Cognitive Change

To Lumosity or not to Lumosity?

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Overview

• Background
  – Cognition: Are some patients more at risk than others for cognitive impairment following treatment?

• What cognitive changes commonly occur?
  – Cognitive complaints versus cognitive impairment
  – Multiple candidate mechanisms for cognitive impairment

• Research
  – Cognition, genetics, brain function and brain structure

• Interventions for cognitive complaints and impairment
Background

• Each year, more than 1.6 million individuals are diagnosed with cancer in the US

• There are almost 14 million US cancer survivors and more than 25 million world wide

• Cognitive complaints are relatively common during and after treatment & may persist for many survivors

• Multiple candidate mechanisms proposed for these complaints and they are often associated with other post-treatment symptoms
Background

• Not Everyone has cognitive changes

• Treatment for cancer is important

• Should not avoid treatment only out of concerns for cognitive changes – should understand the risks and how to work to improve them.
The Amazing Human Brain
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Candidate Mechanisms for Cognitive and Brain Changes

Ahles and Saykin Nature Reviews Cancer 7, 192–201 (March 2007) | doi:10.1038/nrc2073
Risk Factors......

• Age
• Cognitive reserve or vulnerability
• Age and medication interaction (e.g. Tamoxifen has stronger effects on cognition in older patients)
• Whole Brain Radiation
• Genetic predisposition/vulnerability to chemotherapy and/or cognitive impairment

• APOE, COMT
  • poor DNA repair
• Menopause
• Hormonal therapy
• Anxiety, depression,
• Supportive care meds
• Comorbid medical conditions
• Surgery and anesthesia
• Sleep disturbance.
• Blood Brain Barrier Breakdown
In Summary: There is likely a Multi-factorial Etiology

- Anxiety and depression
- Pre-existing genetic factors
- Changes in estrogen levels
- Toxic effects of chemotherapy
- Proinflammatory cytokines influence on brain function
What do the research studies tell us about specific cognitive changes?

- Few studies until about 20 years ago, when research began to increase
- Real consensus in 2003 regarding presence of cognitive change
- Initial cross-sectional designs in survivors
  - Poorer NP performance with chemotherapy exposure
  - No consistently identified domains
  - Self-reported cognitive complaints NOT usually associated with NP performance
  - Various chemotherapy regimens
General Cognitive Findings During or Just Following Treatment (lots of “noise” in research, reflects cortical and subcortical changes)

Attention
  - Concentration
  - Switching attention from one task to another
  - Ignore distractions
  - Attention to detail

Mental Processing speed
  - How quickly one can think, respond

Motor
  - Dexterity, coordination, speed

Memory
  - Short- and Long-term memory
  - Learn and recall words, stories
  - Remember events versus facts
  - Remember designs, faces

Executive function
  - Organizing, planning and carrying out a plan
  - Problem solving
  - Reasoning
  - Multi-tasking

Working memory
  - Mentally manipulate information

Visuospatial functioning
  - Copying, use blocks to make 3-D designs, map reading, hand-eye coordination

Language
  - Naming
  - Word retrieval
Self-Reported Complaints (often related to slowed processing speed and variable attention)

• Difficulty finishing something started
• Inefficient at doing well-known tasks
• Problems planning and carrying out a plan
• Problems multi-tasking; difficulty managing complex tasks
• Difficulty learning and remembering new things
Meta-Analysis of Cognitive Functioning in Breast Cancer Survivors Previously Treated With Standard-Dose Chemotherapy


Visuospatial ability—Figure copy, block designs

Verbal Ability—word generation, naming

On average, across all studies, over time cognitive deficits are limited to these two domains in breast cancer survivors treated with chemotherapy.
Specific Example of Course of Cognitive Symptoms in Breast Cancer Patients Over Time

- Anxiety and depression are common, and associated with cognitive complaints
- Impaired NP test performance found prior to chemotherapy treatment
- Decline in NP function during treatment that recovers by a year
- Symptoms and decrements in quality of life (QOL) are common at end of primary treatment and resolve over time in most patients
- A subset of breast cancer problems have persistent cognitive complaints and poor QOL.
Brain Function: Effects of Chemotherapy on the Brain in Cancer Discordant Twins

Twin Study: A is patient with breast ca and B is her identical twin without breast ca.

Chemotherapy exposed brains may have to work harder to compensate for damage to neural networks   Ferguson et al. JCO 2007
Gray matter reduction associated with systemic chemotherapy for breast cancer: a prospective MRI study

Brenna C. McDonald · Susan K. Conroy · Tim A. Ahles · John D. West · Andrew J. Saykin

Short-term effects of chemotherapy on brain structure

Areas in red indicate gray matter density declines in chemotherapy patients 1 month after treatment.

Fig. 2 Regional gray matter density declines in chemotherapy-treated breast cancer patients from baseline to 1 month after chemotherapy
Chemotherapy Altered Brain Functional Connectivity in Women with Breast Cancer: A Pilot Study

Julie A. Dumas¹,*, Jenna Makarewicz¹, Geoffrey J. Schaubhut¹, Robert Devins¹, Kimberly Albert¹,², Kim Dittus³, and Paul A. Newhouse¹,²

Figure 1.
Functional connectivity in the dorsal attention network ($p < .05; k = 1000$) that decreased at one month and recovered one year after chemotherapy treatment.
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Figure 2.
Functional connectivity in the default mode network ($p < .05; k = 1000$) that decreased one
Potential Treatments

- First, address untreated depression, pain, and anxiety
- Ensure adequate sleep
- Focus on management of fatigue
- If complaints persist, obtain consultation from a trained neuropsychologist familiar with cancer treatment
- Role of pharmacological agents
Treatment with modafinil embedded within a fatigue study, increase wakefulness also see better memory.
To Lumosity or Not to Lumosity?

Research says.....

Not Really
Only if you want to.

The power of play: The effects of Portal 2 and Lumosity on cognitive and noncognitive skills

Valerie J. Shute*, Matthew Ventura, Fengfeng Ke

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So, what can I do?

• Cognitive Rehabilitation: individualized treatment, to address *personal, relevant functional goals* – less emphasis on particular cognitive functions.

• Compensatory Strategies: ways to “work around” or adapt to cognitive weaknesses

• Restorative: retraining of cognitive skills after a loss of function.
Cognitive Rehabilitation Techniques

Determine what is important to you.

The brain thrives on structure/routine, but seeks novelty and learning.

A lot of the recommendations for cognitive rehabilitation are things you’re already doing – to improve automaticity.
Cognitive Rehabilitation: Routine/Structure

- Keep the same sleep/wake schedule every day
  - Sleep hygiene
- Keep a daily planner or calendar. Get into the routine of using it *everyday* for *every activity*.
  - The use of alarms
  - The use of emojis
- Establish a daily schedule at the beginning of your day
- Complete tasks one at a time.
- Environmental Modifications
  - White board in a highly visibly place
  - Things you want to remember together, place together.
- In the beginning, allow yourself some extra time.
Cognitive Rehabilitation: Novelty and Learning

• Change tasks frequently (according to your daily schedule).
  • Take breaks - working while tired will NOT be helpful to anyone!

• Least interesting tasks (or hardest task) when you’re at your “cognitive best”

• Keep your brain and body active!
  • Engage in physical activity daily
  • Seek out cognitive stimulation: reading, problem solving, social interactions, listening to the news, volunteering, employment
  • Find things you find interesting, and do them!

• Get in touch with a therapist or counselor
Memory Specific Rehabilitation Techniques:

- Identify the information to be remembered
  - Say it back
- Minimize the amount of information to be remembered
  - Write it down
  - Chunk similar things together
- Structure the information to learn, make this as meaningful as possible
  - Visual imagery, relate it to a story, etc
- Define a cue to retrieving the information
  - Visual or verbal
- Rehearse what needs to be remembered.
  - Practice!