Safety of Disclosing Amyloid Status in Cognitively Normal Older Adults

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Disclosures: Research funding from NIH, Avid Radiopharmaceuticals / Lilly; Speaker’s Bureau for Amyvid Reader Training
Amyloid PET Appropriate Use Criteria

• Appropriate
  – Persistent and progressive MCI
  – Possible AD with atypical course
  – Atypically early age-of-onset

• Inappropriate
  – Typical AD
  – To determine dementia severity
  – Asymptomatic individuals

Johnson, KA et al, Alzheimer’s and Dementia, 2013
Grill JD, Johnson DK, Burns JM, Neurodeg Dis Manage, 2013
Ethical Issues in Disclosing Amyloid Status

- Clinical significance imprecisely understood
- Psychological risks not studied
- Proven interventions not available
- Social, legal, or healthcare implications
- Not elevated result may give false reassurance

- Autonomy
- Prior research suggests risk info can be delivered without harm
- May facilitate lifestyle changes

Grill JD, Johnson DK, Burns JM. Neurodegenerative Disease Management, 2013
New Era of AD Prevention Trials

• Identify Alzheimer changes prior to onset of symptoms
  – Window of opportunity
• Foundation for AD prevention trials
  – Exercise
    • KU APEX study
  – Anti-amyloid strategies
    • A4 Study; Janssen EARLY Study
Alzheimer’s Prevention Program Exercise Trial (APEX)

- Cognitively normal with elevated brain amyloid
- RCT or 1-year of aerobic exercise
  - Amyloid PET
  - MRI Brain low
  - Cognition
- **Sub-study:** Assess the effect of disclosure on depression, anxiety, and test-related distress
APEX Disclosure and Assessments

• **Disclosure process**
  - Amyloid Imaging Guide
  - Pre-Scan Counseling
  - Disclosure Counseling

• **Screening for anxiety/depression**
  - BAI > 15; GDS > 5
  - Clinician impression

• **Assessments** *(Baseline, Disclosure, 6-week, 6-month)*
  - Depression (CES-D)
  - Anxiety (Beck Anxiety Index)
  - Impact of Genetic Testing Scale – distress subscale
Summary of Results

• Disclosing amyloid PET results to CN appears to be safe and well tolerated
  • n=97 (27 elevated, 70 non-elevated)
    – No effect on depression symptoms
    – Minimal, non-sustained effect on anxiety
    – Minimal effect on test-related distress
  • Predicted by baseline anxiety and depression symptoms

Burns et al, Alzheimer’s & Dementia, 2017
APEX Screening Participants

- N=101: n=1 excluded due to elevated anxiety (BAI>10);
  n=3 encouraged to not continue due to perceived anxiety

Table 1
Descriptive statistics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Amyloid elevated (N = 27)</th>
<th>Amyloid nonelevated (N = 70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>73.1 (4.8)</td>
<td>71.2 (5.7)</td>
</tr>
<tr>
<td>Education, y</td>
<td>16.2 (3.0)</td>
<td>16.8 (2.4)</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>14 (51.9)</td>
<td>45 (64.3)</td>
</tr>
<tr>
<td>Caucasian, N (%)</td>
<td>27 (100)</td>
<td>67 (95.7)</td>
</tr>
<tr>
<td>Hispanic, N (%)</td>
<td>0 (0)</td>
<td>1 (1.4)</td>
</tr>
<tr>
<td>Family history, N (%)</td>
<td>3 (11.1)</td>
<td>11 (15.7)</td>
</tr>
<tr>
<td>MMSE</td>
<td>29.2 (0.9)</td>
<td>29.1 (1.2)</td>
</tr>
</tbody>
</table>

Burns et al, Alzheimer’s & Dementia, 2017
KU Disclosure Talking Points

• **Pre-scan Counseling**
  – Written materials before visit
  – “Amyloid is a risk factor”
    • Review AD risk factors
  – Possible results
    • Elevated (not “positive”)
      – Not a diagnosis of AD
      – Indicates higher risk
      – Don’t know how high the risk or the timeframe
    • Not Elevated (not “negative”)
      – Likely lower risk of AD
      – Does not mean you will never develop AD
  – We do not share with PCP, EMR

• **Disclosure Session**
  – Same clinician
  – Review meaning of possible results
    • Elevated
      • Not elevated
  – Disclose results
    • Review meaning of their result
  – Provide feedback on lifestyle, diet, exercise
  – Information on ongoing prevention studies
Depressive Symptoms (CES-D)

Group
- Black: Elevated
- Gray: Not Elevated

Center for Epidemiologic Studies Depression Scale

Baseline | Post-disclosure | Week 6 | Month 6
---|---|---|---

Burns et al, Alzheimer's & Dementia, 2017
Anxiety Symptoms (BAI)

Burns et al, Alzheimer’s & Dementia, 2017
Disclosure-Related Distress
(Impact of Genetic Testing)

- IGT distress composite higher at 6wk and 6mo in amyloid elevated vs amyloid nonelevated
  - 12 items
    - 0=Never
    - 1=Very Rarely
    - 2=Infrequent
    - 4=Frequent
    - 5=Very Often

Upset about my test results
Sad about my test result
Anxious about test result
Perceived loss of control
Problems enjoying life because of test result
Worry about risk of AD
Uncertain about what test means for my AD risk
Uncertain about what test means for children/family’s AD risk
Frustration due to lack of AD prevention guidelines
Concern regarding how test result will affect insurance status
Perceived difficulty talking about test result with family
Regret about getting test results
Disclosure-Related Distress
(Impact of Genetic Testing)

<table>
<thead>
<tr>
<th>ITEMS</th>
<th>6 Weeks</th>
<th>6 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nonelevated</td>
<td>Elevated</td>
</tr>
<tr>
<td>Upset</td>
<td>0.10 (0.60)</td>
<td>0.60 (1.04)*</td>
</tr>
<tr>
<td>Sad</td>
<td>0.07 (0.40)</td>
<td>0.64 (1.04)*</td>
</tr>
<tr>
<td>Anxious</td>
<td>0.06 (0.38)</td>
<td>0.56 (0.96)*</td>
</tr>
<tr>
<td>Control</td>
<td>0.22 (0.68)</td>
<td>0.24 (0.52)</td>
</tr>
<tr>
<td>Lack Enjoyment</td>
<td>0.0 (0.0)</td>
<td>0.12 (0.44)†</td>
</tr>
<tr>
<td>Uncertain test</td>
<td>0.35 (0.66)</td>
<td>1.24 (1.13)*</td>
</tr>
<tr>
<td>Uncertain risk</td>
<td>0.26 (0.63)</td>
<td>1.00 (1.38)*</td>
</tr>
<tr>
<td>Frustration</td>
<td>0.28 (0.70)</td>
<td>0.88 (1.01)*</td>
</tr>
<tr>
<td>Insurance</td>
<td>0.35 (0.78)</td>
<td>0.88 (1.13)†</td>
</tr>
<tr>
<td>Difficulty talking</td>
<td>0.07 (0.40)</td>
<td>0.20 (0.58)</td>
</tr>
<tr>
<td>Regret</td>
<td>0.01 (0.12)</td>
<td>0.30 (0.76)*</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>1.77 (3.73)</strong></td>
<td><strong>7.17 (8.54)</strong>*</td>
</tr>
</tbody>
</table>

Burns et al, Alzheimer's & Dementia, 2017
Caveats

• Limited generalizability
  – Highly screened group, interested in 1 year aerobic exercise trial, 24 of 27 enrolled in trial
  – Not applicable to clinical population

• Screened for anxiety and depression (n=4 excluded)
  – Clinician judgment not replaced by surveys

• Small sample size

• Impact may change as risk estimates become more precise
Conclusions

• Disclosing amyloid PET results appears safe in setting of clinical trial with pre- and post-counseling
  – No measurable effect on depression
  – Minimal effect on anxiety and test-related distress

• Importance of structured disclosure process
  – Attention to baseline levels of anxiety and depression
  – Repetitive talking points, attention to language

• Future research: behavior change, health literacy

• *Amyloid Imaging Guide, Talking Points available for download: Burns et al, Alzheimer’s and Dementia 13(2017)1024-1030*
KU Alzheimer’s Disease Center

Key KU ADC Collaborators
Russell Swerdlow, MD
Eric Vidoni, PhD
Jill Morris, PhD
Robyn Honea, PhD
David Johnson, PhD
William Brooks, PhD
Jon Mahnken, PhD

Acknowledgements
NIH/NIA funding
The KU ADC team
Our research participants!