The European Health Psychologist

keynote article

Varieties of resilience and their biological underpinnings

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University of Wisconsin-Madison Resilience has been empirically studied for several decades, beginning with work in the 1970s and

1980s focused on children who grew up with mentally ill parents or lived in poverty. In the 1990s, scientists began examining resilience at the other end of the life cycle, with the goal of illuminating why some individuals negotiate the challenges of aging better than others. In both early and later life, the central issue of interest was that some individuals, when faced with hardship, loss, or adversity, do well. That is, they do not succumb to mental or physical illness when subjected to difficulties in life, but instead show profiles of healthy functioning. This article summarizes ongoing research on individuals from a national sample of U.S. adults who have been confronted with a variety of life challenges. The aim is to document that many are resilient, formulated as showing the capacity to maintain, or regain well-being in the face of adversity. Of particular interest are the biological processes and brain mechanisms that underlie such resilience. Thus, an additional set of findings explores these linkages. The model of resilience put forth is fundamentally biopsychosocial in scope. concluding section notes intervention strategies designed to promote resilience among ever larger segments of society.

Prevailing in the face of adversity

At its core, human resilience involves the juxtaposition of the positive and the negative—i.e., how strengths are maintained, if not deepened, in the confrontation with difficult life challenges. Our initial studies formulated the positive in terms of psychological well-being (Ryff,

1989). We were interested in who was able to show high well-being in the face of various types of adversity, such as living with an alcoholic, parenting a child with disabilities, providing care aging parent or spouse, socioeconomic disadvantage, or negotiating the losses of growing old (e.g., relocation, increased chronic conditions) (for a summary see Ryff & Singer, 2003). Our studies emerged in the context of numerous other efforts to advance understanding of the construct of resilience (see Luthar, Cicchetti, & Becker, 2000; Reich, Zautra, & Hall, 2010). More recently, we have examined resilience and its health consequents in the context of a national study of U.S. adults, known as MIDUS (Midlife in the U.S.). Funded by the John D. and Catherine T. MacArthur Foundation, MIDUS was launched in 1995/96 with over 7,000 adults aged 25 to 74. Its primary objectives were to investigate the roles of psychological and social factors in understanding how people age across the decades of adult life. In 2004/05, a longitudinal follow-up was initiated, with funds from the National Institute on Aging. The second wave repeated baseline assessments and added new measures (cognition, biomarkers, brain-based emotional reactivity and recovery). Currently, we are "refreshing" the MIDUS study—i.e. we are recruiting new members to the sample with a focus on studying the impact of the ongoing economic recession on the lives of U.S. adults via comparison of same-aged adults from different historical periods. We are also initiating the third wave of assessments on the existing sample.

Data from MIDUS are publicly available (http://www.midus.wisc.edu). To date, more than 400 publications have been generated from the

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study. They cover a wide array of topics that have appeared in premier journals across the scientific disciplines. For those interested in studying resilience, MIDUS is unique among population-based inquiries, given its unusual depth and breadth in assessments of psychological and social strengths, key ingredients needed to document the presence of wellness in the face of adversity and possibly to explain why, via key protective resources. Three varieties of resilience research from MIDUS are summarized below.

Resilience in the face of socioeconomic inequality. MIDUS is a key forum for investigating social inequalities in health and in so doing, adds to the growing literature documenting more unfavorable health profiles among those with lower standing in the socioeconomic hierarchy (Adler & Stewart, 2010). Many MIDUS studies have, however, documented that some individuals of limited means (low incomes or low educational attainment) are nonetheless doing well. Thus, they do not fit the average profile wherein socioeconomic disadvantage culminates in poor health. For example, Lachman and Weaver (1998) found that low income individuals who possess high levels of personal mastery did not show compromised health. Instead, their self-rated health was comparable to that observed among higher income respondents. In addition, Lachman, Agrigoroaei, Murphy, and Tun (2010) showed that low education adults who engaged in greater cognitive activities (reading, writing, word games) were protected against the lower performance on memory and executive function typically found among the less educated. Ethnic/racial disparities in health are a variant on the theme of inequality. An unexpected finding from the MIDUS baseline data was that minority respondents reported higher psychological well-being than their majority counterparts, independent of differences in educational attainment (Ryff, Keyes, & Hughes, 2003). The minority advantage was even greater after controlling for perceived discrimination, suggesting that some aspects of positive psychological functioning (e.g., purpose in life, personal growth) may, paradoxically, be honed by living with the challenges of minority life.

Resilience vis-à-vis the challenges of aging. Older people (age 65+) are at higher risk for various health problems (e.g., cardiovascular disease, cancer, diabetes, Alzheimer's disease). They also face loss of significant social roles (e.g., widowhood, retirement) as they age. Perhaps related to these challenges, older persons show downward trajectories on numerous aspects of psychological well-being and are at increased risk for depression and cognitive impairment (see Ryff, Friedman, Morozink, & Tsenkova, 2012). Nonetheless, there is notable variability among older adults, such that many do not fit such negative psychological profiles. Moreover, those who maintain high well-being show diminished risk for subsequent morbidity, and they live longer. For example, MIDUS investigators have found that although self-rated health tends to worsen with age, those who report better social relationships and a higher sense of control had better self-rated health at the follow-up assessment (Cotter & Lachman, 2010). In addition, Lachman and Agrigoroaei (2010) found that decline in functional health over time was reduced among those possessing more protective factors (i.e., control beliefs, social support, physical exercise). Other studies from MIDUS have examined behavioral such factors. volunteering, as protective influences on the health and well-being of older individuals. Choi and Kim (2011) found that those who volunteer and make charitable donations had higher wellbeing, with effects possibly attributable to participants' sense of efficacy, altruism and desire to do good deeds. Greenfield and Marks (2004) found that formal volunteering was associated with more positive affect among older adults. Volunteering also buffered against declines in purpose in life associated with loss of major social

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roles. Greenfield (2009) further examined felt obligation to help others as a protective factor vis-à-vis loss of well-being following decline in functional abilities. Seeman et al. (2011) investigated whether social contacts and support were related to cognitive abilities in middle-aged and older adults. Significant positive associations were observed between greater social contact and support with both executive function and episodic memory, whereas declines in social contact were negatively associated with both outcomes. particularly among younger adults. together, the above findings underscore the role of various positive psychosocial factors in reducing the likelihood of health and cognitive decline in later life.

Resilience vis-à-vis targeted life challenges. MIDUS researchers have investigated the impact of specific life events on respondents' health and Experiencing abuse well-being. (emotional, physical, sexual) in childhood has been of considerable interest. Pitzer and Fingerman (2010) invoked the idea of resilience by showing that the impact of severe physical abuse in childhood on adult problems (poor health, negative affect) was reduced among those with a greater sense of agency (sense of control) over their lives. Greenfield and Marks (2010) found that sense of community served to mitigate the impact of child abuse on psychological distress in adulthood. Other studies have examined resilience in the context of dealing with cancer. Costanzo, Ryff, and Singer (2009) found that although depression worsened over time among cancer survivors, they showed resilience in several other ways. Specifically, their profiles of mood, psychological and social well-being, and spirituality over time were no different than what was observed among demographically similar adults not dealing with cancer. In addition, Pudrovska (2010) found that cancer diagnosis among younger cohorts resulted in increases in personal growth compared to individuals without cancer. Loss of spouse constitutes a significant life challenge of interest in MIDUS. Ong et al., (2010) compared a sample of bereaved individuals who lost a spouse between wave 1 and 2 with a demographically matched group of continuously married individuals. Although spousal loss predicted greater decreases in positive emotions across time, those who reporter higher levels of positive reappraisal (conceptualized as a resilience factor) showed less decrease in positive emotions following death of spouse. Thus, across multiple types of life challenge, MIDUS investigators have documented profiles of sustained or enhanced well-being in the face of adversity.

Biological concomitants of resilience

The above examples document the capacity to maintain health and well-being vis-à-vis challenge but do not explicate underlying biological processes. Years ago Dienstbier (1989) put forth the concept of "physiological toughness" to account for a pattern of arousal that works together with effective psychological coping to comprise positive physiological reactivity. It includes low sympathetic nervous system (SNS) arousal base rates combined with strong, challenge-induced SNS-adrenal-medullary arousal and resistance to brain catecholamine depletion and suppression of pituitary adrenal-cortical responses. In addition, Charney (2004) has elaborated the mechanisms of resilience at psychobiological levels via multiple neurochemical patterns of response to acute stress, which he connects to neural mechanisms of reward and motivation as well as adaptive social behaviors. MIDUS includes assessments of biological factors and brain-based measures of emotional reactivity and recovery on subsamples of respondents. It is therefore possible to bring these measures to formulations of resilience, albeit with less mechanistic detail than formulated by Dienstbier (1989) or Charney (2004). Initial empirical tests have focused on whether the maintenance of high psychological well-being in the face of challenge

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translates to better biological regulation (see Ryff & Singer, 2009 for a summary of evidence prior to MIDUS). With the MIDUS national sample, recent findings document that biological costs of socioeconomic inequality are mitigated among low education individuals who have higher levels of psychological well-being (Morozink, Friedman, Coe, & Ryff, 2010). The outcome of interest was interleukin-6 (IL-6), an inflammatory marker implicated in the etiology of numerous adverse outcomes. including cardiovascular disease, diabetes, osteoporosis, and Alzheimer's disease. As predicted, we found that those with lower levels of educational attainment had higher levels of IL-6. However, such patterns were moderated by levels of psychological well-being, such that low education individuals with high levels of purpose in life, environmental mastery, self-acceptance, etc., had lower levels of IL-6 (comparable to those with higher levels of educational attainment). A related study by Miller et al. (2011) showed that although coming from an impoverished childhood environment increases adult risk for metabolic syndrome (MetS, a cluster of cardiovascular risk factors) in middle age, such risk is offset among those who had a nurturing mother in childhood. Thus, individuals from low SES households who reported experiencing high maternal nurturance had a MetS prevalence comparable to those from high SES households in childhood.

Moving to the challenges of aging, Friedman and Ryff (2012) focused on the reality of later life co-morbidity—namely, that with age, individuals are at increased risk for having multiple chronic medical conditions. These conditions are both the consequent of elevated levels of inflammatory proteins (e.g., IL-6, C-reactive protein), and they also contribute to further inflammatory problems. However, we found that among older adults who reported a greater sense of purpose in life and stronger social relationships, the link between chronic conditions multiple and elevated inflammatory markers was mitigated. That is, high well-being protected against elevated inflammation, thereby reducing risk of still further disability ahead as well as earlier mortality.

Brain-mechanisms involved in resilience need to be explicated as well. Urry et al., (2004) examined the neural correlates of psychological well-being and found that those with higher wellbeing had greater left than right superior frontal activation (referred to as EEG asymmetry) compared to those with lower well-being. This activation pattern has been previously linked to positive dispositional styles and reduced risk of depression. Using neuroimaging, van Reekum et al. (2007) found that those who evaluated negative stimuli more quickly showed greater activation of the amygdala. However, such effects varied depending on respondents' levels of psychological well-being. Those with higher wellbeing were slower to evaluate the negative information, and they showed lower amygdala activation. In addition, they showed increased activation of the anterior cingulate cortex (ACC). The interpretation given was that those with high well-being effectively recruit the ventral ACC when confronted with aversive stimuli, manifest reduced activity in the amygdala and appraise such information as less salient (reflected in slower evaluative speed). The two prior studies were not based on MIDUS data, although Heller et al., (2012) used fMRI with MIDUS respondents to show that individuals with more sustained engagement of the ventral striatum in response to positive stimuli (embedded within mixed valence stimuli) reported higher levels of well-being and showed lower levels of cortisol output. The results suggested that being able to repeatedly engage reward circuitry when encountering positive events in the midst of negative ones may underlie eudaimonic well-being, with related implications for adaptive regulation of the hypothalamicpituitary-adrenal axis.

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In summary, the above work has begun to tell a story about resilience that is broad in scientific scope. It begins with the concrete challenges that individuals encounter on their journeys through life and then documents the capacity of some to sustain high well-being despite such adversity. More recent inquiries bring biological risk factors and brain-based mechanisms into the inquiry to show that resilience (i.e., the presence of wellbeing in the face of life difficulties) contributes to better regulation of biological systems as well as to neural mechanisms that underlie healthy patterns of emotional reactivity and recovery. Much work remains to be done in painting the biopsychosocial portrait of resilience. Fortunately, opportunities to contribute to such work are available to all members of the scientific community, given the public availability of data from the MIDUS national (www.midus.wisc.edu).

Acknowledgements

This research was supported by a grant from the National Institute on Aging (P01-AG020166), with prior support from the John D. and Catherine T. MacArthur Foundation. Additional support was provided by the Clinical Research Centers at the University of Wisconsin-Madison (1UL1RR025011), UCLA (M01-RR00865), and Georgetown University (M01-RR023942).

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