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The Effect of Social Isolation on Elder Cognitive, Psychological, and Physical Health

Selina Park[1 *]

[1]Sardis Secondary School, Chilliwack, BC, Canada
*Corresponding Author: selinashpark@gmail.com

Advisor: Dr. Courtney Rivet-Noor, courtney.rivetnoor@duke.edu

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Abstract

Previous studies have concluded that as individuals get older, they become more prone to experiencing loneliness due to significant economical, social, and cognitive changes in their lives. For instance, older adults are more likely to experience more loss in their social network and become reluctant to initiate new networks. Social isolation and loneliness are two major factors damaging elderly adults' health. With the population of elders aged 60 years and older increasing, it is important to understand the root cause of detrimental senior health outcomes in order to minimize its effects. Despite this, seniors' health is often neglected compared to other age groups. Due to lack of sufficient and cohesive data, there is a need for a comprehensive review, to gain a better understanding. The objective of this paper is to analyze the correlation between social isolation of elders and various health issues. Loneliness and social deprivation of elders significantly increased the likelihood of psychological, cognitive, and physical health issues, such as depression, dementia, and cardiovascular diseases.

Keywords: Social isolation, Elderly health, Mental health, Loneliness, Cognitive decline, CVD

1. Introduction

Social isolation and loneliness are major causes of poor mental and physical well-being, especially for older adults. Social isolation can be defined as the absence of social contact and integration into society relative to that of an average person, or to the extent of integration of someone's younger self. However, individuals may still feel socially isolated and experience loneliness with regular social contact. Therefore, loneliness is described as a lack of meaningful friendship (Holmén et al., 2000). It is crucial to differentiate the objective aspect of social isolation from the subjective aspect, since they result in different consequences. Objective isolation refers to the objective measure of social disintegration, such as the number of close friends, whereas subjective isolation refers to one's perception of isolation. Rates of social isolation tend to increase with age nonetheless, as factors such as widowhood and retirement reduce social integration (Cené et al., 2022). With the generation of "baby boomers" (age 65 and above) increasing in our society, over half of this population are at risk of social isolation (Fakoya et al., 2020).

Furthermore, the COVID-19 pandemic has affected individuals worldwide, but the insufficient social contact of the elderly that was amplified seems to be getting little awareness. This population has been considered "most vulnerable" to contract the virus, and hence their isolation was taken more seriously. However, this action may have been a double-edged sword. Social isolation and loneliness are often thought to be interchangeable, but they define different states and are associated with varying outcomes. Some may argue that social isolation has no effect on cognitive decline, whereas loneliness is significantly correlated with it (Holwerda et al., 2014). However, it is reasonable to consider the possibility of both loneliness and social isolation carrying out similar outcomes. In fact, one study showed that individuals with objectively limited social contact had a 60% increased risk of dementia

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(Fratiglioni et al., 2020), while another study claimed only loneliness increases the risk, not isolation (Holwerda et al., 2014). In this review, research discussing isolation is analyzed, some using rodent models to infer the effects on the human body. Although seemingly benign at first glance, social isolation for the elderly population impacts one's quality of life due to cognitive impairment, psychological damage, and cardiovascular health deterioration.

2. Background

2.1 Cognitive Effects

It is already established by numerous studies that people's cognitive functions change throughout their lifespan. The typical aging population may experience mild cognitive decline that does not interfere with day-to-day tasks. A major factor that expedites cognitive decline is social isolation. One recent research study tested this hypothesis by using the measurement of Cambridge Cognitive Examination (CAMCOG) for cognitive health and Lubben Social Network Scale–6 (LSNS-6) for social isolation. CAMCOG is a questionnaire involving 67 items to assess one's cognitive function in eight subscales: orientation, comprehension, expression, memory, attention and calculation, praxis, abstract thinking, and perception. Higher scores on this questionnaire show higher cognitive function. LSNS-6 is a questionnaire to determine one's social isolation by calculating the number of close ties one has. Because LSNS-6 only takes the quantity of social ties that one has, only social isolation can be compared with cognition, not loneliness. They surveyed the elderly population once for baseline data and once more two years later to compare the decline. Results indicate that those with more social contact have higher scores of CAMCOG, which demonstrates the significance of social isolation on one's cognition. Among eight different subscales of CAMCOG, social deprivation was only correlated with regression of orientation, expression, executive functioning, and conception. Although memory was one of the subscales that was not significantly related to social isolation, this uncertainty may have been brought about from their limitation of a relatively short timeframe of the experiment. Despite the other subscales of CAMCOG that did not show significant regression, it is clear that social isolation damages cognition in some way. Moreover, their post-hoc analysis states that there was a statistically significant connection between cognitive health and social isolation for elders with low occupational complexity (Evans et al., 2018). Low occupational complexity can be described as jobs that require less cognitive stimulation. Another recent study found that participants with higher cognitive stimulation jobs had lower levels of inhibition proteins of the central nervous system. This type of protein that inhibits development of nervous tissue appears to increase the likelihood of dementia (Kivimäki et al., 2021). This correlation explains that individuals with lower stimulating jobs are at a far greater risk of dementia, which can be exacerbated with social isolation.

Dementia is an umbrella term which covers many neurological disorders that affect memory and the ability to function in life. Because the elderly population is more vulnerable to this disease, it is important to dissect additional risk factors, such as social isolation, for this rapidly growing age group (Alzheimer's Association, 2023). One recent study found that the loss of gray matter in one's hippocampus is positively correlated with social isolation. Gray matter in the brain plays a significant role in many aspects of one's life, such as movement control, memories, and emotions (Mercadante & Tadi, 2023). Although the gray matter in the hippocampus tends to recede over time regardless of neuropathology, this study demonstrated that having close contact with a social network slows hippocampus aging (Lammer et al., 2023). Since the hippocampus is considered the memory center in the human brain, its reduction in function could eventually lead to memory loss and neurodegenerative disorders related to memory.

This phenomenon has also been described in experimental rodent models. A study was conducted on socially isolated mice to observe the effect on the hippocampus. Rodents are a useful model organism due to their heightened sensitivity to isolation. Therefore, results from studies that use rodents to test the effects of social isolation are applicable to other socially-reliant species. Right and left hippocampus of socially isolated rodents were collected for comparison with rodents that were allowed to socialize. Results show that social isolation was correlated with lower mean weight of the hippocampus. Pathology of the hippocampus, often measured with its weight, is a distinctive characteristic of Alzheimer's Disease (Muntsant & Giménez-Llort, 2020). Alzheimer's Disease accounts for 70% of dementia diagnoses. It is characterized by cognitive decline that can progress to disruption of day-to-day functioning

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(Neuner et al., 2020). Thus, it is reasonable to conclude that social isolation is correlated with not only cognitive decline, but also Alzheimer's Disease (Muntsant & Giménez-Llort, 2020). Due to the outcome of social isolation causing cognitive defects in rodent models, it might be worthy to investigate whether these defects are associated with the physiology of humans.

An experiment conducted in a living-home in Sweden provided similar outcomes. Over the period of around 3 years, over a thousand elders, those with and without dementia, were compared on their social network and their relative risk for developing dementia. Having little social contact increases the risk of dementia by 60%, which further proves the detrimental toll that isolation creates. The factors that determined "social contact" included marital status and social ties with friends and family (Fratiglioni et al., 2000). A more recent study validates this correlation, as over 9 years of experimentation demonstrated that elders who are socially isolated had a 27% increased risk of being diagnosed with Alzheimer's (Johns Hopkins Medicine, 2023). Currently, over 55 million people worldwide are living with Alzheimer's Disease or other dementias (Alzheimer's Association, 2023). It is the seventh leading cause of death globally, and it significantly damages a person's quality of life and their independence (World Health Organization, 2023). Given that social isolation is a risk factor for developing cognitive defects later in life, it is reasonable to conclude that social isolation could have a direct link to dementia. In fact, one study showed that 3.5% of dementia cases can be attributed to social isolation (World Health Organization, 2023). This number of cases attributable to dementia are equivalent to the amount of dementia cases attributed to obesity, hypertension, and diabetes combined (Lammer et al., 2021).

One of the major similarities across Alzheimer's brains is amyloid-β plaque build up. This is created by amyloid precursor proteins that collect between neurons to disrupt their signaling. Another factor that contributes to the disease is neurofibrillary tangles. These are abnormal accumulations of a protein called tau. Although tau can also be abundant in healthy brains, it becomes a problem when the proteins attach to each other, causing tau tangles to block neuronal functions (NIH National Institute on Aging, 2017). Amyloid-β build up, and tau tangles are the two primary criteria for Alzheimer's Disease Diagnosis (Long & Holtzman, 2019). With this information in mind, one study tested whether cortical amyloid burden is associated with higher levels of loneliness. All 79 participants' levels of loneliness were measured using the UCLA Loneliness Questionnaire Scale. This questionnaire has 3 self- reported questions on a scale of 4 to assess one's feelings of loneliness. To assess the amount of amyloid burden, Pittsburgh Compound B-PET scan was used. The results indicate that higher amyloid burden was associated with greater UCLA-loneliness. In fact, participants in the amyloid-positive group had a higher chance of being lonely than the participants in the amyloid-negative group. This correlation was even stronger with APOEε4 carriers, supporting the link between loneliness, plaque buildup, and Alzheimer's Disease. These are individuals that carry one or more alleles of the APOEε4 gene, a gene that increases susceptibility of getting Alzheimer's Disease (Donovan et al., 2016). Although the results do not specify that loneliness causes amyloid build up, it does show a correlation between the two, particularly for those who are genetically predisposed to amyloid build up.

Despite all this evidence, the research still has limitations. It is not clear whether social isolation or loneliness is the direct cause for this decrease in cognitive function, as there are various unaccountable factors that could have changed within the course of an experiment. One study proposed that it is the subjective factor of loneliness that initiates all the harm, such as dementia, not the objective social isolation. In the study conducted by Holwerda et al., there appeared to be no relation between social isolation and increased risk of dementia. Only those that "felt" loneliness had greater risks or plaque buildup (Holwerda et al., 2014). These results make pinpointing a direct cause challenging. When experiments considered the objective view of social isolation, they may have coincidentally found the consequences of loneliness instead, which was caused by isolation. However, there is overwhelming evidence to demonstrate correlation of cognitive decline with both social isolation and loneliness. Social isolation is associated with lower levels of cognitive function, and loneliness is associated with the precursors of Alzheimer's Disease (Evans et al., 2018 & Donovan et al., 2016). Therefore, it is reasonable to conclude that both factors play a role in determining one's quality of life in terms of cognitive effects. Since social isolation is a completely modifiable factor that ultimately leads to adverse health outcomes, there is hope to alleviate some of the impacts (Xiang et al., 2021).

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2.2 Psychological Effects

Although mental illness in the elderly is becoming more prevalent, there is lack of recognition and awareness, causing many to be left untreated (Van Citters & Bartels, 2004). Social isolation greatly affects these illnesses, and this has become more evident through the COVID-19 pandemic.

A recent study found that increase in subjective social isolation is positively correlated with increase in depressive symptoms. Subjective social isolation is measured as an individual's perception of loneliness, rather than numbers of social networks they have. The study indicated no significant result with objective social isolation (Taylor et al., 2018). Therefore, it is important to dissect the effects of perceived social isolation, rather than the isolation itself when considering psychological impacts.

Studies indicate that social isolation is associated with increased mortality rates and linked with worsening mental health (de Sousa et al., 2022). Furthermore, people experiencing low social support tend to be more likely to develop depression disorder (Santini et al., 2020). The World Health Organization proposed that depression is the fourth leading cause of disability worldwide, and by 2030, it will become the most prevalent health issue (Levula et al., 2018). Clinical depression is linked with several other mental illnesses that significantly reduce one's quality of life, such as generalized anxiety disorder, panic disorder, and social phobia (Fulghum Bruce, 2022). In fact, studies show that half of the people with depression experience symptoms of generalized anxiety disorder at least once (Levula et al., 2018). One recent study hypothesized that both perceived isolation and social disconnectedness lead to increase in depression and anxiety symptoms. They also hypothesized that perceived isolation (loneliness) is the connector that links social isolation with poorer mental health. For their experiment, they used 10-year follow-up data from the National Social Life, Health, and Aging Project (NSHAP) to represent a diverse population of older adults. Depressive traits were tested using Center for Epidemiological Studies-Depression Minus Loneliness (CES-D-ML) scale, and anxiety was measured with the seven-item anxiety subscale of the Hospital Anxiety and Depression Scale (HADS-A). Their results indicated that, consistent with the study above, only perceived isolation is positively correlated with depressive and anxiety symptoms. Furthermore, greater social disconnectedness predicted greater perceived loneliness (Santini et al., 2020). This shows that although social isolation and loneliness are not the same, many of those who are objectively isolated tend to feel lonely.

Research indicates that loneliness is one of the three factors leading to depression, the other two being dissatisfaction with life and smoking, especially for older adults (Green et al., 1992). Individuals naturally become more prone to loneliness with age, as likelihood of experiencing age-related loss increases. With time, they inevitably lose friendship networks and find it difficult to initiate new friendships. Therefore, the elderly population is more vulnerable to mental health risks (Singh & Misra, 2009).

Depression is a mental disorder which is often caused by an underactive serotonergic system (Dankoski et al., 2014). The disturbance in production of a neurotransmitter called serotonin or 5-hydroxytryptamine (5-HT), leads to sad, empty, and depressive moods. The balance of 5-HT production from the dorsal raphe nucleus controls an individual's mood. Its inactivity and dysregulation cause depression. Even non-depressed individuals have hindered activation of 5-HT neurons when under stressful conditions. An experiment was done to observe social isolation's effects at a chemical level in mice. Mice were isolated for more than seven weeks and then were tested with whole-cell electrophysiology to observe 5-HT neuron activity. The results showed that mice that were isolated had significantly less action potentials created in 5-HT neurons compared with those of the control. In an attempt to try to reactivate these neurons, optical (blue light) and electrophysiological stimulations were performed. However, there still seemed to be an evident decrease in frequency of neuron firing and activation of 5-HT neurons. Further investigation was done to assess the mice's anxiety levels after isolation. They showed significant increase in overall immobility and anhedonia (Sargin et al., 2016). Therefore, it can be concluded that isolating a social species reduces the function of a vital neurotransmitter involved in emotion regulation.

One recent experiment was conducted in China to observe the relationship between loneliness and suicide risks. They explored psychosocial risk factors for elderly suicide cases to record their data. For each case, one living elder from the same community was used as the control. Their results showed that seniors with high levels of loneliness and hopelessness were twice more likely to commit suicide (Niu et al., 2020). Although loneliness alone did not cause

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active suicide desires (Niu et al., 2020, Tachikawa et al., 2023), with hopelessness being the major symptom of depression, it is evident that loneliness has an impact on suicidal risks. Furthermore, multiple research studies concluded that the motivation of self-harm with intent of suicide for older adults was loss of control, increased loneliness, and burdensome aging. However, it is important to note that not all self-harm actions are intended for suicides. Due to its negative stigma, especially for the elderly, seniors often do not seek out support (Troya et al., 2019).

In addition to the complex intertwining of loneliness and depression, loneliness also seems to be connected with sleep deprivation (Griffin et al., 2020). For one study targeting older Americans, participants completed the Hughes Loneliness Scale for loneliness and sleep disturbance scale every two years. They found a reciprocal, feedback-loop relationship between sleep disturbance and loneliness (Griffin et al., 2020). In other words, loneliness leads to irregular sleep, and irregular sleep leads to loneliness, creating a never-ending cycle. One reason why loneliness would affect the sleep cycle could be due to activation of the hypothalamus-pituitary-adrenal (HPA) axis (Griffin et al., 2020). The HPA axis is a neuroendocrine system that releases a glucocorticoid hormone, cortisol, in the bloodstream to activate the sympathetic nervous system and fight-or-flight response (Hinds & Sanchez, 2022). This hormone is essential to the regular sleep-wake cycle. Thus, over activation of this system may disrupt the typical patterns of sleep (Griffin et al., 2020). Although sleep disturbance in itself poses a great danger to one's quality of life, it also creates another pathway leading to depression. In fact, greater sleep disturbances were associated with greater risk of developing depressive symptoms (Stone & Xiao, 2018). Social isolation and depression are closely linked due to the impact on neurobiology, mood, and sleep.

2.3 Physical Effects

When considering the effect of social isolation on an individual, cognitive decline and psychological disturbances are often thought to be the most common consequences. This could be due to social isolation being intangible - a state of being that cannot cause physical harm to a human body. In comparison with obesity or hypertension, for example, isolation and loneliness seem rather harmless. However, one study indicated that the odds of mortality caused by social isolation and loneliness are greater than the odds of death due to obesity and hypertension combined (Xia & Li, 2018). In fact, social isolation directly puts elders at risk for various illnesses.

Human bodily functions strive toward maintaining homeostasis. Individuals have several systems responsible for this, among which is the HPA axis (Sheng et al., 2021). This neuroendocrine system consists of the interaction among the hypothalamus, pituitary glands, and adrenal glands. The HPA axis is responsible for releasing hormones that regulate the physiologic stress response. Cortisol prepares the body by increasing glucose levels in the bloodstream. This helps the body gain energy to manage a prolonged stressor. It also increases the blood pressure to supply more blood to the body, so that they have more power to escape the stressor through methods such as running away (Evans, 2023). Although the HPA axis and its products are necessary to humans, prolonged activation of the axis can lead to detrimental effects on the body (Heck et al., 2020). Among several ways the HPA axis can be stimulated, social isolation seems to be correlated with higher HPA axis function. In one study, rats were socially isolated chronically for four weeks and their HPA activity was measured. The results showed that the negative feedback inhibition was impaired, and the rats required higher doses of synthetic glucocorticoid for the feedback loop to work (Hawkley et al., 2012). Negative feedback inhibition essentially terminates a signal when the products start to accumulate. Impairment of this system indicates that the HPA axis is continuously activated and producing glucocorticoids (Hawkley et al., 2012).

Humans cannot undergo severe isolation for experiments such as the one using rodents conducted by Hawkley et al. due to ethical concerns. Therefore, for one study, social isolation was measured as the number of close persons in a participant's network. Supporting the study with rats, those that had fewer social networks had greater cortisol outputs. Another study conducted at a socially isolated senior home also showed similar results. Some participants went through a social activation program, and the rest remained in isolation. The control group that remained socially isolated showed increased plasma cortisol during the 3 months follow-up (Hawkley et al., 2012). This is due to the psychological stress that was caused by the isolation, which is an unnatural situation for our social species (Al Omran

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et al., 2022). Furthermore, lonely people tend to perceive more things as stressful. These stressors activate the fight-or-flight response, with the HPA axis and sympathetic nervous system (SNS) working together (Pourriyahi et al., 2021). In prairie voles, for instance, social isolation increased the heart rate and its rhythm dysregulation due to over activation of SNS and inactivation of parasympathetic nervous system (Li & Xia, 2020). Even from evolutionary perspective, humans who are alone are more susceptible to encounter predators, which triggers stress to survive the threats (Scatà et al., 2023). Chronically elevated cortisol levels from isolation not only escalated aging, but also resulted in increased risk for diseases (Stevenson et al., 2019).

When this stress response becomes long-lasting due to circumstances like social isolation, the body begins to increase production of pro-inflammatory cytokines (Scatà et al., 2023). Cytokines are proteins in the body that control inflammation, immune system and response to trauma. Pro-inflammatory cytokines tend to make inflammation worse, and anti-inflammation tends to reduce inflammation (Dinarello, 2000). Release of these molecules leads to immune dysregulation, causing people to acquire diseases more readily and making it more difficult to fight them off (Scatà et al., 2023). Immature classical monocytes begin to accumulate without changing the total number of white blood cells, which is the root of inflammatory function (Li & Xia, 2020).

This pro-inflammatory response initially occurs to fight off threats. Despite the intention of protection, when the inflammation is not short-lived, it increases the risk of cardiovascular diseases (CVD) (Paul et al., 2021). It is important to note that chronic inflammation marks the beginning of CVD. Although the evidence between CVD and social isolation is limited compared with more obvious precursors such as diabetes(Freak-Poli et al., 2021), isolation acts as a pathway to several of these precursors, ultimately increasing the likelihood of getting CVD one way or another. In fact, in a recent study, individuals over the age of 70 had a 66% increased risk of incident CVD, and the percentage doubled if individuals had low social support (Freak-Poli et al., 2021). The cytokine production further harms the body by creating "sickness behaviors," such as social withdrawal (Paul et al., 2021). Evolutionarily, when humans get sick from diseases, they are to isolate from the rest of the community to contain the sickness. Cytokines coordinate this response, which only intensifies social isolation.

A systematic review linking loneliness with cytokine production concluded that loneliness increases a certain type of pro-inflammatory cytokine called interleukin-6 (IL-6) (Paul et al., 2021). When IL-6 production is short- lived, it is very effective at its function of activating immune response. However, when it becomes chronic, as in the case of chronic psychological stress caused by isolation, it becomes toxic to the body. In particular, although acute production of IL-6 for a short term protects the heart's tissues and muscles, prolonged production makes the same effects detrimental. The heart muscle undergoes a change similar to hypertrophy, possibly leading to heart failure (Fontes et al., 2015). In fact, one study found that social isolation increases the cases of heart failure by 21%. Furthermore, those isolated were more likely to die waiting for a heart transplant over the span of one year (Cené et al., 2022). Heart failure often originates from chronic hypertension (Tackling & Borhade, 2023). Hypertension accounts for 18% of total deaths in the United States. To better understand the relation of loneliness with increased systolic blood pressure, a population-based study was conducted over the course of 5 years. Loneliness was measured using the UCLA Loneliness Scale. The results indicate that over a long period of time, lonely people have higher systolic blood pressure than non-lonely people (Hawkley et al., 2010). Although this research did not specify the relationship between loneliness and hypertension, it is evident that loneliness does have a negative effect on the heart. The physical effects of social isolation are extensive due to immune function dysregulation and increased risk in CVD.

3. Future Directions:

Social isolation is a hidden poison that destroys quality of life more severely than some well-known diseases. However, due to lack of awareness on the significance of social isolation and loneliness, not many attempt to find preventative solutions for the most vulnerable population, seniors. Thus, there is a need for extensive research of direct and indirect effects of isolation to solidify our understanding. Unlike countless other untreatable and incurable diseases, social isolation is a modifiable factor that contributes to pathology.

Currently, not only are the consequences of social isolation damaging the quality of lives of millions, they act as a significant burden to the economic social cost. For instance, South Korea is almost a super-aged society, with more

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than 16.8% of the population being 65 years-old and above. Around 10% of the largest healthcare insurance programs accounted for strokes, and 3-5% accounted for depression (Kim et al., 2022). Furthermore, in the United States in 2021, general hospice services for elders with dementia are estimated to be $355 billion (Alzheimer's Association, 2021). These statistics evidently show the magnitude of the elderly healthcare economy. Social isolation is arguably the most preventable factor that can reduce these numbers significantly.

The findings of this review suggest that there is harm for both objective and subjective social isolation, the latter being loneliness. Hence, the need for adequate solutions to each problem is crucial. It can be difficult to operate interventions such as in-person social groups due to health regulations especially for the elderly, so future interventions must be durable for continuous support even during unprecedented times. A scoping review observing the effectiveness of robots as social support for seniors found that qualitatively, the robots not only decreased loneliness but also increased the level of engagement in conversations with others when the robots were present. Many of the participants viewed these robot agents as "social beings" rather than unemotional machines (Gasteiger et al., 2021). Although robots do not add up to all human-like qualities, they can be more reliable when humans are unreachable. Another review focused on internet-based interactions, such as online chat rooms and videoconferencing. Their results were overall inconclusive due to limited resources on this topic (Fakoya et al., 2020). However, these new ideas involving virtual and artificial connections show that person-to-person interventions are not the only possible solutions. There is a clear lack of knowledge surrounding social isolation and its detrimental consequences in elders, despite the sudden surge of it in the past few years. Therefore, exploring solutions and enforcing them are necessary for elderly health.

4. Conclusion

Human beings are social species that require proper social integration. However, as we age, the odds of falling out of integration increases. Older adults undergo significant changes in their social life such as retirement, loss of a significant other, death of friends, and much more. Especially during unprecedented times such as the coronavirus pandemic, people in senior homes lacked access to the outside world in an attempt to protect them. When isolated, consequences are not just reduced to feelings of loneliness. In fact, this review reveals the destructive effects of social isolation cognitively, psychologically, and physically.

Due to lack of stimulation in the brain from not socializing with others, brain aging is expedited. An experiment using rodents showed cognitive decline due to isolation in the form of memory deficits. Similarly, humans showed a decrease in the brain matter of the hippocampus when socially isolated. Not only does social isolation result in lower cognition, it also increases the risks of dementia. Studies found that the precursors of Alzheimer's Disease, amyloid burden and tau pathology, are significantly correlated with loneliness. Although this study did not show significant results with social isolation, the reciprocal relationship between social isolation and loneliness predicts correlation.

Perceived loneliness also greatly affects individuals psychologically. Rodents were used once again to compare the psychological distress caused by social isolation with anxiety and depressive symptoms. This review found two major links that connect loneliness with depression. The first way is the underproduction of the serotonergic neurotransmitter. The second way introduces the sleep cycle. Irregular sleep cycles can be caused by over activation of the HPA axis, which produces cortisol. Chronic production of this hormone significantly increases the likelihood of being diagnosed with depression.

The over activation of the HPA axis also has physical consequences on the body. With prolonged activation of the SNS and cortisol production due to social isolation, the body produces cytokines. These cytokines hinder immune function. One specific type of pro-inflammatory cytokine, Interleukin-6, was studied in the aforementioned review. Chronic production of this protein significantly raises the percentage of cardiovascular diseases such as hypertension, heart failure, and overall morbidity.

With social isolation being a modifiable factor, substantial interventions can reduce these consequences. Until potential solutions are developed, millions of elders' suffering and the healthcare's social cost will only worsen. Fortunately, present day's technology advancement shows the boundlessness of future interventions and gives hope to mitigate social isolation.

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