Maximizing Cognitive Function

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Progress In Oncology

Improved survival time → Improved survivorship

DeSantis et al., 2014; Cancer Research UK
Progress In Brain Tumors

Improved survival time → Improved survivorship

Longer survival in patients with 1p/19q codeleted AO/AOA treated with PCV followed by radiation

Longer survival in patients with GBM treated with Optune and temozolomide after concurrent TMZ/XRT
Multiple Signs and Symptoms

- 75% of patients have 3+ symptoms
  - Cognitive changes
  - Fatigue and sleep disturbance
  - Headache
  - Motor changes
  - Seizure
  - Mood disturbance
  - Personality change
  - Sensory change
- Moderate to severe in <20%
- Functionally limiting (work, walking, ADLs) in 25%

- 28-33% return to competitive employment
  - Reduced hours (part-time)
  - Increased work limitations
  - Increased time off

Litofsky et al., Neurosurgery, 2004; Wellisch et al., Psycho-Onc, 2002; Armstrong et al., Neuro-Onc, 2016
GAP: NBTS Patient Needs Survey

- Online survey of 1411 patients and caregivers (709 patients, 702 caregivers)
  - N=709 patients (30% GBM), N=702 caregivers (68% HGG)
  - Finding information on cognitive changes was rated the most difficult
Family and caregivers surveyed reported cognitive & neurobehavioral problems more troubling than physical problems.

Cognitive decline is associated with and precedes decline in activities of daily living and HRQOL.

TOP PRIORITIES FOR FUTURE BRAIN TUMOR TREATMENTS (other than living longer)

- Retain brain functioning
- Maintain ability to walk and perform basic physical tasks
- Reduce pain, including headaches

GBM/Astrocytoma, Oligodendroglioma, and Meningioma caregivers
Brain Organization and Function

• Cognitive dysfunction is common in brain tumor patients
Brain Organization and Function

- 100 billion neurons, 60 trillion synapses

Simulation: 3M neurons, 476M synapses

Milky Way Galaxy
100-400 billion stars

(<0.00003%)
Contributors to Cognitive Decline

steroids, seizures, anemia, fatigue, endocrinologic disturbance, depression and anxiety, pain medicines, medicines with anticholinergic properties...
Mitigating Cognitive Decline

- Radiation and Chemotherapy
  - Goal: kill tumor cells and control tumor growth
  - Toxicity: Off target (on target, off tumor) normal tissue toxicity

- Risk reduction:
  - Reduce radiation to normal brain
    - IMRT, Proton, SRS, HA-WBRT
  - Cognitive outcomes in trials
  - Molecularly targeted therapy

- Neuroprotection:
  - Memantine, Donepezil
  - Others??

<table>
<thead>
<tr>
<th>Months from Randomization</th>
<th>Memantine</th>
<th>Placebo</th>
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<tr>
<td>3</td>
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</tbody>
</table>

Failures: Memantine 219, Placebo 256
Total: Memantine 256, Placebo 252
p (one-sided) = 0.01
HR = 0.784 (0.621, 0.988)
Management and Intervention Strategies

• Team approach
  • You and your family
  • Physicians and nurses
  • Neuropsychologists
  • Psychiatrists
  • Social workers
  • OT, PT, SLP

• Common comorbidities
  • Fatigue, sleep disturbance, mood disturbance

• Cognitive rehabilitation
  • General and Specific approaches (memory)
Managing Cognitive Dysfunction

Gordon Paul (1969), “The ultimate clinical question”: “What treatment, by whom, is most effective for this individual, with that specific problem, under which set of circumstances, and how does it come about?”
Maximizing Cognitive Function

• Manage cognitive deficits
  • Comorbidities
    • Reversible contributors
  • Maintain Brain Health
    • Diet and Exercise
    • Stress Management, Social Engagement
    • Proper Sleep
  • Pharmacological
    • Stimulants (fatigue, attention, processing speed)
    • Donepezil
  • Behavioral
    • Compensatory strategies
    • Neuroplasticity-based training?
“Reversible” Contributors - Comorbidities

- Metabolic abnormalities
  - Thyroid abnormality
  - Electrolyte abnormality
  - Glucose abnormality
  - Vitamin deficiencies
  - Cushing’s disease
  - Addison’s disease
  - Organ failure (liver, renal, respiratory)

- Medication side effects
  - Anticholinergics, pain meds
  - Seizures
  - Edema
  - Substance use/abuse
    - Poor adherence to medication schedule due to cognitive deficits
    - Pill box, alarms, caregiver support
• Definition of Cancer-Related Fatigue
  • National Comprehensive Cancer Network: “a distressing, persistent, subjective sense of physical, emotional, and/or cognitive tiredness or exhaustion related to cancer that is not proportional to recent activity and interferes with usual functioning”
Manage Comorbidities - Fatigue

• Fatigue
  – Identify and treat underlying correctable medical conditions
  – Regular exercise, sensible diet
  – Activity scheduling and energy conservation
  – Sleep 7-9 hours
  – Stimulants

• Sleep disturbance
  – Sleep hygiene
    • Institute a consistent sleep schedule
    • Limit vigorous activities and caffeine before bed
    • 10 minute toss and turn rule
    • Don’t use daytime naps as substitute
    • Stress management
  – Identify modifiable medical contributors
    • Timing of medications
  – Sleep study
Management and Intervention: Mood Changes

- Depression and Anxiety

- Talk to your health care team
  - Counseling
  - Support groups
  - Behavioral activation
  - Medications

MHS-61: 93% Depressed, 7% Not Depressed
3-Q: 73% Depressed, 27% Not Depressed
Doctors: 85% Depressed, 15% Not Depressed
Management and Intervention: General Brain Health

Get Moving
- Aerobic: 150 minutes moderate / 75 minutes vigorous
- Strength: 2x/week

Eat Smart
- **Dietician
- Low-carb diet
- Mediterranean diet
- DHA/Omega-3
- Coffee/tea
- Turmeric
- Avoid: saturated fat, trans fat, added sugars

Control Risks
- Blood pressure
- Cholesterol
- Avoid smoking
- Moderate alcohol intake

Rest Well
- 7-9 hours sleep

Stay Connected
- Stimulating conversation
- Social support
- Insulates against stress

Keep Sharp
- Stay mentally active
- Remain curious
- Learn new hobby, skill...
- Play: engage your brain

https://healthybrains.org/pillars/
Management and Intervention: Cognitive Rehabilitation

- Goal: reduce the interference of cognitive inefficiencies on everyday life
- Compensatory strategy training
  - Utilize preserved skills to support areas of cognitive weakness
    - Use visual memory capacity to support verbal memory disorder
  - Self-awareness to identify “at-risk” situations for cognitive failures
  - Minimize distractions
- Cognitive prostheses
  - Memory prosthesis - Smart phone (calendar, alarms, etc.)
- Environmental modifications
- Psychotherapy and psychoeducation
  - Improve coping, stress management
  - Brain injury and functional impact
  - Identify high risk situations, anticipate and plan
Management and Intervention: Memory

- Cognitive Prostheses – External memory aides

High Tech

“Memory Prostheses”

Low Tech

“Memory Station”
Management and Intervention: Memory

• Compensatory Strategies – Enhance memory by.…
  – Optimizing Attention
    – New learning takes concentration and effort, find best time of day
    – Slow down, minimize distractions/interruptions, work on 1 thing at a time, paraphrase new information, take frequent short breaks
  – Facilitating Encoding/Learning
    – Repeat to be learned information
    – Make a note
    – Practice Spaced Rehearsal
    – Process information in multiple modalities
      • Speak it, write it, read it
      • Use imagery (3 feet in a yard)
Management and Intervention: Memory

• Compensatory Strategies – Enhance memory by….
  – Making associations, increase organization
    – Mnemonics: e.g., acronyms
      • Goal: How do I remember the Great lakes?
      • Strategy: HOMES (Huron, Ontario, Michigan, Erie, Superior)
  – Chunking: IBMPHDMTVCBS ….. IBMPHDMTVCBS
  – Deep encoding strategies
    • Association: Relate new info to something you already know
    • Elaborative rehearsal: talk in depth about the piece of information to increase familiarity and relevance
  – SQ3R method for reading
Management and Intervention: Executive Function

• Goal management training: increase ability to maintain intentions in goal directed behavior

• S.T.O.P. technique
  • Stop
  • Think
  • Organize
  • Proceed

• Increased externally guided structure
Management and Intervention: Computerized Cognitive Exercises

- A Brain-Plasticity Based Computerized Intervention to Treat Attention and Memory Problems in Adult Brain Tumor Survivors

**Brain tumor survivors**
- cognitive complaint
- attention/memory impairment

**Computerized Training Intervention:**
- 40 PACR sessions: 1 hour per day, 5 days per week for a total of approximately 8 weeks

**Feasible?**
- 60% Feasible
- 40% Not Feasible

**Useful?**
- 22% Very Satisfied
- 33% Somewhat Satisfied
- 44% Neutral

**Recommend?**
- 100% Yes
Management and Intervention: Computerized Cognitive Exercises

- A Brain-Plasticity Based Computerized Intervention to Treat Attention and Memory Problems in Adult Brain Tumor Survivors

<table>
<thead>
<tr>
<th>Test Type</th>
<th>Pre</th>
<th>Post</th>
<th>p-Value</th>
<th>d</th>
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<tbody>
<tr>
<td>Speed of Processing and Attention</td>
<td>p = .02, d = 1.29</td>
<td>p = .04, d = .32</td>
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<tr>
<td>Speed of Processing and Working Memory</td>
<td>p = .07, d = .44</td>
<td>p = .12, d = .52</td>
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<td>Emotional Recognition</td>
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<td>Categorization</td>
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<tr>
<td>Composite, %ile</td>
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* Significant difference
Management and Intervention: Behavior Changes

• Behavioral and Personality Change
  – Determine if the issue is due to the situation, disease, or treatment
  – May require counseling and medications

  • Positively reinforce appropriate behavior that represents progress away from problem behavior

  • Apply adaptive strategies in place of problem behaviors
    • Stressful situations may require you to remove yourself from the activity rather than insist the behavioral reaction is inhibited while remaining in the stressful situation

  • Understandable plan, implement consistently, patience
Caregivers

• RECAPS
  • Reminders (spoken, written, pictures)
  • Environment (don’t change surroundings, memory station)
  • Consistent routines (keep up with familiar routines, make new ones)
  • Attention (avoid distractors, cue to focus)
  • Practice (skills from therapy, and old skills)
  • Simple steps (break tasks into simple, concrete steps, allow extra time)
Caregivers

• **MESSAGE**
  - Maximize their attention
  - Control your **Expression** (show interest)
  - Keep it **Simple** (short, simple, familiar, provide choices)
  - **Support the conversation** (extra time, repeat, rephrase)
  - Assist with visual aids
  - Get the message (interpret, circumlocute, nonverbal as well)
  - Encourage and engage
Caregivers

- Your role in cognitive rehabilitation
- Know how the “deficit” will impact “abilities”
- Learn the strategies
- Support the continuation of progress

Boele et al. (2013) demonstrated that six 1-hour CBT oriented personalized psychoeducation sessions with caregivers resulted in:
  - Better mental function
  - Improved caregiver mastery

Boele et al., JNO, 2013
Other Resources

• Online resources
  • American Brain Tumor Association:
    http://www.abta.org/care-treatment/
  
    http://www.psypress.com/neuropsychological-disorders/resources/

• Bibliotherapy
  
Thank you!