Insulin Resistance, Adiposity and Risk for Alzheimer’s Disease

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Laboratory of Behavioral Neuroscience
National Institute on Aging (NIA)
National Institutes of Health (NIH)
Effective AD treatments

Identify ‘treatable’ mechanisms

Discover ‘biologically relevant’ biomarkers

Understand disease risk mechanisms

Related to disease pathology

Sensitive to clinical heterogeneity

Gene

Environment

‘OMICs’
- Proteomics
- Metabolomics

MICROARRAYS
- Protein-protein interactions
- Autoantibodies

UNIT OF CLINICAL AND TRANSLATIONAL NEUROSCIENCE
LBN, NIA IRP
Background

Not all risk factors are equal
Unpacking the risk factor box

Insulin Resistance

Obesity

A life-course approach to the aetiology of late-onset dementias

Lancet Neurol 2006; 5: 87–96
Background

PERIPHERY
- Normoglycemia
- Impaired glucose tolerance
- Type-II Diabetes

INd u I N R E S I STANCE

BRAIN
- Normal aging
- Mild cognitive impairment
- Alzheimer’s disease
Both Insulin resistance and impaired glucose tolerance are associated with increased risk of AD and all-cause dementia.
Temporal relationship between insulin resistance and AD is unclear

*Schrijvers et al: 2010 Insulin metabolism and the risk of Alzheimer disease
The Rotterdam Study*

• Insulin metabolism influences the clinical manifestation of AD *only within 3 years.*
Is insulin resistance associated with **AD pathology**?
Is insulin resistance associated with AD pathology?

- Established in 1958 by Dr. Nathan Shock
- > 3000 participants enrolled to date
- Current enrolment 1362 subjects
- Neuroimaging substudy in 1994
- 158 participants studied by annual Brain MRI and 15O-water PET
- Since 2005 11C-PiB PET acquired on 75 individuals
- Annual blood samples ad detailed neuropsychological testing
- Typical BLSA subject has 10 annual 15O-water PET and MRI scans with multiple serial blood samples
Is insulin resistance associated with AD pathology?

**STUDY DESIGN** *(Baltimore Longitudinal Study of Aging-Autopsy cohort)*

- Impaired Glucose Tolerance
- Normal Glucose Tolerance

OGTT; 66.0 years  
Age at autopsy; 88.0 years

22.0 years

Plaques  
Neurofibrillary Tangles

CERAD  
BRAAK
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cohort(^a)</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>Autopsy (n = 197)</td>
<td>11C-PiB Scanning (n = 53)</td>
<td></td>
</tr>
<tr>
<td>Age at outcome, y(^b)</td>
<td>88.3 (7.3)</td>
<td>79.2 (5.8)</td>
<td></td>
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<tr>
<td>Sex, No. of participants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>133</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>64</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Age at first OGTT, y</td>
<td>66 (11)</td>
<td>53 (11)</td>
<td></td>
</tr>
<tr>
<td>No. of OGTTs(^c)</td>
<td>6.6 (3.2)</td>
<td>7.1 (2.7)</td>
<td></td>
</tr>
<tr>
<td>No. of OGTTs with insulin value</td>
<td>3.6 (1.9)</td>
<td>4.0 (2.5)</td>
<td></td>
</tr>
<tr>
<td>No. of participants with dementia</td>
<td>101</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Braak score</td>
<td>3.5 (1.3)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Peak CERAD score</td>
<td>1.6 (1.1)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Mean CERAD score</td>
<td>1.3 (1.0)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Composite AD pathology score</td>
<td>3.7 (1.3)</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>11C-PiB DVR score</td>
<td>NA</td>
<td>1.18 (0.27)</td>
<td></td>
</tr>
</tbody>
</table>
Glucose Intolerance, Insulin Resistance, and Pathological Features of Alzheimer Disease in the Baltimore Longitudinal Study of Aging

Madhav Thambisetty, MD, PhD; E. Jeffrey Metter, MD; An Yang, PhD; Hillary Dolan, BA; Christopher Marano, MD; Alan B. Zonderman, PhD; Juan C. Troncoso, MD; Yun Zhou, PhD; Dean F. Wong, MD; Luigi Ferrucci, MD; Josephine Egan, MD; Susan M. Resnick, PhD; Richard J. O'Brien, MD, PhD

Table 2. Effect of Glucose, Insulin, and Insulin Resistance Values on Pathological Features of AD in the Autopsy Cohorta

<table>
<thead>
<tr>
<th>Value</th>
<th>Glucose Group</th>
<th></th>
<th></th>
<th></th>
<th>Insulin Group</th>
<th></th>
<th></th>
<th></th>
<th>HOMA Group</th>
<th></th>
<th></th>
<th></th>
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<th>P Value</th>
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<tr>
<td>Lifetime fasting measure</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>91 (3)</td>
<td>98 (3)</td>
<td>113 (13)</td>
<td>&lt;.001</td>
<td>97 (11)</td>
<td>100 (9)</td>
<td>103 (11)</td>
<td>.02</td>
<td>95 (9)</td>
<td>99 (8)</td>
<td>105 (12)</td>
<td>&lt;.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin, µU/mL</td>
<td>8 (4)</td>
<td>9 (3)</td>
<td>11 (6)</td>
<td>&lt;.001</td>
<td>6 (1)</td>
<td>8 (1)</td>
<td>14 (3)</td>
<td>&lt;.001</td>
<td>5 (1)</td>
<td>8 (1)</td>
<td>14 (5)</td>
<td>&lt;.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HOMA</td>
<td>1.7 (0.8)</td>
<td>2.3 (0.8)</td>
<td>3.0 (1.7)</td>
<td>&lt;.001</td>
<td>1.3 (0.5)</td>
<td>2.0 (0.3)</td>
<td>3.5 (1.5)</td>
<td>&lt;.001</td>
<td>1.3 (0.3)</td>
<td>2.2 (0.2)</td>
<td>3.6 (1.5)</td>
<td>&lt;.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Braak score</td>
<td>3.5 (1.4)</td>
<td>3.6 (1.4)</td>
<td>3.4 (1.2)</td>
<td>.86</td>
<td>3.5 (1.2)</td>
<td>3.4 (1.5)</td>
<td>3.5 (1.3)</td>
<td>.48</td>
<td>3.6 (1.4)</td>
<td>3.4 (1.4)</td>
<td>3.5 (1.3)</td>
<td>.44</td>
<td>.46</td>
<td></td>
</tr>
<tr>
<td>Peak CERAD score</td>
<td>1.5 (1.1)</td>
<td>1.5 (1.1)</td>
<td>1.7 (1.1)</td>
<td>.50</td>
<td>1.6 (1.1)</td>
<td>1.6 (1.1)</td>
<td>1.5 (1.0)</td>
<td>.83</td>
<td>1.6 (1.2)</td>
<td>1.6 (1.1)</td>
<td>1.5 (1.0)</td>
<td>.30</td>
<td>.30</td>
<td></td>
</tr>
<tr>
<td>Mean CERAD score</td>
<td>1.3 (1.0)</td>
<td>1.3 (1.0)</td>
<td>1.4 (1.0)</td>
<td>.79</td>
<td>1.3 (1.0)</td>
<td>1.3 (1.0)</td>
<td>1.3 (1.0)</td>
<td>.71</td>
<td>1.3 (1.0)</td>
<td>1.3 (1.0)</td>
<td>1.2 (1.0)</td>
<td>.48</td>
<td>.48</td>
<td></td>
</tr>
<tr>
<td>Composite AD pathology score</td>
<td>3.7 (1.3)</td>
<td>3.7 (1.3)</td>
<td>3.7 (1.2)</td>
<td>.80</td>
<td>3.7 (1.2)</td>
<td>3.7 (1.4)</td>
<td>3.6 (1.2)</td>
<td>.81</td>
<td>3.7 (1.3)</td>
<td>3.7 (1.3)</td>
<td>3.6 (1.2)</td>
<td>.28</td>
<td>.79</td>
<td>.36</td>
</tr>
</tbody>
</table>

| Lifetime 120-min measure     |               |            |            |            |               |            |            |            |            |            |            |            |            |         |
| Glucose, mg/dL               | 114 (12)      | 146 (11)   | 198 (34)   | <.001      | 140 (41)      | 152 (32)   | 164 (35)   | .05        | 128 (28)   | 152 (40)   | 176 (35)   | <.001      |           |         |
| Insulin, µU/mL               | 45 (21)       | 60 (30)    | 73 (49)    | <.001      | 30 (7)        | 50 (6)     | 99 (34)    | <.001      | 31 (9)     | 51 (12)    | 96 (40)    | <.001      |           |         |
| HOMA                         | 13 (6)        | 22 (11)    | 36 (25)    | <.001      | 11 (6)        | 18 (5)     | 43 (23)    | <.001      | 10 (3)     | 18 (3)     | 42 (21)    | <.001      |           |         |
| Braak score                  | 3.4 (1.3)     | 3.6 (1.4)  | 3.4 (1.2)  | .59        | 3.3 (1.3)     | 3.7 (1.2)  | 3.6 (1.4)  | .26        | 3.3 (1.3)  | 3.6 (1.4)  | 3.5 (1.5)  | .28        | .79       | .36       |
| Peak CERAD score             | 1.5 (1.0)     | 1.6 (1.1)  | 1.5 (1.1)  | .67        | 1.4 (1.1)     | 1.6 (1.0)  | 1.6 (1.1)  | .53        | 1.5 (1.1)  | 1.6 (1.1)  | 1.6 (1.1)  | .36        | .53       |         |
| Mean CERAD score             | 1.3 (1.0)     | 1.3 (1.0)  | 1.2 (1.0)  | .49        | 1.2 (1.0)     | 1.3 (0.9)  | 1.3 (1.0)  | .65        | 1.3 (1.0)  | 1.4 (1.0)  | 1.2 (1.0)  | .36        | .53       |         |
| Composite AD pathology score | 3.6 (1.3)     | 3.8 (1.3)  | 3.6 (1.2)  | .53        | 3.5 (1.2)     | 3.7 (1.2)  | 3.7 (1.3)  | .39        | 3.5 (1.3)  | 3.8 (1.2)  | 3.7 (1.4)  | .53        |           |         |
Conclusions

- Insulin resistance is not associated with severity of AD pathology
- May point to molecular events downstream of Aβ fibril formation and tau aggregation
Unpacking the risk factor box

Insulin Resistance

Obesity

A life-course approach to the aetiology of late-onset dementias

Lancet Neurol 2006; 5: 87–96
“By 2030, almost 90% of American adults will be overweight”

- Wang Y et al. Will all Americans become overweight or obese? estimating the progression and cost of the US obesity epidemic.

Midlife obesity has been consistently associated with increased risk of AD

<table>
<thead>
<tr>
<th>Study</th>
<th>Population Details</th>
</tr>
</thead>
</table>

- Interval-censored data
- Cox proportional hazards

“Obese people had a 74% increased risk of dementia (hazard ratio 1.74, 95% confidence interval 1.34 to 2.26), while overweight people had a 35% greater risk of dementia (1.35, 1.14 to 1.60) compared with those of normal weight (body mass index 18.6-24.9).”
Midlife obesity has been consistently associated with increased risk of AD

However...

What is the effect of midlife adiposity on Age-at-onset (AAO) of AD?

- Most studies ignore AAO
- Focus on Age-specific incidence rates
- Rely on AD diagnosis years after measuring exposure
- When BMI data are unavailable, they rely upon self-reported weight and height at age 50 years
AAO is a phenotype with a distinct heritability
AAO is a phenotype that is important

- **NATIONAL ALZHEIMER’S PROJECT ACT**
  - **GOAL**
    - TO EFFECTIVELY TREAT ALZHEIMER’S DISEASE
    - DELAY ONSET
    - SLOW PROGRESSION BY 2025

In the United States alone, delaying AD onset even by one year will result in annual savings of 10 billion dollars at 10 years after initiating the intervention.
Does midlife adiposity affect the AAO of AD?

• N=1394 BLSA participants cognitively normal at baseline

• 8643 visits, average follow up interval; 13.9 years

• 142 cases of newly diagnosed AD

• AD diagnosis made at consensus conferences according to NINCDS-ADRDA criteria using detailed neuropsychological tests and clinical history

• Linear mixed effects model was applied on the entire BLSA longitudinal sample (N=2985; 21014 BMI observations) with body mass index (BMI) as the dependent variable to derive Best Linear Unbiased Estimates of BMI at 50 years of age.
Does midlife adiposity affect the AAO of AD?

- Parametric survival analysis using Accelerated Failure Time (AFT) models
- Midlife BMI as predictor and models adjusted for sex, APOE ε4 carrier status, education and cardiovascular risk
# Midlife adiposity and AAO of AD

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Age at baseline, mean(SD)</td>
<td>59.5 (15.6)</td>
</tr>
<tr>
<td>Male, No. (%)</td>
<td>512 (36.7)</td>
</tr>
<tr>
<td>White, No. (%)</td>
<td>1,040 (74.6)</td>
</tr>
<tr>
<td>Education, mean(SD)</td>
<td>16.0 (2.7)</td>
</tr>
<tr>
<td>Follow-up years, mean(SD)</td>
<td>13.9 (9.5)</td>
</tr>
<tr>
<td>Cardiovascular comorbidities,</td>
<td>1.06 (0.99)</td>
</tr>
<tr>
<td>BMI at age 50, kg/m²</td>
<td>25.8 (4.1)</td>
</tr>
<tr>
<td>Age at onset of AD</td>
<td>83.3 (6.8)</td>
</tr>
</tbody>
</table>
Higher midlife adiposity is associated with earlier AAO of AD

**Midlife BMI and AAO of Alzheimer’s Disease (AD) (N=158)**

<table>
<thead>
<tr>
<th></th>
<th>Fully Adjusted Model$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acceleration factor† (SE) P-value</td>
<td>Male</td>
</tr>
<tr>
<td>Age at onset of AD (time to event)</td>
<td>0.024 (0.012) 0.042</td>
</tr>
</tbody>
</table>
Higher midlife adiposity is associated with earlier AAO of AD

Midlife BMI and AAO of Alzheimer’s Disease (AD) (N=142)

Each increment of one unit in midlife BMI is associated with an earlier age-of-onset of AD by an average of 6.7 months.

Relationship between 10th percentile survival time for Alzheimer’s dementia (AD) and midlife BMI with 90% confidence intervals.
Does midlife adiposity affect AD neuropathology?

• N=191 participants with neuropathological assessment

• Clinical diagnoses prior to autopsy:
  – AD (N=71)
  – Normal (N=68)
  – MCI (N=26)
  – Non-AD dementia (N=24)
  – Cognitive impairment; not MCI (N=2)

• Age at death: 88.8(7.0)
• APOE ε4 carriers No. (%): 37 (25)
• BMI at age 50, kg/m², mean(SD): 24.9 (3.5)
Higher midlife adiposity is associated with greater AD neuropathology

<table>
<thead>
<tr>
<th>β (SE) P-value</th>
<th>Sex (1=male, 0=female)</th>
<th>Midlife BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Braak</td>
<td>-0.64 (0.34) 0.062</td>
<td>0.071 (0.027) 0.0087</td>
</tr>
<tr>
<td>CERAD</td>
<td>-0.57 (0.31) 0.063</td>
<td>0.026 (0.024) 0.27</td>
</tr>
</tbody>
</table>

Plaques

Neurofibrillary Tangles

CERAD  BRAAK
Midlife adiposity is associated with

- Earlier AAO of AD
- Greater AD Neuropathology

Yi-Fang Chuang et al. Molecular Psychiatry, 2015
Is there a common biology underlying obesity and obesity-related behaviors during aging?
The headless, hungry, unhealthy stereotype of obesity

Headless, Hungry, and Unhealthy: A Video Content Analysis of Obese Persons Portrayed in Online News

REBECCA M. PUHL, JAMIE LEE PETERSON, JENNY A. DePIERRE, AND JOERG LUEDICKE

Rudd Center for Food Policy and Obesity, Yale University, New Haven, Connecticut, USA
Is there a common biology underlying obesity and obesity-related behaviors during aging?
Is there a common biology underlying obesity and obesity-related behaviors during aging?
The fat mass and obesity (*FTO*) gene

- Strongest known susceptibility locus for obesity
- Population-attributable risk of obesity due to *FTO* is estimated to be about 20%
- 16% of individuals of European ancestry are homozygous for obesity related risk alleles of *FTO* and are at 67% higher risk for obesity
- Was originally discovered in a GWAS of diabetes
- Is associated with increased risk of AD
How *FTO* influences BMI trajectory in older adults is not clear.
Study Design

A. FTO and longitudinal changes in BMI during aging

BLSA (N=697)

1958 1960 2012
*** every 2 years ***

Baseline

B. FTO and longitudinal changes in brain function

BLSA (N=697) → BLSA-NI
N=69; 560 scans; follow-up interval 8.1 years.

[18O] water PET scans

1958 1994
Baseline

C. FTO and longitudinal changes in impulsivity and dietary patterns during aging

BLSA (N=692)

1958
Baseline

NEO-PI-R

Impulse control regions

Secondary taste area

Excitement seeking

*** every 2 years ***

7-day dietary record

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Table 1. Demographic characteristics of participants in the BLSA cohort*

<table>
<thead>
<tr>
<th></th>
<th>Whole sample (n = 697)</th>
<th>TT (n = 226)</th>
<th>TC (n = 336)</th>
<th>CC (n = 135)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at baseline, years</td>
<td>45.8±16.8 (17-96)</td>
<td>45.6±15.7</td>
<td>45.9±17.2</td>
<td>47.0±17.5</td>
<td>0.404</td>
</tr>
<tr>
<td>Female</td>
<td>325 (46.6)</td>
<td>109 (48.2)</td>
<td>1 (15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Education, years</td>
<td>16.7±2.2</td>
<td>16.7±2.1</td>
<td>1 (15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean follow-up years</td>
<td>23.1±12.0</td>
<td>23.8±11.8</td>
<td>22.7±12.2</td>
<td>23.2±11.8</td>
<td>0.512</td>
</tr>
<tr>
<td>Mean follow-up visits</td>
<td>10.5±6.0</td>
<td>10.8±6.1</td>
<td>10.3±6.2</td>
<td>10.4±5.7</td>
<td>0.596</td>
</tr>
<tr>
<td>Physical activity at baseline</td>
<td></td>
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<td></td>
<td>0.134</td>
</tr>
<tr>
<td>Sedentary</td>
<td>39 (7.6)</td>
<td>16 (9.3)</td>
<td>19 (8.2)</td>
<td>4 (3.8)</td>
<td></td>
</tr>
<tr>
<td>Light</td>
<td>191 (37.4)</td>
<td>74 (42.8)</td>
<td>80 (34.3)</td>
<td>37 (35.6)</td>
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<tr>
<td>Moderate-high</td>
<td>280 (54.9)</td>
<td>83 (48.0)</td>
<td>134 (57.5)</td>
<td>63 (60.6)</td>
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<tr>
<td>Smoking</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.652</td>
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<tr>
<td>Never</td>
<td>323 (46.3)</td>
<td>106 (46.9)</td>
<td>159 (47.3)</td>
<td>58 (43.0)</td>
<td></td>
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<tr>
<td>Former</td>
<td>296 (42.5)</td>
<td>98 (43.4)</td>
<td>135 (40.2)</td>
<td>63 (46.7)</td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>78 (11.2)</td>
<td>22 (9.7)</td>
<td>42 (12.5)</td>
<td>14 (10.4)</td>
<td></td>
</tr>
<tr>
<td>Baseline BMI†</td>
<td>24.5±3.6</td>
<td>24.5±3.8</td>
<td>24.4±3.5</td>
<td>24.6±3.4</td>
<td>0.817</td>
</tr>
</tbody>
</table>

* Continuous characteristics are expressed as mean±SD. Categorical characteristics are expressed as no. (%)
FTO and longitudinal changes in BMI during aging

\[ \chi^2 = 13.7, \text{ df} = 4, p = 0.008 \]
N=69 cognitively normal participants (43 men and 26 women; mean age 69 ± 7.3 years with mean follow-up 8.1 ± 1.1 years and total 560 scans)

Differences in longitudinal changes in regional resting state cerebral blood flow (rCBF) between obesity risk allele carriers (FTO+) and non-carriers (FTO-). Blue areas indicate brain regions that show significantly greater longitudinal decreases in rCBF in the FTO+ group.
Obesity risk allele carriers of *FTO* have reduced mPFC function during aging

<table>
<thead>
<tr>
<th>Region</th>
<th>Side</th>
<th>Coordinates x</th>
<th>y</th>
<th>z</th>
<th>T value</th>
<th>P value</th>
<th>Number of voxels</th>
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<tbody>
<tr>
<td>Decreases in rCBF</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior cingulate gyrus (32)</td>
<td>L</td>
<td>-12</td>
<td>46</td>
<td>14</td>
<td>3.54</td>
<td>&lt;0.001</td>
<td>116</td>
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<tr>
<td>Medial orbitofrontal gyrus (11)</td>
<td>R</td>
<td>10</td>
<td>34</td>
<td>-12</td>
<td>3.32</td>
<td>&lt;0.001</td>
<td>260</td>
</tr>
<tr>
<td>Anterior cingulate gyrus (24)</td>
<td>R</td>
<td>2</td>
<td>30</td>
<td>4</td>
<td>3.28</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Inferior parietal gyrus (40)</td>
<td>R</td>
<td>42</td>
<td>-60</td>
<td>42</td>
<td>3.12</td>
<td>0.001</td>
<td>56</td>
</tr>
<tr>
<td>Superior temporal gyrus (21)</td>
<td>R</td>
<td>64</td>
<td>-16</td>
<td>2</td>
<td>3.58</td>
<td>&lt;0.001</td>
<td>96</td>
</tr>
<tr>
<td>Parahippocampal gyrus (35)</td>
<td>L</td>
<td>-22</td>
<td>-24</td>
<td>-16</td>
<td>3.21</td>
<td>0.001</td>
<td>117</td>
</tr>
</tbody>
</table>
Reduced mPFC function is associated with Increased Impulsivity

- 1. Behavioral disinhibition
- 2. Risky decision-making
- 3. Delay discounting
mPFC also contains ‘taste-responsive’ neurons

Functions of the orbitofrontal and pregenual cingulate cortex in taste, olfaction, appetite and emotion

ET Rolls

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Study Design

A. FTO and longitudinal changes in BMI during aging

BLSA (N=697)

1958 1960 *** every 2 years *** 2012

Baseline

B. FTO and longitudinal changes in brain function

BLSA (N=697) BLSA-NI

N=69; 560 scans; follow-up interval 8.1 years.

[18O] water PET scans

1958 *** 1994

Baseline

C. FTO and longitudinal changes in impulsivity and dietary patterns during aging

Excitement seeking

Impulse control regions

BLSA (N=692)

1958 1989 *** every 2 years *** NEO-PI-R

Secondary taste area

7-day dietary record
NEO-PI-R
240-item questionnaire; gold standard of personality assessment
FFM of Personality (Costa and McCrae, 1990)

• Four distinct facets capture ‘Impulsivity’
  – 1. Impulsiveness: moody, irritable, and excitable
  – 2. Self-discipline: people high in impulsiveness cannot resist doing what they do not want themselves to do'
  – 3. Excitement seeking: pleasure-seeking, daring, adventurous
  – 4. Deliberation: hasty, impulsive, careless, and impatient

“\textit{I have sometimes done things just for "kicks" or "thrills."}"

“\textit{I love the excitement of roller coasters.”}"

“\textit{I have trouble making myself do what I should.”}"

“\textit{I think things through before coming to a decision.”}
**FTO** and longitudinal changes in impulsivity and dietary patterns during aging

![Graphs showing changes in excitement-seeking and fat intake over age](image)

**Excitement-seeking**

$\beta=0.06$, $t=2.21$, $P=0.027$

**Fat intake**

$\beta=0.06$, $t=2.41$, $P=0.016$
• **FTO** is a key biological basis of obesity during aging

• **Reduced medial prefrontal cortical function** – a common neural mechanism underlying obesity-related behaviors including impulsivity and food intake
Is there a common biology underlying obesity and obesity-related behaviors during aging?

FTO Genotype
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Unit of Clinical and Translational Neuroscience

• Post-doctoral fellowships available

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