. The SDS used in this manner has demonstrated excellent utility in detecting

dementia syndromes (Mundt, Freed, & Greist, 2000). We used this measure as an indicator of participants' cognitive functioning prior to the health events that led to nursing home admission.

Social advantage

We defined social embeddedness as the degree to which the individual is embedded in a social network, using the Social Support Questionnaire 6-item version (SSQ6) (Sarason, Sarason, Shearin, & Pierce, 1987; Rascle, Bruchon-Schweitzer, & Sarason, 2005) to measure the size and satisfaction with the social network. The SSQ6 is a six-item version of the larger Social Support Questionnaire. Respondents are asked to list the number of people they can count on to perform various relationship functions, then to rate their satisfaction in each category. The SSQ number score is the mean number of people per item, and the SSQ Satisfaction score is the mean satisfaction rating per item (range 1−6). The SSQ6 has excellent internal consistency, with average inter-item correlations around .55, and alphas near .95. Because the SSQ does not directly measure religious involvement, and religious involvement has been related to nursing home adjustment (Bickerstaff, Grasser, & McCabe 2003; Lee, Woo, & Mackenzie, 2002), we also included six additional items describing religious participation from the work of Pargament and his colleagues (Pargament, Koenig, & Perez, 2000; Pargament, Van Haitsma & Ensing, 1995). These items assess time spent in religious services and activities, contact with clergy, and number of acquaintances affiliated with the same religious community. They are scored from 1 to 9 based on frequency of engagement in each activity.

Measures of well-being at Baseline

The Personal Health Questionnaire-9 (PHQ-9 (Kroenke & Spitzer, 2002) is a nine-item, well-validated, depression screener that has been incorporated in the MDS 3.0 (Löwe, Kroenke, Herzog, & Gräfe, 2004). Scores on the PHQ-9 range from 0 to 27, with 8 considered the cut-off for clinically significant depressive symptoms. We extracted PHQ-9 scores, coded by facility staff, from the baseline MDS-3.

Because there is no MDS-3 indicator of anxiety, we incorporated the rating anxiety in dementia (RAID) (Shankar, Walker, Frost, & Orrell, 1999) into our initial interview. The RAID is an 18-item scale; each item is rate 0−3, producing a possible range of 0−54. We chose the RAID because of its ease of administration to mildly to moderately impaired respondents. Internal consistency is good (full scale .83, subscales range from .51 to .74), and test−retest stability was .53 (Shankar et al.,1999.

The Quality of Life-AD scale (Logsdon, Gibbons, McCurry, & Teri, 2002) is a 13-item self -report instrument designed for persons with cognitive impairment; scores range from 13 to 52, with higher scores indicating better quality of life. It incorporates dimensions including physical condition, mood, relationships, ability to participate in meaningful activities, patient's financial situation, the self as a whole, and life quality as a whole. Responses are structured in a four-choice format (poor to excellent). The scale demonstrated good internal consistency (alpha = .88), test−retest reliability (ICC = .76), and good validity as indicated by lower correlations with depression, and higher correlations with day-to-day functioning and activity levels (Logsdon et al., 2002).

Analyses

We first generated descriptive statistics along with coefficient alpha (reliability) statistics where appropriate for each of the study variables. We next generated a correlation matrix for the set of psychological, social resource, and well-being variables.

Allostasis

To see whether the individual indicators of allostasis related to our proposed psychosocial resources and well-being indicators, we generated the set of correlations between the biomarkers and the other model variables. Beyond these correlations, we used two methods for determining the degree to which a combination of biomarkers were associated with resources and well-being variables. To compute the optimal predictive capability of the biomarkers, we used multiple regression. This approach created a linear combination of the biomarkers that maximized the squared correlation (R^2) between the biomarkers and the other variables. We were also interested in constructing a summary index of allostasis as a combination of biomarkers. Our rationale for this index was based on work previously done at Johns Hopkins. We used the approach developed at Johns Hopkins to calculate scores summarizing multiple inflammatory biomarkers. Using a principal components approach, latent variable analysis based on a biological model that counterbalances up- and down-regulation processes (Bandeen-Roche, Walston, Huang, Semba, & Ferrucci, 2009) showed that a first principal component accounted for a substantial proportion of the common variance of the biomarkers. This suggested that a single summary score could adequately represent allostasis. Given the different scalings of the biomarkers, converted them to *z*-scores and then summed the *z*-scores to create the index, *z-stasis*. Comparing the squared correlation (r^2) between this index and each of the outcomes to the R^2 from the corresponding multiple regressions would indicate how the optimal regression scaling compared to the *z*-stasis index in terms of prediction. The Hopkins investigative team derived principal component scores that approximated their biological process constructs; these, along with individual markers, were evaluated as predictors of impairment and frailty status in regression analyses, adjusting for key confounders.

Results

Table 1 shows the means, standard deviations, and ranges of the principal study variables. The range of cognitive

Table 1. Descriptive statistics for key study variables. Alpha statistics are also presented for self-report variables.

Variable	*n*	Mean	SD	Range	Alpha
Age	25	76.68	10.23	58−91	
Education in years	25	10.98	2.76	6−16	
		Physical resources			
Frailty sum score	25	1.92	1.15	0−4	
CIRS-G severity (possible range 1−4)	25	2.24	0.33	1.71−2.9	
Activities of daily living self-performance	26	23.81	10.58	4.0−39.11	
		Allostasis			
Dehydroepiandrosterone sulfate micrograms/ml	22	0.2273	0.15	.06−.80	
Insulin-like growth Factor_1 ng/ml	22	0.56	1.03	0−3.67	
C reactive protein ng/ml	22	34,613.05	32,777.44	931−92,776	
Soluble IL_6R ng/ml	22	129.82	45.06	61.36−247.64	
Interleukin 10 pg/ml	22	0.5	0.8	0−2.9	
Myeloperoxidase ng/ml	22	14.06	13.25	0−53.04	
		Psychological resources			
Dementia rating scale total (AMSS)	23	4.48	3.12	2−12	
Symptoms of dementia screener	14	17.24	3.20	11−22	0.85
Number of past mental health diagnoses	24	1.04	1.4	0−5	
Number of current mental health diagnoses	24	0.67	1.01	0−3	
Hope agency	25	12.2	3.65	4−16	0.86
Hope pathways	25	12.24	3.18	4−16	0.85
Hope total score	25	24.44	6.42	9−32	0.91
Optimism	25	6.2	2.86	3−12	0.71
Pessimism	25	8.96	3.58	3−15	0.73
		Social resources			
SSQ number	25	1.91	1.38	.17−6.33	0.80

impairment on the DRS-2 total score was from normal to severe, and 56% scored in the severely impaired range. Nonetheless, as shown in the far right-hand column of Table 1, the internal consistency estimates for the self-report indicators of psychological and social resources and well-being were acceptable to excellent, with alphas of 0.7−0.9. We show in Table 2 the inter-correlations among the psychosocial and social resources and baseline well-being measures. From this table, we see that social resources do not appear to correlate well with either psychological resources or well-being outcomes. Among the psychological resources, we have highlighted groupings of positive and negative resources in Table 2, with the positive resources including hope and optimism, and the negative resources including mental health history variables; the table shows that the positive resources tend to inter-correlate, as do the negative resources. Variables in both positive and negative resource groups have significant relationships with quality of life. Only the negative resource group shows significant relationships with anxiety, as measured by the RAID, and only two variables, optimism and mental health history (one from each resource group), are significantly related to depression symptoms measured by the PHQ-9. These findings further demonstrate that the self-report measures of social and psychological resources perform well in this sample despite the broad range of cognitive impairment. That is, their relationships with one another are consistent with predictable groupings of positive and negative resources.

We examined the relationships among the six proposed biomarkers (DHEAS-R, CRP, IGF-1, sIL-6r, IL-10, and MPO) and other resilience resources. Table 3 shows these results. The first six columns of Table 3 show the zero-order correlations between each biomarker and other resilience resources, as well as the correlations among the biomarkers (in the shaded band below the demographic variables). Each resource variable was regressed on the entire set of biomarkers, and the next column in the table shows the resulting R^2s from these multiple regressions. The eighth column of Table 3 shows the effect sizes of these R^2 statistics. Taken as a group of predictors, the biomarkers performed well: the effect sizes of their relationships with other resources ranged from .09 for the Adult Hope Scale to .49 with social network size.

We derived a summation of *z*-scores for the biomarkers that allowed for them to be treated as a single index of allostasis (*z-stasis*). Correlations between the *z*-stasis summation score and each individual biomarker, shown in the last column of Table 3, ranged from .22 to .66; three of these reached statistical significance (for DHEAS, IGF-1, and MPO). Even with this small sample size, we found significant correlations between our *z-stasis* index and indicators of frailty (.54), illness severity (.50), mental health history (−.48), and for social support (.48). Other correlations were non-significant but of sufficient magnitude to suggest the presence of medium effect sizes: −.42 with symptoms of dementia, and .33 with the Adult Hope Scale. The *z-stasis* variable was not correlated,

Table 2. Correlations among psychological and social resources and well-being at baseline.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1. SSQ number																
2. SSQ satisfaction	.52**															
3. Religious involvement	.08	.11														
4. Hope total	.23	.17	−.04													
5. Hope agency	.16	.15	.02	.95**												
6. Hope pathways	.28	.16	−10	.93**	.77**											
7. Optimism	−.16	.00	−.07	−.66*	−.70**	−.53**										
8. Pessimism	−.07	−.10	−.22	−.40	−.35	−.41*	.14									
9. DRS total	.19	−.18	−.07	−.10	−.12	−.06	−.15	.03								
10. Symptoms of dementia screener	.07	.09	−.15	−.11	−.20	.01	.33	−.10	−.41							
11. Presence of any current mental health diagnosis	−.15	−.56*	−.32	−.43*	−.55**	−.23	.45*	.32	.10	.25						
12. Number of current MH diagnoses	−.07	−.39	−.31	−.49*	−.64**	−.25	.43*	.27	.18	.28	.87**					
13. Presence of any past MH diagnosis	−.08	−.40	−.33	−.45*	−.57**	−.26	.46*	.06	.39	.06	.71**	.62**				
14. Number of past MH diagnoses	−.16	−.45	−.28	−.33	−.47*	−.14	.28	.18	.40	.18	.73**	.84**	.70**			
15. PHQ−9	.04	.26	−.14	−.22	−.20	−.23	.43*	−.19	−.15	.09	.22	.07	.49*	.12		
16. RAID	.21	−.13	−.36	−.15	−.29	.04	.20	.28	.16	−.10	.74**	.71**	.54**	.63**	.24	
17. Quality of life − AD	−.09	−17	−.14	.52*	.57*	.39	−.46*	−.41	−.32	−.31	−.35	−.51	−.34	−.54**	−.17	−.41*

Note: SSQ = Social Support Questionnaire; DRS = Mattis Dementia Rating Scale; PHQ-9 = Public Health Questionaire-9; and RAID = rating anxiety in dementia.
*$p < .05$.
**$p < .01$.

however, with baseline well-being. The PHQ-9 scores correlated .45 with one biomarker, IGF-1, and the R^2 was .21 ($f^2 = .27$) for the overall prediction of PHQ-9 with biomarkers, but this relationship did not emerge with the *z*-stasis variable.

Discussion

The goal of this paper was to examine relationships among variables represented in the left side of the framework depicted in Figure 1, variables that represent resilience resources that should affect the well-being of nursing home residents, as a first step in testing the overall longitudinal framework in prospective research. Our primary purpose was to examine the performance of an index of allostasis developed with biomarkers that had good prior research support for their association with well-being outcomes. The zero-order correlations of the individual biomarkers with other resilience resources were of sufficient magnitude to suggest that each individual biomarker was associated with at least one other resilience resource. Although not many reached statistical significance in this pilot sample, the effect sizes of the multiple regressions, along with overall magnitude of the correlations, suggest that our choice of biomarkers was appropriate to represent allostasis as a resilience resource. These biomarkers did not have high correlations with one another, but as a group they showed good correspondence with the majority of other resource variables. We found that the *z*-stasis summation score was associated with physical, social, and psychological resilience resources, including those reflecting physical and mental health vulnerability as well as positive resources of social support, optimism, and hope; again, although a number of these associations reached statistical significance, others were of a magnitude that would yield statistical significance with a larger sample, assuming they prove stable in further research. There was no resource variable other than demographics that was not related to at least one biomarker variable. In the derived summation; however, it is often not possible to observe which biomarker is responsible for the significant relationships, and unique variance estimates showed different patterns of relationship for each biomarker. This implies that the *z*-score summation of the biomarkers, though valuable, can obscure the role of the individual biomarkers in the analyses.

We also examined the performance of our self-report measures of resilience resources in this nursing home sample. As shown in Table 1, the internal consistency of these measures was good, and consistent with reports of internal consistency with other samples. The measures inter-correlated in predictable ways, with the psychological resources in particular grouped along positive and negative mental health lines. These correlations, and the correlation of these measures with our index of allostasis, further support the integrity of the self-report measures for this sample. Our findings are consistent with findings from the MDS field testing and validation studies that

Table 3. Relationships among measures of allostasis and all other resilience resources.

	Zero-order *r*						Multiple regression		
Variables	DHEAS	IGF_1	CRP	sIL_6r	IL_10	MPO	R^{2a}	Effect size of R^{2b}	z-Sum (z-stasis)
Age	−.04	.13	−.22	.35	−.17	.26	.12	.13	.11
Education	−.06	.15	.16	−.02	.19	−.02	.09	.09	.04
Income	.00	−.03	−.30	.15	−.27	−.06	.09	.10	−.17
Gender	.20	.13	.12	.04	.03	.15	.10	.11	.26
Frailty sum	.25	.25	.40	−.15	.22	.46*	.32	.47	.54*
CIRS-G severity	.36	.30	.06	−.02	.08	.19	.24	.32	.37
CIRS-G total	.34	.19	.04	.15	.17	.43*	.21	.27	.50*
ADL self-perform.	.08	.11	.17	.32	−.04	.25	.10	.11	.34
DHEAS	1.00						.29	.35	.46*
IGF-1	−.07	1.00					.25	.34	.52*
CRP	−.10	−.21	1.00				.35	.53	.22
sIL_6r	.06	.23	−.43*	1.00			.22	.28	.35
IL_10	−.11	.15	.20	.00	1.00		.15	.18	.41
MPO	.42	.26	.13	.07	−.15	1.00	.37	.59	.66*
DRS AMSS	−.02	−.07	.45*	−.11	.07	.27	.20	.25	.21
Symptoms of dementia screener	−.51	.26	−.27	−.06	−.05	−.19	.28	.39	−.42
Number of past mental health diagnoses	−.35	−.10	−.16	−.21	−.12	−.31	.16	.19	−.48*
Presence of any past diagnosis	−.42	.20	−.14	−.02	.15	−.30	.19	.23	−.19
Number of current mental health diagnoses	−.31	−.13	−.15	−.10	−.11	−.39	.18	.22	−.45*
Presence of any current mental health diagnosis	−.38	.05	−.18	−.10	−.02	−.48*	.27	.37	−.42
Hope scale agency	.34	−.11	.20	−.02	.09	.23	.12	.13	.29
Hope scale pathways	.22	−.05	.27	.04	.25	.13	.21	.26	.33
Hope scale total	.30	−.08	.24	.01	.16	.20	.09	.10	.32
Optimism	−.37	.32	−.34	.05	.09	−.13	.28	.39	−.15
Pessimism	−.02	−.02	−.16	−.10	.16	−.03	.13	.14	−.07
SSQ-N	−.08	−.05	.70*	−.14	.26	.27	.49	.96	.37
SSQ-S	.22	.19	.23	−.05	.34	.34	.27	.37	.48*
Religious involvement	.11	−.21	.25	−.29	−.38	.06	.24	.32	−.18

Note: CIRS-G = Cumulative Illness Rating Scale, Geriatric; ADL = activities of daily living (self-support); SSQ = Social Support Questionnaire (number and satisfaction); and DRS = Mattis Dementia Rating Scale.

*$p < .05$.

[a]R^2 was generated for each variable regressed on the six biomarkers, and the effect sizes were derived from each *r*-square. Likewise, each biomarker was multiply regressed on the other five biomarkers.

[b]Effect sizes for the multiple regressions were calculated as $f^2 = R^2/(1-R^2)$; a small $f^2 = .02$, a medium $f^2 = .15$ and a large $f^2 = .35$. Asterisks do not reflect significance of effect sizes.

demonstrated preserved ability of residents with cognitive impairment to respond to self-report items on standardized assessment of mood symptoms (Saliba et al., 2012)

The major limitation to this study is the very small sample that was diverse with respect to time since admission. Time since admission, and thus the distance between the assessed resources, particularly allostasis, and the precipitating health event could have ranged from 10 days to 3 months, thus blurring the boundary between a static baseline resource and ongoing efforts at adaptation. Nevertheless, these preliminary findings clearly demonstrate linkages among different types of resources that may affect the longitudinal trajectory of nursing home residents, including significant relationships among biomarkers of allostasis, resilience resources, and well-being indicators. While we do not want to make too much of the patterns of correlation in a sample this small, our composite index of allostasis showed surprisingly large effect sizes not only with frailty and illness variables, but also with social and emotional resources that should be strongly linked to well-being indicators. It is especially interesting that the allostasis index had moderate effect sizes in relation to social embeddedness variables, despite the fact that these variables were not related strongly to psychological resources. Demonstrating the inter-relatedness among physiological, social, and psychological resilience resources is a preliminary step towards developing longitudinal models that might predict resilience trajectories and help identify nursing home residents most at risk and in need for interventions. Biomarkers of allostasis may also provide a novel means of assessing intervention outcomes. We view these findings as encouraging and suggestive that further work including the allostasis markers within our multidimensional longitudinal framework is merited.

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No potential conflict of interest was reported by the authors.

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