

PET IMAGING OF BRAIN FUEL UPTAKE: MOVING TOWARDS UNDERSTANDING THE LINK BETWEEN COGNITION AND BRAIN METABOLISM IN THE ELDERLY

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BACKGROUND:

Brain glucose uptake –

- Decreases in Alzheimer's disease (AD).
- Decreases with age, apparently even in the healthiest elderly.
- Is the earliest reported pathophysiological change associated with AD.

Ketone bodies (ketones) –

- Brain's principal alternative fuel to glucose.
- Nothing is known of brain ketone metabolism during healthy aging or in AD.
- Beneficial effects on cognition in AD.

QUESTION:

- Is low brain glucose uptake in the elderly specific to glucose or is it a marker of a broader metabolic problem?

APPROACH:

- Study healthy young and elderly subjects with normal glucose tolerance.
- Use positron emission tomography (PET) to compare brain uptake of the ketone – carbon-11-labeled acetoacetate (¹¹C-AcAc) – to that of glucose (18-fluorodeoxyglucose; ¹⁸F-FDG) sequentially in the same PET experiment.

RESULTS:

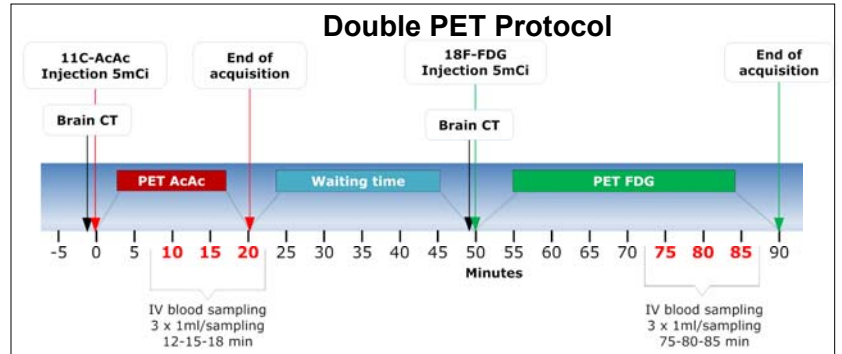
- Compared to the young (n=4) subjects, the elderly (n=3) had higher fasting plasma ketones (AcAc – 56 vs. 127 μM; β-HBA - 149 vs. 259 μM) but the same fasting glucose (~5.3 mM).
- Globally, in the elderly, brain ¹⁸F-FDG uptake was 11% lower while ¹¹C-AcAc uptake was 3% lower (statistics to be done at n=5/group).
- Aging least affected uptake of both these fuels in the thalamus and striatum.

DISCUSSION and FUTURE STUDIES:

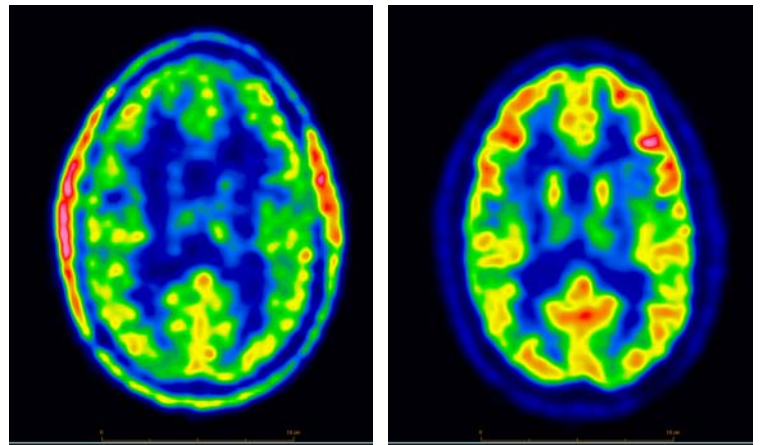
- Whether impaired brain glucose is a specific defect in aging that contributes to the risk of AD or is simply underlies a broader problem has important therapeutic implications.

• We will –

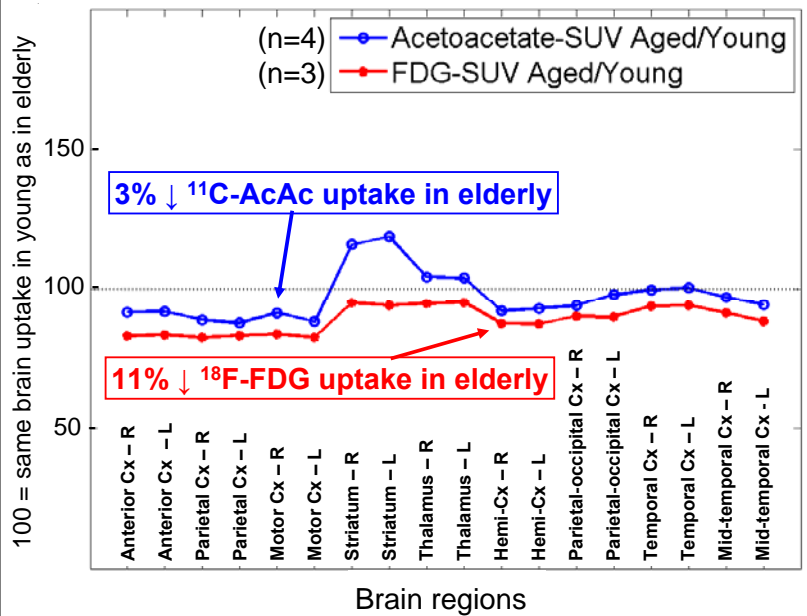
1. continue brain PET studies in the healthy elderly, and in those with mild cognitive impairment, AD, and type 2 diabetes, a major risk factor for AD.



Brain PET images of ¹¹C-acetoacetate uptake (left) and ¹⁸F-fluorodeoxyglucose uptake (right) in the same person



Fuel uptake in 18 brain regions in the healthy elderly



2. establish the merit of strategies aiming to improve the availability of fuels to the brain in order to mitigate the risks of cognitive decline in the elderly.

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