ACT I: Assessment of Cancer Related Brain Fog using the Test of Strategic Learning

Principal Investigator

Adam L. Cohen, MD, MS

Sub-Investigator(s)

Ebtahal Al Shami B.A.
Michelle Ferretti, MSW, LCSW, OSW-C

Patient Advocate
Deriece Harrington

Sponsor

Inova Schar Cancer Institute
Inova Neurosciences

April 20, 2022

Version 2

ABSTRACT

Title: ACT I: Assessment of Cancer Related Brain Fog using the Test of Strategic Learning

Short Title: ACT I.

Rationale: To determine the ability of the Test of Strategic Learning (TOSL) to detect cognitive impairment in people complaining of brain fog.

Objectives: We hypothesize that we can recruit 3 people per month and that the TOSL will have high correlation with PAOFI higher level cognition subscore. The primary objectives are: Time to recruit the first 10 patients and the correlation of TOSL Synthesizing Summary score with PAOFI score at time 0

Study Type: This is a prospective observational cohort

Study Design: 55 people will be recruited who are 18 years of age and older and diagnosed with stage I-III breast cancer within the last 5 years and who can operate a computer and read and understand English.

Study Methodology: Participants will complete the TOSL, the PAOFI, and the FACT-COG at enrollment and then 3 months later. Completion can be done in person or on a computer.

Statistical Methodology: After the 1st 10 people we will pause to consider the recruitment rate and feasibility. If we can recruit 10 people in 4 months (recruitment rate 2.5 people/month) that will be considered sufficient recruitment rate to proceed to the full study. If the recruitment rate and dropout rate are sufficient for completing the main study in the allotted time, we will proceed to stage 2, which is the full study. We will use a Spearman correlation coefficient to compare the TOSL subscales with the PAOFI subscales. 50 people will also give 80% power to reject the null hypothesis of 0 correlation if the actual correlation is at least 0.4, at a significance level of 0.05. Assuming 10 percent drop out, we will recruit 55 people.

INTRODUCTION

1.1. Specific Aims

Aim 1: To demonstrate the feasibility of recruiting patients to a brain fog study at Inova

Aim 2: To correlate BHI gist reasoning and complex narrative memory domains with overall Patient Reported Outcome measures at baseline

Aim 3: To correlate change in BHI gist reasoning and complex narrative memory domains with change in Patient Reported Outcome Measures

1.2. Hypothesis

We hypothesize that the Brain Health Index domains of gist reasoning and complex narrative memory will negatively correlate with higher cognitive subscale of the PAOFI and changes in BHI will negatively correlate with changes in the higher cognitive subscale of the PAOFI

1.3. Background and Significance

1.3.1. BACKGROUND

Breast cancer remains the most common cancer in women, with an estimated incidence of 2,261,419 new cases reported globally in 2020. Breast cancer in men is rare; in 2019 in the United States, less than 1% of new breast cancer diagnosis occurred in men. Cancer-related cognitive impairment (CRCI) in breast cancer patients, sometimes called "brain fog" is now a recognizable concern, and an important problem to address. In 2018, 3.1 million women were reported to live with breast cancer in the United States and up to 75% experience CRCI. CRCI in patients with breast cancer causes problems with attention, working memory, executive function linked to a region in the brain called the prefrontal cortex, as well as processing speed. CRCI has a negative impact on quality of life (QOL) and detrimental effects on daily activities. The etiology of CRCI is not yet well understood, it can be related to the disease or treatments, such as surgery, chemotherapy, radiation, hormone therapy, and immunotherapy.

Patient complaints of CRCI symptoms have been reported and documented mostly by Self-Assessments, directly from patients, and Patient-reported outcomes (PROs). One of the few formal neuropsychological tests that assesses a spectrum of cognitive abilities in breast cancer patients is the Patient's Assessment of Own Functioning Inventory (PAOFI). PROs have consistently documented brain fog. However, there is a lack of evidence of detected concordance between CRCI self-reported complaints and formal neuropsychological assessments that are currently being implemented. In addition, the specific attribution of PAOFI to standardized neurocognitive metrics is not well examined and understood. Further, analyses the correlation of PAOFI to "objective" standardized neurocognitive assessments. The study also aims to examine the ability of standardized psychometrics to detect CRCI complaints, thus establishing a strong agreement between cognitive complaints and neuropsychological performance.

1.3.2. BACKGROUND ON PAOFI and FACT-COG

The Patient Assessment of Own Functioning Inventory (PAOFI) is a subjective measure of cognitive function. PAOFI is a widely used application in a diverse set of clinical population. The PAOFI was developed in reflection of commonly reported complaints and the cognitive domains typically assessed in neuropsychological evaluations. The PAOFI consists of 33 categories designed to assess the different aspects of cognitive function with the goal of capturing the diverse characteristics of self-assessed cognitive complaints. Categories are aggregated into four subscales: Higher Level Cognitive and Intellectual Functions (HLC) tapping executive functioning (nine questions); Memory (ten questions); Language (nine questions); and Motor/Sensory-Perceptual (five questions). Items are rated on a Likely scale from 1 ("almost always") to 6 ("almost never"). The scoring system involves summing only the items with high severity number (i.e., scores of 1, 2, or 3) into a domain score. There have been limited studies evaluating the psychometric properties

and reliability/validity of PAOFI. To better understand its usefulness in this patient population, a study conducted by Van Dyk et al. examined the scaling structure, reliability, and construct validity of the PAOFI in breast cancer survivors. The study found that certain aspects of the assessment, such as the scoring method are not sensitive enough to detect the more subtle cognitive changes that are frequently reported by breast cancer patients.

Self-reporting instruments have been widely administered across a diverse range of clinical settings. This approach has been regularly applied in experimental studies and is validated by clinicians to be a practical and effective method for collecting data (Van Dyk et al., 2017). The Functional Assessment of Cancer Therapy-Cognitive (FACT-Cog) is a certified method for identifying patients' cancer-related cognitive impairments. FACT-Cog is a self-reported questionnaire designed for cancer patients to assess perceived cognitive function and its impact on quality of life (Costa et al., 2018). The FACT system was first developed in 1980 by David Cella, a postdoctoral student in Memorial Sloan Cancer Center (www.facit.org). FACT has now become a licensed measurement system with many categories of assessments, one being the FACT-COG. The FACT-COG consists of 37 questions evaluating four different components of perceived cognitive function; perceived cognitive impairments (CogPCI: 20 items); perceived cognitive abilities (CogPCA: 9 items); comments from others (CogOth: 4 items); and the impact of perceived cognitive impairments on quality of life (CogQOL: 4 items). It is aimed at assessing patients' memory, attention, concentration, language, and thinking skills and the impact of cognition disturbances on the quality of life. Participants' rate the question based on how many times a given situation has occurred the past week. This is constructed on a five-point scale, from never/not at all (0) to several times a day/very much (4). The total FACT-Cog score is the sum of the four subscales and ranges from 0-148. The higher the total score, the better the cognitive function, and the lower the impact on patients' quality of life (Hajj et al. 2020, Costa et al. 2018). Studies evaluating the FACT-Cog found appropriate construct validity for the total score of neuropsychological weaknesses in cancer patients and survivors. The assessment has specific strengths in detecting signs of depression and anxiety rather than cognition function, such as memory. (Hajj et al. 2020) Thus in orders to detect cognitive dysfunction, suggestions have been made to refine the assessment. A recommended best approach is incorporating assessing cognitive abilities (Dyk et al., 2017). Others found the calculation structure uncertain, and a big consideration was tailored to future efforts focusing on scoring specific cognitive domains separately (Van Dyk et al., 2020). Overall, there are significant concerns in regard to the FACT-Cog lacking targeted subjective abilities.

1.3.3. BACKGROUND ON BHI

The Brain Health Index (BHI) is a standardized performance benchmark that was developed by scientists at the Universities of Edinburgh and Glasgow. BHI was designed to assess whole brain deterioration and help predict cognitive function. BHI has been successful in detecting cognitive decline in stroke patients significantly more accurate than methods that were previously established. This performance benchmark allows an effective observation of changes in key cognitive abilities over time. BHI includes various assessment domains that incorporate a series of written and verbal tasks, specifically targeting the frontal lobe. It aims at to determining the performance of critical frontal lobe processes, which are responsible for executive functions such as planning, decision making, and problem solving.

An assessment domain of BHI called the Test of Strategic Learning (TOSL) measures gist reasoning, an assessment that directs participants to construct as many abstract ideas as possible from a lengthy text. The scoring is based on the number of abstract ideas the participants cultivated. TOSL also includes a measurement of memory for text details called the Memory for Details. Participants are asked to recall specific details of the text used to assess gist. Previous studies have found that the gist reasoning test may be sensitive enough to help clinicians identify previously undedicated subtle cognitive changes that could explain the difficulties of daily life experienced by patients with cognitive impairments. This was found to be true in patients with traumatic brain injury. Gist reasoning is also found to be a subsequently guide for appropriate therapies.

The Visual Selective Learning Task (VSLT) is a selective learning task in which the participant's ability to learn select information among other items is assessed (Hanten et al., 2004; Hanten, Zhang, & Levin, 2002). Individuals are presented with multiple trials of single words, 20 words each, 10 of which are a high-point value and 10 of which are a low-point value. Individuals are instructed to remember as much as they can, with

the goal being to earn points. The ability to filter low-value and focus on high-value information is reliant on attention, working memory, and inhibition and has been shown to be sensitive to frontal lobe dysfunction, including attention deficit disorders and traumatic brain injury.

1.3.4. Rationale of ACT1

Prior studies have found a lack of association between neuropsychological performance and documentation of subjective cognitive complaints in breast cancer patients. This could be reflective to the lack of specificity and sensitivity of the self-reported tools. Gist reasoning is predicted to be a better evaluator of frontal lobe cognitive function. Thus, it provides us with a better way to detect cognitive complaints in breast cancer patients. Cognitive complaints indicate neuropsychological decline but efforts to establish this relationship in cancer survivors have produced ambiguous results. It is believed that subjective cognitive assessment is not a substitute for objective performance. Cognitive complaints in breast cancer survivors are unique, expressive symptoms that alert clinicians of threats to poor cognitive functioning. Future research should focus on the effects of objective instruments to assess neurocognitive performance in breast cancer population. Establishing a strong correlation between neurocognitive performance and cognitive complaints will allow increased awareness of cognitive decline in breast cancer patients. This is imperative in the quest of studying this adverse event. There are a few studies that assess CRCI in a heterogeneous matter using an adequate size of sample population and diverse set of breast cancer patients. This study hypothesizes that TOSL is an objective indicator of brain fog which yields increased sensitivity and superior results.

2. STUDY DESIGN AND SUBJECT SELECTION

2.1. Study Type
This is an observational prospective cohort study

2.2. Setting/Location
Subjects will be recruited from clinics at ISCI, LWC sessions, and community groups.

Consenting: A study team member to contact patient, introduce the study, and schedule a convenient time to consent. Consent can be done in one of the consult rooms and /or CTO conference rooms or over the phone.

Assessments: Assessments can be done either in person or on computer from home. If they are done in person they will be done:

BHI , PAOFI and FACT-COG can be done Clinic consult rooms/various rooms in ISCI or in the life with cancer lounge rooms on floor 2. All assessments will be done on a computer.

2.3. Duration of Study
There will be two assessments, three months apart. The expected duration of recruitment is 18 months.

2.4. Number of Subjects
55 people

2.5. Study Population

2.5.1. Gender of Subjects
Men or women with stage I-III breast cancer.

2.5.2. Age of Subjects
>18 years
No upper limit

2.5.3. Racial and Ethnic Origin

No restrictions. To increase the recruitment of a diverse subject population, all assessments are available both online or on paper. We have also involved a patient advocate on the leadership committee to help with community outreach.

2.5.4. Vulnerable Populations

As this study is no more than minimal risk, vulnerable populations will not be excluded.

2.6. Inclusion Criteria

1. 18 years of age or older
2. ECOG performance status ≤ 2
3. Patients diagnosed or with a history of breast cancer within the last 5 years.
4. Life expectancy of at least 3 months
5. Subject reports experiencing brain fog or cognitive impairment that the subject attributes to cancer or cancer therapy
6. Able to sit for one hour and attend and respond to verbal and written instructions.
7. Able to use a computer

2.7. Exclusion Criteria

1. Brain metastases from breast cancer
2. Severe hearing or visual impairment
3. Unable to give informed consent
4. Unable to read and write in English
5. Those diagnosed with history of neurologic injuries or disorders (e.g. seizures, strokes, traumatic brain injury, brain surgery, neurodegenerative disorders) other than those attributable to cancer or cancer therapy.

STUDY METHODS AND PROCEDURES

3.1. Setting/Location

3.2. Recruitment

In close collaboration with ISCI breast clinical physicians (Dr. Mauro, Dr. Harnden, and Dr. Pennisi) and breast surgery clinic (Dr. Wiley). CRC can also prescreen physician schedule and contact patients directly. The patient advocate will also assist in outreach efforts to community organizations.

3.3. Study Treatment/Intervention

This is a non-interventional study.

At both time points, patients will be administered the TOSL, the PAOFI, and the FACT-COG. Testing will take approximately 30-50 minutes to complete. Each participant will be tested individually in a quiet room by a trained examiner or at home via computer. Subjects will complete the PAOFI and FACT-COG before the VSLT and TOSL. The PAOFI and FACT-COG are included in the appendix.

The Visual Selective Learning Test:
The VSLT will be administered to examine the ability to filter low-value and select high value information. In the VSLT the examinee is presented with a series of words, one at a time. Some words are in all caps and some are in all lower case. There are three rounds. In two of the rounds, words in all caps are valued at 10

points and words in lower case are valued at 1 point. In the third round, the values are reversed. The examinee is instructed to remember the words to maximize their point value.

The Test of Strategic Learning:
The Test of Strategic Learning (TOSL, Chapman, Gamino, & Cook, under review; S. Chapman, J. Hart, H. Levin, L. Cook, J. Gamine, unpublished data, 2009) will be administered to examine the higher-order cognitive control function of gist reasoning (the ability to abstract novel integrative interpretations from complex information) and to examine memory for core details/facts.

The TOSL consists of a one-page text in the form of an expository, biographical narrative. The narrative is dense with details of the person's life. Taken beyond the surface level, the texts contain multiple high-level themes that encapsulate the key concepts within the story. For example, one of the TOSL texts was about a man (John Pierpoint's) life and the eight jobs he attempted throughout his life in an effort to improve life for others (Chapman et al. 2002). The text also contained detailed information about the reasons for his failure in each career. There are 3 different TOSL text narratives which can be used alternately: Malcolm Muggeridge, Sarah Hale, John Pierpont. One of the texts can be used at time point 1 and a different text can be used at time point 2 to minimize practice effects.

The three components of the TOSL are:
1) A high-level overview of the text.

2) Life lessons or take-away messages that could be learned from the text (Interpretive statements)

3) Detail-level questions about the text

The first two components yield two measurements of the ability to use gist reasoning to abstract the central message and glean interpretations from complex information. The third component provides a measure of the ability to recall the important facts/details.

Participants will be tested individually in a quiet room by a trained examiner. Before presenting the text, the examiner familiarizes participants with the task. The participants are informed: "The text conveys a lot of high-level meanings. After reading the passage, I will first ask you to write a high-level overview. Then I will ask you to generate numerous lessons that can be learned. So be thinking about the bigger ideas as you read the text. Also, I will ask you some specific questions."

Participants are then provided with a copy of the narrative text to read. Participants read the text silently. The participant is allowed to re-read the narrative and may underline or take notes if they desire, but they are informed they will not be allowed to refer back to the text once they are done reading. Upon completion, the text is removed from sight so that participants do not have the option to refer to it further. The participant is then asked to write a condensed version of the passage they just read that includes as many high-level ideas as possible within a 6-minute time limit. They are instructed they do not need to include all of the details, but instead to write highlights that convey ideas of substance from the text. If participants begin making a list or writing down bullet points of information, they are cued to instead write down their ideas in the form of a paragraph. In addition to the abstracted overview/synopsis, to further assess the ability to abstract meaning, participants derive one-sentence interpretive statements from the text. The participant is next asked to write down as many lessons or take-home messages that can be gleaned from the information as he or she can think of within a 6-minute time limit.

Subsequently, the participant is given the "memory for detail" recall measure of the TOSL, which entails a series of cued questions to assess recall of specific details from the complex narrative text that was used to assess gist reasoning. Participants are first asked a question that requires listing key points from the text. They are then asked 8 cued questions that require short answers regarding detail information about 8 key points from the text. For example, for participants given the TOSL text about John Pierpoint, participants are first asked to recall all the careers that John Pierpont had. They are then asked cued questions to specify what happened in each of the 8 careers.

The TOSL has a manualized objective scoring system in which written overviews/synopses conveying abstracted gist meanings receive a higher score than those that focused on the stated details of the text. Participants receive 1 point for each key thematic concept/abstracted idea conveyed in their overview of the text in their own words; verbatim or paraphrased ideas receive no points. With regard to scoring the interpretive statements, concrete interpretations of the text that were directly tied to the explicit content also receive no points. Abstract interpretations that express a generalized takeaway that can be inferred from the narrative and are stated in the client's own words rather than via a cliché or rote saying receive 1 point. When scoring the "memory for detail' recall measure of the TOSL, a cumulative score can range from 0 to 24 total points possible, with 24 points representing the best possible score. One point is given for each of the 8 possible key points recalled. In addition, for each prompt to provide more specific detail about the key points, participants can receive a score from 0 to 2 points depending on the accuracy and completeness of the response. Participants receive 2 points for providing 2 or more details specific to the given prompt, 1 point for accurately capturing one detail, and no points for incorrectly recalled details. For example, on the TOSL text about John Pierpoint, participants receive 1 point for each of the eight careers they recall and 2 points for giving a complete reason for each career's failure, 1 point for giving a partial reason, or 0 points for giving an incorrect reason.

Two trained raters independently score the TOSL overviews, interpretative statements, and responses to probes about their memory for details. Disagreements between raters are resolved through discussion and mutual consensus. The scoring will be discussed with a clinician from the Center for BrainHealth at UT Dallas over telephone or video call, with no identifying patient information provided. Raters are blinded to the participants' scores on the patient-reported outcome measures.

Responses to detail-level questions about the text (TOSL Part 3) will be tape-recorded and later transcribed for verbatim scoring for all participants. Written responses will be elicited for the overviews/synopses and interpretive statements (TOSL Parts 1 and 2) for all participants except for those who are unable to write their responses due to physical constraints. For these participants, oral responses on these tasks will also be audio-recorded and later transcribed for verbatim scoring. Participants will also be asked to read aloud their written overviews/synopses and interpretive statements for audio-recording and later transcription if their handwriting is difficult to read. Audio recordings will be deleted after transcription.

Brief Description of Variables from Cognitive Testing

Name of Measure	**Variables/what is being assessed by the measures**	**Description**	**Scoring**	**Scoring information:**
Test of Strategic Learning (TOSL) Part 1: Synthesizing summary	Gist reasoning	Participant construct as many abstracted ideas as possible (in a summary format) from a 1-page text	Number of abstracted ideas	Performance ranges: 0 – 1: Lower 30% 2 – 3: Middle 40% 4+ Upper 30%
Test of Strategic Learning (TOSL) Part 2: Lessons/one-sentence interpretative statements	Gist Reasoning	Patient provides as many one-sentence interpretations as possible from a 1-page text	Number of interpretation statements	0-1: Lower 25% 2-3: Middle 50% 4-10+: Upper 25%

Test of Strategic Learning (TOSL) Part 3: Memory for Details	Memory for details/facts from a complex narrative text	Participant recalls (on cued questions) specific details of the text used to assess gist reasoning	Recall of facts 0-24	0-8 points: Lower 25% of clients 9-16: Middle 50% of clients 17-24: Upper 25% of clients

3.4. Endpoints/Outcomes Measurements

3.4.1. **Primary outcomes**.

Primary Outcome:
Stage 1: Time to recruit the first 10 patients
Stage 2: Correlation of TOSL Synthesizing Summary score with PAOFI score at time 0

Primary end-points:
Stage 1: Number of months between opening of recruitment and recruitment date of the 10^{th} subject
Stage 2: Spearman correlation coefficient between the TOSL Lessons score and the PAOFI higher level cognition subscale score.

3.4.2. Secondary outcomes

1. Correlation of the TOSL Lessons score with the PAOFI total score and the FACT-COG cognitive impairments subscore and total score
2. TOSL synthesizing summary score and TOSL memory for details score and the PAOFI higher level cognition score, PAOFI total score, and FACT-COG cognitive impairments subscore and total score at time 0
3. Correlation of the change in the TOSL Lessons score, synthesizing summary score, and memory score with the change in PAOFI total score, higher level cognition subscore, and FACT-COG cognitive impairment subscore and total score between session 1 and session 2, 3 months apart

3.5. Consent/Assent

Delegated study investigators who received consent training will approach eligible subjects for enrollment into the study. A copy of the signed consent form will be given to the patient, the original signed consent will be kept in a study binder. No study procedures will occur prior to obtaining informed consent.

3.6. Monitoring Subjects and Criteria for Withdrawal of Subjects from the Study.

Subjects may voluntarily stop at any time.

STATISTICAL CONSIDERATIONS/DATA ANALYSIS

4.1. Sample Size

Stage 1 (internal pilot):

After the 1st 10 people we will pause to consider the recruitment rate and feasibility.

10 people with also give 80% confidence that we will encounter in the pilot study at least one incident of some unanticipated problem that may arise with a probability of 15%. (Vichtbauer 2015)
We will estimate the recruitment rate as 10 divided by the number of months to recruit 10 people. For the full study to recruit 55 people in 18 months requires an average recruitment of 3 people per month. If we can recruit 10 people in 4 months (recruitment rate 2.5 people/month) that will be considered sufficient recruitment rate to proceed to the full study.

10 people will also allow an estimate of the dropout/noncompletion rate. If the observed dropout rate is 10%, a sample size of 10 people will provide an 80% two-sided confidence interval of 1 to 34%.

If the recruitment rate and dropout rate are sufficient for completing the main study in the allotted time, we will proceed to stage 2, which is the full study.

Stage 2
The TOSL lessons score is a numeric score from 0 to 10 that can then be split in quartiles. In cognitively normal seniors, the mean score is 3.35 with SD 1.29. The complex narrative memory subscale is a numeric score from 0 to 24. In cognitively normal seniors, the mean score is 16.35 with SD 3.88. (Anand 2010) The PAOFI has 33 questions, each measured on a 1-6 score. The higher cognitive learning subscale has 12 items, and the reported score is an average of these items. In healthy controls the mean was 1.32 with SD 0.40. In women with breast cancer with cognitive complaints, the mean score was 2.68 with standard deviation 0.9. The Higher Level Cognition subscore has a Spearman correlation of ~ 0.47-0.71 with other memory tests in women with breast cancer without cognitive complaints. We will use a Spearman correlation coefficient to compare the BHI subscales with the PAOFI subscales. If the correlation coefficient is 0.7, to have 95% confidence interval width of 0.33 or less, we need 50 people. 50 people will also give ~85% power to reject the null hypothesis of 0 correlation coefficient if the actual correlation is at least 0.4, at a one-sided significance level of 0.05. Assuming a 10 percent drop out, rate we will recruit 55 people.

Given the small number of evaluations, the coordinator will confirm there are no missing items on the FACT-COG and PAOFI.

FACT-COG will be scored using the version 3 scoring document (https://www.facit.org/measures-scoring-downloads/fact-cog-scoring-downloads) without scoring the 4 items indicated as "NOT CURRENTLY SCORED."

Study participants' VSLT score, TOSL score, the PAOFI score, FACT-COG score and their subscale score at baseline and follow-up will be summarized using descriptive statistics (N, min, max, mean, median, SD).

The following Spearman's correlation coefficients will be calculated
between the TOSL Lessons score/VSLT score and the PAOFI higher level cognition subscale score
between the TOSL lessons score/VSLT score and the PAOFI total score, the FACT-COG cognitive impairment subscale score and total score
between TOSL synthesizing summary score, TOSL memory for details score and the PAOFI higher level cognition score, PAOFI total score, FACT-COG cognitive impairments subscale score and total score at baseline.
between the change (from baseline to follow-up assessments) in the VSLT score, TOSL Lessons score, synthesizing summary score, memory score and the change (from baseline to follow-up assessments) in PAOFI total score, higher level cognition subscale score, the FACT-COG cognitive impairment subscale score and total score.

4.2. Data Storage

4.2.1. Data Management

Information about patients will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Privacy and confidentiality of all patients enrolled must be maintained.

Study data will be collected and managed using REDCap electronic data capture tools hosted at Inova Health System. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

The VSLT and TOSL will be administered through Qualtrics hosted on the UT Dallas server. This Qulatrics server is password protected and HIPAA compliant. The subject records on that server will be coded by subject ID number, and the key will be kept at Inova in the REDCap EDC, so no identifiable information will be stored at UT Dallas.

4.2.2. Records Retention

Data will be stored for three years following study completion and then destroyed. If data is used for future research and analysis, all identifiers will be removed.

HUMAN SUBJECTS PROTECTION (RISKS, BENEFITS, AND ALTERNATIVES)

5.1. Risks

Potential loss of privacy. The risk will be minimized by shielding the participant's by unlinking his or her identity from his or her personal health information.

Psychological risk. Patients may experience potential anxiety, stress, and depression as well as uncomfortable emotions such as anger, fear, sadness, discomfort.

5.2. Benefits

There are no direct benefits to the patient. All subjects will be informed about Life With Cancer free resources for brain fog.

5.3. Alternatives

The alternative is not to participate in the research.

5.4. Confidentiality

Confidentiality of the data will be ensured as follows:

- Only the research team will have access to electronic databases with the patient data. The electronic database will be held on a password-protected server within the Inova Health System firewall.
- Data will be made available only to the investigators and staff working on this database, all of whom are appropriately trained.
- Data for participants who take the Test of Strategic Learning electronically will have their responses stored on Qualtrics. Access to systems is restricted to specific individuals who have a need-to-know such information and who are bound by confidentiality obligations. Access is monitored and audited for compliance. Qualtrics uses Transport Layer Security (TLS) encryption (also known as HTTPS) for all transmitted data. Surveys may be protected with passwords. Qualtrics' services are hosted by trusted data centers that are independently audited using the industry standard SSAE-18 method.

SUBJECT COMPENSATION

6.1. Costs

There are no costs to participants.

6.2. Payment

$25 gift card at completion of second assessment.

ADVERSE EVENT REPORTING

As this is a minimal risk, non-interventional study, adverse events will not be recorded.

FUNDING

Inova Schar Cancer Institute and Inova Neurosciences Service Line.

CONFLICTS OF INTEREST

The research group has no conflicts of interest.

FACILITIES AND EQUIPMENT

Inova Schar Cancer Institute
8081 Innovation Park Drive
Fairfax, Virginia 22031

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APPENDIX

FACT-Cognitive Function (Version 3)

Below is a list of statements that other people with your condition have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

	PERCEIVED COGNITIVE IMPAIRMENTS	**Never**	**About once a week**	**Two to three times a week**	**Nearly every day**	**Several times a day**
CogA1	I have had trouble forming thoughts0	0	1	2	3	4
CogA3	My thinking has been slow0	0	1	2	3	4
CogC7	I have had trouble concentrating0	0	1	2	3	4
CogM9	I have had trouble finding my way to a familiar place0	0	1	2	3	4
CogM10	I have had trouble remembering where I put things, like my keys or my wallet0	0	1	2	3	4
CogM12	I have had trouble remembering new information, like phone numbers or simple instructions 0	0	1	2	3	4
CogV13	I have had trouble recalling the name of an object while talking to someone	0	1	2	3	4
CogV15	I have had trouble finding the right word(s) to express myself0	0	1	2	3	4
CogV16	I have used the wrong word when I referred to an object0	0	1	2	3	4
CogV17b	I have had trouble saying what I mean in conversations with others0	0	1	2	3	4
CogF19	I have walked into a room and forgotten what I meant to get or do there0	0	1	2	3	4
CogF23	I have had to work really hard to pay attention or I would make a mistake..... 0	0	1	2	3	4

CogF24	I have forgotten names of people soon after being introduced0	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

		Never	**About once a week**	**Two to three times a week**	**Nearly every day**	**Several times a day**
CogF25	My reactions in everyday situations have been slow0	0	1	2	3	4
CogC31	I have had to work harder than usual to keep track of what I was doing0	0	1	2	3	4
CogC32	My thinking has been slower than usual0	0	1	2	3	4

CogC33a	I have had to work harder than usual to express myself clearly0	0	1	2	3	4
CogC33c	I have had to use written lists more often than usual so I would not forget things0	0	1	2	3	4
CogMT1	I have trouble keeping track of what I am doing if I am interrupted0	0	1	2	3	4
CogMT2	I have trouble shifting back and forth between different activities that require thinking0	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to the <u>past 7 days</u>.

	COMMENTS FROM OTHERS	Never	**About once a week**	**Two to three times a week**	**Nearly every day**	**Several times a day**
CogO1	Other people have told me I seemed to have trouble <u>remembering information</u>0	0	1	2	3	4
CogO2	Other people have told me I seemed to have trouble <u>speaking clearly</u>..... 0	0	1	2	3	4
CogO3	Other people have told me I seemed to have trouble <u>thinking clearly</u>..... 0	0	1	2	3	4

CogO 4	Other people have told me I seemed confused	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	PERCEIVED COGNITIVE ABILITIES	Not at all	A little bit	Some-what	Quite a bit	Very much
Cog PC1	I have been able to concentrate	0	1	2	3	4
Cog PV1	I have been able to bring to mind words that I wanted to use while talking to someone	0	1	2	3	4
Cog PM 1	I have been able to remember things, like where I left my keys or wallet	0	1	2	3	4
Cog PM 2	I have been able to remember to do things, like take medicine or buy something I needed	0	1	2	3	4
Cog PF1	I am able to pay attention and keep track of what I am doing without extra effort	0	1	2	3	4
Cog PC H1	My mind is as sharp as it has always been	0	1	2	3	4
Cog PC H2	My memory is as good as it has always been	0	1	2	3	4
Cog PM T1	I am able to shift back and forth between two activities that require thinking	0	1	2	3	4
Cog PM T2	I am able to keep track of what I am doing, even if I am interrupted	0	1	2	3	4

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	IMPACT ON QUALITY OF LIFE	Not at all	A little bit	Some-what	Quite a bit	Very much
CogQ 35	I have been upset about these problems0	0	1	2	3	4
CogQ 37	These problems have interfered with my ability to work0	0	1	2	3	4
CogQ 38	These problems have interfered with my ability to do things I enjoy..... 0	0	1	2	3	4
CogQ 41	These problems have interfered with the quality of my life0	0	1	2	3	4