Characterizing Biased Cancer-Related Cognitive Processing: Relationships With BRCA1/2 Genetic Mutation Status, Personal Cancer History, Age, and Prophylactic Surgery

Kristen M. Carpenter
The Ohio State University

Stacy Eisenberg
University of Southern California

Sharone Weltfreid
American University

Carissa A. Low
University of Pittsburgh

Tammy Beran and Annette L. Stanton
University of California, Los Angeles

Objective: This study evaluated associations of cancer-related cognitive processing with BRCA1/2 mutation carrier status, personal cancer history, age, and election of prophylactic surgery in women at high risk for breast cancer. *Method:* In a 2 (BRCA1/2 mutation carrier status) $\times$ 2 (personal cancer history) matched-control design, with age as an additional predictor, participants ($N = 115$) completed a computerized cancer Stroop task. Dependent variables were response latency to cancer-related stimuli (reaction time [RT]) and cancer-related cognitive interference (cancer RT minus neutral RT). RT and interference were tested as predictors of prophylactic surgery in the subsequent four years. *Results:* RT for cancer-related words was significantly slower than other word groups, indicating biased processing specific to cancer-related stimuli. Participants with a cancer history evidenced longer RT to cancer-related words than those without a history; moreover, a significant Cancer History $\times$ Age interaction indicated that, among participants with a cancer history, the typical advantage associated with younger age on Stroop tasks was absent. BRCA mutation carriers demonstrated more cancer-related cognitive interference than noncarriers. Again, the typical Stroop age advantage was absent among carriers. Exploratory analyses indicated that BRCA+ status and greater cognitive interference predicted greater likelihood of undergoing prophylactic surgery. Post hoc tests suggest that cancer-related distress does not account for these relationships. *Conclusions:* In the genetic testing context, younger women with a personal cancer history or who are BRCA1/2 mutation carriers might be particularly vulnerable to biases in cancer-related cognitive processing. Biased processing was associated marginally with greater likelihood of prophylactic surgery.

Keywords: breast cancer, BRCA testing, cognitive bias, Stroop, prophylactic surgery

Clinical genetic testing for BRCA1 and BRCA2 (BRCA1/2) mutations is increasingly an option for individuals with high hereditary breast and ovarian cancer risk. Healthy women with deleterious BRCA1/2 mutations are estimated to have substantially elevated lifetime risk of breast and ovarian cancers: 56–84% (vs. 7–10% in the general population) for breast cancer and 10–50% (vs. 1–2% in the general population) for ovarian cancer (U.S. Preventive Services Task Force, 2005). Moreover, breast cancer patients with deleterious BRCA1/2 mutations are at increased risk for developing contralateral disease (Metcalfe et al., 2004) and ovarian cancer (Struewing et al., 1997). With regard to psychological consequences, most researchers have concluded that clinical genetic testing has little adverse impact for most women (e.g., (Hamilton, Lobel, & Moyer, 2009; Meiser, 2005). Large within-group variability in distress exists, however, with a subgroup of BRCA1/2 mutation carriers vulnerable to high or sustained cancer-

related distress (Beran et al., 2008; Croyle, Smith, Botkin, Baty, & Nash, 1997; Halbert et al., 2011; Kinney et al., 2005; Watson et al., 2004). Examination of additional psychological consequences of genetic testing is warranted, in particular within those realms that carry potential clinical implications. One important domain is cancer-specific cognitive processing, the focus of the current research.

Some evidence suggests that heightened cancer risk can result in attentional bias toward cancer-related stimuli. To examine cancer-related cognitive processing, Erblich and colleagues (Erblich, Montgomery, Valdimarsdottir, Cloitre, & Bovbjerg, 2003) developed a cancer variation of the Stroop task. In two studies outside the genetic testing context, one involving manual presentation of stimuli ($N = 168$; Erblich et al., 2003) and the other using a computerized task ($N = 68$; DiBonaventura, Erblich, Sloan, & Bovbjerg, 2010), women with a family history of breast cancer displayed longer response latencies when presented with cancer-related stimuli than with control stimuli (positively valenced words, negatively valenced words, neutral words, and cardiovascular-disease related words) and as compared with women without a familial cancer history. The association of cognitive processing with BRCA1/2 status, a stronger indicator of cancer risk than familial cancer history, has not been explored. In addition, those two studies excluded women with a personal history of cancer. To our knowledge, only one study has addressed cancer-related cognitive processing in individuals with cancer. In a sample of adults with insomnia secondary to cancer diagnosis (Taylor, Espie, & White, 2003), participants ($N = 33$) demonstrated attentional bias for cancer-related stimuli, as evidenced by longer response latencies for cancer-related versus sleep-related and neutral stimuli. Taken together, these three studies suggest that women at increased risk for cancer are susceptible to biased cancer-related cognitive processing and that, among those with personal cancer histories, biases in processing are more pronounced for cancer-related information than for other personally relevant stimuli.

Biased cognitive processing such as this has been construed by some as excessive attention to threat cues and is important in causation and maintenance of anxiety, depression, and other forms of distress (for a review, see Williams, Matthews, & Macleod, 1996). Essentially, biased processing results in excessive vigilance toward distress-related stimuli in the environment (e.g., physician office, cancer awareness ribbon), which leads to increased distress, which further exacerbates vigilance and impairs information processing. Inefficient or otherwise biased cancer-related cognitive processing could have a variety of important downstream effects for those at elevated risk, including poor uptake of information related to cancer risk and/or preventive options (Lerman et al., 1997) and interference with day-to-day activities and/or goals due to excessive attention to cancer-related stimuli (i.e., disproportionate use of cognitive resources; Koster, Crombez, Van Damme, Verschuere, & De Houwer, 2004; Koster, De Raedt, Goeleven, Franck, & Crombez, 2005). Given the complexity of the decisions facing women presenting for clinical BRCA1/2 testing, biased cancer-related cognitive processing could have significant implications for their overall health, well-being, and quality of life.

Relatively little research has addressed consequences of biased cognitive processing as indicated by Stroop performance. We are aware of no studies in which the links between biased cognitive processing and health outcomes have been investigated in the cancer context, but Jessop, Rutter, Sharma, and Albery (2004) reported that individuals with asthma evidencing high cognitive interference related to their illness are less adherent to treatment than individuals evidencing moderate cognitive interference. BRCA1/2 mutation carriers are advised to consider prophylactic mastectomy and/or oophorectomy to reduce their cancer risk. In the genetic testing context, engagement in risk-reducing behaviors represents an important clinical outcome. An increase in the uptake of prophylactic surgeries is evident in recent years, with 37% of carriers electing mastectomy (Schwartz et al., 2012) and 45–65% electing oophorectomy (Schwartz et al., 2012; Sidon et al., 2012). It remains unclear, however, why some patients elect surgical prophylaxis and others do not. The genetic testing context provides a unique opportunity to examine not only the phenomenon of biased cancer-related cognitive processing, but also its clinical implications.

The principal aim of the current study was to test whether cancer-related cognitive processing varied as a function of BRCA1/2 carrier status and personal cancer history. Specifically, we hypothesized that (a) women who carry a BRCA1/2 mutation would evidence more biased cancer-related cognitive processing than noncarriers, and (b) women with a personal history of breast or ovarian cancer would evidence more biased cancer-related cognitive processing than women without a personal cancer history, as women in both of these groups are at relatively higher risk for subsequent cancers. The secondary aim was to explore whether biased cognitive processing is associated with lower participation in cancer-related protective health behaviors, specifically the decision to elect prophylactic surgery. We also evaluated whether cancer-related distress can account for any obtained relations between cancer-related cognitive processing and other variables.

Method

Participants

Participants were recruited from among women enrolled in the UCLA Familial Cancer Registry and Genetic Evaluation Program. Eligibility criteria for the Registry include (a) age ≥ 18 years and (b) personal or familial history of cancer consistent with BRCA1/2 heredity and/or having at least a 10% prior probability of being a BRCA1/2 mutation carrier based on published risk assessment data. As a part of the Registry protocol, all participants provided informed consent to be contacted about studies related to their cancer risk.

Registry participants were eligible for the present study if they (a) were female; (b) elected to undergo BRCA1/2 testing through the Registry; and (c) if negative for a mutation, the participant was considered an "uninformative negative" (i.e., the participant did not have a first-degree family member who had previously tested positive for a BRCA mutation). Those who test negative and are related to a BRCA-mutation carrier are considered "definitive" or "true" negatives and typically advised that their lifetime breast and ovarian cancer risk is comparable to that of women in the general population (Antoniou et al., 2003; Risch et al., 2006; Thompson & Easton, 2001; Wacholder, Streuwing, Hartage, Greene, & Tucker, 2004; Whittemore, Gong, & Itnyre, 1997). We chose to exclude these women from the present study to increase homogeneity in

the negative subgroup, opting to include uninformative negative because it is the most frequent result of BRCA1/2 genetic testing.

Eligible Registry participants were defined as "cases" if they tested positive for a BRCA1 or BRCA2 mutation (BRCA+). Each case was matched to a Registry participant who tested negative for a BRCA mutation (BRCA-; control). These were sorted according to personal cancer history (yes vs. no). Next, matching was conducted on age (in decades), educational attainment (college graduate vs. less than college graduate), and months since receiving genetic testing results (within 60 months). If a case could not be matched to an appropriate control on these variables, slight mismatches were allowed, such that a mismatch of the control participant was allowed to the closest "unit" on no more than one variable (e.g., the next decade in age).

Within the boundary condition of the number of BRCA+ cases available in the Registry ($n = 100$), a priori power analysis was conducted to estimate necessary sample size. The number of participants required for a 2 (BRCA testing status) × 2 (personal cancer history) design to yield a large effect ($f = .40$) with 95% power is 112, which represented the minimum target sample size. Recruitment of all eligible BRCA+ cases (along with a one-to-one matched control) was attempted to detect a smaller effect.

Cancer Stroop Task

The Stroop task is one of the most widely used measures of cognitive processing in psychology (MacLeod, 1991). In the classic paradigm, participants are successively presented with color names and are asked to identify the (primarily conflicting) typeface color as quickly as possible. The Stroop is believed to assess selective attention, cognitive flexibility, and processing speed (MacLeod, 1991). Several variations of the task have been developed (e.g., Emotional Stroop; Williams et al., 1996), all of which require participants to suppress responses to distracting word information while maintaining attention on typeface color. However, unlike the classic task, stimuli in these variations capture attention through personal relevance of the words for the responder (e.g., addiction [Cox, Fadardi, & Pothos, 2006]; attention deficit hyperactivity disorder [Lansbergen, Kenemans, & van Engeland, 2007]; chronic pain [Schoth, Nunes, & Liossi, 2012]; depression [Epp, Dobson, Dozois, & Frewen, 2012]). Longer response latencies (i.e., slower RT) and more cognitive interference (i.e., longer RT to target words vs. neutral words) are considered an indication of cognitive bias for target stimuli.

We used the variation of the Stroop task developed by Erblich and colleagues (DiBonaventura et al., 2010; Erblich et al., 2003), administered via computer. Stimuli included five 10-word lists: *cancer* (e.g., biopsy, tumor), *cardiovascular disease* (e.g., bypass, coronary), *general threat* (e.g., afraid, shaky), *positive content* (e.g., glad, love), and *neutral content* (e.g., fountain, powder). Average item response latency (i.e., RT) was calculated for each word list. As in other studies using a keyboard interface to measure RT (e.g., (McNally et al., 1994), trials with response latencies of <300 msec or >2000 msec were considered outliers and excluded. As is common in the Stroop literature (MacLeod, 1991), a cognitive interference score (average cancer RT minus average neutral RT) was also included as an outcome.[1]

Prophylactic Surgery

Receipt of prophylactic mastectomy and oophorectomy was ascertained by self-report at the baseline interview for the present study. As part of their annual Registry follow-up evaluations, participants also reported whether they underwent prophylactic mastectomy or oophorectomy in the preceding year. Responses from the four annual evaluations subsequent to participants' Stroop session were combined to indicate whether they underwent any prophylactic surgery (yes/no) during the 4-year follow-up period.

Additional Measures

Verbal skill. Because verbal fluency can affect Stroop task performance, the North American Adult Reading Test (NAART; (Spreen & Strauss, 1991) was used to assess verbal skills. Participants were asked to pronounce a list of 60 words without the aid of phonetic cues (e.g., sieve, zealot, epitome). The number of words pronounced incorrectly is tallied; higher scores indicate poorer verbal fluency.

Cancer-specific distress. The Impact of Event Scale (IES; Horowitz, Wilner, & Alvarez, 1979) was used to assess intrusive thoughts (7 items) and avoidant behaviors (8 items) "related to your cancer risk" during the preceding seven days (0 = *not at all* to 5 = *often).* Total scores range from 0 to 75, with higher scores reflecting greater intrusion/avoidance related to cancer risk. Internal consistency reliability (Cronbach's alpha) for the total score for the present sample was .88.

Procedures

Eligible participants ($N = 196$) were contacted by Registry personnel via an introductory letter and follow-up phone call. The study was described, and those who verbally consented ($N = 133$, 68%) were scheduled for a testing session. Twelve women subsequently canceled and were unable to be rescheduled, yielding a final participation rate of 62% ($N = 121$). Of those who completed a testing session, six were excluded after the fact due to red-green color deficiency ($n = 2$); incomplete questionnaire data ($n = 1$); identification as a "true negative" ($n = 1$); and computer error in Stroop administration ($n = 2$), yielding a final N of 115.

The testing session took place in a private room in dedicated laboratory space in the Psychology Department ($n = 83$, 72%) or in the participant's home ($n = 32$, 28%) if she was unable or

---

[1] Researchers also have examined errors in naming the color of the personally relevant stimulus word, but generally do not find a significant difference in errors for relevant versus irrelevant words (MacLeod, 1991). This is consistent with previous studies using the cancer Stroop (DiBonaventura et al., 2010; Erblich et al., 2003) and the broader Stroop literature. Similarly, no significant difference in errors in color naming was evident in preliminary analyses, and this variable is not discussed further. For the reader's reference, we have included descriptive statistics for errors in Table 2.

unwilling to travel to the research site.[2] Following a detailed description of study procedures, written informed consent was obtained by a female research assistant at the beginning of the testing session. Each testing session lasted approximately 60 minutes and included completion of a brief author-constructed interview, questionnaires, and a computerized Cancer Stroop task. To eliminate the possibility of bias in administering the Stroop task resulting from knowledge of the participant's cancer history or carrier status, the research assistant who administered the interview was not the assistant who administered the Stroop task. Participants were offered $40 for their effort and reimbursed for parking as applicable.

Participants completed the computerized Stroop task in a quiet room with a female research assistant present but out of view. The computer task began with a practice trial of 10 words. Participants were instructed to indicate the color of the typeface (red, green, or blue) for each word by pressing designated keys on the keyboard as quickly as possible. Participants were then presented with the five experimental word lists. List order was counterbalanced across participants. Words within each list were presented randomly, 10 times each, for a total of 100 trials per list. Typeface color varied randomly. Each word appeared onscreen until the participant responded by pressing a key; participants received no feedback about the accuracy or speed of their responses. The duration of the task varied based on participants' response latencies, but generally lasted 12–15 min, including four 1-min breaks between lists.

Analytic Strategy

To examine the relationship between BRCA status, cancer history, and the cognitive processing dependent variables, we performed two univariate general linear model analyses (GLM)—one predicting Cancer RT, the other predicting interference—with BRCA mutation carrier status (BRCA+, BRCA−) and personal breast/ovarian cancer history (Br/Ov+, Br/Ov−) as between-subjects factors. A priori, we reasoned that it would be important to include age as a moderator in these analyses for two reasons: First, age is an important covariate when studying cognitive processing. On RT tasks, including the Stroop, younger age is consistently associated with faster RT (Ludwig, Borella, Tettamant, & de Ribaupierre, 2010; MacLeod, 1991; Van der Elst, Van Boxtel, Van Breukelen, & Jolles, 2006). Second, younger age is associated with higher levels of, and more persistent, psychological distress in the genetic testing context (Halbert et al., 2011; Watson et al., 2004) and among cancer patients and survivors (Howard-Anderson, Ganz, Bower, & Stanton, 2012; Mosher & Danoff-Burg, 2005). Thus, age was included as a continuous variable, and the models included all two-way interactions among BRCA status, cancer history, and age, as well as the three-way interaction (BRCA Status × History × Age). Linear regression was used to probe significant interaction effects. The other two matching variables—months since genetic testing and years of education—and verbal fluency (NAART) were considered as covariates for these analyses; none had a significant univariate relationship with Cancer RT or interference and thus were not included in the final models.[3]

To explore predictors of prophylactic surgery at 4 years, multinomial logistic regression was used. Receipt of prophylactic surgery was treated as a dichotomous dependent variable (1 = *received prophylactic mastectomy and/or oophorectomy*; 0 = *no prophylactic surgery*). The predictors of interest were the Stroop outcomes (Cancer RT, interference). BRCA status (BRCA+ = 1) and personal cancer history (yes = 1) were also included. Other covariates considered for inclusion were age, marital status (yes vs. no), months since genetic testing, years of education, and parity (yes vs. no); univariate analyses indicated that none of these sociodemographic variables were significantly correlated with receipt of prophylactic surgery (all p's > .40) and so none were retained for analysis. Odds ratios were calculated to test the association between each of the predictor variables and receipt of surgery (Kirkwood & Sterne, 2003). Given the number of outcome events, we reasoned that no more than two variables should be retained in the final model. We thus used a stepwise elimination procedure (IBM SPSS v. 19). The entry probability was set at $p =$ .25 and the removal probability was set at $p =$ .10, as this was an exploratory analysis. The model was also constrained to no more than two predictor variables per recommendations for logistic regression (Vittinghoff & McCulloch, 2007).

Results

Sample Description

Table 1 displays sample sociodemographic and BRCA-related characteristics. Four balanced groups were obtained such that the sample had approximately equal numbers of women who tested BRCA+ and had breast and/or ovarian cancer ($n = 31$); BRCA+ with no history of breast or ovarian cancer ($n = 26$); BRCA- with a history of breast or ovarian cancer ($n = 30$); and BRCA- with no history of breast or ovarian cancer ($n = 28$). Between-groups comparisons (one-way analysis of variance [ANOVA]; χ^2 test for personal cancer history) on the matching variables suggest that the match was successful (personal cancer history: $p = .78$; age: $p = .14$; education: $p = .88$; months since testing: $p = .71$).

With regard to the sample available for analysis of prophylactic surgery at follow-up, 17 women had undergone both prophylactic mastectomy and oophorectomy prior to the Stroop session and were therefore excluded. An additional 6 were excluded due to receipt of therapeutic mastectomy and/or oophorectomy prior to the Stroop session. Seven developed a new cancer after the Stroop session and 7 were lost to follow-up, resulting in a 4-year follow-up sample of 78 (68% of the total *N*), 13 (17%) of whom had undergone prophylactic surgery subsequent to the Stroop session.

---

[2] No significant group (laboratory vs. home visit) differences in Stroop RT, errors, or cognitive interference score emerged, so data were collapsed across test location for all analyses.

[3] For completeness, we repeated the principal analyses with all of the matching variables included as controls. The effects of years of education and months since genetic testing were not significant and the effects of our variables of interest—BRCA status, personal cancer history, and age—remained; thus only the variables of interest were retained for the analyses.

Table 1
Sociodemographic and Medical Characteristics of the Sample

Characteristic	Full sample ($N = 115$)	Breast/ovarian cancer history (negative)		Breast/ovarian cancer history (positive)	
		BRCA$-$ ($n = 28$)	BRCA$+$ ($n = 26$)	BRCA$-$ ($n = 30$)	BRCA$+$ ($n = 31$)
Age (years)	48.5 (10.7)	45.6 (9.8)	42.9 (11.0)	54.1 (9.0)	50.5 (9.1)
Education (years)	16.9 (2.5)	17.3 (2.1)	17.3 (2.4)	16.6 (2.6)	16.5 (2.8)
Married (% yes)	80 (70%)	82%	62%	63%	71%
Children ≤18 years (% yes)	38%	64%	35%	30%	26%
Months since genetic testing	30.6 (23.9)	24.4 (19.3)	21.1 (22.4)	38.0 (25.8)	37.1 (24.0)
Months since cancer diagnosis (Mdn)	61.0 (87.4)	n/a	n/a	72.0 (73.5)	48.0 (100.2)
Cancer site (%):					
Breast	56 (49%)			100%	84%
Ovary	5 (4%)			0%	16%
Stage (%):					
0	10 (9%)			20%	13%
I	21 (18%)			33%	35%
II	22 (19%)			33%	39%
III	2 (2%)			0%	6%
Unavailable	6 (5%)			14%	6%

Note. Unless otherwise indicated, values represent *M* (*SD*).

Preliminary Analysis

Descriptive statistics for the Stroop-related outcomes are displayed in Table 2.[4] To verify that participants evidenced bias for cancer-related stimuli, we performed a repeated-measures ANOVA (GLM) with list (cancer, cardiac, threat, positive, neutral) as a within-subjects factor. Results revealed a significant main effect of list, $F(4, 456) = 15.11$, $p < .001$. Planned comparisons (paired t tests, $\alpha = .01$ to control for familywise error) indicated that RT for the cancer list was significantly slower than RT for all other lists, indicating that, as expected and consistent with the Erblich studies (DiBonaventura et al., 2010; Erblich et al., 2003), women in the present sample evidenced biased cognitive processing specific to cancer-related stimuli.

Principal Analyses: Stroop Outcomes

For cancer RT, there was no significant main effect of BRCA status, $F(1, 107) = .13$, $p = .72$, though there were significant main effects of personal cancer history, $F(1, 107) = 4.77$, $p = .03$, partial $\eta^2 = .04$, and age, $F(1, 107) = 10.94$, $p < .01$, partial $\eta^2 = .09$. A significant Cancer History × Age interaction qualified these main effects, $F(1, 107) = 3.89$, $p = .05$, partial $\eta^2 = .04$. The other two-way (i.e., Cancer History × BRCA Status; BRCA Status × Age) interactions were not significant, nor was the three-way interaction between cancer history, BRCA status, and age. Figure 1 provides an illustration of the significant interaction. In a post hoc linear regression analysis including only those with no personal cancer history, younger age was associated with faster cancer RT ($p < .001$). Among those with a personal cancer history, age was not a significant predictor of Cancer RT ($p = .43$).

Regarding the interference score, there was a significant main effect of BRCA status, $F(1, 107) = 4.21$, $p = .04$, partial $\eta^2 = .04$. Main effects for cancer history, $F(1, 107) = 1.19$, $p = .28$, and age, $F(1, 107) = .00$, $p = .99$, were not significant. The main effect for BRCA status was qualified by a significant BRCA Status × Age interaction, $F(1, 107) = 3.95$, $p = .05$, partial $\eta^2 = .04$, which is illustrated in Figure 2. The other interaction terms were not statisti-

cally significant. Among BRCA mutation carriers, younger women evidenced greater interference than did older women, whereas among those who were not mutation carriers, older women evidenced greater interference than did younger women. Post hoc regression analyses yielded results similar to those for personal cancer history on RT; among BRCA+ women, age was not a significant predictor of interference ($p = .25$), whereas older women evidenced nonsignificantly more interference ($p = .07$) among noncarriers.

Exploratory Analysis: Receipt of Prophylactic Surgery at 4 Years

As described in the Analytic Strategy, a stepwise elimination procedure was used for the logistic regressions, with the final model constrained to include no more than two predictor variables. Variables entered were (a) Cancer RT, (b) interference, (c) BRCA status (BRCA+ = 1), and personal cancer history (yes = 1). In the final model, BRCA status and interference were retained. Results indicated that BRCA+ status was significantly associated with having prophylactic surgery during the 4-year follow-up period (OR = 17.45; 95% CI, 3.11 to 97.86; $p = .001$) and interference score was marginally significant (OR = 1.01; 95% CI, 1.00 to 1.02; $p = .06$). Taken together, these results indicate that BRCA+ status and greater cognitive interference were associated with increased likelihood of undergoing prophylactic surgery.

Post Hoc Analyses

Given the posited association between distress related to cancer and biased cancer-related cognitive processing, we assessed whether cancer-related distress accounted for the observed rela-

---

[4] Additional analyses demonstrated that women who already had received risk-reducing surgery at baseline did not differ significantly from women who had not undergone such surgeries prior to baseline on Cancer RT or interference (all $p < .22$).

Table 2
Descriptive Statistics: Stroop Outcomes

	Full sample (N = 115)	Breast/ovarian cancer history (negative)		Breast/ovarian cancer history (positive)	
		BRCA− (n = 28)	BRCA+ (n = 26)	BRCA− (n = 30)	BRCA+ (n = 31)
Average response latency (RT), msec					
Cancer	817.8 (146.0)	778.5 (127.4)	781.3 (135.6)	868.1 (134.5)	835.1 (167.8)
Cardiac	791.8 (128.4)	760.7 (126.2)	758.3 (127.1)	845.4 (115.1)	796.1 (131.5)
General threat	786.3 (136.6)	757.2 (130.0)	762.1 (122.2)	828.5 (116.5)	791.9 (164.3)
Positive	786.1 (137.6)	752.9 (119.4)	764.4 (145.5)	833.0 (116.5)	788.9 (157.2)
Neutral	773.6 (133.2)	754.3 (123.2)	739.5 (122.3)	809.2 (113.4)	785.1 (161.6)
Errors (number per list)					
Cancer	2.8 (4.4)	2.5 (2.1)	2.5 (2.0)	3.8 (7.4)	2.4 (3.3)
Cardiac	2.3 (2.4)	2.1 (1.9)	2.2 (1.8)	2.9 (3.7)	1.8 (1.4)
General threat	2.6 (4.1)	2.7 (2.5)	1.8 (1.5)	3.4 (5.9)	2.4 (4.6)
Positive	2.5 (2.4)	2.2 (1.9)	2.2 (1.6)	2.8 (3.1)	2.5 (2.5)
Neutral	2.7 (2.9)	2.5 (1.7)	2.6 (2.2)	3.4 (4.1)	2.4 (3.0)
Interference (Cancer RT-Neutral RT), msec	44.2 (72.4)	24.2 (72.8)	41.7 (52.9)	58.8 (82.8)	50.0 (74.6)
Impact of Event Scale (IES)					
Avoidance subscale	6.2 (6.4)	5.3 (6.4)	6.1 (5.1)	6.9 (7.8)	6.6 (6.2)
Intrusion subscale	5.9 (6.0)	4.1 (5.3)	7.2 (6.0)	6.5 (6.3)	6.0 (6.0)
Total score	12.2 (11.5)	9.4 (11.1)	13.3 (9.7)	13.4 (13.5)	12.6 (11.1)

Note. Values represent mean (*SD*).

tionships. Thus, we repeated all of the analyses reported herein, including cancer-specific distress as a covariate (IES total score). Descriptive statistics for the IES are included in Table 1 for reference. Results of these analyses indicated that (a) cancer-specific distress was not a significant unique predictor of Cancer

RT, interference score, or receipt of prophylactic surgery; and (b) the pattern of significance for the other predictors was identical in all models.

We also explored whether cancer-related distress served as a mediator of either of the relationships observed in the principal
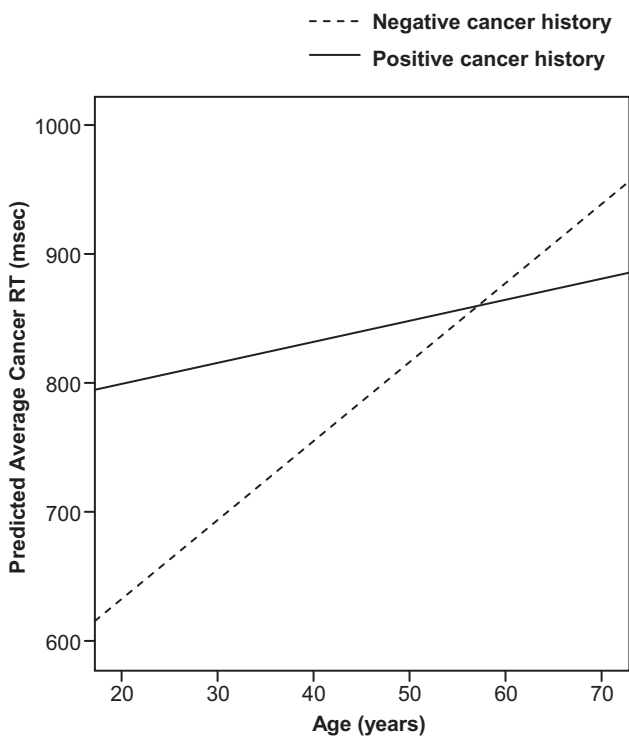

Figure 1. Predicted average cancer reaction time (RT) as a function of the significant interaction between personal cancer history and participant age.
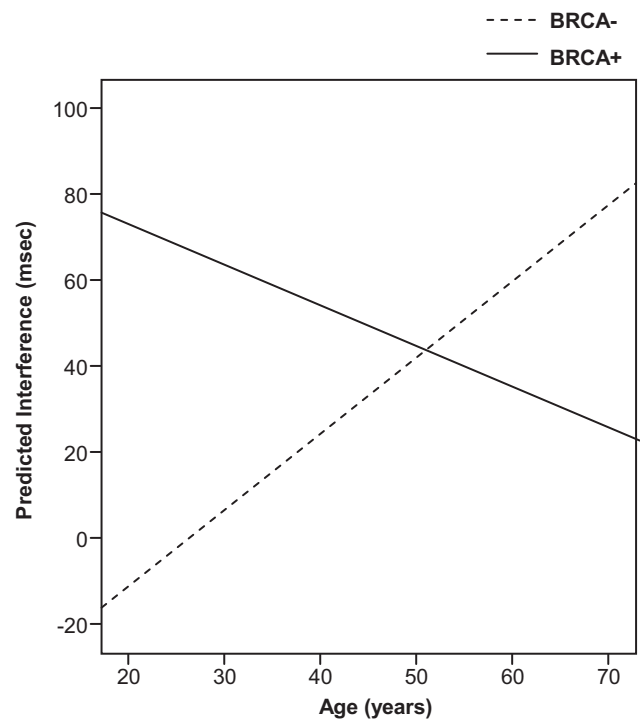

Figure 2. Predicted cognitive interference as a function of the significant interactions between BRCA status and participant age.

analyses (i.e., BRCA status and interference; cancer history and cancer RT). The model testing the relationship between cancer history and cancer-specific distress was not significant, $F(1, 113) = .65$, $p = .42$, and the relationship between BRCA status and cancer-specific distress was not significant [$F(1, 113) = .47$, $p = .50$]. Thus, cancer-specific distress did not mediate the observed relationships between BRCA status/cancer history and biased cancer-related cognitive processing.

Discussion

The primary aim of the current study was to examine cancer-related cognitive processing among women who had undergone BRCA1/2 genetic testing and to test whether such processing varied as a function of BRCA1/2 carrier status and personal cancer history. Our hypotheses were supported: women with deleterious BRCA1/2 mutations evidenced more biased cancer-related cognitive processing (more interference) than noncarriers, and women with a personal history of breast or ovarian cancer evidenced more biased cancer-related cognitive processing (longer response latencies) than women with no such history. In both cases, however, age moderated the effects (see Figures 1 and 2). In the broader Stroop literature, older participants tend to evidence longer RT and more interference than younger participants (Ludwig et al., 2010; MacLeod, 1991; Van der Elst, et al., 2006). In the present study, the typical age advantage was effectively eliminated for cancer RT and interference, but this varied by predictor. We propose subtly different explanations for the two Stroop outcomes, with the caveat that they are speculative.

Regarding response latency and personal cancer history, it is possible that women with a personal cancer history responded more slowly to cancer-related stimuli, regardless of age, because the words themselves were more familiar, salient, and/or personally relevant to survivors. Women in the present sample without a personal history of cancer might evidence comparable knowledge of cancer-related information, given their familial history/risk profile (Mouchawar, Byers, Cutter, Dignan, & Michael, 1999), but exposure to cancer-related information is different for women who have been diagnosed and treated for the disease (Zakowski et al., 1997). For these patients, the Stroop stimuli tap not only content knowledge, but episodic memory, activating multiple pathways that might slow responding (Anderson, Bothell, Lebiere, & Matessa, 1998).

Regarding the results for cognitive interference, we believe that the suspension of goals related to cancer risk reduction among younger BRCA+ participants creates a set of circumstances in which cognitive interference is not only possible but quite likely. It is common for medical teams working with BRCA+ patients to recommend surveillance over prophylactic surgery until completion of planned childbearing (Eisen, Rebbeck, Wood, & Weber, 2000). Decades of evidence suggests that when a goal has been suspended, several mental processes remain focused on the goal, that is, the Zeigarnik effect (1927). Recent research has demonstrated that even experimentally induced goals occupy cognitive resources, (e.g., working memory; Masicampo & Baumeister, 2011). Others have demonstrated that goals are more likely to intrude into consciousness when progress toward them is difficult or problematic (Bongers, Dijksterhuis, & Spears, 2010). The age range for the present sample was 27 to 70 years old, and a

substantial portion of younger participants did not have children. It is also the case that younger (vs. older) participants in the present study were less likely to have undergone preventive mastectomy ($p = .04$) or oophorectomy ($p = .03$) prior to the Stroop session and more likely to report plans to do so in the future (mastectomy: $p < .01$; oophorectomy: $p = .05$; data not shown). Put another way, younger participants in the present study were more likely to have unfulfilled goals related to reducing their cancer risk, which could explain their higher levels of interference.

Though they were contrary to our expectations, the prophylactic surgery results provide support for the notion that cognitive interference was associated with goal suspension, as greater interference was associated with increased likelihood of prophylactic surgery in the four years following the Stroop session. Indeed, a greater proportion of women who reported at the baseline assessment that they intended to undergo prophylactic mastectomy and/or oophorectomy in the future actually did so during the follow-up period, compared to those who reported they did not plan to undergo prophylactic surgery: mastectomy: $\chi^2(2, N = 77) = 17.35$, $p < .001$; oophorectomy: $\chi^2(2, N = 77) = 17.51$, $p < .001$].[5] It would be interesting to see whether cognitive interference resolved following surgery for these women, although the design of the present study did not allow for this. Of course, these results were exploratory and the effect of interference on receipt of surgery should be interpreted with caution in light of the small sample size and restrictions on the number of relevant controls we were able to include in the analysis.

Interestingly, we did not find evidence for an association between cancer-specific distress and biased cancer-related cognitive processing, nor did we find evidence supporting cancer-specific distress as a mediator of the relationship between biased processing and BRCA status or personal cancer history. These results are consistent with Erblich et al. (2003) and with recent evidence that biased attention toward threatening material can exist independent of a subjective affective response (Blanchette & Richards, 2012), though we believe there is still insufficient evidence to conclude that distress does not play an important role here. The genetic testing clinical scenario is complex. All of the women in the present study were at increased risk for breast and/or ovarian cancer by virtue of their personal cancer history, familial cancer history, ethnicity, or some combination thereof ("true negatives" were excluded). Nonetheless, these women represent four different patient groups, with varying levels of cancer risk. In light of this and the observed interactions among age, BRCA status, and cancer history, the role of cancer-specific distress might be better illustrated using a moderated mediation approach (Muller, Judd, & Yzerbyt, 2005). Our study was not powered for such an analysis, but future research should consider this possibility, as identifying factors that contribute to or maintain such distress will ultimately improve understanding of patient uptake and utilization of genetic risk information.

The present study provides evidence for nuanced relationships among cancer-relevant predictors, individual differences (notably,

---

[5] In response to a reviewer's comment, we examined the possibility of whether baseline surgical intentions eliminated the predictive effect of biased processing by including it as a covariate in the logistic regression analysis. Inclusion of the variable in the final models did not impact the significance or pattern of results for BRCA status or interference.

age), cognitive processing, and patients' decisions to undergo prophylactic surgery. Moreover, these results suggest that research that endeavors to advance understanding of the uptake and consequences of receiving genetic risk information must move beyond documenting negative affective responses. Cancer-related cognitive processing appears to be an important, clinically relevant target; however, limitations of the design and methods should be noted. Power to detect small to moderate effects was limited. A larger sample would have allowed more flexibility to explore additional predictors and/or moderators. In addition, data were not obtained at the time of testing/diagnosis; instead, all variables were assessed, on average, two to three years following genetic testing and, for those with a personal history of cancer, an average of five years following diagnosis. There were no significant associations between time elapsed since genetic testing or cancer diagnosis and cognitive processing in the present sample; however, studies that aim to elucidate the relationship between biased cancer-related cognitive processing and distress—and their clinical implications—should likely be conducted at various points during the genetic testing process and, optimally, include longitudinal follow-up. Future studies could provide valuable insight into individuals' behavioral responses to genetic information, which will become all the more important as clinical genetic testing options expand to other cancers and diseases.

References

Anderson, J. R., Bothell, D., Lebiere, C., & Matessa, M. (1998). An integrated theory of list memory. *Journal of Memory and Language, 38,* 341–380. doi:10.1006/jmla.1997.2553

Antoniou, A., Pharoah, P. D., Narod, S., Risch, H. A., Eyfjord, J. E., Hopper, J. L., . . . Easton, D. F. (2003). Average risks of breast and ovarian cancer associated with BRCA1 or BRCA2 mutations detected in case series unselected for family history: A combined analysis of 22 studies. *American Journal of Human Genetics, 72,* 1117–1130. doi:10.1086/375033

Beran, T. M., Stanton, A. L., Kwan, L., Seldon, J., Bower, J. E., Vodermaier, A., & Ganz, P. A. (2008). The trajectory of psychological impact in BRCA1/2 genetic testing: Does time heal? *Annals of Behavioral Medicine, 36,* 107–116. doi:10.1007/s12160-008-9060-9

Blanchette, I., & Richards, A. (2013). Is emotional Stroop interference linked to affective responses? Evidence from skin conductance and facial electromyography. *Emotion, 13,* 129–138.

Bongers, K. C. A., Dijksterhuis, A., & Spears, R. (2010). On the role of consciousness in goal pursuit. *Social Cognition, 28,* 262–272. doi:10.1521/soco.2010.28.2.262

Cox, W. M., Fadardi, J. S., & Pothos, E. M. (2006). The Addiction-Stroop test: Theoretical considerations and procedural recommendations. *Psychological Bulletin, 132,* 443–476. doi:10.1037/0033-2909.132.3.443

Croyle, R. T., Smith, K. R., Botkin, J. R., Baty, B., & Nash, J. (1997). Psychological responses to BRCA1 mutation testing: Preliminary findings. *Health Psychology, 16,* 63–72. doi:10.1037/0278-6133.16.1.63

DiBonaventura, M. D., Erblich, J., Sloan, R. P., & Bovbjerg, D. H. (2010). A computerized stroop task to assess cancer-related cognitive biases. *Behavioral Medicine, 36,* 37–43. doi:10.1080/08964280903521321

Eisen, A., Rebbeck, T. R., Wood, W. C., & Weber, B. L. (2000). Prophylactic surgery in women with a hereditary predisposition to breast and ovarian cancer. *Journal of Clinical Oncology, 18,* 1980–1995.

Epp, A. M., Dobson, K. S., Dozois, D. J. A., & Frewen, P. A. (2012). A systematic meta-analysis of the Stroop task in depression. *Clinical Psychology Review, 32,* 316–328. doi:10.1016/j.cpr.2012.02.005

Erblich, J., Montgomery, G. H., Valdimarsdottir, H. B., Cloitre, M., & Bovbjerg, D. H. (2003). Biased cognitive processing of cancer-related information among women with family histories of breast cancer: Evidence from a cancer stroop task. *Health Psychology, 22,* 235–244. doi:10.1037/0278-6133.22.3.235

Halbert, C. H., Stopfer, J. E., McDonald, J., Weathers, B., Collier, A., Troxel, A. B., & Domcheck, S. (2011). Long-term reactions to genetic testing for BRCA1 and BRCA2 mutations: Does time heal women's concerns? *Journal of Clinical Oncology, 29,* 4302–4306. doi:10.1200/JCO.2010.33.1561

Hamilton, J. G., Lobel, M., & Moyer, A. (2009). Emotional distress following genetic testing for hereditary breast and ovarian cancer: A meta-analytic review. *Health Psychology, 28,* 510–518. doi:10.1037/a0014778

Horowitz, M. J., Wilner, N., & Alvarez, W. (1979). Impact of Event Scale: A measure of subjective stress. *Psychosomatic Medicine, 41,* 209–218.

Howard-Anderson, J., Ganz, P. A., Bower, J. E., & Stanton, A. L. (2012). Quality of life, fertility concerns, and behavioral health outcomes in younger breast cancer survivors: A systematic review. *Journal of the National Cancer Institute, 104,* 386–405. doi:10.1093/jnci/djr541

Jessop, D. C., Rutter, D. R., Sharma, D., & Albery, I. P. (2004). Emotion and adherence to treatment in people with asthma: An application of the emotional Stroop paradigm. *British Journal of Psychology, 95,* 127–147. doi:10.1348/000712604773952386

Kinney, A. Y., Bloor, L. E., Mandal, D., Simonsen, S. E., Baty, B. J., Holubkov, R., . . . Smith, K. (2005). The impact of receiving genetic test results on general and cancer-specific psychologic distress among members of an African-American kindred with a BRCA1 mutation. *Cancer, 104,* 2508–2516. doi:10.1002/cncr.21479

Kirkwood, B. R., & Sterne, J. A. C. (2003). *Essential medical statistics.* Hoboken, NJ: Wiley.

Koster, E. H., Crombez, G., Van Damme, S., Verschuere, B., & De Houwer, J. (2004). Does imminent threat capture and hold attention? *Emotion, 4,* 312–317. doi:10.1037/1528-3542.4.3.312

Koster, E. H., De Raedt, R., Goeleven, E., Franck, E., & Crombez, G. (2005). Mood-congruent attentional bias in dysphoria: Maintained attention to and impaired disengagement from negative information. *Emotion, 5,* 446–455. doi:10.1037/1528-3542.5.4.446

Lansbergen, M. M., Kenemans, J. L., & van Engeland, H. (2007). Stroop interference and attention-deficit/hyperactivity disorder: A review and meta-analysis. *Neuropsychology, 21,* 251–262. doi:10.1037/0894-4105.21.2.251

Lerman, C., Biesecker, B., Benkendorf, J. L., Kerner, J., Gomez-Caminero, A., Hughes, C., & Reed, M. M. (1997). Controlled trial of pretest education approaches to enhance informed decision-making for BRCA1 gene testing. *Journal of the National Cancer Institute, 89,* 148–157. doi:10.1093/jnci/89.2.148

Ludwig, C., Borella, E., Tettamant, M., & de Ribaupierre, A. (2010). Adult age differences in the Color Stroop Test: A comparison between an item-by-item and a blocked version. *Archives of Gerontology and Geriatrics, 51,* 135–142. doi:10.1016/j.archger.2009.09.040

MacLeod, C. M. (1991). Half a century of research on the Stroop effect: An integrative review. *Psychological Bulletin, 109,* 163–203. doi:10.1037/0033-2909.109.2.163

Masicampo, E. J., & Baumeister, R. F. (2011). Consider it done! Plan making can eliminate the cognitive effects of unfulfilled goals. *Journal of Personality and Social Psychology, 101,* 667–683. doi:10.1037/a0024192

McNally, R. J., Amir, N., Louro, C. E., Lukach, B. M., Riemann, B. C., & Calamari, J. E. (1994). Cognitive processing of idiographic emotional information in panic disorder. *Behavior Research and Therapy, 32,* 119–122. doi:10.1016/0005-7967(94)90092-2

Meiser, B. (2005). Psychological impact of genetic testing for cancer susceptibility: An update of the literature. *Psycho-Oncology, 14,* 1060–1074. doi:10.1002/pon.933

Metcalfe, K., Lynch, H., Ghadirian, P., Tung, N., Olivotto, I. A., Warner, E., . . . Narod, S. A. (2004). Contralateral breast cancer in BRCA1 and BRCA2 mutation carriers. *Journal of Clinical Oncology, 22,* 2328–2335. doi:10.1200/JCO.2004.04.033

Mosher, C. E., & Danoff-Burg, S. (2005). A review of age differences in psychological adjustment to breast cancer [Review]. *Journal of Psychosocial Oncology, 23,* 101–114. doi:10.1300/J077v23n02_07

Mouchawar, J., Byers, T., Cutter, G., Dignan, M., & Michael, S. (1999). A study of the relationship between family history of breast cancer and knowledge of breast cancer genetic testing prerequisites. *Cancer Detection and Prevention, 23,* 22–30. doi:10.1046/j.1525-1500.1999.00065.x

Muller, D., Judd, C. M., & Yzerbyt, V. Y. (2005). When moderation is mediated and mediation is moderated. *Journal of Personality and Social Psychology, 89,* 852–863. doi:10.1037/0022-3514.89.6.852

Risch, H. A., McLaughlin, J. R., Cole, D. E., Rosen, B., Bradley, L., Fan, I., . . . Narod, S. A. (2006). Population BRCA1 and BRCA2 mutation frequencies and cancer penetrances: A kin-cohort study in Ontario, Canada. *Journal of the National Cancer Institute, 98,* 1694–1706. doi:10.1093/jnci/djj465

Schoth, D. E., Nunes, V. D., & Liossi, C. (2012). Attentional bias towards pain-related information in chronic pain: A meta-analysis of visual-probe investigations. *Clinical Psychology Review, 32,* 13–25. doi:10.1016/j.cpr.2011.09.004

Schwartz, M. D., Isaacs, C., Graves, K. D., Poggi, E., Peshkin, B. N., Gell, C., . . . Perley, L. (2012). Long-term outcomes of BRCA1/BRCA2 testing: Risk reduction and surveillance. *Cancer, 118,* 510–517. doi:10.1002/cncr.26294

Sidon, L., Ingham, S., Clancy, T., Clayton, R., Clarke, A., Jones, E. A., . . . Evans, D. G. R. (2012). Uptake of risk-reducing salpingo-oophorectomy in women carrying a BRCA1 or BRCA2 mutation: Evidence for lower uptake in women affected by breast cancer and older women. *British Journal of Cancer, 106,* 775–779. doi:10.1038/bjc.2011.573

Spreen, O., & Strauss, E. (1991). *A compendium of neuropsychological tests.* New York, NY: Oxford University Press.

Struewing, J. P., Hartge, P., Wacholder, S., Baker, S. M., Berlin, M., McAdams, M., . . . Tucker, M. A. (1997). The risk of cancer associated with specific mutations of BRCA1 and BRCA2 among Ashkenazi Jews.

New England Journal of Medicine, 336, 1401–1408. doi:10.1056/NEJM199705153362001

Taylor, L. M., Espie, C. A., & White, C. A. (2003). Attentional bias in people with acute versus persistent insomnia secondary to cancer. *Behavioral Sleep Medicine, 1,* 200–212. doi:10.1207/S15402010BSM0104_3

Thompson, D., & Easton, D. F. (2001). Variation in cancer risks, by mutation position, in BRCA2 mutation carriers. *American Journal of Human Genetics, 68,* 410–419. doi:10.1086/318181

Van der Elst, W., Van Boxtel, M. P. J., Van Breukelen, J. P., & Jolles, J. (2006). The Stroop color-word test: Influence of age, sex, and education and normative data for a large sample across the adult age range. *Assessment, 13,* 62–79. doi:10.1177/1073191105283427

Vittinghoff, E., & McCulloch, C. E. (2007). Relaxing the rule of ten events per variable in logistic and Cox regression. *American Journal of Epidemiology, 165,* 710–718. doi:10.1093/aje/kwk052

Wacholder, S., Streuwing, J. P., Hartage, P., Greene, M. H., & Tucker, M. A. (2004). Breast cancer risks for BRCA1/2 carriers. *Science, 306,* 2187–2191.

Watson, M., Foster, C., Eeles, R., Eccles, D., Ashley, S., Davidson, R., . . . Evans, D. G. R. (2004). Psychosocial impact of breast/ovarian (BRCA1/2) cancer-predictive genetic testing in a UK multi-centre clinical cohort. *British Journal of Cancer, 91,* 1787–1794. doi:10.1038/sj.bjc.6602207

Whittemore, A. S., Gong, G., & Itnyre, J. (1997). Penetrance and contribution of BRCA1 mutations in breast cancer and ovarian cancer: Results from three U.S. population-based case-control studies of ovarian cancer. *American Journal of Human Genetics, 60,* 496–504.

Williams, J. M., Matthews, A., & Macleod, C. M. (1996). The emotional Stroop task and psychopathology. *Psychological Bulletin, 120,* 3–24. doi:10.1037/0033-2909.120.1.3

Zakowski, S. G., Valdimarsdottir, H. B., Bovbjerg, D. H., Borgen, P., Holland, J., Kash, K., . . . Zee, K. V. (1997). Predictors of intrusive thoughts and avoidance in women with family histories of breast cancer. *Annals of Behavioral Medicine, 19,* 362–369. doi:10.1007/BF02895155

Zeigarnik, B. (1927). Das Behalten erledigter und unerledigter Handlungen. *Psychologische Forschung, 9,* 1–85.