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FATIGUE AND ANXIETY IN BREAST CANCER: THE RELATIONSHIP WITH INTERPRETATION BIAS

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Abstract

Background: Research has highlighted both fatigue and anxiety to be two of the most debilitating symptoms of breast cancer that prevail for years into its survivorship, and suggests that these symptoms influence how people interpret information. Harbouring negative interpretation biases also helps to maintain self-destructive beliefs resulting in increased severity of symptoms and disability in those already affected by the illness. This study is the first utilizing an experimental measure of assessing interpretation bias in a population of breast cancer to investigate the contribution of fatigue and anxiety.
Method: A cross-sectional study design was used. 53 breast cancer survivors and 62 female healthy controls were recruited via opportunistic sampling. Participants completed an online questionnaire assessing basic demographics, fatigue via the Chalder Fatigue Questionnaire (CFQ) and anxiety using the Hospital Anxiety and Depression Scale (HADS). Following this, an in-person testing session assessed interpretation bias (IB) using a computerised task.
Results: Independent sample t-tests found a non-significant result in the comparison of IB indices between populations ($t(112.60) = .28$, $p = .783$; $d = .05$). Significant differences were observed in mean fatigue and anxiety scores in the breast cancer population compared to the healthy controls. Pearson correlation identified a statistically significant positive correlation between CFQ scores and negative interpretation bias ($r = .34$, $n = 53$, $p = .013$), however not for anxiety. Hierarchical multiple regression was calculated to predict negative interpretation biases based on potential confounding variables (age, relationship status and level of education), CFQ, HADS anxiety scores (separately). All four regression models were non-significant. The only significant predictor of negative interpretation bias was fatigue ($\beta = .39$, $t(53) = 2.71$, $p = .009$).
Conclusion: The identified significant correlation between fatigue and negative interpretation bias in this study corroborates findings from existing literature. However other results proved inconsistent with the vast body of research suggesting that breast cancer survivors would make more negative interpretations of ambiguous stimuli on an IB task compared to healthy controls. These results highlight the potential for future research investigating strategies of inherent self-adaptive and coping mechanisms that are or could be adopted by these participants to overcome this cognitive bias.

Keywords: *Fatigue, anxiety, breast cancer, interpretation bias.*

1. Introduction

Breast cancer is the most common cancer amongst females worldwide affecting approximately 1 in 8 women in their lifetime (Rojas K, 2016). According to Cancer Net, the average 5-year survival rate of women with invasive breast cancer is ~90%, and the 10-year survival rate is ~83%. It is therefore essential to understand and attempt to address the significant issues in cancer survivorship to minimise distress and improve patient quality of life (QOL). Following remission of breast cancer, the most common concern is fear of cancer recurrence. Fatigue has been reported by 30-50% of breast cancer survivors within the first five years post-treatment (Kingston B, 2016). It is one of the most prevalent symptoms experienced by those in remission of breast cancer and is present at significantly higher rates compared to age-matched controls.

One of the core processes, believed to maintain and perpetuate anxiety, is how people interpret and process information. A consistent finding amongst psychological literature is the tendency of individuals to process information preferentially according to their perspective of the world and perception of themselves (Beck A.T, 1988). Cognitive schemas are complex internally stored representations of ideas derived from previous experiences which, when operationalised, lead people to

construct their own psychological realities (Pace T, 1988). Beck theorised that when activated schemas are disproportionate to life events, information processing becomes erroneous, therefore affecting other systems resulting in inappropriate affect or behaviour (Beck AT, 1988). These schemas become reflected in the subjective interpretation of stimuli. These information-processing biases are frequently found in anxious individuals who generally sustain a view of the world that is more dangerous and threatening to them.

Cognitive models of anxiety show that cognitive biases such as interpreting ambiguous information in a negative manner, known as an interpretation bias, can serve as a strong maintaining factor of maladaptive anxiety (Lichtenthal W.G, 2017). Furthermore, Hughes et al., (2016) established that people with chronic fatigue syndrome (CFS), a condition characterised by persistent and debilitating physical and mental fatigue, tended to interpret ambiguous information as more illness-related and threatening in comparison to healthy individuals.

To date, no studies have utilised experimental measures with breast cancer survivors to explore how they interpret ambiguous information and how this relates to anxiety and fatigue. This study will be the first to take measures of both fatigue and anxiety cumulatively in the context of information processing. We hypothesised that: *"Breast cancer survivors would make more negative somatic/ illness-related interpretations of neutral stimuli on an interpretative bias task, compared to healthy controls"*; accounting for potential confounding variables (age, relationship status and highest level of education). Secondly, we also hypothesised that *"Interpretation biases would have positive correlations to increased levels of anxiety and fatigue in breast cancer survivors."*

2. Methods

2.1. Design

A cross-sectional observational study design was used to investigate interpretation bias in breast cancer survivors compared to a healthy control population.

2.2. Participants

Over the period October 2018 – February 2020, a total of 58 participants in remission of breast cancer and 122 healthy controls were recruited via opportunistic sampling. Breast cancer participants were recruited primarily from oncology clinics at Guys and St Thomas' Trust (GSTT), whilst the healthy control population was recruited primarily through word of mouth, social media, poster distribution, an online portal via Kings College London (KCL) and applications including 'Next Door' and 'Gumtree'.

2.3. Materials

The software Qualtrics was used to create a survey assessing basic demographics, including age, ethnicity, relationship status and the highest level of education. The CFQ is an 11-item questionnaire assessing severity of physical and mental fatigue (Chalder et al., 1993). A Likert scoring system measured the severity of the fatigue using a scale where less than usual scored (0), no more than usual (1), more than usual (2) and much more than usual (3). The HADS is a commonly used reliable self-report scale assessing psychological distress in non-psychiatric, consisting of 16 items evaluating anxiety and depression on two separate subscales. Each item has a Likert response scale and is scored from 0 to 3, which gives a score from 0-24 for each scale. Interpretation bias was assessed using a task developed by Mathews and Mackintosh (2000). It involved the endorsement of statements that have either positive or negative interpretations to an ambiguous scenario presented to them in the form of a short four-line story. Participants were asked to recall the scenarios in a 'memory test' and decide how similar four new statements were in comparison to the original text. These statements included a positive interpretation, a negative interpretation, a false but positive statement (positive foil) and a false but negative statement (negative foil).

2.4. Procedure

Ethical approval was granted by the Berkshire B NHS Ethics Committee (REC reference: 14/SC/0172) at King's College London. Participation in the study was voluntary, however, to maximize the sample size, £20 was given as a partial incentive and to cover travel expenses into the site of testing.

2.5. Analysis

The data was analyzed using IBM SPSS Statistics (Version 26) software. Descriptive analysis was conducted for participant characteristics of both groups including age, gender, time since diagnosis, relationship status, highest level of education, CFQ, HADS depression and HADS anxiety scores and IB Index. Independent sample t-tests were used to compare mean CFQ scores, HADS depression and anxiety

scores, between the IV 'health status' with two levels (breast cancer and healthy control populations). An independent t-test was also used in assessing the primary hypothesis to determine whether there were any statistically significant differences in mean IB index, positive interpretations and negative interpretations between breast cancer survivors and healthy controls. Pearson product-moment correlation coefficients (PMCC) were carried out to assess the strength of the relationship between levels of anxiety and IB performance (including overall index, positive and negative interpretations separately); and levels of fatigue and IB. In order to determine whether there were any significant effects of confounding variables on negative interpretation biases in breast cancer survivors, a hierarchical multiple regression analysis was performed with CFQ scores, HADS anxiety scores, relationship status, highest level of education and age as predictors and negative IB as the DV variable.

3. Results

After matching age/gender of the healthy controls to the breast cancer population, the final analysis included 62 healthy controls and 53 breast cancer survivors. Significant differences were observed in mean fatigue and anxiety scores in the breast cancer population compared to the healthy controls. Fatigue = ($t(66.70)=6.88$, $p <.001$, $d=.76$). HADS anxiety = ($t(110.55)= 3.48$, $p=.001$; $d=.64$). HADS depression = ($t(94.29)=3.618$, $p <.001$; $d=.76$). Statistics show these both to have a medium effect size. Independent sample t-tests found a non-significant result in the comparison of IB indices between populations ($t(112.60) =.28$, $p=.783$; $d=.05$). Equally this was the same for positive and negative interpretations. The second hypothesis: 'Interpretation bias would be positively correlated with increased levels of anxiety and fatigue in the breast cancer population', was assessed using Pearson product-moment correlation (PMCC). Pearson correlation identified a statistically significant positive correlation between CFQ scores and negative interpretation bias ($r=.34$, $n=53$, $p=.013$), however not for anxiety ($r=.20$, $n=53$, $p=.158$). Hierarchical multiple regression was calculated to predict negative interpretation biases based on potential confounding variables (age, relationship status and level of education), CFQ, HADS anxiety scores (separately). All four regression models were non-significant. The only significant predictor of negative interpretation bias was fatigue ($ß =.39$, $t(53)=2.71$, $p=.009$).

4. Discussion

The significant difference in mean fatigue and anxiety levels between the two populations corroborate findings from existing literature, which consistently recognise these symptoms to be two of the largest threats to psychological well-being amongst breast cancer survivorship (Lichtenthal W.G, 2017). This rejection of the primary hypothesis challenges findings of existing literature. From the results of the interpretation bias task, it may be inferred that the cognitive schemas of the breast cancer participants were not maladaptive as Beck's theory suggested, yet perhaps the contrary. Interestingly, research has suggested that positively interpreting ambiguous information may constitute a protective marker of psychological well-being, particularly during stressful circumstances. Using the principles of cognitive bias modification, individuals who adopt this positive mentality are typically more resilient to stress which provides them with great cognitive flexibility and they're able to endorse more positive comping styles in the face of adversity, thus explaining the non-significant difference in interpretation bias performance compared to healthy controls.

The finding that fatigue was positively correlated with making more negative interpretations on the IB task is consistent with current research supporting the association between fatigue and negative IB (Kleim B., 2014). Whilst research has focused on chronic fatigue syndrome populations in the past, it is proposed that factors maintaining fatigue are transdiagnostic to a range of other long-term conditions. Although it may appear paradoxical, studies have proposed that physical exercise can serve as a beneficial intervention, which may help women survivors of breast cancer to recognise and reorganise their interpretations of fatigue thereby reducing its intensity. Other studies suggest yoga and mindfulness interventions are powerful tools in combating cancer-related fatigue.

The non-significant correlation between anxiety and negative IB falls contradictory to a lot of literature as the cognitive models of anxiety disorders propose that information processing has a vital role in developing emotional psychopathology. This finding may be due to the HADS anxiety scale which has reduced sensitivity and specificity compared to a 'gold standard' structured clinical interview. *4.2 – Limitations*: The study was underpowered with unequal sample sizes of 53 and 62, instead of desired 64 as determined using G* Power software (Erdfelder E., 1996). The subjectivity of fatigue and anxiety may further contribute to a bias in results; therefore, it would be appropriate to consider potential objective measures of these variables focusing on physiological processes, i.e. sympathetic arousal or performances including reaction times. The self-reported execution of these questionnaires introduces

both social desirability bias and recall bias as many questions rely on the participant being able to recall symptoms over the past month accurately. Additionally, some participants in the breast cancer group were taking hormone therapy for which there is empirical evidence supporting its correlation to increased levels of fatigue, mood swings and depression. Finally, there were differences in variability of time passed since being in remission and the results do not account for some patients being at different stages of remission. This could be improved by including it as a confounding variable.

5. Conclusion

Overall, this study was able to detect a significant positive correlation between higher levels of fatigue and negative interpretation biases. Confirmation of this association should provoke inquiry into interventions such as various techniques of CBM incorporating positive interpretation training and other strategies such as exercise and mindfulness. Our findings draw inquisition into potential ways by which survivors of breast cancer can adapt and cope with the effects of their illness. The future direction of research within this field should focus on determining a more specific and direct relationship between one's mechanisms of coping and the effects on interpretation bias in survivors of breast cancer. Identifying these strategies will prove essential to community psychiatric and clinical practice. It may, in turn, apply to the broader scope of all long-term conditions to ease the burden of fatigue and anxiety, two of their most profound symptoms.

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