Modeling California Heat Wave Exposure and Links to Dementia-like Neurodegeneration in Elderly

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The California heat waves of 2022 were the most severe on record and will likely increase in the coming years. The increasing heat wave intensities, a common worldwide phenomenon in coastal regions, is predicted to result from climate change. Interestingly, about 40% of the population in the US lives near coastal areas or 100 miles of the coast. Notably, In California, the population aged 60 years and over is expected to grow more than three times as fast as the total population, and this growth will vary by region. Studies suggest that elderly with co-morbidities might be more susceptible to the effects of heat waves. I hypothesized that preclinical modeling with heat wave-mimicking exposure may serve as an indicator of neurodegenerative disease risks in the elderly. Mice aged 24 months (65 yrs of human age) were subjected to 40˚ C exposure for 15 days, and the brain tissues were assessed for neurodegeneration by assessing argyrophilic structures, neuroinflammation by assessing microglial activation and a specific small molecule neuroimmune cytokine lipocalin-2. Results showed that there was a significant increase in argyrophilic structures, microglial activation and lipocalin-2 levels in the heat-stressed elderly mice when compared to non-exposed controls. Further serum levels of Lipocalin-2 correlated with increased microglial activation, suggesting heat exposure showed marked susceptibility to dementia-like neurodegeneration in the elderly. It can serve as a future clinical roadmap for predicting risk in the elderly following severe heat waves due to climate change.