Climate Change and Global Warming: Are Individuals with Dementia - Including Alzheimer's Disease - At a Higher Risk?

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1. INTRODUCTION

Climate change represents a global issue, and it has become a challenge not only for climatolo-

recently debated on an increased risk for people with chronic diseases [1]. Climate change also involves various extreme events, such as floods, forest wildfires, storms, and others. In particular, hot weather and heat extremes have gained the attention of the scientific and clinical community since they can increase mortality and morbidity, negatively affect mental health, and reduce physical work capacity and motor-cognitive performances [2]; such attention to the impact of heat on health has resulted in series from the Lancet journals (https://www.thelancet.com/series/heat-and-health) and a network promoted by the World Health Organization (WHO), World Meteorological Organization (WMO), and other partners (https://ghhin.org/). In this perspective paper we aimed to discuss the possible effects of climate change on the risk of accelerating the progression of diseases causing dementia, and health-related risks in those with dementia in the context of climate change and global warming.

Among different chronic clinical conditions, cognitive impairment and neurodegenerative diseases could be affected by global warming through different mechanisms, as heat stress might result in increased excitotoxicity, oxidative stress, and neuroinflammation. Taken together, in the pathophysiology of dementia of Alzheimer's type (AD) these effects might promote amyloid β (Aβ) peptide and phosphorylated Tau protein accumulation [3]. In addition, people with AD could be characterized by altered circadian patterns, which include a shift or disruption of the normal pattern of body temperature [4], and thermoregulatory abnormalities might be associated with the development of the disease [5, 6]. Nevertheless, compared to other neurodegenerative conditions such as Parkinson's disease, actually, there is not a clear correlation between global warming and epidemiological indices of dementia and AD, and future studies should confirm if this is due to the different neurons' vulnerability to heat stress [3].

Epidemiological analysis of previous heat waves has suggested that elderly persons are at a higher risk of mortality due to hot weather, and the risk increase among those with comorbidities, including dementia [7]. Even a small increase in mean ambient temperature (1.5°C) has been suggested to increase the risk of hospital dementia-associated admissions [8]. Taken together, these findings suggest poor physical health and the prevalence of cognitive disturbances might represent serious risk factors for heat-related illnesses, and the latter might depend on altered risk perception and capacity to care during an extreme heat event properly. Indeed, it has been suggested that the excess in mortality for serious cognitive deficits (dementias of various origins, including that resulting from stroke or Alzheimer's disease) during previous heat waves could be caused by a person's impaired perception of environmental conditions, threshold of suffering, and physiological defense mechanisms, including thirst [7]. In addition, some pharmacological treatments have been shown to affect some thermoregulatory responses, and in particular sweating, therefore increasing the risk of heat-associated illnesses, in particular when sweating becomes a fundamental heat loss mechanism (*e.g.,* during heat waves or physical activity) [9]. For example, cholinesterase inhibitors, selective serotonin reuptake inhibitors, opioids and tricyclic antidepressants might result in hyperhydrosis (therefore representing a possible risk for dehydration). In contrast, antimuscarinic anticholinergic agents, carbonic anhydrase inhibitors and tricyclic antidepressants can result in sweating deficiency [10]. Therefore, it should be recommended to

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evaluate the effects on thermoregulation of the different (including novel) drugs that are commonly used to treat dementia and other neurodegenerative disorders. As such, adaptative responses, both physiological and behavioral, are necessary to cope with environmental conditions that might represent a risk to people's health, and lack of adaptation (which might be present in the elderly or in people with neurodegenerative disorders) could therefore represent a risk factor for environmental temperature related illnesses.

For survival, behavioral thermoregulation may be even more important than autonomic nervous system responses [11] and might be helpful to compensate for environmental stimuli, as in the cold [12]. To prevent heat illness, humans also heavily rely on behavioral thermoregulation, such as seeking shade or buildings with air conditioning, increasing fluid intake, removing clothing, or taking a cooling shower [13-17]. The ability to make behavioral regulations when exposed to low or high temperatures declines with aging [18, 19], as well as thermal and wetness perception [20]. This fact contributes to the discomfort experienced by the elderly [21] and to their higher vulnerability (*i.e.,* being easily influenced/harmed by) to hypo- or hyperthermia [22]. Correct thermal selection is essential for optimal nighttime energy savings and for a good quality night's sleep [23, 24]; indeed. According to Raymann *et al.* even a slight drop in skin temperature reduces the tendency to fall asleep and may contribute to the night awakenings so common in the elderly [24].

Behavioral changes to environmental temperatures seem to be determined by thermal discomfort [25], but since the elderly, despite being physiologically challenged, have a diminished perception of discomfort and an impaired ability to sense their own thermal state, particularly in summer [26, 27], they may be disinclined to reduce the thermal challenge by adapting their behavior (*e.g.,* they regulate their indoor ambient temperature less precisely) [28]. In addition, they may be unwilling to take simple measures like opening windows because of cost, fear of crime, or concerns about noise and pollution [29].

Although behavioral change recommendations (*e.g.,* "stay hydrated," "avoid the heat," *etc.*) are a priority in public health interventions, only a few elderly people actually alter their practices [30]. This may have something to do with the fact that many elderly people do not think to be at risk or that the advice is relevant to them. Only a few aged people may acknowledge their own risk, despite recognizing the heat and medical risks in others [31]. Older people didn't think they were old or threatened by heat, but they thought other people of their age were at risk. This distorted self-perception makes them less likely to adopt protective behavior [32-35]. In addition, people with dementia and AD, especially in the elderly, can be characterized by behavioural and psychological symptoms, requiring specific actions that include pharmacological and non-pharmacological treatments; in particular, non-pharmacological approaches include psychosocial interventions, nursing care, physical activity, sensory stimulation, and cognitive training [36]. Taken together, these findings suggest that, in order to influence behavior, interventions must incorporate education and awareness measures to match people's risk to self-perceptions and experiences [16].

Unfortunately, there are very few controlled studies on age-related behavioral thermoregulation changes. Aujard *et al.* (2006) demonstrated that behavioral thermoregulation changes with age in the mouse lemur. This nonhuman primate model has also been proposed as an Alzheimer's disease model because it resembles the aging processes in people, such as brain atrophy, cognitive decline, hormonal changes, and a fragmentation of the circadian rhythm similar to those observed in human aging and dementia [37]. In all conditions, older animals chose ambient temperatures significantly higher than adult animals, with the exception of the "winter days", when it was most needed since both the circadian and seasonal phases dictate low activity levels and low ambient temperatures [38]. Due to impaired physiological and behavioral responses to heat, age is cited as a major significant intrinsic risk factor in all studies (Grewe and Blättner, 2011), but psychiatric illness was the factor most strongly associated with death in terms of pre-existing medical conditions [13].

Several studies have shown a relationship between senile dementia of the Alzheimer's type and abnormalities in temperature homeostasis. Diamond and Diamond (1991) reported the case of a patient whose severe cold intolerance symptom onset and progression mirrored her disease course [39]. As depicted by Fletcher *et al.* (2015) and conceptualized in neurobiological models, in dementia, altered behavioral responses to temperature reflect complex psychological constructs, including, altered awareness, tolerance, motivation, behavioral organization, or some combination of these factors [40]. Temperature processing requires transforming sensory data into complex experiential constructs. These stimuli are loaded with subjective emotional, mnestic, and semantic associations in addition to having fundamental biological significance. Brain regions involved in altered temperature processing closely overlap with those involved in social cognition, highlighting the tight coupling of homeostasis and social signaling and their shared vulnerability in mental disease states [40-42].

CONCLUSION

To sum up, due to impaired cognitive and/or functional capacities, the elderly may be unable to alter their behavioral thermoregulation: Such perceptual, cognitive, and behavioral factors are critical and should be studied in more detail, as the effectiveness of methods that can be applied to improve people's abilities to implement behavioral changes may ultimately depend heavily on people's motivation (*e.g.,* awareness of their own vulnerability, intention to adhere), capabilities (*e.g.,* physical and mental conditions, literacy, skills, and knowledge), and opportunities (*e.g.,* actual access to services and solutions, financial means) [43]. In addition, global warming may be indirectly associated with the development of other clinical conditions, including kidney or infectious disease, that might further complicate the vulnerable individual's health due to increased risk of dehydration [44, 45] and the spread of infections promoting factors [46, 47]. Therefore, considering the novel challenges imposed by climate change and global warming becomes fundamental to better understand the relationship between environmental conditions and health, in particular in those with cognitive impairments and neurodegenerative disorders, and to develop plans and public health actions to monitor and mitigate such risks [46].

RECOMMENDATIONS AND TAKE-HOME MESSAGES

Increased ambient temperature represents a health risk, especially in the elderly and in people with neurological conditions, such as neurodegenerative disorders and cognitive impairment.

During heatwaves, people with dementia or AD living at home should be monitored by their caregivers of health services to check the indoor environment conditions and propose countermeasures to cool the environment (*e.g.,* electric fan use).

Smart-home systems could be developed and adopted to support the elderly and people with impaired cognitive functions, in particular those with altered behavioral responses, by automatically operating cooling/warming systems based on validated algorithms.

Healthcare professionals working in institutions should be trained to correctly recognize potential environmental risks (also supported by local alerts), identify the individuals at a higher risk due to a lack of physiological/behavioral adaptation, and rapidly implement countermeasures and mitigation strategies.

Particular attention should be given to fluid balance, promoting healthy hydration strategies, and monitoring those at risk of dehydration. It may be beneficial to develop smart watches or similar devices that can provide remote body temperature monitoring in elderly and demented individuals with a loss of awareness.

Future research should focus on both physiological and behavioral responses to different environmental conditions in the elderly and in those with cognitive deficits and neurological disorders.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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