ann. behav. med. (2010) 40:218–227
DOI 10.1007/s12160-010-9210-8

ORIGINAL ARTICLE

Loneliness Matters: A Theoretical and Empirical Review of Consequences and Mechanisms

Louise C. Hawkley, Ph.D. · John T. Cacioppo, Ph.D.

Published online: 22 July 2010

Abstract As a social species, humans rely on a safe, secure social surround to survive and thrive. Perceptions of social isolation, or loneliness, increase vigilance for threat and heighten feelings of vulnerability while also raising the desire to reconnect. Implicit hypervigilance for social threat alters psychological processes that influence physiological functioning, diminish sleep quality, and increase morbidity and mortality. The purpose of this paper is to review the features and consequences of loneliness within a comprehensive theoretical framework that informs interventions to reduce loneliness. We review physical and mental health consequences of loneliness, mechanisms for its effects, and effectiveness of extant interventions. Features of a loneliness regulatory loop are employed to explain cognitive, behavioral, and physiological consequences of loneliness and to discuss interventions to reduce loneliness. Loneliness is not simply being alone. Interventions to reduce loneliness and its health consequences may need to take into account its attentional, confirmatory, and memorial biases as well as its social and behavioral effects.

Keywords Loneliness · Regulatory loop · Physiology · Health behavior · Sleep · Intervention

This research was supported by Grant R01-AG036433-01 and R01-AG034052 from the National Institute on Aging and by the John Templeton Foundation.

L. C. Hawkley · J. T. Cacioppo
Center for Cognitive and Social Neuroscience,
University of Chicago,
Chicago, IL, USA

L. C. Hawkley (✉)
Department of Psychology, University of Chicago,
940 E. 57th St,
Chicago, IL 60637, USA
e-mail: hawkley@uchicago.edu

Introduction

Loneliness is a common experience; as many as 80% of those under 18 years of age and 40% of adults over 65 years of age report being lonely at least sometimes [1–3], with levels of loneliness gradually diminishing through the middle adult years, and then increasing in old age (i.e., ≥70 years) [2]. Loneliness is synonymous with perceived social isolation, not with objective social isolation. People can live relatively solitary lives and not feel lonely, and conversely, they can live an ostensibly rich social life and feel lonely nevertheless. Loneliness is defined as a distressing feeling that accompanies the perception that one's social needs are not being met by the quantity or especially the quality of one's social relationships [2, 4–6]. Loneliness is typically measured by asking individuals to respond to items such as those on the frequently used UCLA Loneliness Scale [7]: "I feel isolated," "There are people I can talk to," and "I feel part of a group of friends." The result is a continuum of scores that range from highly socially connected to highly lonely.

Each of us is capable of feeling lonely, and loneliness is an equal opportunity tenant for good reason. We have posited that loneliness is the social equivalent of physical pain, hunger, and thirst; the pain of social disconnection and the hunger and thirst for social connection motivate the maintenance and formation of social connections necessary for the survival of our genes [8, 9]. Feelings of loneliness generally succeed in motivating connection or reconnection with others following geographic relocation or bereavement, for instance, thereby diminishing or abolishing feelings of social isolation. For as many as 15–30% of the general population, however, loneliness is a chronic state [10, 11]. Left untended, loneliness has serious consequences for cognition, emotion, behavior,

and health. Here, we review physical and mental health consequences of perceived social isolation and then introduce mechanisms for these outcomes in the context of a model that takes into consideration the cognitive, emotional, and behavioral characteristics of loneliness.

Loneliness Matters for Physical Health and Mortality

A growing body of longitudinal research indicates that loneliness predicts increased morbidity and mortality [12–19]. The effects of loneliness seem to accrue over time to accelerate physiological aging [20]. For instance, loneliness has been shown to exhibit a dose–response relationship with cardiovascular health risk in young adulthood [12]. The greater the number of measurement occasions at which participants were lonely (i.e., childhood, adolescence, and at 26 years of age), the greater their number of cardiovascular health risks (i.e., BMI, systolic blood pressure (SBP), total, and HDL cholesterol levels, glycated hemoglobin concentration, maximum oxygen consumption). Similarly, loneliness was associated with increased systolic blood pressure in a population-based sample of middle-aged adults [21], and a follow-up study of these same individuals showed that a persistent trait-like aspect of loneliness accelerated the rate of blood pressure increase over a 4-year follow-up period [22]. Loneliness accrual effects are also evident in a study of mortality in the Health and Retirement Study; all-cause mortality over a 4-year follow-up was predicted by loneliness, and the effect was greater in chronically than situationally lonely adults [17]. Penninx et al. [15] showed that loneliness predicted all-cause mortality during a 29-month follow-up after controlling for age, sex, chronic diseases, alcohol use, smoking, self-rated health, and functional limitations. Sugisawa et al. [18] also found a significant effect of loneliness on mortality over a 3-year period, and this effect was explained by chronic diseases, functional status, and self-rated health. Among women in the National Health and Nutrition Survey, chronic high frequency loneliness (>3 days/week at each of two measurement occasions about 8 years apart) was prospectively associated with incident coronary heart disease (CHD) over a 19-year follow-up in analyses that adjusted for age, race, socioeconomic status, marital status, and cardiovascular risk factors [19]. Depressive symptoms have been associated with loneliness and with adverse health outcomes, but loneliness continued to predict CHD in these women after also controlling for depressive symptoms. Finally, loneliness has also been shown to increase risk for cardiovascular mortality; individuals who reported often being lonely exhibited significantly greater risk than those who reported never being lonely [14]. In sum, feelings of loneliness mark increased risk for morbidity and mortality, a phenomenon that arguably reflects the social essence of our species.

Loneliness Matters for Mental Health and Cognitive Functioning

The impact of loneliness on cognition was assessed in a recent review of the literature [9]. Perhaps, the most striking finding in this literature is the breadth of emotional and cognitive processes and outcomes that seem susceptible to the influence of loneliness. Loneliness has been associated with personality disorders and psychoses [23–25], suicide [26], impaired cognitive performance and cognitive decline over time [27–29], increased risk of Alzheimer's Disease [29], diminished executive control [30, 31], and increases in depressive symptoms [32–35]. The causal nature of the association between loneliness and depressive symptoms appears to be reciprocal [32], but more recent analyses of five consecutive annual assessments of loneliness and depressive symptoms have shown that loneliness predicts increases in depressive symptoms over 1-year intervals, but depressive symptoms do not predict increases in loneliness over those same intervals [36]. In addition, experimental evidence, in which feelings of loneliness (and social connectedness) were hypnotically induced, indicates that loneliness not only increases depressive symptoms but also increases perceived stress, fear of negative evaluation, anxiety, and anger, and diminishes optimism and self-esteem [8]. These data suggest that a perceived sense of social connectedness serves as a scaffold for the self—damage the scaffold and the rest of the self begins to crumble.

A particularly devastating consequence of feeling socially isolated is cognitive decline and dementia. Feelings of loneliness at age 79 predicted "lifetime cognitive change" as indicated by lower IQ at age 79 adjusting for IQ at age 11, living arrangements at age 11 and at age 79, sex, marital status, and ideal level of social support [27]. This finding does not rule out a reverse causal direction; cognitive impairments may hamper social interactions, prompt social withdrawal, and thus lead to loneliness. Other studies, however, have indicated that loneliness is a precursor of cognitive decline. For instance, the cognitive functioning of 75–85-year-olds (as assessed by the Mini-Mental State Examination) did not differ as a function of loneliness at baseline but diminished to a greater extent among those high than low in loneliness over a 10-year follow-up [28]. In a prospective study by Wilson et al. [29], loneliness was inversely associated with performance on a battery of cognitive measures in a sample of 823 initially dementia-free older adults. Moreover, loneliness at baseline was associated with a faster decline in cognitive performance on most of these measures over a 4-year follow-up. This was

not true of the converse: cognitive status at baseline did not predict changes in loneliness. In addition, incidence of Alzheimer's disease (76 individuals) was predicted by degree of baseline loneliness after adjusting for age, sex, and education; those in the top decile of loneliness scores were 2.1 times as likely to develop Alzheimer's disease than those in the bottom decile of loneliness scores. Depressive symptoms had a modest effect on Alzheimer's disease risk, but loneliness continued to exert a significant and much larger influence on Alzheimer's disease than depressive symptoms when depressive symptoms were included in the model [29]. Overall, it appears that something about our sense of connectedness with others penetrates the physical organism and compromises the integrity of physical and mental health and well-being. What that "something" might be is the topic to which we next turn.

How Loneliness Matters: Mechanisms

The Loneliness Model Our model of loneliness [8, 9] posits that perceived social isolation is tantamount to feeling unsafe, and this sets off implicit hypervigilance for (additional) social threat in the environment. Unconscious surveillance for social threat produces cognitive biases: relative to nonlonely people, lonely individuals see the social world as a more threatening place, expect more negative social interactions, and remember more negative social information. Negative social expectations tend to elicit behaviors from others that confirm the lonely persons' expectations, thereby setting in motion a self-fulfilling prophecy in which lonely people actively distance themselves from would-be social partners even as they believe that the cause of the social distance is attributable to others and is beyond their own control [37]. This self-reinforcing loneliness loop is accompanied by feelings of hostility, stress, pessimism, anxiety, and low self-esteem [8] and represents a dispositional tendency that activates neurobiological and behavioral mechanisms that contribute to adverse health outcomes.

Health behaviors One of the consequences of loneliness and implicit vigilance for social threat is a diminished capacity for self-regulation. The ability to regulate one's thoughts, feelings, and behavior is critical to accomplish personal goals or to comply with social norms. Feeling socially isolated impairs the capacity to self-regulate, and these effects are so automatic as to seem outside of awareness. In a dichotic listening task, for instance, right-handed individuals quickly and automatically attend preferentially to the pre-potent right ear. Latency to respond to stimuli presented to the non-dominant ear can be enhanced, however, by instructing participants to attend to their left ear. Among young adults who were administered this task, the lonely and nonlonely groups did not differ in performance when directed to attend to their pre-potent right ear, but the lonely group performed significantly worse than the nonlonely group when directed to shift attention to their non-prepotent left ear [30]. In other words, automatic attentional processes may be unimpaired, but effortful attentional processes are compromised in lonely relative to socially connected individuals.

Of relevance for health is the capacity for self-regulation in the arena of lifestyle behaviors. Regulation of emotion can enhance the ability to regulate other self-control behaviors [38], as is evident from research showing that positive affect predicts increased physical activity [39]. In middle-aged and older adults, greater loneliness was associated with less effort applied to the maintenance and optimization of positive emotions [31]. Compromised regulation of emotion in lonely individuals explained their diminished likelihood of performing any physical activity, and loneliness also predicted a decrease in physical activity over time [31]. Physical activity is a well-known protective factor for physical health, mental health, and cognitive functioning [40], suggesting that poorer self-regulation may contribute to the greater health risk associated with loneliness via diminished likelihood of engaging in health-promoting behaviors. A related literature shows that loneliness is also a risk factor for obesity [41] and health-compromising behavior, including a greater propensity to abuse alcohol [42]. To the extent that self-regulation accounts for poorer health behaviors in lonely people, better health behaviors may be more easily accomplished in the actual or perceived company of others. Interestingly, animal research has shown that social isolation dampens the beneficial effects of exercise on neurogenesis [43], implying that health behaviors may better serve their purpose or have greater effect among those who feel socially connected than those who feel lonely. This hypothesis remains to be tested, but research on the restorative effects of sleep is consistent with this notion.

Sleep Countering the physiological effects of the challenge of daily emotional, cognitive, and behavioral experiences, sleep offers physiological restoration. Experimental sleep deprivation has adverse effects on cardiovascular functioning, inflammatory status, and metabolic risk factors [44]. In addition, short sleep duration has been associated with risk for hypertension [45], incident coronary artery calcification [46], and mortality [47].

What is less appreciated is that sleep quality may also be important in accomplishing sleep's restorative effects. Nonrestorative sleep (i.e., sleep that is non-refreshing despite normal sleep duration) results in daytime impairments such as physical and intellectual fatigue, role

impairments, and cognitive and memory problems [48]. We have noted that loneliness heightens feelings of vulnerability and unconscious vigilance for social threat, implicit cognitions that are antithetical to relaxation and sound sleep. Indeed, loneliness and poor quality social relationships have been associated with self-reported poor sleep quality and daytime dysfunction (i.e., low energy, fatigue), but not with sleep duration [49–52]. In young adults, greater daytime dysfunction, a marker of poor sleep quality, was accompanied by more nightly micro-awakenings, an objective index of sleep continuity obtained from SleepCaps worn by participants during one night in the hospital and seven nights in their own beds at home [53]. The conjunction of daytime dysfunction and micro-awakenings is consistent with polysomnography studies showing a conjunction, essentially an equivalence, between subjective sleep quality and sleep continuity [54], and substantiates the hypothesis that loneliness impairs sleep quality.

In an extension of these findings, loneliness was associated with greater daytime dysfunction in a 3-day diary study of middle-age adults, an association that was independent of age, gender, race/ethnicity, household income, health behaviors, BMI, chronic health conditions, daily illness symptom severity, and related feelings of stress, hostility, poor social support, and depressive symptoms. Cross-lagged panel analyses of the three consecutive days indicated potentially reciprocal causal roles for loneliness and daytime dysfunction: lonely feelings predicted daytime dysfunction the following day, and daytime dysfunction exerted a small but significant effect on lonely feelings the following day [55], effects that were independent of sleep duration. In other words, the same amount of sleep is less salubrious in individuals who feel more socially isolated and, ironically, less salubrious sleep feeds forward to further exacerbate feelings of social isolation. This recursive loop operates outside of consciousness and speaks to the relative impenetrability of loneliness to intervention.

Physiological functioning The association between loneliness and cardiovascular disease and mortality [13, 14, 19] may have its roots in physiological changes that begin early in life. As noted earlier, chronic social isolation, rejection, and/or feelings of loneliness in early childhood, adolescence, and young adulthood cumulated in a dose–response fashion to predict cardiovascular health risk factors in young adulthood (26 years old), including elevated blood pressure [12]. In our study of young adults, loneliness was associated with elevated levels of total peripheral resistance (TPR [49, 56]). TPR is the primary determinant of SBP until at least 50 years of age [57], which suggests that loneliness-related elevations in TPR in early to middle-adulthood may lead to higher blood pressure in middle and older age. Consistent with this hypothesis, loneliness was associated with elevated SBP in an elderly convenience sample [49], and in a population-based sample of 50–68-year-old adults in the Chicago Health, Aging, and Social Relations Study [21]. The association between loneliness and elevated SBP was exaggerated in older relative to younger lonely adults in this sample [21], suggesting an accelerated physiological decline in lonely relative to nonlonely individuals. Our recent study of loneliness and SBP in these same individuals over five annual assessments supported this hypothesis. Short-term (i.e., 1 year) fluctuations in loneliness were not significant predictors of SBP changes over 1-year intervals, but a trait-like component of loneliness present at study onset contributed to greater increases in SBP over 2-, 3-, and 4-year intervals [22]. These increases were cumulative such that higher initial levels of loneliness were associated with greater increases in SBP over a 4-year period. The prospective effect of loneliness on SBP was independent of age, gender, race/ethnicity, cardiovascular risk factors, medications, health conditions, and the effects of depressive symptoms, social support, perceived stress, and hostility [22]. Elevated SBP is a well-known risk factor for chronic cardiovascular disease, and these data suggest that the effects of loneliness accrue to accelerate movement along a trajectory toward serious health consequences [20].

The physiological determinants responsible for the cumulative effect of loneliness on blood pressure have yet to be elucidated. TPR plays a critical role in determining SBP in early to mid-adulthood, but other mechanisms come into play with increasing age. Candidate mechanisms include age-related changes in vascular physiology, including increased arterial stiffness [58], diminished endothelial cell release of nitric oxide, enhanced vascular responsivity to endothelial constriction factors, increases in circulating catecholamines, and attenuated vasodilator responses to circulating epinephrine due to decreased beta-adrenergic sensitivity in vascular smooth muscle [59–61]. In turn, many of these mechanisms are influenced by lifestyle factors such as diet, physical inactivity, and obesity—factors that alter blood lipids and inflammatory processes that have known consequences for vascular health and functioning [62, 63].

Neuroendocrine Effects

Changes in TPR levels are themselves influenced by a variety of physiological processes, including activity of the autonomic nervous system and the hypothalamic-pituitary adrenocortical (HPA) axis. The sympathetic branch of the autonomic nervous system plays a major role in maintaining basal vascular tone and TPR [64, 65] and elevated sympathetic tone is responsible for the development and maintenance of many forms of hypertension [66]. To date, loneliness has not been shown to correlate with SNS activity at the myocardium (i.e., pre-ejection period [21, 56]) but was associated

with a greater concentration of epinephrine in overnight urine samples in a middle-aged and older adult sample [21]. At high concentrations, circulating epinephrine binds α-1 receptors on vascular smooth muscle cells to elicit vasoconstriction and could thereby serve as a mechanism for increased SBP in lonely individuals.

Activation of the HPA axis involves a cascade of signals that results in release of ACTH from the pituitary and cortisol from the adrenal cortex. Vascular integrity and functioning are beholden, in part, to well-regulated activity of the HPA axis. Dysregulation of the HPA axis contributes to inflammatory processes that play a role in hypertension, atherosclerosis, and coronary heart disease [67–69]. Loneliness has been associated with urinary excretion of significantly higher concentrations of cortisol [70], and, in more recent studies, with higher levels of salivary or plasma cortisol [71, 72]. Pressman et al. [72] found that loneliness was associated with higher early morning and late night levels of circulating cortisol in young adult university students, and Steptoe et al. [71] found that chronically high levels of trait loneliness in middle-aged adults (M=52.4 years) predicted greater increases in salivary cortisol during the first 30 min after awakening (i.e., cortisol awakening response) such that the cortisol awakening response in individuals in the highest loneliness tertile was 21% greater than that in the lowest tertile. In our study of middle-aged and older adults, day-to-day fluctuations in feelings of loneliness were associated with individual differences in the cortisol awakening response. For this study, diary reports of daily psychosocial, emotional, and physical states were completed at bedtime on each of three consecutive days, and salivary cortisol levels were measured at wakeup, 30 min after awakening, and at bedtime each day. Parallel multilevel causal models revealed that prior-day feelings of loneliness and related feelings of sadness, threat, and lack of control were associated with a higher cortisol awakening response the next day, but morning cortisol awakening response did not predict experiences of these psychosocial states later the same day [73]. Social evaluative threat is known to be a potent elicitor of cortisol [74], and our theory that loneliness is characterized by chronic threat of and hypervigilance for negative social evaluation [9] is consistent with the finding that loneliness predicts increased cortisol awakening response. The relevance of the association between loneliness and HPA regulation is particularly noteworthy given recent evidence that loneliness-related alterations in HPA activity may occur at the level of the gene, a topic to which we turn next.

Gene Effects

Cortisol regulates a wide variety of physiological processes via nuclear hormone receptor-mediated control of gene transcription. Cortisol activation of the glucocorticoid receptor, for instance, exerts broad anti-inflammatory effects by inhibiting pro-inflammatory signaling pathways. Given that loneliness is associated with elevated cortisol levels, loneliness might be expected to reduce risk for inflammatory diseases. However, as we have noted above, feelings of loneliness and social isolation are associated with increased risk for inflammatory disease. This finding may be attributable to impaired glucocorticoid receptor-mediated signal transduction; failure of the cellular genome to "hear" the anti-inflammatory signal sent by circulating glucocorticoids permits inflammatory processes to continue relatively unchecked. We found evidence consistent with glucocorticoid insensitivity in our examination of gene expression rates in chronically lonely versus socially connected older adults [75]. Genome-wide microarray analyses revealed that 209 transcripts, representing 144 distinct genes, were differentially expressed in these two groups. Markers of immune activation and inflammation (e.g., pro-inflammatory cytokines and inflammatory mediators) were over-expressed in genes of the lonely relative to the socially connected group (37% of the 209 differentially expressed transcripts). Markers of cell cycle inhibitors and an inhibitor of the potent pro-inflammatory NF–κB transcript were under-expressed in genes of the lonely relative to the socially connected group (63% of the differentially expressed transcripts). The net functional implication of the differential gene transcription favored increased cell cycling and inflammation in the lonely group [75].

Subsequent bioinformatic analyses indicated that loneliness-associated differences in gene expression could be attributable to increased activity of the NF–κB transcription factor. NF–κB is known to up-regulate inflammation-related genes, and its activity is antagonized by the glucocorticoid receptor. Bioinformatic analyses also indicated a possible decrease in glucocorticoid receptor-mediated transcription in the lonely group, despite the fact that there were no group differences in circulating glucocorticoid levels. These results are consistent with the hypothesis that adverse social conditions result in functional desensitization of the glucocorticoid receptor, which permits increased NF–κB activity and thereby induces a pro-inflammatory bias in gene expression. Group differences in NF–κB/glucocorticoid receptor-mediated transcription activity were not attributable to objective indices of social isolation, nor were they explained by demographic, psychosocial (i.e., perceived stress, depression, hostility), or medical risk factors [75]. These results suggest that feelings of loneliness may exert a unique transcriptional influence that has potential relevance for health.

In an extension of this work, a recent study showed that feelings of social isolation were associated with a proxy measure of functional glucocorticoid insensitivity [76]. The composition of the leukocyte population in circulation is

subject to the regulatory influence of glucocorticoids; high cortisol levels increase circulating concentrations of neutrophils and simultaneously decrease concentrations of lymphocytes and monocytes. In a study of older Taiwanese adults, this relationship was reflected in a positive correlation between cortisol levels and the ratio of neutrophil percentages relative to lymphocyte or monocyte percentages. However, in lonely individuals, this correlation was attenuated and nonsignificant, consistent with a diminished effect of cortisol at the level of leukocytes.

The precise molecular site of glucocorticoid insensitivity in the pro-inflammatory transcription cascade has yet to be identified, and additional longitudinal and experimental research are needed to determine the degree to which chronic feelings of social isolation play a causal role in differential gene expression. However, the association between subjective social isolation and gene expression corresponds well to gene expression differences in animal models of social isolation (e.g., [77–79]), suggesting that a subjective sense of social connectedness is important for genomic expression and normal immunoregulation in humans. Impaired transcription of glucocorticoid response genes and increased activity of pro-inflammatory transcription control pathways provide a functional genomic explanation for elevated risk of inflammatory disease in individuals who experience chronically high levels of loneliness.

Immune Functioning

Loneliness differences in immunoregulation extend beyond inflammation processes. Loneliness has been associated with impaired cellular immunity as reflected in lower natural killer (NK) cell activity and higher antibody titers to the Epstein Barr Virus and human herpes viruses [70, 80–82]. In addition, loneliness among middle-age adults has been associated with a smaller increase in NK cell numbers in response to the acute stress of a Stroop task and a mirror tracing task [71]. In young adults, loneliness was associated with poorer antibody response to a component of the flu vaccine [72], suggesting that the humoral immune response may also be impaired in lonely individuals. Among HIV-positive men without AIDS, loneliness was associated with a lower count of CD4 T-lymphocytes in one study [83] but was not associated with the CD4 count in another study [84]. However, in the latter study, loneliness predicted a slower rate of decline in levels of CD4 T-lymphocytes over a 3-year period [84]. These data suggest that loneliness protects against disease progression, but no association was observed between loneliness and time to AIDS diagnosis or AIDS-related mortality [84]. Additional research is needed to examine the role of loneliness chronicity, age, life stress context, genetic predispositions, and interactions among these factors to determine when and how loneliness operates to impair immune functioning.

Future Loneliness Matters

Interventions for Loneliness Six qualitative reviews of the loneliness intervention literature have been published since 1984 [85–90], and all explicitly or implicitly addressed four main types of interventions: (1) enhancing social skills, (2) providing social support, (3) increasing opportunities for social interaction, and (4) addressing maladaptive social cognition. All but one of these reviews concluded that loneliness interventions have met with success, particularly interventions which targeted opportunities for social interaction. Findlay [87] was more cautious in his review, noting that only six of the 17 intervention studies in his review employed a randomized group comparison design, with the remaining 11 studies subject to the shortcomings and flaws of pre-post and nonrandomized group comparison designs.

We recently completed a meta-analysis of loneliness intervention studies published between 1970 and September 2009 to test the magnitude of the intervention effects within each type of study design and to determine whether the intervention target moderated effect sizes (Masi et al., unpublished). Of the 50 studies eligible for inclusion in the meta-analysis, 12 were pre-post studies, 18 were non-randomized group comparison studies, and 20 were randomized group comparison studies. Effect sizes were significantly different from zero within each study design group, but randomized group comparison studies produced the smallest effect overall (pre-post=−0.37, 95% CI −.55, −.18; non-randomized control=−0.46, 95% CI −0.72, −0.20; randomized control=−0.20, 95% CI −0.32, −0.08).

Our model of loneliness holds that implicit hypervigilance for social threat exerts a powerful influence on perceptions, cognitions, and behaviors, and that loneliness may be diminished by reducing automatic perceptual and cognitive biases that favor over-attention to negative social information in the environment. Accordingly, we posited that interventions that targeted maladaptive social cognition (e.g., cognitive behavioral therapy that involved training to identify automatic negative thoughts and look for disconfirming evidence, to decrease biased cognitions, and/or to reframe perceptions of loneliness and personal control) would be more effective than interventions that targeted social support, social skills, or social access. Moderational analyses of the randomized group comparison studies supported our hypothesis: the effect size for social cognition interventions (−0.60, 95% CI −0.96, −0.23, N=4) was significantly larger than the effect size for social support (−0.16, 95% CI −0.27, −0.06, N=12), social skills (0.02, 95% CI −0.24, 0.28, N=2), and social access (−0.06,

95% CI −0.35, 0.22, N=2); the latter three types of interventions did not differ significantly from each other. The results for social cognitive therapy are promising, but this intervention type appears not to have been widely employed to date relative to other types of loneliness therapy. Moreover, existing social cognitive therapies have had a small effect overall (0.20) relative to the meta-analytic mean effect of over 300 other interventions in the social and behavioral domains (0.50) [91]. A social cognitive approach to loneliness reduction outlined in a recent book [92] may encourage therapists to develop a treatment that focuses on the specific affective, cognitive, and behavioral propensities that afflict lonely individuals.

Implications for Health Reducing feelings of loneliness and enhancing a sense of connectedness and social adhesion are laudable goals in their own right, but a critical question is whether modifying perceptions of social isolation or connectedness have any impact on health. VanderWeele et al. (unpublished) recently examined the reduction in depressive symptoms that could be expected if loneliness were successfully reduced and found there would be significant benefits that would accrue for as long as two years following the intervention. Would a successful intervention to lower loneliness produce corresponding benefits in physiological mechanisms and physical health outcomes? The only extant data to address this question comes from a recent study in which 235 lonely home-dwelling older adults (>74 years) were randomly assigned to an intervention or control group. In the treatment arm of the study, closed small groups of seven to eight individuals met with two professional facilitators once a week for 3 months to participate in group activities in art, exercise, or therapeutic writing. The control group continued to receive usual community care. Relative to the control group, individuals in the treatment group became more socially active, found new friends, and experienced an increase in feeling needed [93]. This was accompanied by a significant improvement in self-rated health, fewer health care services and lower costs, and greater survival at 2-year follow-up [94]. Feelings of loneliness did not differ between the groups, however [93], indicating that changes in loneliness were not responsible for improvements in health. According to our theory of loneliness, the interventions targeted by the treatment study would not be expected to influence loneliness dramatically because they fail to address the hypervigilance to social threat and the related cognitive biases that characterize lonely individuals. That is, group activities such as those introduced in this intervention provide new social opportunities but do not alter how individuals approach and think about their social relationships more generally. An intervention study of loneliness and health has yet to be designed that addresses the maladaptive social cognitions that make loneliness the health risk factor it increasingly appears to be. Beyond that, additional research is needed to determine the mechanisms through which successful loneliness interventions enhance health and survival, and to examine whether the type of loneliness intervention moderates its health benefits.

Conclusions

Human beings are thoroughly social creatures. Indeed, human survival in difficult physical environments seems to have selected for social group living [95]. Consider that the reproductive success of the human species hinges on offspring surviving to reproductive age. Social connections with a mate, a family, and a tribe foster social affiliative behaviors (e.g., altruism, cooperation) that enhance the likelihood that utterly dependent offspring reach reproductive age, and connections with others at the individual and collective levels improve our chances of survival in difficult or hostile environments. These behaviors co-evolved with supporting genetic, neural, and hormonal mechanisms to ensure that humans survived, reproduced, and cared for offspring sufficiently long that they, too, could reproduce [96–98]. Human sociality is prominent even in contemporary individualistic societies. Almost 80% of our waking hours are spent with others, and on average, time spent with friends, relatives, spouse, children, and coworkers is rated more inherently rewarding than time spent alone [99, 100]. Humans are such meaning-making creatures that we perceive social relationships where no objectifiable relationship exists (e.g., between author and reader, between an individual and God) or where no reciprocity is possible (e.g., in parasocial relationships with television characters). Conversely, we perceive social isolation when social opportunities and relationships do exist but we lack the capacity to harness the power of social connectedness in everyday life. Chronic perceived isolation (i.e., loneliness) is characterized by impairments in attention, cognition, affect, and behavior that take a toll on morbidity and mortality through their impact on genetic, neural, and hormonal mechanisms that evolved as part and parcel of what it means to be human. Future interventions to alleviate the health burden of loneliness will do well to take into account our evolutionary design as a social species.

References

1. Berguno G, Leroux P, McAinsh K, Shaikh S. Children's experience of loneliness at school and its relation to bullying and the quality of teacher interventions. *Qualitative Report*. 2004; 9: 483–499.
2. Pinquart M, Sorensen S. Influences on loneliness in older adults: A meta-analysis. *Basic and Applied Social Psychology*. 2001; 23: 245–266.

3. Weeks DJ. A review of loneliness concepts, with particular reference to old age. *International Journal of Geriatric Psychiatry*. 1994; 9: 345–355.
4. Peplau L, Perlman D. Perspectives on loneliness. In: Peplau L, Perlman D, eds. *Loneliness: A sourcebook of current theory, research, and therapy*. New York: Wiley; 1982.
5. Hawkley LC, Hughes ME, Waite LJ, et al. From social structure factors to perceptions of relationship quality and loneliness: The Chicago Health, Aging, and Social Relations Study. *Journal of Gerontology: Social Sciences*. 2008; 63B: S375–S384.
6. Wheeler L, Reis H, Nezlek J. Loneliness, social interaction, and sex roles. *J Pers Soc Psychol*. 1983; 45: 943–953.
7. Russell D, Peplau LA, Cutrona CE. The revised UCLA Loneliness Scale: Concurrent and discriminant validity evidence. *J Pers Soc Psychol. 1980; 39: 472–480.*
8. Cacioppo JT, Hawkley LC, Ernst JM, et al. Loneliness within a nomological net: An evolutionary perspective. *Journal of Research in Personality*. 2006; 40: 1054–1085.
9. Cacioppo JT, Hawkley LC. Perceived social isolation and cognition. *Trends in Cognitive Sciences*. 2009; 13: 447–454.
10. Heinrich LM, Gullone E. The clinical significance of loneliness: A literature review. *Clin Psychol Rev*. 2006; 26: 695–718.
11. Theeke LA. Predictors of loneliness in U.S. adults over age sixty-five. *Arch Psychiatr Nurs*. 2009; 23: 387–396.
12. Caspi A, Harrington H, Moffitt TE, Milne BJ, Poulton R. Socially isolated children 20 years later: Risk of cardiovascular disease. *Arch Pediatr Adolesc Med*. 2006; 160: 805–811.
13. Eaker ED, Pinsky J, Castelli WP. Myocardial infarction and coronary death among women: Psychosocial predictors from a 20-year follow-up of women in the Framingham Study. *Am J Epidemiol*. 1992; 135: 854–864.
14. Olsen RB, Olsen J, Gunner-Svensson F, Waldstrøm B. Social networks and longevity. A 14 year follow-up study among elderly in Denmark. *Soc Sci Med*. 1991; 33: 1189–1195.
15. Penninx BW, van Tilburg T, Kriegsman DM, et al. Effects of social support and personal coping resources on mortality in older age: The Longitudinal Aging Study Amsterdam. *Am J Epidemiol*. 1997; 146: 510–519.
16. Seeman T. Health promoting effetcs of friends and family on health outcomes in older adults. *American Journal of Health Promotion*. 2000; 14: 362–370.
17. Shiovitz-Ezra S, Ayalon L. Situational versus chronic loneliness as risk factors for all-cause mortality. *Int Psychogeriatr*. 2010; 22: 455–462.
18. Sugisawa H, Liang J, Liu X. Social networks, social support, and mortality among older people in Japan. *J Gerontol*. 1994; 49: S3–13.
19. Thurston RC, Kubzansky LD. Women, loneliness, and incident coronary heart disease. *Psychosom Med*. 2009; 71: 836–842.
20. Hawkley LC, Cacioppo JT. Aging and loneliness: Downhill quickly? *Current Directions in Psychological Science*. 2007; 16: 187–191.
21. Hawkley LC, Masi CM, Berry JD, Cacioppo JT. Loneliness is a unique predictor of age-related differences in systolic blood pressure. *Psychol Aging*. 2006; 21: 152–164.
22. Hawkley LC, Thisted RA, Masi CM, Cacioppo JT. Loneliness predicts increased blood pressure: Five-year cross-lagged analyses in middle-aged and older adults. *Psychol Aging*. 2010; 25: 132–141.
23. DeNiro DA. Perceived alienation in individuals with residual-type schizophrenia. *Issues Ment Health Nurs*. 1995; 16: 185–200.
24. Neeleman J, Power MJ. Social support and depression in three groups of psychiatric patients and a group of medical controls. *Soc Psychiatry Psychiatr Epidemiol*. 1994; 29: 46–51.
25. Richman NE, Sokolove RL. The experience of aloneness, object representation, and evocative memory in borderline and neurotic patients. *Psychoanalytic Psychology*. 1992; 9: 77–91.
26. Goldsmith SK, Pellmar TC, Kleinman AM, Bunney WE. *Reducing Suicide: A National Imperative*. Washington, DC: National Academy Press; 2002.
27. Gow AJ, Pattie A, Whiteman MC, Whalley LJ, Deary IJ. Social support and successful aging: Investigating the relationships between lifetime cognitive change and life satisfaction. *Journal of Individual Differences*. 2007; 28: 103–115.
28. Tilvis RS, Kahonen-Vare MH, Jolkkonen J, et al. Predictors of cognitive decline and mortality of aged people over a 10-year period. *J Gerontol (A Biol Sci Med Sci)*. 2004; 59: M268–M274.
29. Wilson RS, Krueger KR, Arnold SE, et al. Loneliness and risk of Alzheimer disease. *Arch Gen Psychiatry*. 2007; 64: 234–240.
30. Cacioppo JT, Ernst JM, Burleson MH, et al. Lonely traits and concomitant physiological processes: The MacArthur social neuroscience studies. *Int J Psychophysiol*. 2000; 35: 143–154.
31. Hawkley LC, Thisted RA, Cacioppo JT. Loneliness predicts reduced physical activity: Cross-sectional and longitudinal analyses. *Health Psychol*. 2009; 28: 354–363.
32. Cacioppo JT, Hughes ME, Waite LJ, Hawkley LC, Thisted RA. Loneliness as a specific risk factor for depressive symptoms: Cross-sectional and longitudinal analyses. *Psychology and Aging*. 2006; 21: 140–151.
33. Segrin C. Social skills, stressful events, and the development of psychosocial problems. *Journal of Social & Clinical Psychology*. 1999; 18: 14–34.
34. Heikkinen R-L, Kauppinen M. Depressive symptoms in late life: A 10-year follow-up. *Arch Gerontol Geriat*. 2004; 38: 239–250.
35. Wei M, Russell DW, Zakalik RA. Adult Attachment, Social Self-Efficacy, Self-Disclosure, Loneliness, and Subsequent Depression for Freshman College Students: A Longitudinal Study. *Journal of Counseling Psychology*. 2005; 52: 602–614.
36. Cacioppo JT, Hawkley LC, Thisted RA. Perceived social isolation makes me sad: Five year cross-lagged analysis of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations study. *Psychol Aging*. 2010; 25: 453–463.
37. Newall N, Chipperfield J, Clifton R, et al. Causal beliefs, social participation, and loneliness among older adults: A longitudinal study. *Journal of Social and Personal Relationships*. 2009; 26: 273–290.
38. Tice DM, Bratslavsky E. Giving in to feel good: The place of emotion regulation in the context of general self-control. *Psychological Inquiry*. 2000; 11: 149–159.
39. McAuley E, Morris KS, Motl RW, et al. Long-term follow-up of physical activity behavior in older adults. *Health Psychol*. 2007; 26: 375–380.
40. Penedo FJ, Dahn JR. Exercise and well-being: A review of mental and physical health benefits associated with physical activity. *Curr Opin Psychiatr*. 2005; 18: 189–193.
41. Lauder W, Mummery K, Jones M, Caperchione C. A comparison of health behaviours in lonely and non-lonely populations. *Psychology, Health, and Medicine*. 2006; 11: 233–245.
42. Akerlind I, Hornquist JO. Loneliness and alcohol abuse: A review of evidences of an interplay. *Soc Sci Med*. 1992; 34: 405–414.
43. Stranahan AM, Khalil D, Gould E. Social isolation delays the positive effects of running on adult neurogenesis. *Nature Neurosci*. 2006; 9: 526–533.
44. Mullington JM, Haack M, Toth M, Serrador JM, Meier-Ewert HK. Cardiovascular, inflammatory, and metabolic consequences of sleep deprivation. *Prog Cardiovasc Dis*. 2009; 51: 294.
45. Gangwisch JE, Heymsfield SB, Boden-Albala B, et al. Short sleep duration as a risk factor for hypertension: Analyses of the first national health and nutrition examination survey. *Hypertension*. 2006; 47: 833–839.

46. King CR, Knutson KL, Rathouz PJ, et al. Short sleep duration and incident coronary artery calcification. *JAMA*. 2008; 300: 2859–2866.
47. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. *Arch Gen Psychiatry*. 2002; 59: 131–136.
48. Ohayon MM. Prevalence and correlates of nonrestorative sleep complaints. *Arch Intern Med*. 2005; 165: 35–41.
49. Cacioppo JT, Hawkley LC, Crawford LE, et al. Loneliness and health: Potential mechanisms. *Psychosom Med*. 2002; 64: 407–417.
50. Friedman EM, Hayney MS, Love GD, et al. Social relationships, sleep quality, and interleukin-6 in aging women. *PNAS*. 2005; 102: 18757–18762.
51. Jacobs JM, Cohen A, Hammerman-Rozenberg R, Stessman J. Global sleep satisfaction of older people: The Jerusalem Cohort Study. *J Am Geriatr Soc*. 2006; 54: 325–329.
52. Mahon NE. Loneliness and sleep during adolescence. *Perceptual & Motor Skills*. 1994; 78: 227–231.
53. Cacioppo JT, Hawkley LC, Berntson GG, et al. Do lonely days invade the nights? Potential social modulation of sleep efficiency. *Psychol Sci*. 2002; 13: 385–388.
54. Akerstedt T, Hume K, Minors D, Waterhouse J. The meaning of good sleep: A longtitudinal study of polysomnography and subjective sleep quality. *J Sleep Res*. 2009; 3: 152–158.
55. Hawkley LC, Preacher KJ, Cacioppo JT. Loneliness impairs daytime functioning but not sleep duration. *Health Psychol*. 2010; 29: 124–129.
56. Hawkley LC, Burleson MH, Berntson GG, Cacioppo JT. Loneliness in everyday life: Cardiovascular activity, psychosocial context, and health behaviors. *J Pers Soc Psychol*. 2003; 85: 105–120.
57. Franklin SS, Gustin WI, Wong ND, et al. Hemodynamic patterns of age-related changes in blood pressure: The framingham heart study. *Circulation*. 1997; 96: 308–315.
58. Schiffrin EL. Vascular stiffening and arterial compliance: Implications for systolic blood pressure. *Am J Hypertens*. 2004; 17: S39–S48.
59. Cheitlin MD. Cardiovascular physiology-changes with aging. *The American Journal of Geriatric Cardiology*. 2003; 12: 9–13.
60. Folkow B, Svanborg A. Physiology of cardiovascular aging. *Physiol Rev*. 1993; 73: 725–764.
61. Toro L, Marijic J, Nishimaru K, et al. Aging, ion channel expression, and vascular function. *Vascular Pharmacology*. 2002; 38: 73–80.
62. Danesh J, Wheeler JG, Hirschfield GM, et al. C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. *N Engl J Med*. 2004; 350: 1387–1397.
63. Yusuf S. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study). *Lancet*. 2004; 364: 937–952.
64. Beevers G, Lip GY, O'Brien E. ABC of hypertension: The pathophysiology of hypertension. *Br Med J (Clinical research ed)*. 2001; 322: 912–916.
65. Black HR, Bakris GL, Elliott WJ. Hypertension: epidemiology, pathophysiology, diagnosis, and treatment. In: Fuster V, Alexander RW, O'Rourke RA, eds. *Hurst's the Heart*. 10th ed. New York: McGraw-Hill; 2001:1553-604.
66. Guyenet PG. The sympathetic control of blood pressure. *Nature Rev Neurosci*. 2006; 7: 335–346.
67. Girod JP, Brotman DJ. Does altered glucocorticoid homeostasis increase cardiovascular risk? *Cardiovasc Res*. 2004; 64: 217–226.
68. Nijm J, Jonasson L. Inflammation and cortisol response in coronary artery disease. *Ann Med*. 2009; 41: 224–233.
69. Whitworth JA, Schyvens CG, Zhang Y, Mangos GJ, Kelly JJ. Glucocorticoid-induced hypertension: From mouse to man. *Clin Exp Pharmacol Physiol*. 2001; 28: 993–996.
70. Kiecolt-Glaser JK, Ricker D, George J, et al. Urinary cortisol levels, cellular immunocompetency, and loneliness in psychiatric inpatients. *Psychosom Med*. 1984; 46: 15–23.
71. Steptoe A, Owen N, Kunz-Ebrecht SR, Brydon L. Loneliness and neuroendocrine, cardiovascular, and inflammatory stress responses in middle-aged men and women. *Psychoneuroendocrinology*. 2004; 29: 593–611.
72. Pressman SD, Cohen S, Miller GE, et al. Loneliness, social network size, and immune response to influenza vaccination in college freshmen. *Health Psychol*. 2005; 24: 297–306.
73. Adam EK, Hawkley LC, Kudielka BM, Cacioppo JT. Day-to-day dynamics of experience-cortisol associations in a population-based sample of older adults. *Proc Nat Acad Sci USA*. 2006; 103: 17058–17063.
74. Dickerson SS, Kemeny ME. Acute stressors and cortisol responses: A theoretical integration and synthesis of laboratory research. *Psychol Bull*. 2004; 130: 355–391.
75. Cole SW, Hawkley LC, Arevalo JM, et al. Social regulation of gene expression in human leukocytes. *Genome Biology*. 2007; 8: R189.181–R189.113.
76. Cole SW. Social regulation of leukocyte homeostasis: The role of glucocorticoid sensitivity. *Brain Behav Immun*. 2008; 22: 1049–1055.
77. Levine S, Mody T. The long-term psychobiological consequences of intermittent postnatal separation in the squirrel monkey. *Neurosci Biobehav Rev*. 2003; 27: 83–89.
78. Pan Y, Liu Y, Young KA, Zhang Z, Wang Z. Post-weaning social isolation alters anxiety-related behavior and neurochemical gene expression in the brain of male prairie voles. *Neurosci Lett*. 2009; 454: 67–71.
79. Poletto R, Steibel JP, Siegford JM, Zanella AJ. Effects of early weaning and social isolation on the expression of glucocorticoid and mineralocorticoid receptor and 11beta-hydroxysteroid dehydrogenase 1 and 2 mRNAs in the frontal cortex and hippocampus of piglets. *Brain Res*. 2006; 1067: 36–42.
80. Dixon D, Cruess S, Kilbourn K, et al. Social Support Mediates Loneliness and Human Herpesvirus Type 6 (HHV-6) Antibody Titers. *Journal of Applied Social Psychology*. 2001; 31: 1111–1132.
81. Glaser R, Kiecolt-Glaser JK, Speicher CE, Holliday JE. Stress, loneliness, and changes in herpesvirus latency. *J Behav Med*. 1985; 8: 249–260.
82. Kiecolt-Glaser JK, Garner W, Speicher C, et al. Psychosocial modifiers of immunocompetence in medical students. *Psychosom Med*. 1984; 46: 7–14.
83. Straits-Troster KA, Patterson TL, Semple SJ, et al. The relationship between loneliness, interpersonal competence, and immunologic status in HIV-infected men. *Psychology and Health*. 1994; 9: 205–219.
84. Miller GE, Kemeny ME, Taylor SE, Cole SW, Visscher BR. Social relationships and immune processes in HIV seropositive gay and bisexual men. *Ann Behav Med*. 1997; 19: 139–151.
85. Cattan M, White M. Developing evidence based health promotion for older people: A systematic review and survey of health promotion interventions targeting social isolation and loneliness among older people. *Internet Journal of Health Promotion*. 1998; 13: 1–9.
86. Cattan M, White M, Bond J, Learmouth A. Preventing social isolation and loneliness among older people: A systematic review of health promotion interventions. *Aging & Society*. 2005; 25: 41–67.
87. Findlay R: Interventions to reduce social isolation amongst older people: Where is the evidence? *Abstracts in Social Gerontology*. 2004; *47*.
88. McWhirter BT. Loneliness: A Review of Current Literature, with Implications for Counseling and Research. *Journal of Counseling and Development*. 1990; 68: 417–422.

89. Perese E, Wolf M. Combating loneliness among persons with severe mental illness: Social network interventions' characteristics, effectiveness, and applicability. *Issues in Mental Health Nursing*. 2005; 26: 591–609.
90. Rook KS. Promoting social bonding: Strategies for helping the lonely and socially isolated. *Am Psychol*. 1984; 39: 1389–1407.
91. Lipsey MW, Wilson DB. *Practical Meta-Analysis*. Thousand Oaks: Sage; 2001.
92. Cacioppo JT, Patrick B. *Loneliness: Human Nature and the Need for Social Connection*. New York: Norton; 2008.
93. Routasalo PE, Tilvis RS, Kautiainen H, Pitkala KH. Effects of psychosocial group rehabilitation on social functioning, loneliness and well-being of lonely, older people: Randomized controlled trial. *J Adv Nurs*. 2009; 65: 297–305.
94. Pitkala KH, Routasalo P, Kautiainen H, Tilvis RS. Effects of psychosocial group rehabilitation on health, use of health care services, and mortality of older persons suffering from loneliness: A randomized, controlled trial. *J Gerontol (A Biol Sci Med Sci)*. 2009; 64: 792–800.
95. Wilson DS. *Evolution for Everyone: How Darwin's Theory Can Change the Way We Think About Our Lives*. New York: Delacorte; 2007.
96. Cacioppo JT, Amaral DG, Blanchard JJ, et al. Social neuroscience: Progress and implications for mental health. *Perspectives on Psychological Science*. 2007; 2: 99–123.
97. Donaldson ZR, Young LJ. Oxytocin, vasopressin, and the neurogenetics of sociality. *Science*. 2008; 322: 900–904.
98. Lovejoy CO. Reexamining human origins in light of Ardipithecus ramidus. *Science*. 2009; 326: 74e71–74e78.
99. Emler N. Gossip, reputation, and adaptation. In: Goodman R, Ben Ze'ev A, eds. *Good Gossip*. Lawrence: University of Kansas Press; 1994: 34–46.
100. Kahneman D, Krueger AB, Schkade DA, Schwarz N, Stone AA. A survey method for characterizing daily life experience: The day reconstruction method. *Science*. 2004; 306: 1776–1780.