ABSTRACT
Caregivers of individuals with dementia are at risk for chronic stress and social isolation. These exogenous factors may lead to perceived stress and perceived loneliness—psychosocial endogenous (subjective) elements of caregiving experience. Chronic stress and perceived loneliness may disrupt neuroendocrine and neuroimmunological regulation, creating low-grade systemic inflammation, promoting proinflammatory gene expression, and expediting cellular aging (endogenous physiological factors). These disturbances may enhance caregivers’ risk for chronic conditions of inflammatory pathogenesis. Thus, caregivers’ perceived stress and perceived loneliness may form a symptom cluster that can serve as a marker of risks for physical and mental illness. Due to the overwhelming reliance on family caregivers within the increasing population of individuals with dementia, it is essential that clinicians inquire about caregivers’ perceived stress and perceived loneliness, are competent in supporting and educating caregivers, and are knowledgeable about specific resources for caregivers. [Journal of Psychosocial Nursing and Mental Health Services, xx(x), xx-xx.]

More than 15.5 million Americans are informal (i.e., unpaid) caregivers for individuals with Alzheimer’s disease or other dementias (Alzheimer’s Association, 2017). Most individuals with dementia live in the community, relying on family caregivers (Richardson, Lee, Berg-Weger, & Grossberg, 2013). Older adults with cognitive impairment who live at home as opposed to institutions have a better quality of life, cognitive

Chronic Stress, Social Isolation, and Perceived Loneliness in Dementia Caregivers
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function, functional status, and social connectedness, and fewer depressive symptoms (Nikmat, Al-Mashoor, & Hashim, 2015).

On the contrary, dementia caregivers’ adverse outcomes include depressive symptoms, caregiver burden (Richardson et al., 2013), anxiety (Corrêa et al., 2015), decreased health-related quality of life (Garzón-Maldonado et al., 2017), poor subjective health (Andrén & Elmståhl, 2008), social isolation (Vallée & Vallée, 2017), and loneliness (O’Connor, Aritzendi, & Kaszniaak, 2014). Chronic stress is prevalent in this population (Allen et al., 2017) and is associated with increased mortality risk (Russ et al., 2012) and chronic systemic inflammation (Miller et al., 2014), a pathogenetic basis for several conditions, including cardiovascular disease (Fassett & Coombes, 2009), Alzheimer’s disease, cancer, and diabetes (Oishi & Manabe, 2016). The current review explores the relationship between caregiving stressors and social isolation (exogenous factors) and perceived stress and perceived loneliness (endogenous factors). Biologically based disruptions in the context of dementia caregiving are discussed.

OVERVIEW OF CAREGIVERS’ EXPERIENCE

A greater proportion of dementia caregivers assist care recipients with activities of daily living compared to caregivers of older adults without dementia. Such dependency reflects gradual increases in functional and cognitive impairment in dementia (Alzheimer’s Association, 2016). Behavioral and psychological symptoms of dementia (BPSD), which most individuals with dementia experience at some point during illness (e.g., agitation, aggression, hallucinations, delusions, sleep disorders [Desai, Schwartz, & Grossberg, 2012]), are associated with caregivers’ distress, inappropriate pharmacotherapy, and increased health care costs (Cerejeira, Lagarto, & Mukaetova-Ladinska, 2012). Dementia caregivers dedicate more hours weekly for caregiving compared to caregivers of individuals without dementia (Alzheimer’s Association, 2016). Aggression, agitation, and psychosis are among the most burdensome BPSD to caregivers (Rocca et al., 2010). Caregivers’ chronic stress may increase due to their social isolation or perceived loneliness. Social isolation implies an objective, quantifiable state of limited human contact (Steptoe, Shankar, Demakakos, & Wardle, 2013). Perceived loneliness denotes a distressing emotional state arising from lack of social connectedness (Luo, Hawkley, Waite, & Cacioppo, 2012). Both terms are used in the dementia caregiving literature. Caregiving responsibilities may cause social isolation or perceived loneliness because other activities (e.g., socialization) may decline in priority due to lack of time (Vitaliano, Murphy, Young, Echeverria, & Borson, 2011) or caregivers’ depressive symptoms. Perceived loneliness may also result from the lost relationship with the care recipient (Evans & Lee, 2014). Social isolation may worsen caregivers’ well-being and cognition (Vitaliano et al., 2011).

PHYSIOLOGICAL EFFECTS OF CHRONIC STRESS

Neuroendocrine and immune regulation underlies stress adaptation (Wohleb, McKim, Sheridan, & Godbout, 2014). Stress activates the hypothalamic-pituitary-adrenal (HPA) axis (Tomiyama et al., 2012), resulting in cortisol release. The latter exerts negative feedback on the hypothalamus, inhibiting HPA axis activation (Tasker & Herman, 2011), thus decreasing cortisol release. Cortisol has immunosuppressive and anti-inflammatory effects in initial inflammatory response stages (Coutinho & Chapman, 2011). Thus, cortisol is protective in acute stress.

Chronic stress is linked to immune cell dysfunction (Dhabhar, 2014). During chronic stress, white blood cells (WBCs) under-express glucocorticoid receptors that bind cortisol (Hannibal & Bishop, 2014). Without receptors, the unbound hormone cannot exert its anti-inflammatory effect on WBCs, and systemic inflammation persists. Systemic inflammation has been observed in individuals with chronic stress, including spouses of cancer patients (Rohleder, Marin, Ma, & Miller, 2009), individuals with posttraumatic stress disorder (Spitzer et al., 2010), minority or low-income pregnant women experiencing high perceived stress (Corwin et al., 2013), individuals who grew up in poverty (Miller et al., 2009), and those with high lifetime traumatic stress exposure (O’Donovan, Neylan, Metzler, & Cohen, 2012).

In addition, telomere length in peripheral blood mononuclear cells is shortened among dementia caregivers (Damjanovic et al., 2007). Telomeres are protective regions on chromosomes’ terminal ends. Their shortened length is a marker of cellular aging. Perhaps as a marker of allostatic load, dementia caregivers with greater cortisol secretion following an acute laboratory stressor have shorter telomere length (Tomiyama et al., 2012).

LINK BETWEEN CAREGIVING STRESSORS, SOCIAL ISOLATION, PERCEIVED STRESS, AND PERCEIVED LONELINESS

Dementia caregivers are under chronic stress, with stress effects bearing a physiological fingerprint. Social isolation is linked to increased morbidity (Valtorta, Kanaan, Gilbody, Ronzi, & Hanratty, 2016). Some diseases linked to social isolation are of inflammatory pathogenesis (e.g., cardiovascular disease [Holt-Lunstad & Smith, 2016], stroke (Nagayoshi et al., 2014)). Furthermore, subjective social isolation (perceived loneliness) is associated with gene transcription change. Individuals experiencing chronic perceived loneliness have over-expression of pro-inflammatory genes and under-expression of genes conferring anti-inflammatory protection (Cole et al., 2007). In addition, lonelier healthy adults exhibit greater synthesis of inflammatory cytokines following acute stress (Jaremka et al., 2014). With many instances of sudden stress in caregiving (e.g., patient’s aggres-
sion, wandering), caregivers’ chronic stress may undermine their response to acute stress. Other perceived loneliness sequelae include executive function impairment, depression, sleep disruption, and earlier mortality (Hawkley & Capitanio, 2015).

CLINICAL PRACTICE IMPLICATIONS

Caregiving stressors, social isolation, perceived stress, and perceived loneliness may be linked with physiological dysregulation, evidenced by HPA axis overactivity with resultant pro-inflammatory state, exacerbated cellular aging, and gene expression changes. Thus, perceived loneliness and perceived stress may form a symptom cluster—a phenomenon of predictable co-occurrence of at least two symptoms (Aktas, Walsh, & Rybicki, 2010).

A model with caregiving aspects grouped into three categories is proposed (Figure). First, environmental exogenous factors may be, to some extent, objectively identified. These factors include caregiving stressors, such as financial strain due to care recipients’ increasing needs. Caregivers’ employment frequently suffers, as caregiving responsibilities may necessitate changes (e.g., from decreasing work hours to retiring prematurely [Alzheimer’s Association, 2016]). Other stressors are care recipients’ BPSD (Unson, Flynn, Glendon, Haymes, & Sancho, 2015) and amount and complexity of required care (Alzheimer’s Association, 2016). Care may be physically demanding with patients’ paranoia (i.e., unintentional resistance to movement) (Hobbelan, Tan, Verhey, Koopmans, & de Bie, 2011). Decision making may be another stressor (e.g., deciding on institutionalization) (Austrom et al., 2014). Stress may arise from the care recipient’s health care management, as other chronic conditions are common among individuals with dementia (Banerjee, 2015). These stressors may lead to social isolation, the second environmental exogenous factor. Contributors to social isolation may be employment termination, rural residence (Navaie, 2011), and sacrificing social activities (Brodaty & Donkin, 2009). Social isolation may worsen objective stressors; hence, these factors are connected. Caregiving stressors may exacerbate perceived stress, a psychosocial endogenous factor. Social isolation may induce perceived loneliness, which in turn may exacerbate perceived stress, and vice versa. Finally, perceived stress and perceived loneliness undermine physical health (HPA axis dysregulation and genetic and molecular level changes).

Practice implications of the proposed symptom cluster are summarized in the Table. The key question a clinician may ask is whether any adult patient is a caregiver. Caregivers are “hidden patients” (Reinhard, Given, Petlick, & Bemis, 2008, p. 341), who may not reveal that they are caregivers. Clinicians should be knowledgeable about resources for dementia caregivers in their local area. Mere referral to community agencies is better than no attention, but underutilizes resources and effective interventions developed specifically for dementia caregivers. Most caregivers do not access numerous programs for caregivers (Gitlin, Marx, Stanley, & Hodgson, 2015) for reasons ranging from transportation difficulties to caregivers’ employment (Navaie, 2011). Clinicians are in a prime position to connect interventions and resources to caregivers, aiding in translation of research findings into clinical practice and improving use of community agencies. Health care providers should be more specific in answering caregivers’ questions and following up, maintaining continuity of care. Clinicians may develop a list of resources specific to their location with the following information: clinics/providers specializing in dementia management; education for dementia caregivers (including online options); support groups; social work services that can assist with questions ranging from advanced care planning to enlisting paid support to assistance with Medicare and Medicaid; resources for in-home paid assistance and transportation; and help with medications (e.g., GoodRx [access https://www.goodrx.com]). Not all resources may be available in certain geographic areas; hence, clinicians’ up-to-date knowledge of local and national opportunities (e.g., online classes) is key.

Finally, an indirect but essential way to help caregivers is to provide optimal care to patients with dementia using up-to-date guidelines. Given that dementia is an umbrella term for several diseases, including Alzheimer’s disease and vascular, Lewy body, and mixed dementia, specific literature must be consulted. Comprehensive current statements, such as Alzheimer’s Association® reports (Alzheimer’s Association, 2017) and the American Academy of Neurology guidelines (American
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<th>Examples of Interventions/Resources/Strategiesa</th>
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<tr>
<td>Stresses of caregiving</td>
<td>How do you feel as a caregiver? Referral to a local Alzheimer’s Association® chapter.</td>
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<td></td>
<td>What stresses do you experience? Referral to caregiver education programs, such as in-person Savvy Caregiver Courses held in various states.</td>
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|                        | Are you employed? What are your financial concerns? Referral to a social worker; Alzheimer’s Association®; National Institute on Aging (Alzheimer’s Disease Education and Resources website [NIA-ADEAR])
|                        | Are you considering institutionalization? If so, what type of residence, when? Referral to a social worker. Discuss housing options and differences between various options: assisted living, senior living, nursing home, paid home assistance (certified nursing assistants), and skilled nursing health care in the home setting. | Are you considering institutionalization? If so, what type of residence, when? Referral to a social worker. Discuss housing options and differences between various options: assisted living, senior living, nursing home, paid home assistance (certified nursing assistants), and skilled nursing health care in the home setting. |
|                        | Who assists you in the care of your care recipient? What assistance do you need? How physically and/or emotionally difficult is caregiving for you? Discuss options for hiring in-person help and enlisting support from family members, friends, or community (i.e., ask for help with concrete tasks when family members or friends ask if they can help). Discuss options for respite. | Who assists you in the care of your care recipient? What assistance do you need? How physically and/or emotionally difficult is caregiving for you? Discuss options for hiring in-person help and enlisting support from family members, friends, or community (i.e., ask for help with concrete tasks when family members or friends ask if they can help). Discuss options for respite. |
|                        | What do you know about your care recipient’s illness? What questions do you have about it? How do you manage your care recipient’s medications? Educate about dementia using up-to-date sources (Alzheimer’s Association, Uptodate, Beers Criteria). If available, refer the patient to a memory clinic. Advise to attend a class for caregivers, such as the Savvy Caregiver Course. Caregiving education modalities include: psychoeducation; cognitive-behavioral therapy; counseling; acceptance and commitment therapy; environmental programs; and multicomponent approaches. Online interventions may be available. | What do you know about your care recipient’s illness? What questions do you have about it? How do you manage your care recipient’s medications? Educate about dementia using up-to-date sources (Alzheimer’s Association, Uptodate, Beers Criteria). If available, refer the patient to a memory clinic. Advise to attend a class for caregivers, such as the Savvy Caregiver Course. Caregiving education modalities include: psychoeducation; cognitive-behavioral therapy; counseling; acceptance and commitment therapy; environmental programs; and multicomponent approaches. Online interventions may be available. |
|                        | What symptoms does your care recipient manifest? Symptoms may include agitation (e.g., wandering, pacing, repetitive motions); verbal and/or physical aggression; mood disturbance (e.g., depressive symptoms, apathy); psychosis (e.g., hallucinations, delusions); and sleep–wake cycle disruption. Although dementia is incurable, its symptoms are frequently provoked by modifiable factors (e.g., care recipients’ pain, hunger, thirst, need to urinate/defecate, discomfort, boredom, need for social contact and stimulation). Hence, it is important to control the environment to prevent and attenuate symptoms. | What symptoms does your care recipient manifest? Symptoms may include agitation (e.g., wandering, pacing, repetitive motions); verbal and/or physical aggression; mood disturbance (e.g., depressive symptoms, apathy); psychosis (e.g., hallucinations, delusions); and sleep–wake cycle disruption. Although dementia is incurable, its symptoms are frequently provoked by modifiable factors (e.g., care recipients’ pain, hunger, thirst, need to urinate/defecate, discomfort, boredom, need for social contact and stimulation). Hence, it is important to control the environment to prevent and attenuate symptoms. |
| Social isolation        | What is your social network? On whose help can you rely with your caregiving tasks? What activities did you give up after you became a caregiver? Are you socially isolated? If so, what are some ways that have helped you in the past to maintain social connections? Discuss options for the caregiver to strengthen his/her network by engaging in caregiver education and/or support groups. Offer ways in which a caregiver may enlist assistance of others to allow oneself to maintain social connections and fulfill roles outside of caregiving. Offer online caregiver education and/or support groups for caregivers who may be socially isolated due to their inability to attend in-person programs. This may be especially pertinent to caregivers who live in rural areas or lack transportation, as well as caregivers whose care recipients are in advanced dementia stages and require 24/7 care. | Discuss options for the caregiver to strengthen his/her network by engaging in caregiver education and/or support groups. Offer ways in which a caregiver may enlist assistance of others to allow oneself to maintain social connections and fulfill roles outside of caregiving. Offer online caregiver education and/or support groups for caregivers who may be socially isolated due to their inability to attend in-person programs. This may be especially pertinent to caregivers who live in rural areas or lack transportation, as well as caregivers whose care recipients are in advanced dementia stages and require 24/7 care. |
### SUMMARY OF PRACTICE IMPLICATIONS AND INTERVENTIONS FOR DEMENTIA CAREGIVERS

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<th>Domain</th>
<th>Questions Clinicians May Ask</th>
<th>Examples of Interventions/Resources/Strategies[^a]</th>
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<tr>
<td>Perceived stress</td>
<td>What is the most stressful aspect of caregiving for you? What do you find uncertain or anxiety-provoking?</td>
<td>In addition to discussing caregivers’ stress, use validated instruments to quantify caregivers’ stress[^t], anxiety[^s], depression[^t], and burden[^u], and care recipient’s dementia symptom frequency and severity[^v]. The Revised Memory and Behavior Problem Checklist[^v] provides quantifiable information on care recipients’ behavioral symptoms and caregivers’ associated distress. This instrument can help clinicians elucidate which symptoms the care recipient is manifesting and which of those symptoms are most distressing to the caregiver. Hence, clinicians may precisely advise on symptom management. It is important to combine discussion-based assessment of caregivers’ psychological well-being with quantitative assessment, as caregivers may be reluctant to admit their distress.</td>
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<tr>
<td>Perceived loneliness</td>
<td>Do you find yourself lonely? What do you think contributes to it?</td>
<td>Validate that perceived loneliness is a common phenomenon among dementia caregivers. Loneliness may stem from the loss of the relationship with the care recipient and family conflict.</td>
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<tr>
<td>Caregivers’ physical health</td>
<td>When was your last physical examination? Do you experience fatigue, chronic pain, and/or sleep disturbance?</td>
<td>Reinforce the importance for caregivers to attend to their own physical health (e.g., physician visits, annual diagnostic tests recommended according to caregiver’s age and gender). Validate the importance of respite.</td>
</tr>
</tbody>
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[^a]: Interventions and strategies listed are frequently applicable to numerous questions (e.g., the Alzheimer’s Association[^b] has resources for caregivers’ financial questions, issues related to dealing with dementia symptoms).

[^b]: Alzheimer’s Association (2018a).
[^c]: Alzheimer’s Association (2018b).
[^e]: Family Caregiver Alliance (n.d.).
[^f]: Alzheimer’s Association (2017).
[^g]: UptoDate (2018).
[^i]: Hepburn, Lewis, Sherman, & Tomatore (2003).
[^k]: Gallagher-Thompson, Gray, Dupart, Jimenez, & Thompson (2008).
[^l]: Fauth et al. (2017).
[^m]: Losada et al. (2015).
[^n]: Gitlin, Winter, Dennis, Hodgson, & Hauck (2010).
[^o]: Graham-Phillips, Roth, Dilworth-Anderson, & Gitlin (2016).
[^q]: Desai et al. (2012).
[^r]: Cohen, Kanarck, & Memelstein (1983).
[^t]: Radloff (1977).
[^u]: Zarit, Reever, & Bach-Peterson (1980).
[^v]: Teri et al. (1992).
Academy of Neurology, n.d.), are good starting points. Provision of high-quality dementia care and/or referral to dementia care experts will counteract the common experience among dementia caregivers who find clinicians’ assistance with dementia management suboptimal and caregivers’ needs unmet (Jennings et al., 2015). Psychiatric nurses are at the forefront of care for individuals with dementia and their caregivers and can make concrete contributions to the quality of life of these growing population clusters.

REFERENCES


Hawley, L.C., & Capitanio, J.P. (2015). Perceived social isolation, evolutionary fitness...


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