Changing patterns of attention network in Breast Cancer Survivors

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Background

- Cognitive impairment is common among breast cancer survivors receiving systemic treatments, especially chemotherapy and endocrine therapy.
- Attention comprises three distinct networks—alerting, orienting, and executive—which are mediated by different neurocognitive systems.
- Prior studies on chemotherapy *or* tamoxifen alone showed network-specific effects, but dynamic patterns during combined systemic therapy remain unknown.
- Understanding how attention networks change over treatment duration may clarify mechanisms of cognitive impairment and guide cognitive risk monitoring and rehabilitation.

Key Knowledge Gap: The trajectory and temporal pattern of attention network changes in real-world breast cancer survivors treated with both chemotherapy and tamoxifen have not been systematically characterized.

Methods and Materials

Participants

- Cross-sectional study conducted 2018–2024.
- 435 breast cancer survivors who completed chemotherapy followed by tamoxifen；242 age-matched healthy controls.
- Chemo-regimens: CMF (40.9%), TAC (26.4%), FEC (32.7%).
- Exclusion: neurological/psychiatric disorders, substance abuse, visual impairment.

Assessment of Attention

- Attention Network Test (ANT) used to quantify: Alerting efficiency, Orienting efficiency and Executive control efficiency
- Reaction times were log-transformed to reduce skewness.

Clinical & Neuropsychological Measures

- MoCA, HAMA, HAMD, menopausal status, radiation history, pathological stage, Herceptin use.

Statistical Analysis

- Linear mixed-effects regression adjusting for demographic and clinical covariates.
- Restricted cubic spline models to detect nonlinear patterns.

Results

- The two groups did not differ in age, education, or menopausal status. Compared with controls, survivors showed lower MoCA scores (P < .001) and higher anxiety and depression scores on HAMA and HAMD (both P < .001), indicating overall reduced cognitive performance and increased psychological distress.
- Breast cancer survivors exhibited lower alerting network scores than healthy controls (P < .001), suggesting that the alerting network of breast cancer survivors may be compromised. Breast cancer survivors exhibited elevated executive network scores (P < .001), indicating decreased executive network efficiency. However, no discernible differences were detected in the orienting network scores between the groups (P = .212). (Figure 1)
- The effects of treatment duration on the efficiency of the three networks are depicted in Figure 2. Compared with healthy controls, breast cancer survivors exhibited significantly reduced efficiency in the alerting (P < .001) and executive (P < .001) networks, while the orienting network efficiency remained intact.

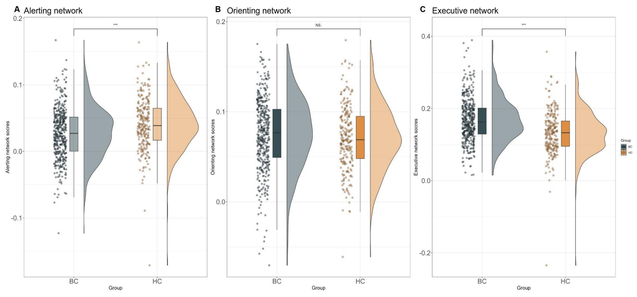


Figure 1. The three attention network scores of patients with breast cancer and healthy controls. The (A) alerting network scores, (B) orienting network scores, and (C) executive network scores of patients with breast cancer and healthy controls.

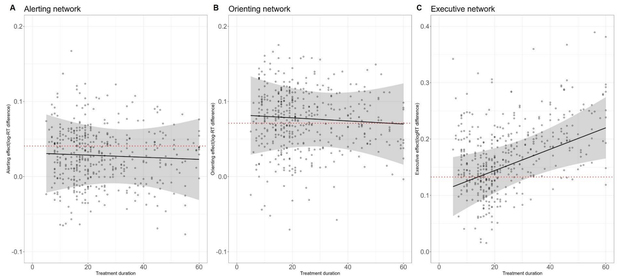


Figure 2. Linear effects of treatment duration on each attention network. (A) alerting network, (B) orienting network, and (C) executive network. The red dotted line is the average of the score of the three attention networks in healthy controls; shaded areas represent 95% confidence intervals.

The executive network demonstrated a nonlinear (V-shaped) trajectory over treatment duration, characterized by an initial improvement peaking around at approximately 15 months, followed by a subsequent decline (nonlinear P < .001). (Figure 3)

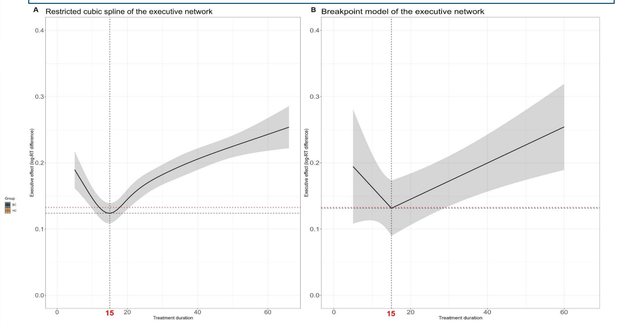


Figure 3. Nonlinear effects of treatment duration on the executive network. (A) The restricted cubic spline regressions of the executive network. (B) The breakpoint model of the executive network with a breakpoint at 15 months. The red dotted line is the average of the score of the three attention networks in healthy controls; shaded areas represent 95% confidence intervals..

This pattern was consistent across different chemotherapy subtypes. The alerting network showed persistent impairment throughout the five years observation period (linear P = .247), potentially indicative of underlying neural alterations. (Figure 4)

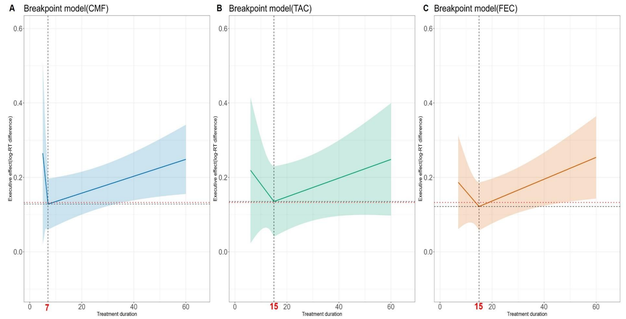


Figure 4. Nonlinear effects of treatment duration on the executive network across the three chemotherapy regimens. The breakpoint model of the executive network with a breakpoint of (A) month 7 in the CMF regimen, (B) month 15 in the TEC regimen, and (C) month 15 in the FEC regimen.

Conclusions

- Breast cancer survivors exhibit selective attention network impairments.
- The executive network follows a distinctive V-shaped pattern: early improvement after chemotherapy; later decline likely related to tamoxifen-associated frontal dopaminergic modulation.
- Alerting deficits appear persistent, potentially reflecting long-term alterations in norepinephrine-related pathways.
- These findings highlight: the complex temporal dynamics of cognitive effects from systemic therapy; the importance of cognitive monitoring beyond the first year; the need for longitudinal studies to clarify mechanisms and support targeted cognitive rehabilitation.

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