Natural Trajectory Subclasses of Cancer Related Cognitive Impairment

Oxana Palesh[1], Tina Truong[2], Adithi Gandhi[2], Susanne Lee[2], Eliza Thrall[1], Alexa De La Torre Schutz[3], Shelli Kesler[3]

1. Virginia Commonwealth University Massey Cancer Center
2. Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford University
3. University of Texas at Austin

Background

The incidence of cancer-related cognitive impairment (CRCI) ranges widely from 17-75%, due in part to inconsistent definitions of impairment.[1, 2]

Inconsistency may reflect limited sensitivity of currently available standardized cognitive tests.

Objectives

To identify subclasses of CRCI to improve the accuracy of identifying patients most at risk for CRCI, and to assess alternative biomarkers used for identifying cognitive subgroups.

Methods

Participants

- 139 female patients undergoing chemotherapy for breast cancer
- Randomized to receive Brief Behavioral Therapy for Cancer-Related Insomnia (BBT-CI) or Healthy Eating Education Learning for healthy sleep (HEAL) (control intervention)
- Participants were assessed at baseline and post intervention at 6 weeks, 6 months, and 12 months

Neuron Derived Exosome (NDE) Measurement

- NDE assay via blood samples (N=124)

Cognitive Assessment

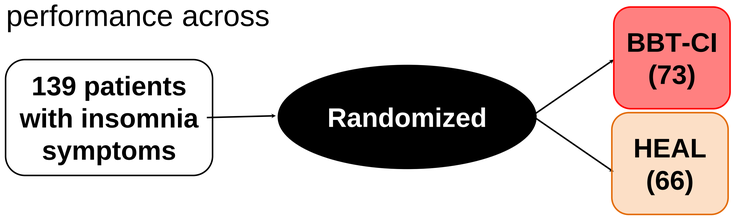
- Standardized measures of verbal declarative memory, attention, processing speed and executive function, and verbal fluency

Statistical Analysis

- Growth mixture modeling (GMM) was used to determine latent subgroups based on different trajectories of cognitive test performance across the four timepoints

	BBT-CI	HEAL	t/X²	p-value
N	73	66		
Age (yrs)	51 (12)	49 (10)	0.751	0.454
Education (yrs)	16 (3)	16 (3)	0.211	0.834
Racial/ethnic minority %	44%	59%	3.23	0.072
Stage at diagnosis 0,I,II,III %	1%,32%,49%,18%	3%,32%,47%,18%	0.486	0.922
Estrogen receptor positive %	74%	72%	0.049	0.826
Progesterone receptor positive %	53%	63%	1.32	0.252
HER2 receptor positive %	37%	50%	2.35	0.125
Chemotherapy cycles	5.7 (5.0)	5.3 (3.6)	0.523	0.602
Locoregional radiotherapy %	13%	12%	0.035	0.852
Hormone blockade %	19%	14%	0.771	0.380

Table 1. Sample Characteristics. Data are shown as mean (standard deviation) unless otherwise noted.



Results

- Mean cognitive performance improved significantly over time (p<0.001).

	Baseline	6 wk	6 mo	12 mo	F	p value
HVLT-Immediate	49.7 (11.3)	49.9 (11.8)	53.5 (10)	56.5 (9.8)	24.5	< 0.001
HVLT-Delayed	49.2 (10.2)	48.0 (11.0)	51.2 (9.7)	52.8 (8.4)	10.0	< 0.001
Trail 1	43.1 (8.1)	47.8 (8.8)	48.3 (9.0)	48.9 (8.0)	38.9	< 0.001
Trail 5	46.6 (9.3)	48.9 (10.3)	51.4 (9.4)	51.5 (9.0)	17.6	< 0.001
COWA	40.7 (11.1)	41.3 (11.9)	44.6 (11.6)	43.7 (11.0)	14.3	< 0.001
NDE (U/ml)	132 (177)	128 (183)	165 (199)	147 (191)	6.6	< 0.001

Table 2. Results of linear mixed models showing the mean effect of time. Data are shown as mean (standard deviation) unless otherwise noted.

- GMM identified 3 distinct latent subgroups: a group of patients with high performance who seemed to benefit from repeated test exposure (Class 1, N = 45, “practice benefiters”), a group of patients with low performance who showed no benefit from practice (Class 2, N = 15, “no net benefiters”), and a group of patients with average performance who were slower to benefit from practice (Class 3, N = 79, “slow benefiters”).

- Cognitive subclass 2 (“no net benefiters”) were characterized by significantly lower education level than the other two classes (F = 7.00, p = 0.001). Cognitive subclass 1 (“practice benefiters”) had fewer racial/ethnic minority patients than the other two classes (F = 8.38, p = 0.015). Cognitive subclasses did not differ significantly in any other available demographic or clinical characteristic. They also did not differ in terms of NDE levels.

Conclusions

- There are multiple distinct longitudinal trajectories of CRCI. These may be influenced by social determinants of health such as education and race/ethnicity.
- Future research is necessary to explore early interventions with those most at risk for CRCI.

Acknowledgements

Funding: This research was supported by NCI R01CA1R01CA239714

References

1. Horowitz TS, Suls J, Trevino M. A Call for a Neuroscience Approach to Cancer-Related Cognitive Impairment. Trends Neurosci. 2018;41(8):493-6.

2. Palesh O, Scheiber C, Kesler S, Mustian K, Koopman C, Schapira L. Management of side effects during and post-treatment in breast cancer survivors. The breast journal. 2018;24:167-75.