Cuadernos de Neuropsicología / Panamerican Journal of Neuropsychology
2020, Vol. 14 Nº 1 129–141
ISSN: 0718-4123
DOI: 10.7714/CNPS/14.1.213

ANXIETY AND COGNITIVE FUNCTIONING IN BREAST CANCER PATIENTS TREATED WITH CHEMOTHERAPY

Ansiedad y Funcionamiento Cognitivo en pacientes con cáncer de mama tratados Con Quimioterapia

Ansiedade e funcionamento cognitivo em pacientes com câncer de mama tratados com quimioterapia

RECIBIDO: 18 noviembre 2019 - ACEPTADO: 28 abril 2020

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Key words:
Breast cancer; anxiety; cognitive impairment; chemotherapy; women's health.

Palabras clave:
Cáncer de mama; ansiedad; deterioro cognitivo; quimioterapia; salud de la mujer.

Palavras-chave:
Cancro da mama; ansiedade; alterações cognitivas; quimioterapia; saúde das mulheres.

A B S T R A C T

Cognitive impairment in breast cancer is frequent and mostly associated to the effects of chemotherapy. Less is known about its association with anxiety symptoms, also prevalent in these patients. This study aimed to explore the possible association between anxiety symptoms and attention, processing speed, memory and executive functions in 20 breast cancer patients treated with chemotherapy. Participants with higher anxiety symptoms showed less sustained attention, higher updating abilities, lower planning skills, and higher cognitive inflexibility than participants with lower anxiety symptoms. Neuropsychological rehabilitation focused on attention and executive functions and psychological intervention on anxiety symptoms, even in women without an anxiety disorder, are needed in order to promote a better quality of life and psychological adjustment in breast cancer patients treated with chemotherapy.

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ISSN: 0718-4123
DOI: 10.7714/CNPS/14.1.213

R E S U M E N

El deterioro cognitivo en el cáncer de mama es frecuente y se asocia principalmente a los efectos de la quimioterapia. Se sabe menos sobre su asociación con los síntomas de ansiedad, también prevalentes en estos pacientes. Este estudio tuvo como objetivo explorar la posible asociación entre los síntomas de ansiedad y la atención, la velocidad de procesamiento, la memoria y las funciones ejecutivas en 20 pacientes con cáncer de mama tratadas con quimioterapia. Las participantes con síntomas de ansiedad más altos han demonstrado baja atención sostenida, capacidades de actualización más altas, habilidades de planificación más bajas y una mayor inflexibilidad cognitiva, que las participantes con síntomas de ansiedad más bajos. La rehabilitación neuropsicológica centrada en la atención y funciones ejecutivas y la intervención psicológica centrada en los síntomas de ansiedad, incluso en mujeres sin un trastorno de ansiedad, son necesarias para promover una mejor calidad de vida y ajuste psicológico en pacientes con cáncer de mama tratados con quimioterapia.

R E S U M O

A ocorrência de alterações cognitivas no cancro da mama é frequente e tem sido associada, em larga medida, aos efeitos da quimioterapia. Menos se sabe sobre a associação destas alterações aos sintomas de ansiedade também prevalentes nestes pacientes. Este estudo teve como objetivo explorar a possível associação entre os sintomas de ansiedade e o funcionamento atencional, processamento de informação, memória e funcionamento executivo em 20 pacientes com cancro da mama tratadas com quimioterapia. As participantes que apresentavam níveis mais elevados de ansiedade evidenciavam também menor atenção sustentada, melhores competências cognitivas de atualização, menores competências de planeamento e maior inflexibilidade cognitiva comparativamente às participantes com menores níveis de ansiedade. Os resultados sugerem a importância da reabilitação neuropsicológica, focada nas funções cognitivas atencionais e executivas, e da intervenção psicológica, dirigida aos sintomas de ansiedade, para promover uma melhor qualidade de vida e ajustamento psicológico em pacientes com cancro da mama tratadas com quimioterapia, mesmo sem perturbação de ansiedade.

Introduction

Breast cancer is the most frequent tumor in women. Although the survival rate of breast cancer is high and associated with a good prognosis, these women experience several sequels of disease and its treatment (Jansen et al., 2011). Among these consequences are changes in cognitive functioning (López-Santiago et al., 2011; Mandelblatt et al., 2014; Von Ah et al., 2013). This cognitive impairment can be visible in several domains, namely in attention (Jansen et al., 2011; Schagen et al., 1999), processing speed (Collins et al., 2009), memory (Collins et. al, 2009; Schagen et al., 1999) and executive functions (Mandelblatt et al. 2014) and affect the quality of life of the patient and compromise the adaptation to the disease (Boykoff et al., 2009; Janelsins et al., 2014), as well as the functional capacity (López-Santiago et al., 2011).

Prior studies have suggested some factors that may contribute to emergence of cognitive deficits. Genetic predisposition and vulnerability, psychosocial variables (e.g. age, education, perceived social support), drugs prescription (Cordellat et al., 2013; López-Santiago et al., 2011), as well as the treatments undergone (chemotherapy, radiotherapy and hormone therapy) (Collins et al., 2009; Shibayama et al., 2014) are some of the factors associated to cognitive deficits. Additionally, the emotional state of patients, particularly anxiety symptoms, has also been identified as a potential explanatory factor for neurocognitive damages (Mandelblatt et al., 2014). A study involving breast cancer women revealed that anxiety may increase vulnerability to cognitive impairment (Vearncombe et al., 2009). In turn, Ramalho et al. (2017) found that one year after diagnosis 8.1% of the breast cancer women had evidence of cognitive impairment, and also observed that the association between chemotherapy and cognitive impairment could be influenced by anxiety levels. These results are in line with other studies carried out with other clinical populations, in which a worse cognitive performance was associated with anxiety (Constant et al., 2005; Gualtieri and Morgan, 2008). Despite these findings, not all studies support the influence of anxiety on cognitive impairment, identifying other explanatory factors (e.g. treatment, age, education, comorbidity, and more advanced stages of the disease) (Hedayati et al., 2012; Mandelblatt et al., 2014; Schagen et al., 1999).

Considering these inconsistent results, it is important to deeply explore the possible association between anxiety symptoms and cognitive impairment, regardless of oncological treatments implemented, in order to increase knowledge about patients' psychological and cognitive difficulties and contribute to neuropsychological intervention planning. Greater clarity about the possible association between these two factors would enhance our ability to recognize patients' difficulties and to intervene. This study intends to identify the prevalence of anxiety and cognitive impairment in a sample of breast cancer patients treated with chemotherapy and to analyze the possible association between anxiety symptoms and cognitive functioning (attention, memory, processing speed and executive functions) in these women.

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Method

Participants

This study included 20 Portuguese women diagnosed with breast cancer, recruited in a center for holistic treatment of this disease, sited in the North of Portugal. Inclusion criteria included: clinical diagnosis of breast cancer, ages ≥ 18 years old and ability to read and write in Portuguese. Participants who presented another oncological diagnosis than breast cancer, neurological disease, those who were terminally ill, had a clinical condition incompatible with the capacity to participate and had a previous history of substance abuse that might affect cognitive performance were excluded from the study.

The mean age of participants was 48.4 years (*SD* = 8.98; Min=37; Max= 66). Most participants were married, lived with the nuclear family, had a higher education level, were employed and had annual incomes between € 7.000 and € 200.000. The majority were diagnosed between 2015 and 2016, being in stages II and III of the disease without metastases. At the time of the first evaluation of this study, most participants are in ongoing oncological treatments. All participants underwent chemotherapy, with surgery and hormone therapy being two of the most frequently performed oncological treatments. The mean duration of chemotherapy treatment was 5 months (*M* = 4.80); internal radiotherapy, 2 months (*M* = 1.80); external radiotherapy, 1 month (*M* = 1.40); hormone therapy, 6 years (*M* = 70.80); and immunotherapy, 12 months (*M* = 12). Eight participants reported suffering from some psychological or psychiatric illness, namely anxiety and depression (see Table1).

Procedure

Data collection occurred between September 2016 and January 2017. The ethical principles established for research with human beings have been fulfilled. After the approval of the study, participants' recruitment was implemented by health professionals of the holistic center, by the researchers at the day of patients' appointments, during seminars and lectures planned by the holistic and addressed to the patients, through leaflets and social networks. When the participants accepted to participate, researchers presented the purpose of the study and informed consent was signed by women.

The research protocol was implemented over three sessions, each lasting an average of 1.5 hours. The scheduling of these sessions was conducted according to the participants' availability. In the first session, participants were informed about the study aim, procedures and confidentiality. Sociodemographic and clinical data were also collected during the first session. At the end of this session, self-report questionnaires were given to participants in order to assess their mental health status. These questionnaires were fulfilled at home and returned in the second session. In the second and third sessions, the neurocognitive assessment of participants was completed.

Materials

A sociodemographic and a clinical questionnaire were constructed and implemented in order to collect sociodemographic information and data about breast cancer disease and treatment.

The **Zung Self-rating Anxiety Scale (SAS)** was applied to evaluate the anxiety state of participants, allowing the analysis of anxious reactions of subjects towards situations triggering anxiety. The test has 20 items divided in four dimensions of anxiety (cognitive, vegetative, motor and of the central nervous system). The score range from 20 to 80 points. The higher the score represent the higher anxiety level (Serra et al., 1982).

The **Stroop Color and Word Test (Stroop)** was used to assess verbal fluency, cognitive efficacy, cognitive processes related to selective attention, cognitive flexibility and resistance to interference. The tasks involved imply to read each word aloud, ignoring its print color, and to do so as quickly as possible, and to name the print color of each word aloud, ignoring the word itself, again doing so as quickly as possible. (In)congruent conditions – using words (in)congruent with the print colors were tested. In the quotation were used T notes, with mean of 50 and standard deviation of 10. The Portuguese version has good internal consistency (Cronbach's alpha of .663) (Fernandes, 2013).

The **Trail Making Test (TMT)** was used to evaluate the processing speed, cognitive flexibility, visual demand, motor performance and executive functions (Perianez et al., 2007). It is divided in two parts. Part A evaluated selective attention. Test B aims to evaluate executive functions (Carvalho et al., 2012). A computer software http://neuropsi.up.pt was used to transform the raw scores into percentiles and scalar scores. For data analysis were considered the scalar scores (M = 10; SD = 3) (Cavaco et al., 2013).

ISSN: 0718-4123
DOI: 10.7714/CNPS/14.1.213

Table 1

Sociodemographic and clinical characteristics of the sample (N=20)

Characteristic	***N*** **(%)**
Marital Status	
Single	2 (10.0)
Married/ Cohabitation	15 (75.0)
Divorced/Separation	3 (15.0)
Household	
Participant	2 (10.0)
Participant and partner	6(30.0)
Participant and children	1(5.0)
Nuclear family	10(50.0)
Extended family	1(5.0)
Education	
Basic education	2 (10.0)
Secondary education	1(5.0)
Higher education	17 (85.0)
Occupational status	
Employee	15 (75.0)
Unemployed/Household	3 (15.0)
Retired	2 (10.0)
Annual income	
Until 7000	1 (5.9)
Between 7000 and 20000	7 (41.2)
Between 20000 and 40000	6 (35.3)
Between 40000 and 80000	2 (11.8)
Above 80000	1 (5.9)
Stages of disease	
Stage II	8 (47.1)
Stage III	9 (52.9)
Treatments	
Surgery	19 (95.0)
Chemotherapy	20 (100)
Internal Radiotherapy	4 (20.0)
External Radiotherapy	12 (60.0)
Hormone therapy	17 (85.0)
Immunotherapy	4 (20.0)
Current situation regarding cancer disease	
Treatment interruption	1 (5.0)
Remission	2(10.0)
Treatment with hormone therapy	15 (75.0)
Treatment with chemotherapy and immunotherapy	
Treatment with radiotherapy and immunotherapy	1(5.0)
	1(5.0)

The **Wechsler Adult Intelligence Scale (WAIS-III)** was developed to assess individuals' intelligence quotient and the intellectual functioning, being constituted by 14 subtests organized in two subscales (verbal and realization). The obtained raw scores were transformed into standardized results to characterize participants' performance. The standardized results are distributed on a scale with mean 10 and standard deviation 3. This instrument presents excellent internal consistency (Cronbach's alpha of the subtests between .74 and .95) (Rocha, 2008). In the present study were implemented the follow

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DOI: 10.7714/CNPS/14.1.213

subtests: Digits memory (to assess to assess immediate memory retention capacity - digits in direct order – and memory and reversibility - digits in reverse order), Code (to assess processing speed, mental flexibility, selective and focused attention), Symbol search (to assess fluid ability, processing speed, perceptual organization, mental operation speed, psychomotor speed, attention, concentration, short-term visual memory, visual-motor coordination and cognitive flexibility), Similarities (to evaluate logical reasoning and abstract thinking and the development of language and verbal fluency), Arithmetic (to evaluate computational capacity and speed in calculus management, auditory memory, school background, concentration, abstract reasoning and contact with reality) and Letters and numbers sequence (to evaluate visual processing, perceptual velocity and synthesis capability of an integrated set).

The **Rey-Osterrieth Complex Figure (FCR-O)** was used to evaluate the visual activity and visual memory, being constituted by two geometric figures (A e B). Only the figure A was used, since the sample was composed by adult women. The maximum score obtained is 36 points, being evaluated the 18 units that compose the figure. The subject's raw scores were transformed in percentiles (Rey, 2002).

The **Benton Visual Retention Test (TRVB)** was used to assess visual perception, visual memory, and visuoconstructive abilities. The form C, type A, was used consisting in presenting each card to the participant for 10 seconds, requesting the immediate memory reproduction. The score was calculated taking into account the number of correct drawings. The estimated pre-morbid IQ and the age of each participant should be taken into account in order to identify whether the number of correct reproductions and the number of errors are below or above expectations and whether there is impairment of cognitive function. The Spanish version presents good internal consistency, with Cronbach's alpha ranging between .79 and .84, for the three forms (C, D and E) of application A (Benton, 2002).

The **Wisconsin Card Sorting Test (WCST)** was applied to the assessment of the executive functions, especially the problem solving ability and cognitive flexibility. It requires that the participant plan strategies and allow to analyze his ability to use environmental feedback to modify these strategies The test have four stimulus cards and 128 cards that present different configurations (color, shape and number). The responses should be considered separately in three dimensions (correct-incorrect, ambiguous-not ambiguous and persevering-not persevering). After verifying the errors and perseverative answers, the scores should be calculated. Subsequently, the direct scores are transformed in typical scores, T scores and percentiles. These scores are obtained through the tables in the handbook and taking into account the age and education of the participants. The WCST presents good internal consistency with Cronbach's alpha ranging between .72 and .90 (Heaton et al., 2001).

The Rey Auditory Verbal Learning Test (RAVLT) was developed to evaluate verbal memory and learning. The task consists in memorizing fifteen words, in a series of five repetitions. A computer software program http://neuropsi.up.pt was used to transform raw scores into percentiles and scalar scores. For data analysis we took into account the scalar scores (M = 10; SD = 3) (Cavaco et al., 2015).

The **Behavioral Assessment of the Dysexecutive Syndrome (BADS)** had the purpose of evaluate the executive functioning in general, as well as the specific components, such as problem solving skills, planning and intentional behavior organization over extended periods of time. It is composed of six subtests. The key search and zoo map tests were used. The maximum score that can be obtained is 16 points. In the Zoo Map the raw scores will be transformed in a profile score, in which 16 corresponds to 4; 11-15 corresponds to 3; 6-10 corresponds to 2; 1-5 corresponds to 1; 0 corresponds to 0. Profile scores between 3 and 4 are considered normal, while scores lower than two indicate some cognitive impairment. This instrument has a fidelity value of .41 (Barbosa et al., 2011). In the present study were implemented the follow subtests: Zoo map (to assess the impairment of the executive functions, namely cognitive planning) and Search for keys (to evaluate the action strategy according to the functionality and likelihood of success).

Statistical analyses

Analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 20. Descriptive statistics (means, standard deviations, frequencies, minimum and maximum) were used to sample characterization. To analyze the prevalence of cognitive deficits in different cognitive domains the cut-off points established for each neuropsychological test were applied. Spearman's correlation matrices were implemented to test the association between anxiety levels and patients' cognitive functioning (memory, attention, processing speed and executive functions).

ISSN: 0718-4123
DOI: 10.7714/CNPS/14.1.213

Results

Prevalence of anxiety and cognitive impairment in breast cancer patients

Considering the cutoff point established for the Zung Self-rating Anxiety Scale (40 points) none of the participants presented anxiety symptoms at clinically significant levels. More than half of the participants exhibited deficits in attention (sustained and divided / alternating), verbal processing speed, long-term verbal and short-term visual memory and executive functions (inhibition and cognitive flexibility) (see Table 2; participants with cognitive deficits were signalized in bold). Despite none of the participants have presented anxiety symptoms at clinically significant levels, possible associations between anxiety levels and patients' cognitive performance were tested.

Table 2

Performance in neuropsychological evaluation tests (N=20)

Área of Cognitive Functioning		**Neuropsychologic Tests**	**With deficit N (%)**	**Without deficit N (%)**
Attention	**Sustained**	STROOP Color	**13(68.4)**	6(31.6)
		TMT A	**12(63.2)**	7(36.8)
	Divided/ Alternating	TMT B	**15 (78.9)**	4(21.1)
		STROOP Color/Word	7 (36.8)	12(63.2)
		WAIS-Letters and numbers	3(15.0)	17(85.0)
Processing Speed	**Verbal**	STROOP word	**12(63.2)**	6(31.6)
	Motor	WAIS-Symbol search	1(5.0)	19(95.0)
		WAIS- code	4(20.0)	16(80.0)
Memory	**Short-term verbal**	WAIS-Digits memory	6(30.0)	14(70.0)
		AVLT 1	8(42.1)	11(57.9)
	Long-term verbal	AVLT 30 minutes	**11(57.9)**	8(42.1)
	Short-term visual	Benton Total Correct Reproductions	3(15.8)	16(84.2)
		Expected errors	3(15.8)	16(84.2)
		Rey-Osterrieth Complex Figure - memory	**12(63.2)**	7(36.8)
Executive Functions	**Updating**	WAIS Inverse Digits Memory	6 (30.0)	14 (70.0)
		Letters and numbers	3(15.0)	17(85.0)
		Arithmetic		
		Similarities	9(45.0)	11(55.0)
		Matrices	1(5.0)	19(95.0)
			2(10.0)	18(90.0)
	Planning	Search for keys	0 (0)	19(100)
		Zoo map	1(5.3)	18(94.7)
	Inhibition	STROOP Color/Word	7 (36.8)	12(63.2)
		TMT B	**15(78.9)**	4(21.1)

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		WISCONSIN No of total errors	**11(57.9)**	8(42.1)
		Perseverative answers	**12(63.2)**	7(36.8)
		Perseverative errors	**12(63.2)**	7(36.8)
		Non-perseverative errors	9(47.4)	10(52.6)
	Cognitive flexibility	No. of complete categories	2(10.5)	17(89.5)
Executive Functions (continuation)		No. of cards to complete 1st category	3(15.8)	16(84.2)
		Failure to maintain criteria	8(42.1)	11(57.9)
		Learn Learn	5 (26.3)	14 (73.7)
		STROOP Interference	4 (21.1)	15 (78.9)

Associations between anxiety symptoms and cognitive functioning in breast cancer patients

Higher levels of vegetative anxiety were associated to lower levels of sustained attention. Associations between anxiety levels and executive functioning were also found, namely between the participants' scores on the vegetative dimension of anxiety, on anxiety at the level of the Central Nervous System, and on total scores of anxiety and the performance in some tests of WCST, suggesting higher cognitive inflexibility in women with higher anxiety levels. Statistically significant associations were also found between total scores of anxiety and performance in the Zoo Map test, indicating that the higher anxiety levels are related to worse planning ability. Statistically significant correlations were moreover found between the motor dimension of the SAS and the test of similarity of WAIS-III, suggesting that higher motor anxiety levels are associated to higher participants' ability to update.

No statistically significant associations were found between anxiety levels (neither considering the total scores nor scores in cognitive, vegetative, motor and central nervous system dimensions) and the participants' performance in divided / alternating attention, executive function inhibition, memory and processing speed tasks (see Table 3)

Discussion

Cognitive impairment has been focus of attention and concern in breast cancer women (Schagen et al., 1999). In the present study, a high percentage of participants (more than an half) reported deficits in attention (sustained and divided / alternating), verbal processing speed, long-term verbal memory and short-term visual memory, and in cognitive inhibition and flexibility. Despite disparities found in the prevalence of cognitive impairment across different studies, namely due to methodological differences, definitions of cognitive impairment, the assessment measures used, characteristics of the samples, moments of evaluation and treatments, difficulties detected in the present study in cognitive functioning are in line with previous findings. One study that intended to determine the trajectory of cognitive function over time (prior to the initiation of chemotherapy one week after the completion of four cycles of chemotherapy with doxorubicin and cyclophosphamide, approximately one week after taxane chemotherapy and six months after completion of treatment) in breast cancer women revealed that 23% of the participants had cognitive impairment prior to chemotherapy, of which 6% in the attention domain. This study also indicated that 6 months after completion of chemotherapy 20% of the sample had a deficit, particularly 14% in attention (Jansen et al., 2011). Von Ah et al. (2013) who evaluated the experiences of 22

ISSN: 0718-4123
DOI: 10.7714/CNPS/14.1.213

Table 3

Association between anxiety and cognitive performance in breast cancer patients: Spearman correlations

Cognitive functioning domain		Neuropsychologic tests	Cognitive dimension of anxiety *r(p)*	Vegetative dimension of anxiety *r(p)*	Motor dimension of anxiety *r(p)*	Central Nervous System dimension of anxiety *r(p)*	Total anxiety *r(p)*
Attention	Sustained	STROOP Color	-.257 (.288)	**-.511 (.025)**	-.197 (.420)	-.206 (.398)	-.322 (.178)
		TMT A	-.200 (.412)	-.237 (.328)	-.055 (.822)	-.065 (.791)	-.082 (.738)
	Divided/ Alternating	TMT B	.039 (.873)	-.302 (.209)	-.016 (.947)	-.024 (.922)	-.061 (.804)
		STROOP Color/Word	-.051 (.837)	-.393 (.126)	.013 (.959)	.013 (.959)	-.104 (.673)
		WAIS-Letters and numbers	.011 (.965)	.013 (.958)	-.182 (455)	-.323 (177)	-.107 (.663)
Processing Speed	Verbal	STROOP Word	-.181 (.457)	-.345 (.148)	-.039 (.875)	-.059 (.811)	-.188 (.441)
	Motor	WAIS-Symbol search	-.238 (312)	-.350 (130)	-.248 (.291)	-.074 (757)	-.316 (.175)
		WAIS- Code	-.022 (.928)	-.203 (.391)	.010 (.967)	.030 (.900)	-.033 (.890)
	Short-term verbal	WAIS-Digits memory	-.193 (.414)	-.267 (.256)	.047 (.844)	-.062 (.795)	-.147 (.538)
		AVLT 1	-.182 (.456)	.175 (.475)	.136 (.578)	-.114 (.642)	.027 (.914)
	Long-term verbal	AVLT 30 minutes	-.008 (.973)	-.049 (.842)	.267 (.268)	.024 (.922)	.086 (.725)

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Memory		Benton Total Correct Reproductions	-.047 (.848)	-.097 (.692)	-.185 (.440)	.028 (.910)	-.112 (.647)
	Short-term Visual	Total errors	-.079 (.749)	-.012 (962)	.165 (.501)	-.112 (.648)	.029 (.906)
		Rey-Osterrieth Complex Figure -Memory	.407 (.084)	.164 (.501)	.037 (.113)	.113 (.644)	.210 (.388)
Executive Functions	Updating	WAIS Inverse Digits Memory	-.135 (.570)	-.233 (.322)	.215 (363)	.180 (447)	.033 (.889)
		Letters and numbers	.011 (.965)	.013 (.958)	-.182 (455)	-.323 (177)	-.107 (.663)
		Arithmetic	.117 (.623)	.013 (.956)	-.119 (.617)	-.146 (.539)	-.057 (.813)
		Similarities	.122 (.609)	-.007(.976)	**.466 (.039)**	.149 (.530)	.277 (.238)
		Matrices	.290 (.214)	-.267 (.255)	-.078 (.743)	.012 (.959)	-.014 (.954)
	Planning	Search for keys Total	-.244 (.315)	-.418 (.075)	-.009 (.972)	-.344 (.149)	-.327 (.172)
		Search for keys Time	-.169 (.489)	.274 (.257)	.053 (.830)	.123 (.615)	.008 (.976)
		Zoo Map	-.345 (.149)	-.395 (.094)	-.369 (.120)	-.245 (.312)	**-.485 (.035)**
	Inhibition	STROOP Color/Word	-.051 (.837)	-.393 (.126)	.013 (.959)	.013 (.959)	-.104 (.673)
		TMT B	.039 (.873)	-.302 (.209)	-.016(.947)	-.024(.922)	-.061(.804)

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		WISCONSIN					
		No of letters applied	.274 (.256)	**.501 (.029)**	.163 (.504)	**.547 (.015)**	.441 (.059)
Executive Functions (continuation)		Correct Answers	.211 (.386)	**.554 (.014)**	.206 (.397)	.446 (.055)	.426 (.069)
		No of total errors	.342 (.151)	.435 (.063)	.158 (.518)	**.569 (.011)**	.455 (.050)
		Perseverative answers	.277 (.251)	**.497 (.030)**	.194 (.426)	**.696 (.001)**	**.509 (.026)**
		Perseverative errors					
	Cognitive flexibility	Non-pers. Errors	.270 (.263)	**.492 (.032)**	.178 (.466)	**.706 (.001)**	**.495 (.031)**
		Conceptual level answers	.286 (.235)	.366 (.124)	.141 (.564)	.453 (.051)	.383 (.106)
		No. of complete categories	-.027 (.913)	**.517 (.023)**	-.068 (.784)	-.068 (.784)	.217 (.372)
		No. of cards to complete 1st category	-.062 (.800)	-.024 (.923)	.035 (.886)	.035 (.886)	-.157 (.520)
		Failure to maintain criteria					
		Learn	.262 (.279)	-.243 (.316)	-.128 (.602)	-.128 (.602)	-.062 (.802)
	Cognitive flexibility (continuation)	STROOP Interference					
			-.002 (.993)	.181 (.459)	.061 (.804)	.061 (.804)	.180 (.460)
			.208 (.392)	-.404 (.080)	-107 (.663)	-107 (.663)	-.129 (.559)
			-.208 (.393)	.064 (.794)	.158 (.519)	.158 (.519)	.170 (.487)

ISSN: 0718-4123
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surviving women with breast cancer and their perception about cognitive impairment, reported concerns about long-term memory (91%), processing speed (73%), executive functions (22%) and attention (55%).

Results of the present study also revealed that none of the participants had clinically significant anxiety levels. This is inconsistent with prior studies, where the prevalence of anxiety varies between 16% at 58% in breast cancer patients (Harris et al., 2017; Lueboonthavatchai, 2007). This could be due to the specific characteristics of the sample. In fact, most of the participants are in treatment with hormone therapy, with a stable clinical condition and health supported in the holistic center where the study was implemented, where psychological counseling is also provided. Even though, as empirical evidence suggests that the anxiety can be a determinant factor of cognitive deficits, being often associated with poor performance in cognitive tasks (Mandelblatt et al., 2014), associations between anxiety symptoms and cognitive functioning were still tested. Study results reinforces previous findings showing an association between anxiety and cognitive functioning of breast cancer patients, namely in sustained attention. This association can be explained by the impact of anxiety in diminishing the control of attention and in impairment of the efficient functioning of the attentional system directed to a certain objective (Eysenck et al., 2007).

Associations were also found between anxiety and the executive functioning, related to flexibility, planning ability and updating. Findings concerning cognitive flexibility and planning ability are in line with the literature showing an impairment in these processes in association to anxiety symptomatology (Park and Moghaddam, 2017; Vearncombe et al., 2009). This can be understood by the association of anxiety symptoms to the malfunctioning of prefrontal brain structures, the same as involved in executive functioning (Visu-Petra et al., 2013). Considering that anxiety and executive processes share the same neuroanatomical region, it is possible to anticipate that these psychological processes can influence one another (Beaudreau and O'hara, 2008; Vearncombe et al., 2009).

The ability to update was also associated to anxiety levels, being higher in participants with higher motor anxiety levels. It is possible that patients with higher anxiety levels feel a "greater motivation to minimize the state of aversive anxiety by promoting greater effort and use of resources and auxiliary processing strategies" (Eysenck et al., 2007), being this responsible for a better performance in tasks involving updating capacity (Visu-Petra et al., 2013). The updating process also involves memory processes (Derakshan and Eysenck, 2009) and as memory was not directly affected by anxiety in present study this could contribute to the explanation of the inexistence of a negative impact of anxiety on this executive function.
No significant associations were found between anxiety levels and memory or processing speed, being these results in agreement with other studies (e.g., Hedayati et al., 2012; Schagen et al., 1999). A longitudinal study involving 146 women with early breast cancer and 69 healthy controls, which evaluated some cognitive domains (attention, memory, response speed and processing speed), showed that the memory and response speed presented subtle changes in patients, being time and treatment, but not anxiety, the factors primarily associated to these changes (Hedayati et al., 2012). Similarly, an investigation comparing cognitive impairment in breast cancer women who underwent chemotherapy after surgery and patients who underwent post-surgical radiation therapy indicated that cognitive changes were evident in 28% of the chemotherapy group and 12% in the control group. The most affected areas were attention, mental flexibility, processing speed and visual memory, which occurred as a consequence of and after chemotherapy treatment. In this study, anxiety was not associated with cognitive problems (Schagen et al., 1999).

Some limitations can be pointed out in the present study including a small sample size that only allows generalization of the results to a specific small group of women with breast cancer treated with chemotherapy and determines that results should be interpreted with caution. The cross-sectional design doesn't allow understanding cognitive functioning before the diagnosis of the oncological disease and their relation with anxiety over time. It is suggested to conduct a longitudinal study to understand the evolution of cognitive impairment and its relation to anxiety. Another important limitation was the use of self-reported questionnaires in the evaluation of anxiety, which may have contributed for the patients making more negative appraisals about their emotional state.

Despite previously limitations, this exploratory study contributed to understand the relation between anxiety and cognitive functioning of breast cancer patients, regardless of oncological treatments implemented. The extensive evaluation of neurocognitive functioning of participants, involving different cognitive domains (attention, memory, processing speed and executive functions), allowed to deeply explore patients' needs and cognitive difficulties with impact in daily life and its relationship with anxiety that is typically higher in women with breast cancer.

In conclusion, anxiety was associated to cognitive impairment in breast cancer patients treated with chemotherapy, namely with sustained attention and executive functions (planning and cognitive flexibility). Findings of this study suggest the need to implement both neuropsychological rehabilitation and psychological intervention programs in order to effectively

ISSN: 0718-4123
DOI: 10.7714/CNPS/14.1.213

reduce cognitive impairment and anxiety and to promote a better quality of life and psychological adjustment in women with breast cancer treated with chemotherapy.

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ISSN: 0718-4123
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