Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Brain, Behavior, and Immunity 107 (2023) 401–402

Contents lists available at ScienceDirect

Brain Behavior and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Letter to the Editor

Comment regarding: "COVID-19 vaccination may enhance hippocampal neurogenesis in adults"

ARTICLE INFO

Keywords
Vaccination
Influenza
BCG
Neurogenesis
Low dose ionizing radiation
Alzheimer's disease
Hippocampus

The interesting viewpoint of Kumar and colleagues (Kumar et al., 2023) based on animal studies and entitled, "COVID-19 vaccination may enhance hippocampal neurogenesis in adults," is supported by observational human data (Bukhbinder et al., 2022; Klinger et al., 2021), thus raising prospects concerning memory and the treatment of Alzheimer's disease (AD). Notably, the authors discuss the different effects of infection versus vaccination on hippocampal microglial activation. Specifically, viral infection leads to M1 microglial activation resulting in proinflammatory cytokines released by the microglia, culminating in the attenuation of adult hippocampal neurogenesis; by contrast, vaccinations, such as influenza and Bacillus Calmette-Guérin (BCG), lead to M2 microglial activation resulting in anti-inflammatory cytokines released by the microglia, culminating in the augmentation of adult hippocampal neurogenesis (Kumar et al., 2023).

As mentioned, human data bolster the concept of vaccinations promoting adult hippocampal neurogenesis. For example, a recently published retrospective cohort study reported the risk of incident AD diagnosis among individuals ≥65 years, comparing those with and without prior influenza vaccination, in a large US claims database during a median follow-up of 46 months (Bukhbinder et al., 2022). During that time, 5.1 % of the influenza-vaccinated and 8.5 % of the influenza-unvaccinated were diagnosed with AD yielding a significant absolute risk reduction of 3.4 % and relative risk reduction of 40 %; this corresponds to an *absolute* decrease in AD diagnosis approaching 1 % each year among influenza-vaccinated versus not influenza-vaccinated adults. Moreover, a retrospective study comprising three cohorts of bladder cancer patients from Israel and the US (Klinger et al., 2021) reported on the risk of subsequent AD in those treated with intravesical BCG instillations versus those treated with transurethral resection of the bladder tumor (TURBT). Compared to those treated with TURBT, the BCG treated patients ≥75 years exhibited a significant decrease of 30.6 % in relative risk of AD diagnosis over a 3.5-to-7-year follow-up. Hence, these studies suggest vaccination induced immune mechanisms may decrease AD incidence.

Interestingly, in AD mouse models, low-dose ionizing radiation (LDIR) has been shown to modulate microglia change from proinflammatory M1 to anti-inflammatory M2 phenotypes, reduce amyloid-β deposition, and improve cognitive deficits (Kim et al., 2020). Furthermore, LDIR has shown positive results in treating severe AD in a small pilot study (Cuttler et al., 2021). The radiation exposure included two brain CT scans at baseline, one at 2 weeks and one at 4 weeks; each CT scan delivered 40 mGy of radiation. Amazingly, three out of the four patients studied exhibited striking improvements in behavior and alertness within days to weeks.

Taken together, there are commonly used, inexpensive and safe therapeutic modalities that, in animal models, phenotypically modulate hippocampal microglial cells to reduce neuroinflammation and favor adult hippocampal neurogenesis. Moreover, emerging evidence suggests these modalities may translate to humans by providing clinical benefit to those suffering from a devastating disease. Finally, the field is ripe for testing combinations of existing vaccines and LDIR protocols for the treatment of various stages of AD and perhaps for the prevention of AD in those at genetically high-risk.

Funding

There was no funding for this manuscript.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

No data was used for the research described in the article.

DOI of original article: https://doi.org/10.1016/j.bbi.2022.09.020.

https://doi.org/10.1016/j.bbi.2022.11.010
Received 10 November 2022; Accepted 13 November 2022
Available online 17 November 2022

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