GOALS:
1. Discuss the types of cognitive problems that patients experience and how those problems are related to the functioning of different brain networks and systems.
2. Explain the process of neuropsychological evaluation and describe how it may be helpful for an individual who is dealing with cognitive symptoms.
3. Describe the (very limited) scientific literature regarding the nature and causes of these problems.
4. Provide suggestions for coping with these problems on a day-to-day basis.
Cognitive Functions

What is ‘Cognition’
• All of the skills of thought
  – Concentration
  – Language skills
  – Visual Spatial Skills
  – Memory
  – Executive Functions
    • Reasoning & Problem Solving
    • Judgment
    • Impulse Control
    • Flexibility
    • Planning, Sequencing & Organizing

How do aplastic anemia, MDS and PNH effect cognition?
• Anemia and related fatigue
• Immune Response Activity
• Treatment & Related Factors
Attention and Concentration

- Ability to focus and sustain attention
- Ability to ignore distractions
- Hold and manipulate information in short term memory
Attention and Concentration

- “Gateway” for information flow to the brain*
- There are limits on the amount of material you can process at one time
- Attention Span
  - Rehearsing a series of numbers forwards and backwards


Processing Speed

- Speed of processing is related to attention
  - How quickly one “processes” information
  - Simple vs. complex
  - Multi-tasking
Processing Speed - ‘Simple’

- Visual Scanning

Processing Speed - ‘Complex’
Language

- Reading
  - Word recognition
  - Comprehension
- Language Production
  - Fluency
  - Phrase Length
- Naming (Word Finding)
- Comprehension
- Writing

Visuospatial

- “Where” pathway (blue)
  - Location of objects in space
- “What” pathway (yellow)
  - Identify objects
  - Recognize faces
- Integration/construction
  - Image rotation
  - Drawing
Visuospatial

[Images of geometric shapes and drawings]
Memory

Recent memory:
• Encoding (Ability to learn new information)
  – Getting the information in – highly related to attention
  – Depends on focus and processing speed
• Storage (Consolidation)
  – Free recall of information after a delay/distractor interval
  – % retention
  – Depends on the hippocampus
• Recognition
  – Use recognition paradigm (yes/no) to distinguish retrieval from consolidation based memory deficits.
Memory

Executive functions

• “Frontal lobe” tests
  – Reasoning & problem solving
  – Inhibition
  – Shifting
  – Initiation, cessation, perseveration
• Other qualitative executive skills
  – Awareness/insight
  – Judgment
• Requires integration of other domains, efficiency
### Stroop Color Word Test

#### Read word

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Personality/Emotion

- Clinical interview
- Standardized measures
  - Mood measures
    - Beck Depression Inventory
    - Beck Anxiety Inventory
    - Patient Health Questionnaire
  - Personality measures
    - MMPI
    - Personality Assessment Inventory

How do AA and MDS effect cognition?

- Anemia and related Fatigue
- Immune Response Activity
- Treatment & Related Factors
How do aplastic anemia, MDS and PNH effect cognition?

Anemia

- Fatigue
  - Results in a reduction in arousal
    - Attention/Concentration
    - Processing speed
  - People experience a “memory” problem
    - Due to reduced encoding
- In severe anemia, low hemoglobin can result in hypoxemia (low oxygen levels) in the brain, but this is very rare.
Scientific study of Cognitive Impairment in MDS (& AML)

- Many people with cancer have problems with memory, fatigue, and depression
- Treatment often worsens these symptoms
- The symptoms may not go away after treatment is finished
- These symptoms may have to do with cytokine-immunologic activation.

Meyers et al., 2005 Cancer; 104: 788-793.
Scientific study of Cognitive Impairment in MDS (& AML)

- Cytokines have significant effects on brain function.
- Individuals with MDS/AML have elevated levels of cytokines.
- Individuals with MDS/AML are treated aggressively with multi-agent chemotherapy that may also increase cytokine production.

Meyers et al., 2005 Cancer; 104: 788-793.

Scientific study of Cognitive Impairment in MDS (& AML)

- Gave neuropsychological tests to 54 people with MDS/AML before chemotherapy
  - 26 returned for follow up testing 1 mo after completing treatment
- **Age:** Average = 60 years (range = 21-84)
- **Gender:** 30 male/24 female
- **Diagnosis:**
  - Myelodysplastic syndrome = 35
  - Acute Myelogenous Leukemia = 19
- **Response: (1 month)**
  - Complete = 19 (14 seen at follow up)
  - Partial or no response = 23 (8 seen at follow up)
  - Not evaluated = 12 (4 seen at follow up)

Meyers et al., 2005 Cancer; 104: 788-793.
Scientific study of Cognitive Impairment in MDS (& AML)

• Cognitive domains tested:
  – Attention
  – Processing Speed
  – Recent Memory
  – Cognitive Flexibility
  – Motor Dexterity

• Other areas assessed:
  – Activities of daily living
  – Fatigue
  – Quality of Life

Meyers et al., 2005 Cancer; 104: 788-793.

Scientific study of Cognitive Impairment in MDS (& AML)

• Biological variables
  – Levels of various Cytokines in blood
    • Interleukins 1, 6, 8
    • Tumor Necrosis Factor – Alpha
  – Hemoglobin levels

Meyers et al., 2005 Cancer; 104: 788-793.
Scientific study of Cognitive Impairment in MDS (& AML)

• Results
  – Many people had cognitive symptoms before treatment
  – Treatment did not have a significant impact on cognitive function but fatigue levels tended to increase

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<thead>
<tr>
<th>Test</th>
<th>Baseline (n = 54)</th>
<th>Follow-up (n = 26)</th>
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<td>Psychomotor speed</td>
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<tr>
<td>Total recall</td>
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<td>58</td>
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<tr>
<td>Immediate recogn</td>
<td>7</td>
<td>25</td>
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<tr>
<td>Delayed recall</td>
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<tr>
<td>Verbal fluency</td>
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<td>Visual scanning</td>
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<tr>
<td>Executive</td>
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<td>46</td>
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<tr>
<td>Dexterity</td>
<td>37</td>
<td>54</td>
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</tbody>
</table>

*Impairment was defined as ≥ 1.5 standard deviation below the normative mean.

Meyers et al., 2005 Cancer; 104: 788-793.

Scientific study of Cognitive Impairment in MDS (& AML)

• Take home points
  – Individuals with MDS/AML are at risk for cognitive dysfunction as a consequence of their disease
  – Cognitive impairments were not related to fatigue or anemia
  – There is a relationship between cognitive symptoms and cytokine levels, suggesting that the symptoms may be related at least in part to cytokine-immunologic activation.

Meyers et al., 2005 Cancer; 104: 788-793.
How do aplastic anemia, MDS and PNH effect cognition?

- Anemia and related Fatigue
- Immune Response Activity
- Treatment & Related Factors

How do aplastic anemia, MDS and PNH effect cognition?

- Treatments
  - Chemotherapy
  - Immunotherapy
  - Stem cell Transplant
- Complications of Treatment
  - Infection
How do aplastic anemia, MDS and PNH effect cognition?

• Emotional reactions to diagnosis and treatment
  – Increased stress
  – Anxiety
  – Depression
• Medication Side Effects
  – Pain medications

Cognitive Effects of Chemotherapy

• Concept of ‘chemo brain’ is controversial
• Widely used term but it’s not clear whether chemotherapy is the cause of concentration and memory problems
• Individuals with memory problems may still perform well on cognitive tests
Cognitive Effects of Chemotherapy

• Chemo agents damage the white matter

• White matter = brain's fibers of connection
• Chemotherapy may damage myelin
• Reduces attention, processing speed

Chemo brain

• Signs and symptoms may include:
  – Difficulty concentrating/short attention span
  – Short term memory problems
  – Difficulty finding the right word
  – Difficulty learning new skills
  – Difficulty multitasking
  – Being unusually disorganized
Chemo brain

• Signs and symptoms (cont):
  – Taking longer than usual to complete routine tasks
  – Trouble with memory, such as recall of a conversation or an image

Chemo brain

• Signs and symptoms of cognitive difficulties vary from individual to individual
• Usually temporary
• Often subside within 2 years of treatment
Treatment for cognitive problems

- Medications
  - Attention enhancers
  - Memory enhancers

- Does brain ‘exercise’ help?
  - It’s better than nothing…
  - …but not necessarily better than anything else
  - Buyer beware

Maintaining Brain Health

- Physical exercise
  - Helps promote overall brain health
  - Improves blood flow to the brain
  - Can help reduce the loss of brain with aging
- Talk to your doctor about the level of exercise that is safe
  - General guidelines are similar to those for heart health
Maintaining Brain Health

- The value of exercise

![Graph showing hippocampus volume changes](image)

Erickson et al., 2011, *Proceedings of the National Academy of Sciences*

Maintaining Brain Health

- Compensatory strategies are most effective method
  - Use a daily organizer
  - Write down information
  - Avoid distractions
  - Ask people to repeat information
  - Get plenty of rest
  - Practice tasks
Maintaining Brain Health

• If you experience memory thinking problems that are troubling or significantly interfere with daily function, discuss with your doctor.

• Keep a journal of signs and symptoms so your doctor can better understand how these problems are affecting your everyday life.

Maintaining Brain Health

• Neuropsychological Evaluation

• Cognitive Rehabilitation Specialists
  • Speech therapy
  • Occupational therapy
Summary

• The brain is not considered a primary site of pathology in AA and MDS
• Despite that, many factors combine to effect brain function and cognition
• Primary issues include:
  – Fatigue
  – Immune system processes
  – Treatment side effects
  – Emotional reactions to diagnosis

Summary (cont)

• Cognitive problems are best managed by maintaining good general brain health and developing strategies on an individual basis

• Neuropsychological evaluation is a useful way to understand if there is a cognitive problem, the nature of it, and strategies to deal with it
Questions?