

Are Hot Flashes Associated with Cognitive Impairments in Breast Cancer Patients?



Acknowledgements: This study was supported by a research grant from the Canadian Breast Cancer Research Alliance held by the second author, a scholarship from the Canadian Institutes of Health Research and from the Fonds pour la recherche en santé du Québec held by the first and fourth author, and a research scientist award from the FRQS awarded to the second author.

Marie-Hélène Savard, Ph.D.^{1;3-4}

1. Laval University Cancer Research Center

Josée Savard, Ph.D.^{1-2;4}

2. School of Psychology, Université Laval

Hans Ivers, Ph.D.^{1-2;4}

3. Unité de recherche en santé des populations

Aude Caplette-Gingras, Ph.D.³⁻⁴

4. Centre de recherche du CHU de Québec, Québec, Québec, Canada

INTRODUCTION

- It has been hypothesized that menopausal hot flashes trigger a counter-regulatory mechanism in the central nervous system as a reaction to insufficient glucose delivery to the brain, and that this may have a beneficial effect on cognitive functioning in postmenopausal women (Dormire, 2003, 2009).
- Consistent with this hypothesis, postmenopausal women who suffer from hot flashes are often asymptomatic after a meal and hot flashes appear when glucose levels decline (Simpkins & Katovich, 1989).
- Preliminary data from animal models also provide some support for this hypothesis (Katovich & Simpkins, 1990; Simpkins & Katovich, 1990). Indeed, induced hypoglycemia results in a consistent flushing response in rats.
- A large proportion of women treated for breast cancer suffer from hot flashes.
- Many of these patients also complain of attention and memory difficulties.

STUDY GOALS

This cross-sectional study aimed to assess the relationship between hot flashes and cognitive impairments in breast cancer patients, who experience an abrupt menopausal transition following the administration of systemic oncological treatments.

METHODS

Participants

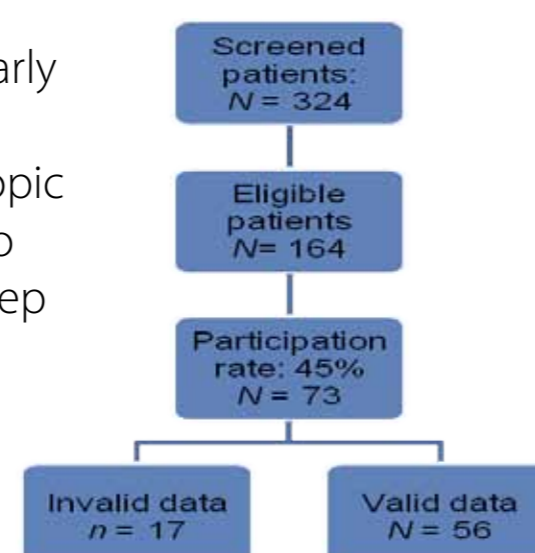
Fifty-six women with breast cancer participated in this study. Patients were recruited from a larger longitudinal study or solicited at the radio-oncology department of L'Hôtel-Dieu de Québec (CHU de Québec).

Inclusion criteria

- Between 30 and 70 years of age
- Having received a first diagnosis of non-metastatic breast cancer
- Having completed in the past four months a treatment protocol combining surgery, chemotherapy and radiotherapy
- Have been receiving hormone therapy for a minimum of five weeks

Exclusion criteria

- A diagnosis of sleep disorder other than insomnia
- Having received neoadjuvant chemotherapy for breast cancer
- Having a score <24 on the Mini-Mental State Examination
- Having any medical, neurological or psychological disorder that is known to significantly alter sleep
- Occasionally or regularly using any medication (other than psychotropic medication) known to significantly affect sleep



Participants' Characteristics by Group

Variable	M	(SD)
Age	51.8	(7.6)
BMI	25.7	(4.8)
		%
Marital Status		
Married/Cohabiting	58.9	
Education		
College or University degree	62.5	
Annual Family Income (CAD)		
\$60 000 and higher	46.5	
Occupation		
Sick leave	60.7	
Menopausal status at diagnosis		
Pre	57.8	
Peri	6.3	
Post	35.9	
Past hormone replacement therapy use	26.6	
Use of a medication to manage hot flashes (venlafaxine, paroxetine, or gabapentin)	23.2	
Use of another psychotropic medication	42.9	
Cancer Stage		
I	23.2	
II	48.2	
III	28.6	

Procedure and Measures

- Participants completed a 24h home-based recording of hot flashes using sternal skin conductance level (SCL) measurement.
- Hot flashes were automatically coded using an increase in SCL of at least 1.2 micro siemens (μmho) within a 30-second period as the criterion (MH Savard et al., submitted).
- Participants were instructed to use an event marker located on the device each time they felt a hot flash was beginning, even during nighttime.

Event marker (participant)	yes	SCL (device)	
		yes	no
yes	true positive	false positive	
no	false negative	true negative	

- After the 24h hot flash recording, participants completed a neuropsychological battery at the cancer research center.

IQ	<ul style="list-style-type: none"> National Adult Reading Test
Episodic Memory	<ul style="list-style-type: none"> Rey-Osterrieth Complex Figure Test Logical Memory I and II Rey Auditory-Verbal Learning Test
Attention and Speed Processing	<ul style="list-style-type: none"> Digit Symbol Trail Making Test A Paced Auditory Serial Addition Task Spatial Span Forward Digit Span Forward Ruff 2 & 7 Selective Attention Test
Executive Functioning	<ul style="list-style-type: none"> Trail Making Test B Verbal Fluency Test Color-Word Interference Test Spatial Span Backward Digit Span Backward

- Participants also completed the Actual State Scale (Broman et al., 1992) and the Performance Rating Scale (Broman et al., 1992) prior to and after the neuropsychological assessment, respectively, as well as the Insomnia Severity Index (Morin, 1993) assessing subjective sleep quality over the last 2 weeks.

Statistical Analyses

- Creation of domains:** To decrease the probability of type I error, results obtained on neuropsychological tests were transformed into z-scores and averaged to create three cognitive domains: (a) episodic memory; (b) attention/speed processing; and (c) executive functioning.
- The relationship between hot flashes and cognitive functioning was examined using Pearson correlation analyses.
- The same analyses were performed taking into account age (young vs. old) and subjective sleep quality (Insomnia Severity Index <8 or >8).

RESULTS

Relationship between objectively-recorded hot flashes and cognitive functioning

Hot flash variable	Neuropsychological domain			Subjective assessment of cognitive functioning	
	Episodic Memory	Attention and Speed Processing	Executive Functioning	Actual State Scale	Performance Rating Scale
Daytime hot flashes (n = 42)					
• True positives	-.23	-.03	-.20	.09	-.01
• Objective hot flashes (true positives + false negatives)	-.21	.01	-.06	.00	-.01
Nighttime hot flashes (n = 56)					
• True positives	-.17	-.01	-.37**	.05	-.17
• Objective hot flashes (true positive + false negatives)	-.12	.14	-.21	.13	-.16

** $p < .01$

- Lower executive functioning scores on the neuropsychological assessment were associated with more frequent objectively-assessed nocturnal hot flashes ($r = -.37, p = .005$).

Relationship between self-perceived hot flashes and cognitive functioning

Hot flash variable	Neuropsychological domain			Subjective assessment of cognitive functioning	
	Episodic Memory	Attention and Speed Processing	Executive Functioning	Actual State Scale	Performance Rating Scale
Daytime hot flashes					
• Event marker	-.11	-.14	-.07	-.03	-.08
• False positives	.06	-.36*	-.03	-.21	.18
Nighttime hot flashes					
• Event marker	-.01	-.11	-.26*	.06	-.11
• False positives	.15	-.21	-.01	.05	-.05

* $p < .05$

- Lower executive functioning scores on the neuropsychological assessment were associated with more manual detections of nocturnal hot flashes ($r = -.26, p = .039$).
- Lower attention and speed processing scores were associated with more false positive diurnal hot flashes ($r = -.36, p = .021$).

All relationships remained significant after controlling for subjective sleep quality.

However, when controlling for age, these relationships remained significant only among older participants.

CONCLUSION

- Breast cancer patients appear to show decreased executive functioning scores following a night characterized by more frequent objective and self-perceived hot flashes.
- These relationships appear to be independent of subjective sleep quality. However, objective sleep quality (i.e., polysomnography) should be included as a potential covariate in future analyses.
- Participants who showed worse attention and speed processing scores also reported more false-positive hot flashes during the previous day, which may indicate that these women also have more difficulties paying attention to physiological symptoms. However, this hypothesis needs further investigation.
- All relationships remained significant only among older participants. Other potential covariates, such as induced menopause following adjuvant treatments among younger participants, may have obscured the results.

RESEARCH AND CLINICAL IMPLICATIONS

- These preliminary data support the hypothesis of a relationship between hot flashes and cognitive impairments among breast cancer patients.
- We found that women with more nocturnal hot flashes tend to have worse cognitive functioning. However, it is still unclear whether increased hot flashes are an indicator of a counter-regulatory mechanism allowing glucose delivery to the brain, as has been previously hypothesized (Dormire, 2003, 2009).
- Further studies are clearly needed in order to replicate these findings. In particular, studies measuring the occurrence of hot flashes in addition to glucose levels during a cognitive task would be helpful to better understand the relationship between hot flashes and cognitive functioning.