Cognition in Cancer Survivorship

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No conflicts of interest to disclose.

Overview

- Cancer Survivorship
- Cognition and Neurocognitive Disorders
- Cancer and Cognition
- Clinical Considerations

Learning Objectives:

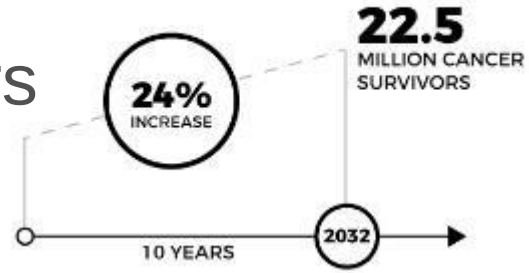
1. Describe evidence for the phenomenon of Cancer-Related Cognitive Impairment
2. Describe how to respond to cognitive symptom reports in cancer survivors.

Survivorship

Survivorship Today

Present and future

- 2022 – 18.1 million cancer survivors in US
- Currently 12.5 million survivors living 5+ years after dx. (nearly 4% of US pop.)
- Projected next decade growth of 5+ year cancer survivors to 16.3 million



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Cognition

Cognition in the Clinic

- **cognition** refers to processes of perceiving, evaluating, recalling and responding to sensory input.

- In practice cognitive ability is evaluated in terms of **domains of cognition**.

Cognition in the Clinic

- **Domains of cognition (each w/subdomains)**

Sensation
Perception
Motor skills and construction
Attention and concentration
Memory
Executive functioning
Processing speed
Language/verbal skills
Social Cognition

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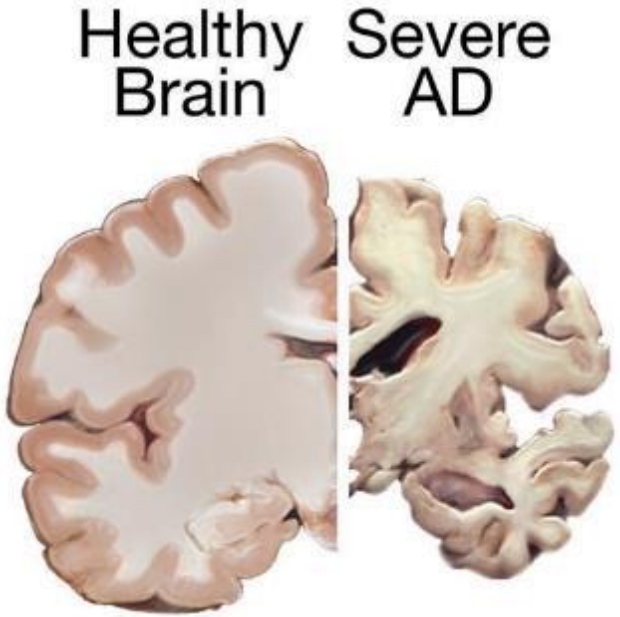
Cognition in the Clinic: Neurocognitive Disorders

Severity is stratified by **functional impairment of IADL and ADL:**

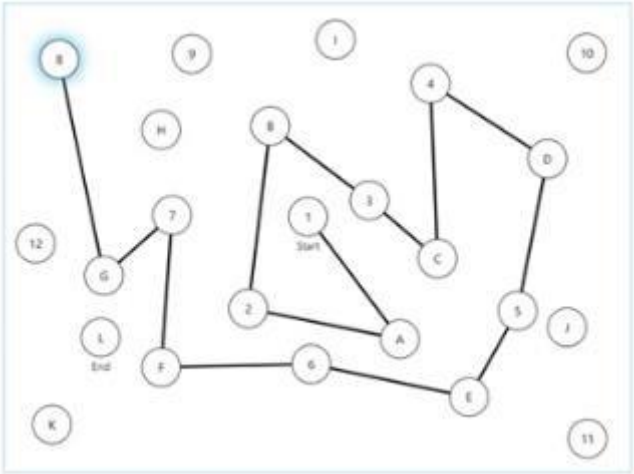
- **Mild:** Difficulties with instrumental activities of daily living (e.g., housework, managing money).
- **Moderate:** Difficulties with basic activities of daily living (e.g., feeding, dressing).
- **Severe:** Fully dependent.



Cognition in the Clinic: Gold Standard for Evaluation

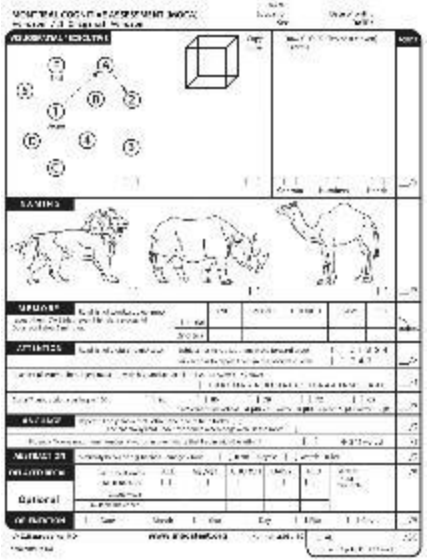
- Neuropsychologists perform **neuropsychological testing (NPT)**
  - a standardized battery of neuropsychological tests to characterize deficits in specific cognitive domains/subdomains.
  - Includes a summative evaluation of deficits and capabilities

- In some areas, NPT may be difficult to access, so clinical measures of cognition may have to suffice.



Cognition in the Clinic: Quantified clinical assessment of cognition

- **Mini Mental Status Evaluation (MMSE)**
- **MiniCOG**
- **Montreal Cognitive Assessment (MoCA)**
- **Saint Louis University Mental Status (SLUMS)**
- **Freund Clock Draw**



- Note each test evaluates specific cognitive domains/subdomains.
- MoCA and SLUMS preferred for sensitivity to mild cognitive impairment.

Cognition and Cancer

Cancer and Cognition

Cancer related cognitive impairment?

- Subjective cognitive slowing and cognitive dysfunction is commonly noted by cancer survivors
  - Described as “brain-fog” or “chemo-brain” by survivors
  - Survivors typically attribute to chemotherapy
  - Current term: Cancer-related cognitive impairment (CRCI)
- What do we know about this phenomenon?

Cancer and Cognition

Mirage or oasis?

- Investigations confirm that **cancer survivors report subjective cognitive problems more frequently** than general population:
  - **Jean-Pierre, et al. 2011**: Analyzed data from National Health and Nutrition Examination Survey (NHANES) N=9819, hx cancer n=1305
  - 14% percent of those with cancer, and 8% of those without, noted past year memory symptoms
  - controlling for demographics, **respondents with cancer were 40% more likely to report memory symptoms** (95% CI, 1.08 to 1.83)
- ALSO… Cancer survivors report **more perceived functional deficits. (Lange et al. 2019)**

Cancer and Cognition

Mirage or oasis?

- Correlation between cognitive symptoms and objective impairment.
  - **Dhillon et al. 2018:** Performed neuropsychological testing and administered the FACT-COG (self-report of cognitive impairment) **in** 362 Australian patients with CRC (localized dz: 289: chemo: 173)
  - Findings: Symptoms did not correlate with cognitive performance.

Cancer and Cognition

Mirage or Oasis?

- The mixed results correlating symptoms to impairments prompted the presumption that other factors may driving cognitive complaints
  - Pain
  - Insomnia
  - Fatigue
  - depression and anxiety

Cancer and Cognition

Mirage or oasis?

- Chemotherapy studies **show strong consistent evidence of cognitive performance deficits**.
- Some evidence for **cognitive recovery**

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Cancer and Cognition

Representative studies of chemotherapy on cognition.

Study	Patients, control group Age	Cognitive assessment	Main CT type (% of patients)	Main outcome
Collins et al.	Breast cancer (n=56, 52 years old ±7.8) versus HC (n=56)	Before, shortly after and 1-year post-CT	FEC-T: 70%	Significant rate of decline to baseline from 1-year post-CT in patients. - 48% of patients had decreased shortly post-CT (9% HC). - **Significant rebound from short-term and 1-year post-CT**
Wouters et al.	Lymphoma (n=106, 47 years old ±12.6) versus HC (n=53)	After CT (median months since completion: 54.5)	CHOP/MOPP-ABV : 76%	Patients**: cognitive impairment in 16%** (most effected were those with lower education and pre-morbid IQ)
Hess et al.	Ovarian cancer (n=231, 40–79 years old)	Before CT, before cycle 4, after cycle 6, and 6 months after completion of primary CT	Palitaxel/carboplatin	At cycle 4**: 25% of patients had cognitive impairment** in at least one domain, 21% and 18% at cycle 6- and 6-months post-CT, respectively

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Some studies show cognitive recovery after treatment, however no significant relationship has been established.

Cancer and Cognition

Brain imaging

Chemotherapy in BC:

- Total brain volume reductions
- Loss of gray matter vol.
- White matter microstructural changes

Koppelmans, 2012

Cancer and Cognition

Deficits and Risk Factors

Most common deficits in CRCI

- Memory – working most affected
- Attention
- Executive function
- Processing speed

Risk factors

- Age
- Preexisting NCD

Cancer and Cognition

Chemotherapies most frequently associated with CRCI

- Doxorubicin
- Paclitaxel
- Methotrexate
- 5-Fluorouracil

Proposed mechanisms:

- Disruption of neurogenesis
- Disruption of myelination and oligodendrocyte function
- Mitochondrial damage
- Increased peripheral and brain cytokine production

Cancer and Cognition

Outstanding questions

What about other therapies?

- **Hormone therapy**
  - Breast
  - Prostate
- **Targeted therapies/Immunotherapy**
- **Surgery**
- **Radiation therapies**

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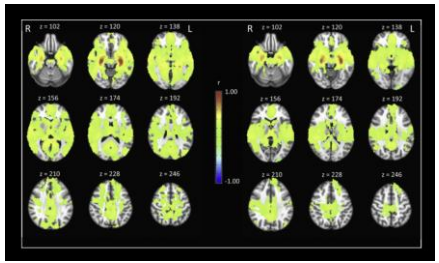
Cancer and Cognition

Outstanding questions

- **Direct effects of cancer on cognition** – non-CNS dz.
  - Breast cancer patients may have increased cognitive impairment **before** treatment. (Ahles et al. 2008)
- What explains **poor overall correlation between survivor symptoms and cognitive performance**?
  - fMRI studies suggest **cognitive adaptation** (recruitment of secondary capabilities into functional networks).



Cognition and Cancer: Clinical Considerations

Cancer and Cognition - Clinical Case:

- A 63-year-old female, recently retired schoolteacher, with a PMH of HLD, well controlled asthma and recently discovered R BC (s/p local resection with LNB showing stage IA ER+/Her2 neg dz) **presents after surgery with no new symptoms to plan treatment.**
- **Pre-treatment**
  - inform about cognitive risks (particularly dt chemotherapy, HT ?)
  - Consider cognitive testing in select patients based on risk/distress?

Cancer and Cognition - Clinical Case:

- A 63-year-old female, recently retired schoolteacher, with a PMH of HLD, well controlled asthma and recently discovered R BC (s/p local resection with LNB showing stage IA ER+/Her2 neg dz, s/p 6 cycles of TAC, NED on most 3/6-month imaging) presents 1 year later with complaints of fatigue, anxiety, and cognitive slowing.

Cancer and Cognition: Clinical Considerations:

Clinical considerations:
Responding to patient concerns about cognitive symptoms

- rule out other actionable causes
  - CNS metastasis
  - Rapidly progressive neurocognitive disorders (e.g. prion dz, etc.)
  - Substance use
  - Medications/polypharmacy
  - Nutritional deficiencies
  - Insomnia / fatigue
  - Uncontrolled pain
  - Psychosocial stressors/psychiatric disorders

Red flags:

- Rapid cognitive decline
- Acute confusion/disorientation
- weight loss, night sweats etc.
- substance use

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Cancer and Cognition: Clinical Considerations:

- Consider clinical cognitive testing (e.g. MoCA, SLUMS) to evaluate extent of impairment.
- Those with more significant cognitive impairment that affects social or occupational function may benefit from formal neuropsychological testing.

Cancer and Cognition: Clinical Considerations:

Interventions for CRCI:

- **Pharmacological -** research is at an early stage, with few large RCT and lacking consistent definitions of CRCI cases
  - Agents studied: methylphenidate, modafinil, donepezil, memantine, gingko biloba, cotinine erythropoietin.

Cancer and Cognition: Clinical Considerations:

Clinical Considerations

What can providers recommend to patients experiencing CRCI?

- **non-pharmacological**
  - Relaxation training
  - Physical exercise programs
  - Cognitive rehabilitation (individual and group)
  - Brain-training programs
  - EEG-based biofeedback
- However, no single treatment is considered a standard.

Conclusion

Conclusion

- Overall progress in cancer has led to greater focus on QoL in survivorship
- Cognitive *symptoms* are common during and after cancer treatment
- Research has identified cognitive impairment (particularly in chemotherapy), however significant questions remain (case definition, treatment, pathogenesis).
- There is no clinical definition of CRCI and no current standard therapy.
- Nevertheless, cognitive symptoms remain an important detractor from QoL.

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