



Clearing the Fog: Optimizing Cancer Trials with Cognitive Assessments



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Cancer is a complex disease, not only affecting the body but also the mind. One often-overlooked aspect is Cancer-Related Cognitive Impairment (CRCI), commonly referred to as “chemo brain” or “cancer fog.” Computerized cognitive assessment systems present a promising avenue for understanding CRCI and optimizing clinical trial protocols.

Insights into CRCI: Beyond Chemotherapy

CRCI refers to changes in cognitive function experienced by cancer patients before, during, or after treatment. Oncology treatments can affect diverse cognitive domains such as memory, attention, processing speed, and executive function.

While the exact mechanisms of CRCI are not fully elucidated, many factors play a role, with the side effects of chemotherapy, radiation therapy, targeted therapy, hormonal therapy, and the cancer itself contributing to cognitive impairment. Additionally, treatment-induced inflammation, hormonal changes, genetic predispositions, aging, and lifestyle factors may also contribute to patients’ cognitive impairment.

Here are some examples of how disease indications and their treatments can cause CRCI symptoms:

- Primary brain tumor (such as glioblastoma): memory and attention deficits due to the tumor’s pressure on brain tissues and disruption of neural pathways.
- Small-cell lung cancer: patients might develop limbic encephalitis, causing severe memory loss and confusion as the immune system mistakenly attacks the brain.
- Chronic Lymphocytic Leukemia (CLL): cognitive difficulties due to systemic inflammation and immune dysregulation can lead to issues with concentration and processing speed.



- Gastrointestinal cancer: weight loss and malnutrition can lead to cognitive decline, affecting brain function.
- Chemotherapy: Patients often experience “chemo brain” characterized by forgetfulness, difficulty concentrating, and slower thinking.
- Lymphoma: A recently diagnosed patient might suffer from anxiety and depression, causing cognitive symptoms such as forgetfulness and trouble concentrating.

CRCI is detected in up to 30% of patients before chemotherapy, up to 75% of patients during treatment, and up to 35% of patients still experience cognitive deficits for years after treatment (Janelsins MC et al., 2014). Cognitive impairment is typically evaluated using psychometric tools including the Mini-Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA), Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), Trail Making Test (TMT), Controlled Oral Word Association (COWAT), and computerized tools.

In addition to these, one promising tool is the CDR system, it is simple to use and can be delivered by non-specialists with test batteries varying between 7 and 30 minutes in duration. With their built-in parallel forms, the tests manage learning effects unlike other paper and pencil tests. Validated in over 50 languages and patient populations.

Signant SmartSignals® Cognitive Drug Research (CDR) System®: a lighthouse in the cognitive fog

The [Signant SmartSignals® Cognitive Drug Research \(CDR\) System®](#) is a widely validated and extremely sensitive computerized tool for comprehensive assessment across essential cognitive domains such as attention, information processing, working memory, executive control, and episodic memory. Moreover, Signant’s market-leading normative database serves as a benchmark, aiding clinical decision-making and ensuring research findings are contextually relevant, including factors such as age, gender, and educational level.

The CDR System enables comprehensive analysis of cognitive assessment data, providing insights into CRCI progression and its impact on trial endpoints. By identifying high-risk individuals, sponsors can implement targeted interventions to mitigate CRCI and improve overall the quality of life for patients with cancer and those in remission. Below are some examples of the potential utility of the CDR System® used in informing indication-specific targeted intervention plans.



Indication	CRCI Symptoms	CDR-System-Supported Interventions
Glioblastoma	Memory and attention deficits	Real-time cognitive assessments to track fluctuations
Limbic Encephalitis	Severe memory loss, confusion	Early detection via CDR system, tailored support
Chronic Lymphocytic Leukemia (CLL)	Issues with concentration and processing speed	Regular cognitive evaluations
Gastrointestinal Cancer	Cognitive decline due to malnutrition	Cognitive monitoring alongside nutritional support
Breast Cancer (Chemotherapy)	Forgetfulness, difficulty concentrating, slower thinking	Objective assessments to quantify cognitive impact
Lymphoma	Forgetfulness, trouble concentrating due to anxiety and depression	Integration of emotional well-being into cognitive endpoints

Assessing Health-Related Quality of Life (HRQOL) questionnaires alongside CRCI provides a comprehensive understanding of how cancer and its treatments influence patients' cognitive function and quality of life, helping provide a necessary holistic oncological care plan.

Revolutionizing Cancer Research with Cognitive Insights

To tackle the cognitive challenges cancer patients face, several therapeutic approaches and lifestyle adjustments can be implemented. These may include:

1. Cognitive rehabilitation programs, including memory training and exercises, can help improve cognitive function.
2. Medications for symptom management like fatigue, depression, and sleep disturbances can impact cognitive function in cancer patients.
3. Memory aids, calendars, organizers, and smartphone apps can help manage daily tasks and appointments.
4. Lifestyle adjustments such as maintaining a healthy diet, staying physically active, managing stress, mindfulness practice, and getting enough sleep can also improve symptoms.



Managing cancer-related cognitive impairment is vital. It improves patient well-being, enhances clinical trial results, and drives innovation in comprehensive cancer care. Explore our SmartSignals® CDR System® and elevate your research protocol with tailored recommendations for optimal results.

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References

Janelins, M., Kesler, S., Ahles, T., & Morrow, G. (2014). Prevalence, mechanisms, and management of cancer-related cognitive impairment. *Int Rev Psychiatry. Int Rev Psychiatry*, 102-13. doi:10.3109/09540261.2013.864260

Kohli, S., Fisher, S., Tra, Y., Adams, M., Mapstone, M., Wesnes, K., . . . Morrow, G. (2009). The effect of modafinil on cognitive function in breast cancer survivors. *Cancer*, 2605-16. doi:10.1002/cncr.24287

Li, Y., Luo, Y., & Song, J. (2023). Optimizing memory performance and emotional states: multi-level enhancement of adult hippocampal neurogenesis. doi:10.1016/j.conb.2023.102693

Pendergrass, J., Targum, S., & Harrison, J. (2018). Cognitive Impairment Associated with Cancer: A Brief Review. *Innovations in Clinical Neuroscience*, 36-44.

Pereira Dias, G., Hollywood, R., Bevilaqua, M., da Luz, A., Hindges, R., Nardi, A., & Thuret, S. (2014). Consequences of cancer treatments on adult hippocampal neurogenesis: implications for cognitive function and depressive symptoms. *Neuro Oncol.*, 476-92. doi:10.1093/neuonc/not321

Walker, L., Wesnes, K., Heys, S., Walker, M., Lolley, J., & Eremin, O. (1996). The cognitive effects of recombinant interleukin-2 (rIL-2) therapy: a controlled clinical trial using computerised assessments. *European journal of cancer*, Vol 32A (13), 2275-83. doi:10.1016/s0959-8049(96)00300-0

Wefel, J., Vardy, J., Ahles, T., & Schagen, S. (2011). International Cognition and Cancer Task Force recommendations to harmonise studies of cognitive function in patients with cancer. *Lancet Oncol.* doi:10.1016/S1470-2045(10)70294-1.



Wesnes, K., Edgar, C., & Brooker, H. (2010). The Disruptions to Cognition, Everyday Function and Quality of Life in Oncology Patients: A Therapeutic Opportunity? ISCTM, 331. doi:10.1016/j.nurt.2010.06.013

Wesnes, K., McNamara, C., & Annas, P. (2016). Norms for healthy adults aged 18-87 years for the Cognitive Drug Research System: An automated set of tests of attention, information processing and memory for use in clinical trials. J Psychopharmacol, 263-72. doi:10.1177/0269881115625116.

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