Understanding Cancer-related Cognitive Impairment

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Agenda

• Types of cognitive problems experience
• What the research says
  – Who is at risk?
  – What is the trajectory of cognitive change?
• How to address cognitive changes
Cognitive Changes That Patients May Experience During and After Chemotherapy

- Difficulty with new learning
- Taking longer to complete tasks
- Trouble multitasking
- Difficulty finding the right word

“Chemo-brain”
Terminology

ChemoBrain / ChemoFog

Cancer-associated Cognitive Change/Impairment
Persisting cognitive complaints are common

Abbreviations: CNST, central nervous system tumor; NHL, non-Hodgkin’s lymphoma; HL, Hodgkin’s lymphoma; CRC, colorectal cancer; HNC, head and neck cancer.

Schmidt et al. (2015) J Cancer Surviv
Cognitive Complaints

More closely linked to mood and fatigue than with performance on tests of cognitive functioning
Not “all in your head”

• Combination of known & currently unknown biological changes (along with stress/mood/health behaviors)
  – Biology of cancer – inflammatory response triggering neurotoxic cytokines
  – Changes in brain structure and function
  – Poor DNA repair
  – Oxidative stress
Risk factors for cognitive decline with cancer treatment

- Genetics
  - APOE (E4 allele) related to microvascular or neural repair processes and is associated with lower cognition in long-term survivors
  - COMT (homozygotic for Val allele) – lower dopamine in frontal cortex and perform more poorly on cognitive testing than Met homozygotes
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- Older age
  - Accumulation of DNA Damage
  - Shortening of telomeres
  - Chronic inflammation
  - Increased oxidative stress
  - Depletion of stem cell reserves

- Average age of study participants is < 50
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- Cognitive reserve
  - Lower IQ and less education is associated with greater vulnerability to cognitive decline
Chemo Dose Effects

- Study looking @ women 2 years since end of chemo
- High dose chemo + tamoxifen
- Standard dose chemo + tamoxifen
- vs. early stage patients (controls)
Chemo Dose Effects

- Study looking @ women 2 years since end of chemo
- High dose chemo + tamoxifen
  - 32% cognitive impairment
- Standard dose chemo + tamoxifen
  - 17% cognitive impairment
- vs. early stage patients (controls)
  - 9% cognitive impairment
Hormone therapies

• Hormone therapies can also lead to cognitive decline
  – The combined treatment of tamoxifen and chemotherapy leads to greater difficulties than chemotherapy alone

• Aromatase inhibitors may have less impact on cognition
Well-designed research studies suggest:

- Magnitude of cognitive change associated with cancer treatment tends to be small to moderate.
Chemotherapy
Chemotherapy
Chemotherapy
Chemotherapy
Chemotherapy
Brain Structure and Function Differences in Monozygotic Twins: Possible Effects of Breast Cancer Chemotherapy

Robert J. Ferguson, Brenna C. MacDonald, Andrew J. Saykin, and Tim A. Ahles

Fig 2. Functional magnetic resonance images of 60-year-old identical twins during a working memory task with incrementally increasing levels of difficulty (left to right). Colored regions denote increased brain activation during working memory relative to a simple vigilance task. (A) Twin treated with chemotherapy; (B) twin who did not receive chemotherapy. Note the expanded spatial extent of cortical activation in the chemotherapy-treated twin.
Cognitive dysfunction is often rated as one of the most problematic post-treatment symptoms.

Survivors report that it contributes to diminished quality of life:
- Economic, emotional, interpersonal costs
- Report greater occupational difficulties

Time Course of Cognitive Dysfunction

• Up to 35% with breast cancer will have “baseline” cognitive deficits
  – Post-diagnosis, pre-chemotherapy

• High rates (≤46%) of “baseline” impairment in prostate cancer, small cell lung cancer, leukemia, testicular cancer
  – No consistent pre-treatment differences in mood, clinical, or demographic variables between those with and without pre-treatment dysfunction

(Schagen 2006; Hurria, 2006; Hermelink, 2007; Wefel, 2004, 2010; Ahles, 2008)
Pre-systemic treatment = 21% showed deficits

Primarily on tests of SPEED

Figure 2. The frequency of baseline impairment is depicted. *Exceeds expectations based on Ingraham and Aiken (1996) binomial distribution curves.
During/just after treatment = 65% showed deficits

Once treatment is initiated MEMORY becomes weak for some patients

Wefel et al., (2010) Cancer
Course of cognitive changes

- Pre-systemic treatment deficits in ~35%

- Deficits during and after treatment in ~65%
  **Largely resolve (return to normal cognitive test scores) in the 12-18 months following treatment**

- Long-term post-chemotherapy cognitive changes persist in a subgroup of 17-34% of cancer survivors

Ahles and Saykin (2007)
Course of cognitive changes

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Ahles and Saykin (2007)
Recommendations, Tips, & Strategies

- **General principles:**
  - Use areas of cognitive strength to compensate for areas of weakness
  - Recognize that you have to do things a bit differently than you normally do, and…
  - Work at it!
    - It’s not always easy to create new habits
Recommendations, Tips, & Strategies

Make it a Habit

• Research shows that habits are more deeply ingrained and resilient than "episodic" memories

• Autopilot
Recommendations, Tips, & Strategies

Pay Attention
Recommendations, Tips, & Strategies

Pay Attention

• Become an active listener
  – Meeting new people, say their name to yourself 5x and use it when you say goodbye
  – Take notes in your own words

• DEEP encoding
  ▫ Make new information as rich as possible
    ◦ Think about it in terms of multiple senses
Learning and Memory is like a file drawer

- Attend to what is going in (open a drawer)
- Make a conscious decision to remember it
- Use an organizational system for your files
  - The info will be in there, but you won’t be able to find it
Give your memory a rest

- Nobody comes through cancer younger, healthier, better rested and with less life stress

- It’s NOT CHEATING to use memory aids!!

- Take notes - organization and consistent use are key
  - Not scattered post-it notes everywhere
  - A regular part of your life (a habit!)

- Develop a system
  - Index cards in a front pocket, iPhone, detailed calendar
  - Apps like EverNote, ToDo, etc.
Recommendations, Tips, & Strategies

Become an active reader

- **PQ4R Method to study and remember factual material**
  - **P** Preview the material
  - **Q** Ask yourself questions
  - **R** Read it
  - **R** Reflect on it
  - **R** Recite answers to your questions
  - **R** Review what you’ve just done
Recommendations, Tips, & Strategies

- Review your day before falling asleep
Recommendations, Tips, & Strategies

Set yourself up for success
Set yourself up for success

- Decrease multitasking
  - Make a list of what you want to do or steps in a large task
  - Pick one to work on & complete before moving on

- Minimize distractions
  - Get your materials together ahead of time
  - Work in a quiet area or use white noise

- Give yourself plenty of time
  - Take breaks as needed so that you stay fresh
Recommendations, Tips, & Strategies

Stay mentally active

• There is not one ‘magic’ activity

• Research shows that diversity and novelty are important
  – Like physical exercise, our brains adjust
  – Socialize, take a class, play card games (preferably with others), do challenging puzzles, play along with TV game shows, go for walks
Recommendations, Tips, & Strategies

Exercise and proper nutrition

• Hatha yoga, Iyengar yoga, Qigong, Tai Chi
  – Improvements in processing speed, memory, executive functioning, quality of life in as little as 1 month

• Can help decrease fatigue
• Improve quality of life
• Reduce stress
Recommendations, Tips, & Strategies

Fatigue, sleep disturbances

- Level of fatigue is more closely tied one’s degree of distress than to the cancer type or treatment

- Activities take longer to complete, decreases mental efficiency
Recommendations, Tips, & Strategies

• Very good evidence that memories are consolidated (made more permanent) during sleep
  – We need about 6 hours of natural sleep to make stable memories

• Beware of sleep medications- some can interfere with memory consolidation
Healthy Sleep Habits

• Keep a regular schedule - meals, meds, exercise, etc.
  – Get up at the same time every morning
• Avoid naps
• No caffeine after lunch
• Avoid alcohol within 6 hours of bedtime
• Don’t smoke or use nicotine before bed
• Don’t be too hungry or too full
Healthy Sleep Habits

• Avoid strenuous exercise in hours before bed
• Establish rituals that help you relax each night before bed (bath, snack, reading)
• Don’t go to bed unless sleepy
• If you’re not asleep after 20 minutes, get up
• Bedroom should be like cave = quiet, dark, cool
• Use the bed only for sleep and sex
Other Causes of Cognitive Difficulties

- **Stress**
  - Reaction to diagnosis
  - Managing treatment challenges
  - Impact on work and family life
  - Financial challenges
  - Changes in self image and autonomy
  - Sexual dysfunction
  - Changes in life course
    - Adjusting to how life might be/is different
Other Causes of Cognitive Difficulties

• **Depression & anxiety undermine cognition**
  – Tend to be under recognized, under diagnosed & under treated
Other Causes of Cognitive Difficulties

• **Depression & anxiety**
  – May coexist with treatment
    • Some medications/treatment contribute
      – Examples = corticosteroids, whole brain radiation
  – May arise because of malignancy itself
    • Example = depression & pancreatic cancer
  – May result from unknown causes
Over the course of a year following diagnosis, 16.6% meet criteria for a depressive disorder.
Mood, Anxiety & Distress

- Cognitive complaints are more closely tied to mood symptoms and distress than they are to actual performance on cognitive testing
  - This does not de-legitimize patient experiences of cognitive lapses
  - Does indicate a form of treatment may be effective at relieving distress and improving cognition
Treatments for Cognitive Decline

• Psychotherapy and supportive counseling
• Medications
  – Antidepressants for mood
  – Anti-anxiety medications
  – Psycho-stimulants for attention and fatigue
  – Sleep aids
  – Memory-enhancing medications
• Formal cognitive rehabilitation programs
# Compensatory Strategies

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Thank You!

Questions

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