Inflammation biomarkers at localized breast cancer diagnosis are associated with cognitive impairment 2 years later

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Introduction

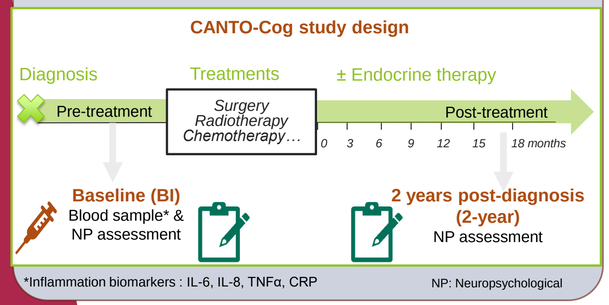
- Inflammation associated to Cancer-Related Cognitive Impairment (CRCI)[1,2]
- Lack of knowledge on the predictive role of inflammatory biomarkers on CRCI[3]

Methods

- French CANTO cohort NCT01993498
- Patients included in CANTO-Cog: breast cancer stage I-III; no previous treatment; no neurological and psychiatric comorbidities; no major cognitive disorders (MMSE≤26, at baseline)
- Inflammation biomarkers (assessed through blood sample):
  - as categorical variables: **IL-6, CRP** (C-Reactive Protein; 3mg/L)
  - as continuous variables: **IL-8, TNFα**
- Cognitive impairment for each domain (based on ICCTF definition, corrected for practice effect with an healthy control group n=119):

episodic memory (HVLT), **working memory** (WAIS-III: digit span, letter-number sequencing), **executive functions** (TMT B, verbal fluency, Stroop), **processing speed** (TMT-A, Stroop), attention (WAIS-III Symbol search, d2)

- **CRC**I: ≥2 impaired cognitive domains
- Covariates: anxiety and depression (HADS), fatigue (FA-12), BMI, endocrine therapy and chemotherapy



*Inflammation biomarkers : IL-6, IL-8, TNFα, CRP

NP: Neuropsychological

Analysis

- **200 patients** analyzed at **BI** and **2-Year**
- Regression models of cognition with each inflammation biomarkers and covariates (adjusted for BI cognitive impairment, age, education)
- Unique multivariable selection model (type backward) including associated variables in previous regression models (p<0.05), adjusted for BI cognitive impairment, age, education

Results

Table1. Characteristics of patients (mean±SD)

Characteristics Demographic	No CRCI at 2-Year n=146	CRCI at 2-Year n=53
Age*	51.9 ± 11	58.1 ± 10
Education*	13.8 ± 2.6	11.7 ± 2.7
BMI*	25.5 ± 4.9	27.5 ± 5.8
Clinical n(%)		
Stage I-II	122 (85)	43 (81)
Chemotherapy	95 (65)	32 (60)
Endocrine therapy	122 (84)	41 (77)
Outcomes 2-Year		
Anxiety	6.8 ± 3.9	6.8 ± 4.3
Depression	3.6 ± 3.1	5.1 ± 4.5
Fatigue (cognitive)	18.2 ± 24	17.0 ± 24

*: p<0.05

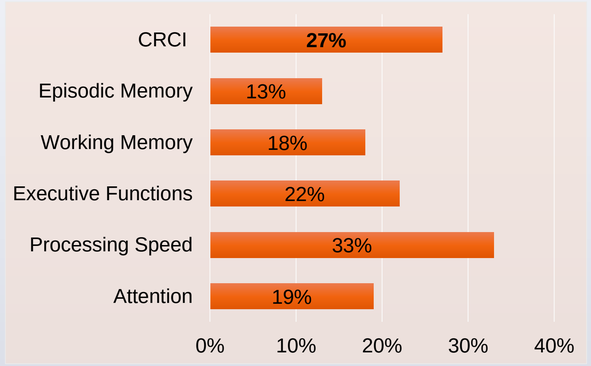


Figure 1. Rate of cognitive impairment at 2-year

Table 2. Significant association between inflammation at baseline and cognitive domains impaired at 2-year

Inflammation markers at baseline	CRCI (unique model)	Episodic memory	Working memory	Processing speed
	OR (95% CI) ; p-value			
IL-6		5.50 (1.43 - 36.60) ; 0.03		
IL-8	0.85 (0.71 – 0.98) ; 0.06			
CRP>3	2.84 (1.06 – 7.64) ; 0.037			2.47 (1.05 - 5.87) ; 0.04
TNFα			0.64 (0.44 -0.89) ; 0.01	

Different model for each marker for episodic memory, working memory and processing speed, adjusted on age, years of education, cognitive impairment at inclusion

Results

- No significant association of inflammation biomarkers with executive function and attention
- High association between BI and 2-year cognitive impairment for each cognitive domain (all OR>6.31)
- No association between BI inflammation biomarkers and BI cognitive impairment (results not shown)

Discussion

- **High levels of CRP** and **IL-6** assessed at diagnosis were associated with **overall CRCI**, processing speed and episodic memory impairments **two years later**
- These findings suggest a potential **inflammatory basis for long-term CRCI**.
- CRP may represent an easily measurable marker in clinical settings and be potentially used to screen patients at greater risk of persistent CRCI.

References

References

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3. Carroll, J. E. et al., 2022 - JCO