Pretreatment Cognitive Function in Women with Newly Diagnosed Breast Cancer

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1. Introduction
- Cognitive function in breast cancer
- Why pretreatment cognitive function matters
- Influence of stress, depression and fatigue

2. Psychosocial Predictors of Cancer-related Cognitive Change
- Goals
- Design & Methods
- Results

3. Implications for Patient Care
- Psychosocial and cognitive screening
- Psychosocial support
- Early intervention
~30-50% of BC patients self-report adverse cognitive changes at some point following diagnosis

- attention
- concentration
- memory
- word finding and way finding

Relatively little is known about

- individual differences
- psychosocial factors

These factors may distinguish patients who experience cognitive difficulties from those who do not.
Incongruity between measures of objective cognitive function and perceived cognitive function

- measurement issue—deficits may be too subtle for traditional neurocognitive tests

Current emphasis on objective testing potentially minimizes women’s lived experience of cognitive loss

Accumulating evidence that subjective cognitive difficulties

- reflect real changes in cognitive function
- correlate with gray and white matter volume changes

We need to look more closely at every day cognitive failures and their impact.
Challenging Research Issues

Another challenge is the lack of systematic patterning in patients’ cognitive function across studies.

- considerable variability in objective neurocognitive performance across the cancer trajectory
- some patients have significant impairment before initiation of chemotherapy and improvement after completion of treatment
- others show decline during and/or after treatment

Clearly, in those patients with pretreatment cognitive difficulties, deficits are not caused by chemotherapy.
Pretreatment Cognitive Function

- prior to surgery, breast cancer patients have more problems with attention than healthy controls
- 17–35% of breast cancer patients have measurable cognitive deficits before starting chemotherapy
- nearly 25% of breast cancer patients meet criteria for cognitive impairment before starting chemotherapy
- low hemoglobin may be a predictor of pretreatment cognitive impairment
- self-reports of poor cognitive function are associated with higher levels of psychological distress and fatigue

[Cimprich, 2005; Desai et al., 2005; Wefel et al., 2004; Wagner et al., 2005; Shapiro et al., 2008]
Patterns of Objective Cognitive Impairment

The PREPARE Trial (Preoperative Epirubicin Paclitaxel Aranesp) for breast cancer patients at 5 centers in Germany (n=104)

- ~30% impaired at baseline
- 27% declined after treatment
- 28% improved after treatment

[Hermalink et al., Cancer, 2007]
Patterns of Perceived Cognitive Function

Longitudinal trial at University of Pennsylvania (N=104)

A. 44% impaired PCF at baseline

B. 32% with mild continuing decline

C. 24% decline during tx and rebound

Variables associated with impaired PCF at BL were:
- college educated ($p = .03$)
- greater distress ($p < .001$)
- greater fatigue ($p = .001$)

[Shapiro, Palmer, Coyne, Wagner, & De Michele, 2008]
What Other Factors Affect Cognition?

- Aging
- Distress
- Fatigue
- Illness
- Medication

Thought (Rodin 1886-89)
Factors Affecting Cognition

- **Aging**
  - Normal age-related declines in memory and processing speed
  - Some volume loss/neuronal shrinkage in 40’s
  - Accelerated loss in 50’s and beyond
  - Cognitive slowing, but not a decline in ability

- **What’s typical?**
  - More time to recall names and words
  - Multi-tasking becomes more difficult
  - Less attention and retention of detail
Factors Affecting Cognition

- Distress

  - Numerous studies demonstrate that distress and depression have adverse effects on cognitive function.

  - Detrimental effects of transient and chronic stress on
    - attention
    - memory
    - spatial learning
    - processing speed

  - Ongoing life stress contributes to neurochemical alterations that impair neural plasticity.
Factors Affecting Cognition

Cancer Specific Distress: Cognitive intrusions/avoidance

- Intrusive thoughts and thought suppression (avoidance) interfere with working memory.
  - excess use of cognitive capacity to control intrusive thoughts
  - reduces attentional resources
  - general retrieval interference

- Essentially, worry and rumination distract from the task at hand.

[Brewin & Smart, 2005; Rassin, Merckelbach, et al., 2000]
Factors Affecting Cognition

- Fatigue
  - most frequent complaint among cancer patients
  - Sleep disruption has profound effects on attention and concentration
  - Fatigue associated with anemia
    - associations between declines in hemoglobin and cognitive function
    - in older adults, mild anemia is a risk factor for executive-function impairment
Psychosocial Predictors of Cancer-related Cognitive Change

Goals

- Examine psychosocial factors associated with both objective and perceived cognitive impairment in women with newly diagnosed breast cancer.
- Describe the nature and frequency of cognitive difficulties these women experience.
- Understand the real-life context in which these difficulties occur.
Method

- Patients maintain 7-day daily diaries of cognitive difficulties (cognitive failure events) and stressors prior to first chemotherapy
- followed by onsite assessment consisting of computerized objective neurocognitive testing and self-report questionnaires
- All testing was completed within 3 days of first chemo, prior to premedication and infusion.
Measures

**Objective Cognitive Function**
- North American Adult Reading Test (NAART)
- Cognitive Stability Index (CSI)
  - Processing Speed, Response Speed, Memory, Attention
- Controlled Oral Word Association Test (COWA)
- Animal Naming

**Perceived Cognitive Functioning**
- Functional Assessment of Cancer Therapy–Cognitive Function (FACT-Cog, V2)
  - cognitive deficiency scale
  - impact on QOL scale
Measures

Psychosocial Measures

- **Depressive Symptoms**: The Centers for Epidemiologic Studies-Depression Scale (CES-D)
- **Cognitive Intrusions /Avoidance**: Impact of events Scale (IES)
- **Fatigue**: Fatigue Symptom Inventory (FSI)
Sample

34 women stages 1-3 consented

29 completed partial data

25 completed testing session
Sample Characteristics

- Mean age = 52 year (33-82).
- 72% identified race as White/Caucasian and 24% as Black/African American
- Well-educated—69% attended college and 13% held terminal graduate degrees
- Majority (65.5%) employed full time
- 24% reported income > $70,000
- NAART estimated premorbid IQ: M =109.2 (95 –126.24)
Age and Objective Cognitive Function

- 33% had deficits ≥ 1SD below norms in one or more areas.
- Younger women’s performance was slightly below that of older women.

<table>
<thead>
<tr>
<th>CSI Domain</th>
<th>Age</th>
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<tbody>
<tr>
<td></td>
<td>Younger &lt;50 (n=13)</td>
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<tr>
<td>Processing Speed</td>
<td>94.13 (18.83)</td>
</tr>
<tr>
<td>Response Speed</td>
<td>98.33 (22.29)</td>
</tr>
<tr>
<td>Memory</td>
<td>103.75 (17.93)</td>
</tr>
<tr>
<td>Distress: CES-D</td>
<td>14.77 (6.64)</td>
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</table>
Distress and Objective Cognitive Function

- CES-D clinical cut-point \( \geq 16 \)
- Processing speed
  - information processing
  - working memory
  - language processing
- Patients often report
  - trouble taking down phone numbers
  - difficulties with mental arithmetic
  - feeling their thinking is slow

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<thead>
<tr>
<th></th>
<th>Distressed (n=13)</th>
<th>Not Distressed (n=12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSI Processing Speed</td>
<td>95.5 (21.1)</td>
<td>102.83 (10.96)</td>
</tr>
</tbody>
</table>

(standard scores: M=100, SD=15)
Cancer Specific Distress & Objective Cognitive Function (IES Cognitive Intrusions/Avoidance)

- Higher IES scores associated with poorer performance on Animal Naming (category fluency)
  - executive function
  - working memory

<table>
<thead>
<tr>
<th>Cognitive Intrusions/Avoidance &amp; Language Fluency</th>
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<tbody>
<tr>
<td>Animal Naming</td>
</tr>
<tr>
<td>IES</td>
</tr>
<tr>
<td>( r = -0.52 ) (( p = 0.027 ))</td>
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Distress, Cancer Specific Distress, PCF & Cog-QOL

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<tr>
<th></th>
<th>IES</th>
<th>PCF</th>
<th>Cog-QOL</th>
</tr>
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<tbody>
<tr>
<td>CES-D</td>
<td>.73 (p &lt; .001)</td>
<td>-.42 (p = .036)</td>
<td>.623 (p = .001)</td>
</tr>
<tr>
<td>IES</td>
<td>-.38 (p = .061 ns)</td>
<td>.37 (p = .07 ns)</td>
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- Depression symptoms were associated with
  - more cognitive intrusions/avoidance
  - Poorer perceived cognitive function
  - Greater perceived cognitive impact on QOL

- IES scores not significantly associated with perceived cognitive function trend?
  - cognitive QOL
Fatigue and Objective Cognitive Function

- FSI cut-point > 4

- Response speed
  - organizing information
  - directing attention to stimulus
  - blocking out other information and distractions

- 1 SD difference

- Only slightly below population norms

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<thead>
<tr>
<th></th>
<th>Fatigued</th>
<th>Not Fatigued</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSI Response Speed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(standard scores: M=100, SD=15)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>94.5 (18.43)</td>
<td>109.4 (16.2)</td>
</tr>
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## Fatigue, Distress & Perceived Cognitive Function

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<tr>
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<th>Fatigue Symptom Inventory Subscales</th>
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<tr>
<td></td>
<td>severity</td>
</tr>
<tr>
<td>Fact-cog</td>
<td>-.569 (p=.021)</td>
</tr>
<tr>
<td>CES-D</td>
<td>.320 (ns)</td>
</tr>
<tr>
<td>IES</td>
<td>.450 (ns)</td>
</tr>
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</table>

- This looks like simple fatigue—just feeling tired—impacts PCF
- FSI severity, current fatigue, and concentration interference drive the association between fatigue and PCF
- FSI concentration and mood interference \(\leftrightarrow\) depressive symptoms
- FSI concentration \(\leftrightarrow\) intrusive thoughts and avoidance
Women with clinically significant intrusive thoughts (IES intrusion subscale ≥ 15) and/or depressive symptoms (CES-D scores ≥ 16) reported an average of 7 cognitive failure events (CFE) per week. Compared to non-distressed women, who reported an average of 3 CFE.
Types of Cognitive Failure Events

Cognitive events were coded by categories defined by Herrmann and Neisser (1978)

- Rote Memory
- Names
- Places
- People
- Intended Actions
- Conversations
- Absentmindedness
- Retrieval of Known Data
Types of Cognitive Failure Events

- Majority of cognitive failure events were associated with absentmindedness (attentional deficits).

- Followed by:
  - Forgetting to perform intended actions
  - Conversational difficulties—particularly, word finding and difficulty expressing one’s self
  - Place and way finding events

- Lapses in retrieval of known data were less frequent, but did occur.
Examples of Cognitive Failure Events

This afternoon I was driving to the plastic surgeon for my last visit. .... I noticed that I braked at a green light for no apparent reason. I was surprised that I did that.

I went to the movies and forgot to pick up one of my friends on the way. And I forgot how to get to her house for around 10 minutes.

The nurse was very kind and asked me about my surgery. I couldn’t find the right vocabulary and began to cry.

Went to pick up flyers for a project- Went slightly blank on the way. Had to rethink the directions to the store- Where to park.

I tried to call a friend and could not remember her phone number. I call this number often. I get very frustrated when I can not function as usual.

I forgot how to spell Wednesday and I learned that in the first grade.
Conclusions

- Taken together, these results suggest that distress, fatigue and cancer-related intrusive thoughts may underlie pretreatment cognitive difficulties.

- Screening for distress and fatigue may identify women at risk for cognitive loss.

- Early intervention targeting these symptoms may improve cognitive function.
  - Psychosocial support
  - Education for symptom management
  - Stress reduction techniques
  - Cognitive skills training
Intervene for Stress and Fatigue

- Suggest Meditation
  - reduces stress
  - improves sleep
Exercise

- reduces stress
- reduces fatigue
- improves mood
- increases oxygen to the brain
- increases chemicals that support cognitive health
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Thank you!