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REVIEW

Loneliness and cognitive function in the older adult: a systematic review

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ABSTRACT

Background: Loneliness is a significant concern among the elderly, particularly in societies with rapid growth in aging populations. Loneliness may influence cognitive function, but the exact nature of the association between loneliness and cognitive function is poorly understood. The purpose of this systematic review was to synthesize current findings on the association between loneliness and cognitive function in older adults.

Method: A comprehensive, electronic review of the literature was performed. Criteria for inclusion were original quantitative or qualitative research, report written in English, human participants with a mean age ≥ 60 years, and published from January 2000 through July 2013. The total number of studies included in this systematic review was ten.

Results: Main findings from the ten studies largely indicate that loneliness is significantly and negatively correlated with cognitive function, specifically in domains of global cognitive function or general cognitive ability, intelligence quotient (IQ), processing speed, immediate recall, and delayed recall. However, some initial correlations were not significant after controlling for a wide range of demographic and psychosocial risk factors thought to influence loneliness.

Conclusions: Greater loneliness is associated with lower cognitive function. Although preliminary evidence is promising, additional studies are necessary to determine the causality and biological mechanisms underlying the relationship between loneliness and cognitive function. Findings should be verified in culturally diverse populations in different ages and settings using biobehavioral approaches.

Key words: aging, elderly, loneliness, cognition, cognitive function

Introduction

Loneliness is a significant concern among the elderly, particularly in societies with rapid growth of aging populations. Loneliness is a complex concept described as a subjectively experienced, aversive emotional state resulting from the perception of unfulfilled personal and social needs, and may result from changing lifestyle with aging, declining health, death of loved ones with decreasing social networks, and worries over institutionalization and financial status (Peplau and Perlman, 1982). Weiss (1973) further theorizes that the experience of loneliness involves both social and emotional facets. Emotional loneliness typically refers to the absence of attachment to a special or beloved person, whereas social loneliness refers to the lack of connectedness or satisfaction with social networks and the absence of a meaningful relationship in one's life.

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Preliminary evidence indicates that loneliness is associated with cognitive decline (Cacioppo and Hawkley, 2009). Cognitive decline, in turn, affects the ability to perform activities of daily living and function independently, including understanding medication instructions, handling finances, arranging transportation, and preparing food. Cognitive decline may progress to dementia or Alzheimer's disease and is not a normal consequence of aging. The aging brain is capable of neurogenesis and neuroplasticity (Salthouse, 2011; Struble and Sullivan, 2011), and better understanding of relevant psychosocial and biological factors that may detrimentally influence cognitive function is important to prevent a decrease in quality of life and improve overall health status in the older adult (Cacioppo and Hawkley, 2009; Salthouse, 2011).

Currently the potential mechanisms underlying the association of loneliness and cognitive function

are poorly understood. Evidence suggests that potential biological mechanisms include prolonged activation of the hypothalamus–pituitary–adrenal (HPA) axis and inflammation. Prolonged activation of the HPA axis with hypercortisolism has been documented with chronic psychological stress and loneliness (Dallman *et al.*, 2004; Steptoe *et al.*, 2004; Adam *et al.*, 2006), and the elderly are particularly prone to experience these psychosocial conditions due to changing personal and social lifestyles with aging (Nies and McEwen, 2011). Lonely elderly people report experiencing a great number of chronic stressors (Hawkley and Cacioppo, 2007) and are more likely to perceive daily events as stressful (Turner, 1989; Cacioppo, 1994). Lonely elderly people are more likely to experience negative thoughts and less positive expectations and persistent negative thoughts and emotions promote stress, further worsening the sense of loneliness (Krause, 1991; Mann, 1997).

Although not universal, loneliness typically has shown significant and negative correlations with cortisol level in college students (Cacioppo *et al.*, 2000; Doane and Adam, 2010) as well as in middle-aged and older adults (Steptoe *et al.*, 2004; Adam *et al.*, 2006). Prolonged hypercortisolism may cause cellular damage in the brain that is associated with altered cognitive function, including dementia or Alzheimer's disease (Epel, 2009). Elevated morning and day salivary cortisol levels have been associated with poor performance in various domains of cognitive function including executive function, episodic memory, and visuo-spatial memory (Fiocco *et al.*, 2006; Peavy *et al.*, 2009; Beluche *et al.*, 2010). Prolonged hypercortisolism also is directly related to reduced dendritic branching, abnormal synapse formation, and neuronal death in the hippocampus and frontal cortex, the areas known for their role in memory and executive function (Steptoe *et al.*, 2004; Adam *et al.*, 2006).

Furthermore, prolonged hypercortisolism disrupts the anabolic/catabolic (A/C) hormonal balance, characterized by lower levels of anabolic hormones (insulin-like growth factor-1, growth hormone, dehydroepiandrosterone, and testosterone) and a high-level of cortisol. The A/C hormonal imbalance leaves the detrimental effects of cortisol unopposed, resulting in negative cellular changes in stress-responsive structures of the brain (Strack *et al.*, 1995; Dallman *et al.*, 2004).

Inflammation is another biological mechanism through which stress and loneliness may impact cognitive function. Lonely individuals are highly reactive to stress, and prolonged and greater activation of glucocorticoids may dysregulate inflammatory responses (Rotenberg *et al.*, 2002; Glaser and Kiecolt-Glaser, 2005). Normally glucocorticoids downregulate inflammatory responses, but prolonged glucocorticoid exposure loses normal regulatory responses and allows higher levels of inflammation to be persistent in lonely individuals (Irwin, 2008; Piazza *et al.*, 2010). Because inflammation has been implicated in pathological processes involved in Alzheimer's disease and dementia (Gorelick, 2010), increased inflammation in lonely individuals may serve as a pathway for impaired cognitive function. Findings of epidemiological studies indicate preliminary correlations between inflammation and cognitive impairment (Gorelick, 2010). Noble *et al.*, (2010) reported that those with higher C-reactive protein levels had higher adjusted odds of impaired memory in the elderly. In addition, elderly who developed Alzheimer's disease at the five-year follow-up showed increased free radical damage from baseline when compared with those who did not (Sonnen *et al.*, 2009). These preliminary findings suggest the need for further research on stress, loneliness, inflammation, and cognitive function.

Although loneliness has been associated with cognitive decline, most of the literature focuses on the association between social networks and cognitive function (Fratiglioni *et al.*, 2000; Bennett *et al.*, 2006; Stoykova *et al.*, 2011). Because loneliness is a subjective feeling related to unfulfilled personal and social needs, simple reliance on the objective measure of social network alone may not adequately represent the concept of loneliness. In fact, a person who is socially isolated may not necessarily feel lonely (Ye *et al.*, 2012), whereas a person surrounded by social network may feel lonely. Thus, emotional loneliness may affect health via biological mechanisms, independent of the size of social network (Steptoe *et al.*, 2013). For this reason, loneliness assessment should include both emotional and social facets. A previous review was focused only on the nature of loneliness within contextual frameworks and general clinical health significance of loneliness across the lifespan (Heinrich and Gullone, 2006). Differing from the previous focus, the purpose of this systematic review was to synthesize current findings on the correlations of loneliness and cognitive function in older adults ≥60 years.

Methods

The literature was searched using PubMed, Medline (Ovid), and Pscycinfo electronic databases. The search keywords included "loneliness," "social isolation," "alienation," "cognition," "elderly," "older adult,' "aging," "geriatric," "cognitive impairment," "cognitive ability," "cognitive decline,"

"cognitive processes," "cognitive function," "cognition," "comprehension," and "memory," in various combinations. Although social isolation is a distinctively different concept from loneliness, it was included as a search term to determine if a measure of loneliness was used in the study. Criteria for inclusion were original quantitative or qualitative research, report written in English, study on human participants with a mean age ≥60 years, and report published from January 2000 through July 2013. Review or opinion papers were excluded.

Initially, 832 articles were identified in PubMed, 795 in Medline (Ovid), and 432 in Pscycinfo. After duplicates were removed and abstracts screened, the total number of studies was reduced to 15. The remaining 15 studies were retrieved for potential use and evaluated on information contained in the full-text version of the study. Upon review, studies not meeting inclusion criteria were eliminated, leaving eight studies. An additional manual search of references yielded another two studies. The total number of studies included in this systematic review was ten (see Table 1).

Results

Description of studies

Design

Out of the ten studies, five were cross-sectional (Holmén *et al.*, 2000; Gilmour, 2011; O'Luanaigh *et al.*, 2012; Schnittger *et al.*, 2012; Gow *et al.*, 2013) and five were longitudinal (Tilvis *et al.*, 2004; Gow *et al.*, 2007; Wilson *et al.*, 2007; Holwerda *et al.*, 2012; Shankar *et al.*, 2013) with a follow-up period ranging from one year (Tilvis *et al.*, 2004) to 68 years (Gow *et al.*, 2007). Eight studies reported findings from participants enrolled in large, population-based studies (Holmén *et al.*, 2000; Tilvis *et al.*, 2004; Gow *et al.*, 2007; Wilson *et al.*, 2007; Holwerda *et al.*, 2012; O'Luanaigh *et al.*, 2012; Gow *et al.*, 2013; Shankar *et al.*, 2013), such as the Amsterdam Study of the Elderly (Holwerda *et al.*, 2012) and The Helsinki Aging Study (Tilvis *et al.*, 2004). Two studies by Gow and colleagues (Gow *et al.*, 2007; 2013) were from the same cohort of participants, The Lothian Birth Cohort, 1921, although approaches and analysis of the data differed with different research questions. There were no qualitative studies that met criteria for inclusion in this review.

Sample

Eight out of ten studies were conducted in Europe, including Ireland (O'Luanaigh *et al.*, 2012; Schnittger *et al.*, 2012), Scotland (Gow *et al.*, 2007; 2013), England (Shankar *et al.*, 2013), Finland (Tilvis *et al.*, 2004), Sweden (Holmén, *et al.*, 2000), and the Netherlands (Holwerda *et al.*, 2012). The remaining two studies were conducted in Canada (Gilmour, 2011) and the United States (Wilson *et al.*, 2007). The number of participants per study ranged from 466 (O'Luanaigh *et al.*, 2012) to 13,176 (Gilmour, 2011) for a total of 26,079 participants across all studies. All authors provided a description of sampling methods and sample size, although specific details varied among studies. Samples included both genders in all studies, and most participants were community dwelling and independently living older adults. One study included participants in nursing homes, but this accounted for only 4% of their sample (Wilson *et al.*, 2007), and 19% of participants in another study were people with dementia (Holmén *et al.*, 2000). The overall health status varied among participants, but most were described as generally healthy with few chronic diseases, such as osteoarthritis, hypertension, coronary artery disease, and hypothyroidism.

Theoretical basis

None of the studies addressed specific theoretical basis for research. However, all authors proposed that certain psychosocial factors, including loneliness, were thought to influence cognitive function in the older adult and this was the implied theoretical basis for research. In addition to loneliness influencing cognitive function, authors of two studies (Tilvis *et al.*, 2004; Holwerda *et al.*, 2012) proposed that psychosocial and biological factors, such as prolonged activation of the HPA axis or inflammation, might interact to detrimentally influence cognitive function. Despite slight variations in theoretical basis, specific aims and hypotheses were consistent to examine the association between loneliness and cognitive function.

Covariates

The most common covariates were factors related to age, gender, educational status, depressive symptoms/depression, and social network factors, such as marital or cohabitation status, significant others, household composition, and social isolation.

Measurement of loneliness

Measurement of loneliness varied among studies, but most researchers utilized one or two Likert-style or yes/no format question(s) to measure loneliness (Holmén *et al.*, 2000; Tilvis *et al.*, 2004; Gow *et al.*, 2007; Gilmour, 2011; Holwerda *et al.*, 2012; O'Luanaigh *et al.*, 2012; Gow *et al.*, 2013). Most

Table 1. Association of loneliness and cognitive function in older adults.

AUTHOR AND YEAR	PURPOSE AND DESIGN	CHARACTERISTICS OF THE SAMPLE AND SETTING	LONELINESS MEASUREMENT	COGNITIVE DOMAIN AND MEASUREMENT	RESULTS
Gilmour (2011)	• To examine correlates of low performance on four cognitive tasks among older adults without Alzheimer disease or dementia. • Cross-sectional	$N = 13{,}176$ • males and females • Age > 65 years • Community dwelling • Canada	• 1 question on a 3-point Likert scale of how often they lacked companionship, felt left out, or isolated.	• Two tasks of immediate and delayed recall of word lists (short-term verbal memory, verbal learning, and post-interference recall) • Two tasks of semantic fluency and the Mental Alteration Test (executive function)	• Loneliness was negatively correlated with worse performance in first recall, executive function, semantic fluency, and processing speed (all $p < 0.01$).
Gow *et al.* (2013)	• To examine associations of diverse measures of social contact and support with cognitive ability. • Cross-sectional	• $N = 1{,}091$ males and females ($M = 70$ years) • Participants were part of the Lothian Birth Cohort, 1936 • Community dwelling • Scotland	• 1 question on a 5 point Likert scale, if they felt lonely at the present time.	• Moray House Test No. 12 (verbal reasoning) • Wechsler Adult Intelligence Scale-III UK and Wechsler Memory Scale-III UK (general cognitive ability, processing speed and memory) • Additional tests of reaction time and inspection time	• Loneliness was negatively correlated with general cognitive ability (Spearman's rho $= -0.14$, $p < 0.0001$), processing speed (Spearman's rho $= -0.12$, $p < 0.001$), and memory (Spearman's rho $= -0.08$, $p < 0.01$). • When all variables were examined in separate ANCOVAs, lower loneliness was significantly correlated with better general cognitive abilities at age 70 ($p < 0.05$).
Gow *et al.* (2007)	• To examine associations between early cognitive ability and later social networks and social support, and to examine associations between social networks, social support, and cognitive change between age 11 and 79. • Longitudinal: 68-year follow-up	• $N = 497$ males (42%) and females ($M = 79$ years) • Participants were part of the Lothian Birth Cohort, 1936 • Community dwelling • Scotland	• 1 question on a 5 point Likert scale, if they felt lonely at the present time. • 1 yes/no question, if they had someone to talk to when they had problems. • Loneliness was measured at follow-up only	• Moray House Test No. 12 (verbal reasoning, arithmetic, analogies) • Raven's Matrices; Scores were converted to IQ scores • Cognitive function was measured at baseline and follow-up	• Loneliness was negatively correlated with age 79 IQ ($r = -0.18$, $p = < 0.001$). • Loneliness was the only significant predictor of lower age 79 IQ ($\beta = -0.15$, $p = < 0.001$). • Loneliness was negatively correlated with significant negative change in cognition ($r = -0.22$, $p = < 0.001$).

Table 1. Continued.

AUTHOR AND YEAR	PURPOSE AND DESIGN	CHARACTERISTICS OF THE SAMPLE AND SETTING	LONELINESS MEASUREMENT	COGNITIVE DOMAIN AND MEASUREMENT	RESULTS
Holmén *et al.* (2000)	• To examine both social and emotional loneliness in people with dementia and people without dementia elderly people. • Cross-sectional	• $N = 589$ males and females. • Age = 75–>90 years ($M = 84$ years) • 81% people without dementia • Participants were part of the Kungsholmen longitudinal study • Community dwelling • Sweden	• One yes/no question for social loneliness, if they often feel lonely/lonesome. • One question for emotional loneliness on a 4-point Likert scale, how often they experience loneliness.	• MMSE (global cognitive function)	• People without dementia subjects reported less social loneliness ($p \leq 0.001$) than people with dementia subjects. • There were no significant differences for emotional loneliness and people with dementia (vs.) people without dementia subjects.
Holwerda *et al.* (2012)	• To examine associations between social isolation, feelings of loneliness, and incident dementia in a cohort of older people without dementia. • Longitudinal = 3-year follow-up	• $N = 2{,}173$ males and females. Age = 65–86 years • Participants were part of the Amsterdam Study of the Elderly (AMSTEL) • Community dwelling • Netherlands	• Answered one yes/no question, if they feel lonely or if they feel very lonely. • Loneliness was measured at baseline and follow-up	• GMS, AGECAT, CAMDEX, MMSE • All instruments assessed global cognitive function • Cognitive function was measured at baseline and follow-up	• The decrease in global cognitive function score from baseline to follow-up was more pronounced in those with greater loneliness (baseline: $M = 27.52$, $SD = 2.12$, follow-up: $M = 25.84$, $SD = 4.11$) when compared to those with less loneliness (baseline: $M = 28.05$, $SD = 1.84$, follow-up: $M = 27.06$, $SD = 2.71$). • Feeling lonely rather than being alone is associated with an increased risk of dementia (OR = 2.56, 95% CI = 1.82–3.61).
O'Luanaigh *et al.* (2012)	• To explore associations between loneliness and cognition and to determine whether specific cognitive domains are associated with loneliness. • Cross-sectional	• $N = 466$ males and females • M age = 75.5 years • Participants were part of The Dublin Healthy Ageing Study • Community dwelling • Ireland	• 1 Likert style, 4-point question, if they feel lonely.	• NART-2 (pre-morbid IQ) • WAIS III (psychomotor processing speed • FAS test and animal fluency (verbal and category fluency) • WMS (verbal learning, interference, delayed recall, visual memory, visual reproduction) • MMSE (global cognitive function)	• Loneliness was negatively correlated with global cognitive function ($p = 0.047$), category fluency ($p < 0.05$), psychomotor processing speed ($p = 0.036$), immediate visual memory ($p = 0.003$), visual memory ($p = 0.003$), pre-morbid IQ ($p < 0.001$), and visual memory savings ($p = 0.003$).

Table 1. Continued.

AUTHOR AND YEAR	PURPOSE AND DESIGN	CHARACTERISTICS OF THE SAMPLE AND SETTING	LONELINESS MEASUREMENT	COGNITIVE DOMAIN AND MEASUREMENT	RESULTS
Schnittger *et al.* (2012)	• To identify the biopsychosocial and cognitive risk factors of emotional loneliness, social loneliness, and social support, and to examine mediating effects in the relationship between social support and outcomes of social and emotional loneliness. • Cross-sectional	• $N = 579$ males and females • M age ≥60 years • Community dwelling • Ireland	• Emotional and social loneliness were both assessed with the De Jong-Gierveld Loneliness Scale	• MMSE (global cognitive function) • Prospective memory, initial word recall, delayed word recall, animal naming (verbal fluency) • Digital span backwards, CAMCOG (recognition, similarities, draw, recall, naming) • TMT-A, B (executive function) • Cognitive Failures Questionnaire Score (attentiveness and memory)	• Emotional loneliness was correlated with worse executive function (Spearman's rho = 0.148), attentiveness, memory (Spearman's rho = 0.185, both $p < 0.002$). • Social loneliness was correlated with worse verbal fluency (Spearman's rho = 0.137, $p < 0.002$). • In multiple regression analyses, cognitive variables were not risk factors for emotional loneliness, but verbal fluency was a risk factor for social loneliness ($p < 0.05$).
Shankar *et al.* (2013)	• To examine the impact of social isolation and loneliness on cognitive function. • Longitudinal: 4-year follow-up	• $N = 6{,}035$ males and females • M age = 65.6 years • Participants were obtained from the English Longitudinal Study of Ageing • Community dwelling • England	• 3-item, short form of the Revised-UCLA Loneliness Scale • Loneliness was measured at baseline and follow-up	• ELSA (verbal fluency, immediate recall, delayed recall) • Cognitive function was measured at baseline and follow-up	• At baseline, loneliness was significantly correlated with worse verbal fluency ($\beta = -0.80$, $p < 0.001$), immediate recall ($\beta = -0.04$, $p = 0.007$), and delayed recall ($\beta = -0.06$, $p < 0.001$). • At follow-up, loneliness was correlated with worse delayed ($\beta = -0.03$, $p = 0.02$) and immediate recall ($\beta = -0.\ 001$, $p < 0.05$) only.
Tilvis *et al.* (2004)	• To identify preventable and treatable risk factors of cognitive decline. • Longitudinal: 1, 5, and 10-year follow-ups	• $N = 650$ males and females, >75 years of age • Participants were obtained from The Helsinki Aging Study • Community dwelling • Finland	• One yes/no question, if they suffer from loneliness. • Loneliness was measured at all time points	• MMSE (global cognitive function) • CDR (Clinical Dementia Rating) • Cognitive function was measured at all time points	• At the 10-year follow-up only, loneliness was significantly correlated with a decline in the MMSE score (RR = 3.0, 95% CI = 1.4–6.8).

Table 1. Continued.

AUTHOR AND YEAR	PURPOSE AND DESIGN	CHARACTERISTICS OF THE SAMPLE AND SETTING	LONELINESS MEASUREMENT	COGNITIVE DOMAIN AND MEASUREMENT	RESULTS
Wilson *et al.* (2007)	• To test the hypothesis that loneliness is associated with increased risk of Alzheimer disease (AD). • Longitudinal: 4 years of annual follow-up	• $N = 823$ males and females (M age = 81 years) • Participants were obtained from the Rush Memory and Aging Project • Community dwelling, nursing homes • United States	• de Jong-Gierveld Loneliness Scale • Loneliness was measured at all time points	• A total of 20 tests were administered annually. • MMSE (global cognitive function) • Seven measures of episodic memory including immediate and delayed recall (Logical Memory Story A, East Boston Story, Word List Memory, Word List Recall, Word List Recognition) • Three tests of semantic memory (Verbal Fluency Test, short forms of the Boston Naming Test and National Adult Reading Test) • Three tests of working memory (Digit Span Forward and Backward, Digit Ordering) • Four tests of perceptual speed (Number Comparison, Symbol Digit Modalities Test, 2 indexes from the modified Stroop Neuropsychological Screening Tests) • Two visuospatial tests (Judgment of Line Orientation, 17-item version of Standard Progressive Matrices)	• Loneliness scores were higher in those who developed AD during follow-up ($p < 0.01$). • Participants with higher loneliness were 2.1 times more likely to develop AD compared to those with low loneliness (RR = 1.51, 95% CI = 1.063–2.14). • Loneliness was negatively correlated with all cognitive domains at baseline, as well as with more rapid decline over time (all $p < 0.01$).

Note: MMSE = Mini-Mental State Examination; GMS = Geriatric Mental State; AGECAT = Automated Geriatric Examination for Computer Assisted Taxonomy; CAMDEX = Cambridge Mental Disorders of the Elderly Examination; NART-2 = National Adult Reading Test; WAIS III = Wechsler Adult Intelligence Scale III; WMS = Wechsler Memory Scale; CAMCOG = Cambridge Cognitive Examination; TMT-A = Trail Making Test-A; TMT-B = Trail Making Test-B; ELSA = English Longitudinal Study of Ageing.

common questions were, "Do you feel lonely at the present time?" and "How often do you experience loneliness?"

In one study, loneliness was measured with the three-item short version of the Revised-University of California at Los Angeles Loneliness scale (R-UCLA Loneliness scale) (Shankar *et al.*, 2013). The R-UCLA Loneliness scale was designed to measure general feelings of social isolation and dissatisfaction with one's social interactions (Russell *et al.*, 1980). The three-item, Likert style questionnaire contains three positively worded items and higher total scores indicate greater levels of loneliness. The instrument is considered reliable across various populations with Cronbach's α ranging from 0.89–0.94 (Russell *et al.*, 1980) and 0.78 (Shankar *et al.*, 2013).

In the remaining two studies, authors measured loneliness with the De Jong Gierveld Scale for Loneliness (Wilson *et al.*, 2007; Schnittger *et al.*, 2012), which was designed to measure overall, emotional, and social loneliness (De Jong Gierveld and van Tilburg, 2006). The six-item, Likert style questionnaire includes three negatively worded items and three positively worded items. Negatively worded items are reverse scored and sum of the scores ranges from 0–24. Higher scores indicate greater levels of loneliness. The instrument is considered reliable in the adult population, with Cronbach's α ranging from 0.70–0.76 (De Jong Gierveld and van Tilburg, 2006) and 0.78 (Wilson *et al.*, 2007), but it was not reported by Schnittger *et al.* (2012).

Measurements of cognitive function

Various domains of cognitive function were measured including global cognitive function, executive function, verbal reasoning, processing speed, immediate and delayed recall, episodic memory, semantic memory, and working memory. The most common instruments used were the Mini-Mental State Examination (MMSE) and Wechsler Adult Intelligence scale-III (WAIS-III). The Moray House Test Number 12 (MHT No. 12) was utilized in two studies.

The MMSE was used to measure global cognitive function in six studies (Holmén *et al.*, 2000; Tilvis *et al.*, 2004; Wilson *et al.*, 2007; Holwerda *et al.*, 2012; O'Luanaigh *et al.*, 2012; Schnittger *et al.*, 2012). The MMSE includes simple tests and problems in the domains of orientation, registration, attention and calculation, recall, and language (Folstein *et al.*, 1975). Scores $\geq$24 are considered normal cognition, and those $\leq$23 correlate closely with dementia. The MMSE is a reliable instrument for the aging population with test–retest reliability of 0.82–0.98 (Folstein *et al.*, 1975). Measures of reliability were not reported for studies included in this review.

The WAIS-III was used in two studies to measure general cognitive ability (O'Luanaigh *et al.*, 2012; Gow *et al.*, 2013). The WAIS-III was designed to measure intelligence in adults and older adolescents (Wechsler, 1997). It provides scores for verbal IQ, performance IQ, and full scale IQ, as well as four secondary indices (verbal comprehension, working memory, perceptual organization, and processing speed). The test is composed of 14 subtests that begin with easy questions and become progressively harder based on the person's performance. All items are summed and transformed into standard scores that represent aggregate abilities (Wechsler, 1997). Administration time for the full test takes approximately 75–110 min. Cronbach's α for individual subtests across all age groups ranges from 0.70–0.93 (Silva, 2008). Cronbach's α for studies included in this review were not reported.

The Moray House Test No. 12 was used in two studies with participants of the same birth cohort to measure intelligence (Gow *et al.*, 2007; 2013). The MHT No. 12 assesses reasoning, arithmetic, following directions, and analogies. In both studies, the test was provided to participants at the age between 11 and 79 years and raw scores were converted into IQ scores, corrected for age. The MHT No. 12 has demonstrated validity with correlations of 0.81 in boys and 0.79 in girls from the Stanford Revision of the Binet scale in 1,000 children of age 11 years (Scottish Council for Research in Education, 1949) and 0.71 with Raven's Matrices among 541 older adults with mean age 79 years (Deary *et al.*, 2004). Measures of reliability were not reported in these studies.

Loneliness and global cognitive function/general cognitive ability

Authors of five studies reported both significant and non-significant associations between loneliness and global cognitive function or general cognitive ability. Mostly, the findings indicated a significant and negative association between the two variables (Holmén, *et al.*, 2000; Tilvis *et al.*, 2004; O'Luanaigh *et al.*, 2012; Gow *et al.*, 2013), but authors of one study reported a non-significant association (Schnittger *et al.*, 2012).

In two cross-sectional studies, O'Luanaigh *et al.* (2012) and Gow *et al.* (2013) analyzed data from large, population-based studies and reported similar findings. Loneliness was significantly and negatively associated with global cognitive function after controlling for depression and social network status (O'Luanaigh *et al.*, 2012). In addition, loneliness

was significantly and negatively associated with general cognitive ability, however, when depression symptoms were controlled for the association, it was no longer significant (Gow *et al.*, 2013). In two other cross-sectional studies, authors measured global cognitive function in relation to two specific domains of loneliness, emotional and social loneliness (Holmén, *et al.*, 2000; Schnittger *et al.*, 2012). Holmén *et al.* (2000) compared the association of loneliness with global cognitive function between people without dementia (81% of sample) and people with dementia participants and found that social loneliness was significantly more common in people with dementia participants ($p \leq 0.001$), but non-significant findings were reported for emotional loneliness in both people with dementia and people without dementia participants. Schnittger *et al.* (2012), on the other hand, included people without dementia participants only and did not find a significant association between social or emotional loneliness and global cognitive function. In one longitudinal study, Tilvis *et al.* (2004) assessed loneliness and global cognitive function at baseline, 1, 5, and 10 years. At the ten-year time point only, after controlling for age, greater baseline loneliness was a significant predictor of cognitive decline in regression analysis (RR = 3.0, 95% CI = 1.4–6.8).

Loneliness and dementia/Alzheimer's disease

In two longitudinal studies over with 3–4 year follow-up times (Wilson *et al.*, 2007; Holwerda *et al.*, 2012), authors found similar significant associations between loneliness and dementia (Holwerda *et al.*, 2012), and between loneliness and Alzheimer's disease (Wilson *et al.*, 2007). Authors of both studies examined if the baseline association of loneliness predicted dementia or Alzheimer's disease at 3 and 4-year follow-up time points (Wilson *et al.*, 2007; Holwerda *et al.*, 2012). In both studies, authors found greater loneliness significantly predicted the increased risk for dementia and Alzheimer's disease at follow-up (OR = 2.56, 95% CI = 1.82–3.61 (Holwerda *et al.*, 2012); RR = 1.51, 95% CI = 1.063–2.14 (Wilson *et al.*, 2007)). The association between loneliness and dementia persisted even after controlling for demographic, somatic, and psychiatric risk factors (Holwerda *et al.*, 2012). Additionally, the association between loneliness and Alzheimer's disease also persisted after controlling for objective measures of social isolation, such as social support and solitary living (Wilson *et al.*, 2007).

Loneliness and memory

Authors of six studies reported both significant and non-significant associations between loneliness and various domains of memory that included immediate and delayed recall, visual and general memory, and episodic, semantic and working memory (Wilson *et al.*, 2007; Gilmour, 2011; O'Luanaigh *et al.*, 2012; Schnittger *et al.*, 2012; Gow *et al.*, 2013; Shankar *et al.*, 2013).

In three cross-sectional population-based studies, immediate recall and delayed recall were examined (Gilmour, 2011; O'Luanaigh *et al.*, 2012; Schnittger *et al.*, 2012). Gilmour (2011) and Schnittger *et al.* (2012) measured immediate recall and delayed recall, while O'Luanaigh *et al.* (2012) measured delayed recall only. Gilmour (2011) found significant and negative correlations of loneliness with immediate recall only ($p < 0.01$), whereas O'Luanaigh *et al.* (2012) reported greater loneliness was associated with worse performance on delayed recall ($p < 0.05$). In contrast, Schnittger *et al.* (2012) found non-significant associations of loneliness with immediate recall and delayed recall.

Similar findings were reported in two longitudinal studies over a four-year follow-up period (Wilson *et al.*, 2007; Shankar *et al.*, 2013). Shankar *et al.* (2013) measured immediate and delayed recall and reported significant and negative associations with loneliness at both baseline and 4-year follow-up (all $p < 0.05$). For delayed recall, higher levels of isolation and loneliness were associated with poorer recall in individuals with lower levels of education only. Wilson *et al.* (2007) measured episodic, semantic, and working memory, and reported significant and negative associations with loneliness at baseline, but only semantic memory remained significant at the fourth year follow-up ($p = 0.01$) when controlling for age, gender, and level of education.

When other domains of memory, such as visual memory and general memory were measured, O'Luanaigh *et al.* (2012), Schnittger *et al.* (2012), and Gow *et al.* (2013) found that loneliness was associated with memory in initial bivariate models. However, only O'Luanaigh *et al.* (2012) found that increased loneliness was significantly associated with reduced visual memory ($p < 0.05$) in both bivariate and multivariate models when controlling for depression and a wide range of demographic, social network factors. Similarly, in initial bivariate correlations, Schnittger *et al.* (2012) found that emotional loneliness was significantly and negatively associated with memory ($p < 0.01$), however, memory was not a significant risk factor for emotional loneliness in final multiple linear regression models. Additionally, Gow *et al.*

(2013) found that loneliness was significantly and negatively associated with memory in bivariate correlations ($p < 0.01$), but loneliness was not significantly associated with memory, independent of age, gender, childhood IQ, and social class in final ANCOVA models.

Loneliness and executive function

For executive function, authors of two population-based cross-sectional studies reported similar significant associations between loneliness and executive function (Gilmour, 2011; Schnittger *et al.*, 2012). In the study with the largest sample size ($N = 13,176$), Gilmour (2011) reported a significant and negative association between loneliness and executive function ($p < 0.01$); however, when social interaction was included in multivariate models, the negative association between loneliness and executive function no longer persisted (Gilmour, 2011). Similarly, Schnittger *et al.* (2012) found a significant negative correlation between emotional loneliness and executive function ($p < 0.05$), but executive function was not a significant risk factor for emotional loneliness independent of psychosocial (depression, neuroticism, and perceived stress) and social network factors (solitary living, accommodation status) in final multiple linear regression models.

Loneliness and intellect

Authors of two population-based studies measured cognitive domains related to intellect and reported similar findings (Gow *et al.*, 2007; O'Luanaigh *et al.*, 2012). Gow *et al.* (2007) used an exceptionally long follow-up of 68 years in the Lothian Birth Cohort, 1921 to determine the association between early cognitive ability and loneliness in late life. Cognitive function was assessed at the age between 11 and 79 years, and loneliness was assessed at the age of 79 years only. Findings indicated that greater loneliness at the age of 79 years was significantly and negatively correlated with IQ at this age ($p < 0.001$). Additionally, loneliness at the age of 79 years was the only significant predictor ($p < 0.001$) of cognitive ability in old age, and demographic and social network factors did not significantly add to this prediction. These findings may indicate that participants who showed more cognitive change over their lifespan were lonelier in late life (Gow *et al.*, 2007). O'Luanaigh *et al.* (2012) used a cross-sectional approach with participants in The Dublin Healthy Ageing Study and measured loneliness with IQ at one time point. Findings revealed that greater loneliness was significantly correlated with worse pre-morbid IQ ($p < 0.05$).

Loneliness and verbal fluency

Authors of three studies analyzed loneliness and verbal fluency and reported mixed findings (O'Luanaigh *et al.*, 2012; Schnittger *et al.*, 2012; Shankar *et al.*, 2013). Schnittger *et al.* (2012) reported that verbal fluency was a significant risk factor of social loneliness ($p < 0.05$). However, O'Luanaigh *et al.* (2012) reported no significant associations between verbal fluency and loneliness when controlling for depression, social networks, and a range of demographic factors. In a longitudinal study with a four-year follow-up, greater loneliness was significantly associated with low levels of verbal fluency at baseline ($p < 0.001$), but not at follow-up (Shankar *et al.*, 2013).

Loneliness and processing speed

In three cross-sectional studies, similar significant correlations were reported between loneliness and processing speed (Gilmour, 2011; O'Luanaigh *et al.*, 2012; Gow *et al.* 2013). Although authors used similar research designs, the sample size varied widely from $N = 466$ (O'Luanaigh *et al.*, 2012) to $N = 13,176$ (Gilmour, 2011). Despite a large difference in sample size, all three groups of authors found significant and negative associations of loneliness and processing speed (all $p < 0.05$). These significant and negative associations persisted after controlling for or including factors such as depression, social network, and a wide range of cognitive and demographic factors.

Discussion

The purpose of this systematic review was to examine associations of loneliness and cognitive function in the aging population. Overall findings from the ten studies largely indicate that loneliness is negatively associated with cognitive function. Main findings were significant and negative correlations of loneliness with global cognitive function or general cognitive ability (Holmén *et al.*, 2000; Tilvis *et al.*, 2004; Wilson *et al.*, 2007; Holwerda *et al.*, 2012; O'Luanaigh *et al.*, 2012; Gow *et al.*, 2013), IQ (Gow *et al.*, 2007; O'Luanaigh *et al.*, 2012), processing speed (Gilmour, 2011; O'Luanaigh *et al.*, 2012; Gow *et al.*, 2013), immediate recall (Gilmour, 2011; Shankar *et al.*, 2013), and delayed recall (O'Luanaigh *et al.*, 2012; Shankar *et al.*, 2013). When loneliness was examined as two different dimensions, social and emotional loneliness, similar significant negative correlations persisted between loneliness and various cognitive domains including verbal fluency (Schnittger *et al.*, 2012) but social loneliness seemed to have a stronger correlation

with global cognitive function than did emotional loneliness (Holmén *et al.*, 2000). On the contrary, some initial correlations of loneliness and cognitive function were not significant after controlling for a wide range of demographic and psychosocial risk factors thought to influence loneliness (Wilson *et al.*, 2007; Gilmour, 2011; O'Luanaigh *et al.*, 2012; Schnittger *et al.*, 2012; Gow *et al.*, 2013; Shankar *et al.*, 2013).

The findings of the ten studies were surprisingly consistent, despite the use of different methodologies to assess loneliness. A majority of the authors used only one or two direct questions in the form of yes/no or Likert style, while three authors used a psychometric instrument with more items. Although the measure with one or two direct questions is minimally burdensome and practical in large cohort studies, this approach implies that loneliness is a one-dimensional concept differing only in the intensity of the experience (Fees *et al.*, 1999). This simplistic approach may not allow for cultural differences or interpretations (Fees *et al.*, 1999). In addition, loneliness might have been thought to be stigmatizing to older people and study participants might have down-scored their loneliness levels when direct questions were used (Victor *et al.*, 2005).

Another common method of measuring loneliness was using a psychometric instrument comprised of a series of Likert-style items exploring personal perception of loneliness. The two loneliness instruments used in the studies, the De Jong Gierveld Scale for Loneliness and the R-UCLA Loneliness scale, treat loneliness as a multidimensional concept and include both positive and negative dimensions of loneliness (Victor *et al.*, 2005). The De Jong Gierveld Scale for Loneliness, for example, includes questions relating to three distinct dimensions of loneliness: deprivation relating to loss of intimate attachment, temporal perspective examining the extent of change in loneliness over time, and range of emotional components of loneliness such as sadness, guilt, frustration, and desperation (Victor *et al.*, 2005). This multi-dimensional approach may represent a true response more comprehensively. A disadvantage is that the multi-item tool may increase the burden on aging participants who may already have health issues.

Confounding variables such as demographic, depressive symptoms/depression, and social network did not influence the relationship between loneliness and cognitive function. For example, despite controlling for demographic risk factors, the association between greater loneliness and worse cognitive function persisted in domains of global cognitive function, dementia, Alzheimer's disease, semantic memory, and visual memory (Tilvis *et al.*, 2004; Wilson *et al.*, 2007; Gilmour, 2011; Holwerda *et al.*, 2012; O'Luanaigh *et al.*, 2012). In addition, despite controlling for depression/depressive symptoms, the association between greater loneliness and worse visual memory and global cognitive function persisted (O'Luanaigh *et al.*, 2012; Schnittger *et al.*, 2012). Lastly, when controlling for social network, the association between greater loneliness and worse global cognitive function and Alzheimer's disease (Wilson *et al.*, 2007; O'Luanaigh *et al.*, 2012) did not significantly add to loneliness predicting cognitive function (Gow *et al.*, 2007).

The current literature does not clarify the cause-and-effect relationship between loneliness and cognitive function. Loneliness may lead to cognitive decline, perhaps from limited social interactions and intellectual stimuli, but it is also possible that cognitive deficits may lead to decreased social interactions and greater loneliness subsequently. Schnittger *et al.* (2012) found that decreased verbal fluency was a significant predictor of social loneliness supporting the latter case. Poor communication skills associated with worse verbal fluency may discourage conversation, hinder the development and maintenance of meaningful relationships, and thus increase loneliness. On the other hand, Shankar *et al.* (2013) found that greater loneliness predicted worse cognitive function, and this finding was more pronounced in participants who had lower educational levels. Lack of resources may increase vulnerability for negative consequences of loneliness on cognitive function and more readily activate biological responses. Loneliness may trigger prolonged activation of the HPA axis to decrease neural reserve through decreased dendritic arborization in the hippocampus and prefrontal cortex, leading to decreased memory and learning (Holwerda *et al.*, 2012). The causal relationship between loneliness and cognitive function should be further investigated using rigorous designs with longitudinal data collection. Equally critical would be better determination for biological mechanisms underlying the causality of loneliness on cognitive function. In that line, persistent hypercortisolism and inflammation are two likely pathways along with discovery of new biomarkers.

Future directions

Most studies have been conducted in Western European countries. Because of different cultural and social environment, findings from one region may not be applicable to populations in other

regions. More studies should be done in diverse settings with multiple populations across diverse cultures and locations, including the United States (Theeke, 2009; De Jong Gierveld and Tesch-Römer, 2012). Future studies should be conducted to elucidate the causality of loneliness on cognitive function using a controlled rigorous prospective design. Biomarkers of hypercortisolism and inflammation along with new biomarkers need to be incorporated in the design. Findings of these studies should serve as a foundation for developing culturally appropriate interventions to decrease loneliness and improve cognitive function in the elderly.

Conclusion

Overall, greater loneliness is associated with lower cognitive function, in which increased cortisol and inflammation may play an important role. Although the preliminary evidence is promising, additional studies are necessary to determine the causality and biological mechanisms underlying the relationship between loneliness and cognitive function. Findings should be verified in culturally diverse populations in different ages and settings.

Conflict of interest

None.

Description of authors' contributions

L. Boss designed the systematic review, performed the literature search, and wrote most of the manuscript. D.H. Kang guided the conception for the review and the process of performing the literature search, assisted with writing the manuscript, and edited the manuscript. S. Branson assisted with writing the manuscript.

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