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Low-dose radiation reduces amyloid-beta plaques and tau in animal models of Alzheimer's disease

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Abstract

Statement of the Problem: AD has a substantial impact on health and health care budgets and new cost-effective treatments are needed.

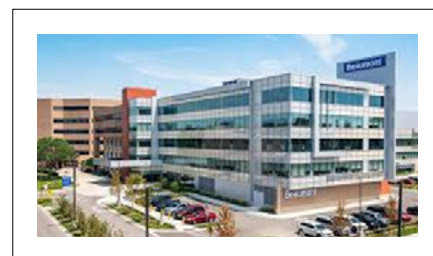
Given the complex neuropathology of AD more effective treatments of AD may be possible using combinations of therapy that target different facets of the disease. An alternative approach would be to discover a treatment modality that is pleotropic in its effect and interferes with the pathophysiology of AD at several levels. In this research we report the effect of low-dose radiation on amyloid-beta and tau in two animal models of AD.

Methodology & Theoretical Orientation: We have studied the effect of 5 fractions of 2 Gy, delivered using a hemi-brain irradiation (HBRT) technique (Fig. 1) on B6.Cg-Tg (APPswePSEN1dE9)85Dbo/J (005864) mice (APP/PS1) and B6;129-Tg(APPswe,tauP301L)1Lfa Psen1tm1Mpm/Mmjax mice (3xTg-AD) and used immunohistochemistry to stain amyloid-beta and tau model. Findings: Five fractions of 2 Gy reduced amyloid-beta plaques by $71.8\% \pm 23.4$ in the brains of APP/PS1 mice ($p > 0.01$). There was also a significant reduction in the size of the plaques in this model from $42.95 \mu\text{m}^2 \pm 12.8$ to $14.52 \mu\text{m}^2 \pm 11.6$. In the 3xTg-AD model there was a consistent and significant ($p=0.028$) reduction in plaque number in the irradiated side of the brain with an average of 40.2 ± 8.9 on the unirradiated side and 23.6 ± 5.2 on the irradiated side. In this model there was considerable variation between mice in the number of tau-positive neurons from as low as 50 to a maximum of 154. However, each mouse showed a reduction tau on the irradiated side with the average change being a 20% reduction ($p=0.0024$).

Conclusion & Significance: Radiotherapy is a well-established and safe medical modality and is not hampered by the blood-brain barrier. Moreover, radiation therapy as a treatment approach for AD could be implemented quickly and inexpensively.

Biography

George Wilson PhD is Chief of Radiation Biology at Beaumont Hospital, Royal Oak. He also serves as Scientific Director of the Beaumont BioBank & Director of the Erb Family Molecular and Genetics Laboratory and is a Professor of Biomedical Research at the Oakland University William Beaumont School of Medicine. He has more than 40 years of experience in biomedical research and over 260 peer-reviewed publications. Dr. Wilson has focused his work primarily on the clinical application of radiobiology dealing with predictive assays and new treatment schedules. He has a particular interest in biological responses to radiation therapy and combining radiation with molecular targeted agents. Dr. Wilson is currently spearheading the animal model studies into the use of low-dose radiation in the treatment of Alzheimer's disease along with, Drs. James Fontanesi, Alvaro Martinez, Dan Michael, Michael Maddens and others.



Publications

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