DEPARTMENT OF PSYCHOLOGY

COGNITIVE AND AFFECTIVE MECHANISMS OF ILLNESS ANXIETY: HOW DO ILLNESS-ANXIOUS INDIVIDUALS PROCESS HEALTH-THREATENING INTEROCEPTIVE AND EXTEROCEPTIVE CUES?

DOCTOR OF PHILOSOPHY DISSERTATION

CHRYSANTHI LEONIDOU

2018

University of Cyprus

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MAY 2018

VALIDATION PAGE

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Doctoral Thesis Title: *Cognitive and affective mechanisms of illness anxiety: How do illness-anxious individuals process health-threatening interoceptive and exteroceptive cues?*

The present Doctoral Dissertation was submitted in partial fulfilment of the requirements for the Degree of Doctor of Philosophy at the Department of Psychology and was approved on the 03/05/2018 by the members of the Examination Committee.

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The present doctoral dissertation was submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy of the University of Cyprus. It is a product of original work of my own, unless otherwise mentioned through references, notes, or any other statements.

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ABSTRACT [in Greek language]

Η επεξεργασία πληροφοριών απειλητικών για την υγεία παίζει σημαντικό ρόλο στο μηχανισμό ανάπτυξης και συντήρησης του άγχους υγείας/ασθένειας, το οποίο ορίζεται ως η ανησυχία για την ύπαρξη μιας σοβαρής ιατρικής πάθησης παρά την αντίθετη ιατρική διαβεβαίωση. Η συστηματική ανασκόπηση της βιβλιογραφίας, η οποία διεξήχθη στο πλαίσιο του παρόντος ερευνητικού προγράμματος, προσπάθησε να επικυρώσει βασικές εισηγήσεις του γνωστικο-συμπεριφορικού μοντέλου για το άγχος υγείας βάσει 54 δημοσιευμένων μελετών. Τα αποτελέσματα υποστηρίζουν το γνωστικο-συμπεριφορικό μοντέλο, παρόλα αυτά, κάποιοι μηχανισμοί οι οποίοι εμπλέκονται στην επεξεργασία πληροφοριών λαμβάνουν μερική μόνο υποστήριξη λόγω της έλλειψης σχετικών μελετών, επομένως χρήζουν περαιτέρω διερεύνησης. Ακολουθώντας τις εισηγήσεις της βιβλιογραφικής ανασκόπησης, η πρώτη εμπειρική μελέτη εξέτασε την επίδραση της αυξημένης προσοχής στις σωματικές αισθήσεις στις συναισθηματικές αντιδράσεις κατά τη διάρκεια της νοερής απεικόνισης καταστάσεων σχετικών με ασθένεια, βάσει υποκειμενικών εκτιμήσεων για συναισθηματική διέγερση, σθένος και σωματικές αισθήσεις, και ψυχοφυσιολογικών μετρήσεων. 101 φοιτητές με χαμηλό, μέτριο και ψηλό επίπεδο άγχους υγείας, συμμετείχαν σε πειραματικό έργο με νοερή απεικόνιση καταστάσεων σχετικών με ασθένεια, και τυποποιημένων φοβικών, χαρούμενων και ουδέτερων καταστάσεων, αφού τους ζητήθηκε να εστιάσουν την προσοχή τους είτε στις σωματικές τους αισθήσεις είτε σε περιβαλλοντικά ερεθίσματα. Τα αποτελέσματα έδειξαν αυξημένες αναφορές συναισθηματικής διέγερσης, αρνητικών συναισθημάτων και σωματικών αισθήσεων, καθώς και αρνητικές συναισθηματικές εκφράσεις προσώπου, αλλά ένα μοτίβο ψυχοφυσιολογικής υπο-διέγερσης κατά τη διάρκεια της νοερής απεικόνισης καταστάσεων σχετικών με ασθένεια, ανεξαρτήτως επιπέδου άγχους υγείας. Η συναισθηματική αντίδραση υπό τις πιο πάνω συνθήκες πιθανόν να αυξάνει το ρίσκο ανάπτυξης άγχους υγείας. Η δεύτερη εμπειρική μελέτη εξέτασε το χρονοδιάγραμμα της μεροληπτικής προσοχής και της σχέσης της με τις συναισθηματικές αντιδράσεις κατά την επεξεργασία εικόνων σχετικών με ασθένεια. 100 φοιτητές με χαμηλό, μέτριο και ψηλό επίπεδο άγχους υγείας συμμετείχαν σε πειραματικό έργο όπου επεξεργάστηκαν ζεύγη εικόνων σχετικών με τη ασθένεια, φοβικών και ουδέτερων καθώς και σε ένα πειραματικό έργο όπου εστίασαν σε μια από τις δύο εικόνες (σχετική με ασθένεια ή ουδέτερη), ενώ καταγράφηκαν οι κινήσεις των ματιών και ψυχοφυσιολογικές μετρήσεις. Ανεξαρτήτως επιπέδου άγχους υγείας, οι συμμετέχοντες παρουσίασαν μεροληπτική κατεύθυνση της προσοχής στις σχετικές με ασθένεια και στις φοβικές εικόνες και διατήρησαν την προσοχή τους στις σχετικές με ασθένεια συγκριτικά με τις ουδέτερες εικόνες στο πρώτο πειραματικό έργο. Αντιθέτως, στο δεύτερο πειραματικό έργο, οι συμμετέχοντες παρουσίασαν ένα μοτίβο αποφυγής των σχετικών με την ασθένεια εικόνων, κάτι το οποίο πιθανόν να αποτελεί ένδειξη

ότι η μεροληπτική προσοχή στα σχετικά με την ασθένεια ερεθίσματα επηρεάζεται από τη φύση του πειραματικού έργου και την πιθανή του επίδραση στον αντιλαμβανόμενο από το άτομο έλεγχο στην κατανομή της προσοχής του. Η τάση αποφυγής των σχετικών με την ασθένεια ερεθισμάτων και στα δύο πειραματικά έργα σχετιζόταν με αυξημένη υποκειμενική και ψυχοφυσιολογική συναισθηματική διέγερση, κάτι που παρέχει προκαταρκτικές ενδείξεις για την κατανομή της προσοχής ως ένα μηχανισμό για συναισθηματική ρύθμιση. Συμπερασματικά, τα αποτελέσματα υπογραμμίζουν την αλληλεπίδρασή μεταξύ γνωστικών και συναισθηματικών μηχανισμών που εμπλέκονται στην επεξεργασία εσωτερικών και εξωτερικών ερεθισμάτων σχετικών με την ασθένεια. Παρά τα μη αναμενόμενα αποτελέσματα για την απουσία επίδρασης του επιπέδου άγχους υγείας, τα αποτελέσματα συμβάλλουν σημαντικά στη θεωρία και στην κλινική πράξη στο σχετικό τομέα.

ABSTRACT [in English language]

Health-threatening information processing has been suggested to play an important role in the mechanism that underlies the development and maintenance of illness anxiety, the preoccupation with having or acquiring a severe medical disease despite appropriate medical reassurance. A systematic literature review conducted in the context of the present research project, attempted to validate central tenets of the cognitive-behavioral conceptualization model of illness anxiety based on 54 published studies. Findings partly support the cognitive-behavioral model, but several of its hypothetical mechanisms that refer to health-threatening information processing receive only weak support, due to the scarcity of relevant studies, and invite further research. Following the systematic review's directions, the first empirical study of this project investigated the influence of heightened attention on somatic sensations of arousal on the emotional responses during illness imagery, based on subjective ratings of arousal, valence and somatic sensations, and psychophysiological measures of heart-rate, heart-rate variability, skin conductance level, and facial electromyography. 101 students with low, moderate and high levels of illness anxiety, participated in an experimental task where they had to imagine personally-relevant illness scenarios and standardized fearful, joyful and neutral scenarios, after they underwent an attention manipulation to focus their attention either on somatic sensations or on environmental stimuli. Findings showed increased reports of emotional arousal, negative affect and somatic symptoms, accompanied by negative emotion expressions but a hypo-arousal physiological response pattern during illness imagery after focusing on somatic sensations, irrespective of illness anxiety levels. The observed emotional response to illness imagery under these conditions may increase the risk for developing and perpetuating illness anxiety. The second empirical study investigated the presence and time-course of components of attentional bias and their association to emotional reactivity during processing of illness-related pictorial stimuli. 100 students with low, moderate and high levels of illness anxiety underwent a free viewing task with illness, fearful and neutral picture pairs and a cued viewing task with illness and neutral picture pairs, during which eye-tracking and psychophysiological measures of arousal were recorded. Irrespective of illness anxiety levels, participants showed an orienting bias towards illness and fearful compared to neutral stimuli, and sustained vigilance to illness compared to neutral stimuli during the free viewing task. Whereas, they showed an avoidant attentional processing pattern of illness compared to neutral stimuli during the cued viewing task. This may suggest that attentional bias to illness stimuli may be influenced by the task nature and its potential influence on perceived control over attention allocation. More avoidance tendencies in both tasks were associated with higher subjective ratings and physiological measures of emotional arousal, providing preliminary evidence about attention allocation as a mechanism in regulating emotion. In all,

findings highlight the interactions between cognitive and affective aspects of processing interoceptive and exteroceptive health-threatening cues. Despite the unexpected null results about the effect of illness anxiety levels, findings have major contributions to theory and clinical practice in the related field.

Acknowledgements

Firstly, I would like to express my sincere gratitude to my supervisor Dr. Georgia Panayiotou for the continuous support during my PhD studies and related research, for her patience, motivation, and immense knowledge. I thank her, among other reasons, because through her guidance I recognized the importance of using experimental methodology to understand human behavior and its link to cognition and emotion in the field of clinical and health psychology. I especially appreciate that she has been always keeping the balance between being very supportive and providing help when needed and encouraging independent work and taking initiatives when permitted. This have much helped me to extend my knowledge in the relevant to my research field and to further develop my research and critical thinking skills. I could not have imagined having a better supervisor and mentor during my PhD studies.

Besides my supervisor, I would like to thank the rest of my dissertation committee: Dr. Maria Karekla and Prof. Dr. Olga Pollatos, for their insightful comments and encouragement from the time that I have presented my research proposal. I also thank Dr. Maria Karekla for sending articles from time to time that have helped to keep into contact with updates in the related literature. In addition, I thank Dr. Marios Avraamides and Dr. Delphine Grynberg from my dissertation committee as I am certain that their knowledge and contribution will be much valuable to widen my research from various perspectives.

My sincere thanks also goes to my fellow labmates, Marios Theodorou and Dora Georgiou for answering my questions on how to program my experiments, and to Klavdia Neophytou and Eva Pettemeridou for the stimulating discussions and for all the fun we have had while working together on our dissertation projects during the last two years. I also thank my research assistants, Andrea Demetriou, Anastasia Hatzigiannakou, Evanthia Kepola, Antigoni Mallouri, and Kalodoti Nicolaou. Without their assistance it would not be possible to finish data collection and data scoring within the planned time-frame.

Of course, without participants it would not be possible to conduct this research. Therefore, I am grateful to the students who have spent some of their time to participate in my experiments. Gratitude also goes to both the Cyprus Scholarship Foundation and the School of Postgraduate Studies at the University of Cyprus for the scholarships that they have awarded for my PhD studies and to the Youth Organization of Cyprus, who provided funding for part of my dissertation research through their project 'Fitites se Drasi'.

And finally, last but by no means least, I would like to thank my family: my parents and my sisters who have supported me all in their own way during my PhD studies, and especially during writing this dissertation, although it is likely they have never really grasped what it is all about.

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CHAPTER 1 | Introduction

Having concerns and being conscious about personal health status, including looking after one's health and receiving medical advice if needed, is thought to be an adaptive attitude as it predicts preventive healthcare behaviors (Jayanti & Burns, 1998). However, when concerns about health become excessive, then the preoccupation with having ill health or interpreting innocuous somatic sensations as signs of a medical disease may be linked to illness anxiety (IA). Individuals with high levels of IA exhibit persistent worries about their physiological health, and about having or acquiring a severe, life-threatening medical disease despite medical assessment and reassurance (Rachman, 2012). The mechanisms that are involved in the development and maintenance of IA received more attention recently, however, due to the scarcity of incisive evidence, they remain to be further investigated. This is the focus of the present research project.

Illness Anxiety Disorder

IA presents on a continuum from low to high levels in the general population. Illness Anxiety Disorder is the new category of symptoms included in the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; American Psychiatric Association, 2013) that corresponds to severe/pathological levels of IA and to the symptomatology previously presented by individuals meeting the Hypochondriasis criteria (American Psychiatric Association, 1994), who do not present somatic symptoms. In addition to excessive levels of anxiety about health, diagnostic criteria include a preoccupation with having or acquiring a serious illness being present for at least six months, lower threshold of alarms about personal health status, excessive health-related behaviors, such as repeated checks of the body for signs of an illness, and maladaptive avoidance (i.e. of doctors or hospitals). For the diagnosis, these criteria should be met while somatic symptoms, medical conditions or high risk of developing a medical condition are absent or if present, they are only mild in intensity or the preoccupation is excessive. This new diagnostic category also proposes two specifiers of the disorder: The Care-seeking type, i.e. individuals who frequently seek medical care, and the Care-avoidant type, i.e. individuals who rarely use medical care because they are too anxious to seek medical attention.

In a recent study examining the prevalence of the Illness Anxiety Disorder and the validity of the new diagnosis, findings showed that 47% of individuals who seek treatment for IA meet the diagnostic criteria for Illness Anxiety Disorder, 45% meet criteria for Somatic Symptom Disorder, and 8% meet the criteria for both disorders (Newby, Hobbs, Mahoney, Wong, & Andrews, 2017). DSM-5 presents a prevalence of 1.3-10.0% in the general population and 3-8% in medical clinic populations (American Psychiatric Association, 2013). The impact of IA in both clinical and subclinical populations is detrimental. IA was linked to lower quality of life and high levels of psychological distress (Chaturvedi, Desai, & Shaligram, 2006; Leonidou, Panayiotou, Karekla, & Bati, 2016; Sempértegui, Karreman, van Hout, & Bekker, 2017). Since this symptomatology starts developing in early adulthood, better understanding of the factors that play a role in its development and maintenance will help in designing interventions that prevent its development and impact, interrupt its maintenance cycle and reduce the suffering of individuals with severe levels of IA.

The Cognitive-Behavioral Model

The conceptualization and the mechanisms involved in the development and maintenance of IA were proposed by the Cognitive-Behavioral model of hypochondriasis and health anxiety (an alternative construct used in the literature for IA) (Warwick & Salkovskis, 1990). This model has its roots on the cognitive model of panic disorder (Clark, 1986) and the cognitive model of obsessive-compulsive disorders (Salkovskis, 1985), hence, the processes that were linked to IA show an overlap with the processes linked to anxiety disorders (Rachman, 2012). This model suggests that individuals with high levels of IA form dysfunctional cognitive schemas and beliefs based on previous experiences related to health or illness. Dysfunctional beliefs often include an overestimated possibility of having a severe disease or overestimation of the severity of a disease, an increased number of perceived negative consequences and difficulties when facing a health problem (Rachman, 2012) and perceived limited availability of medical and healthcare resources in one's environment (Hadjistavropoulos et al., 2012). When they experience ambiguous symptoms, illness-anxious individuals interpret them as catastrophic and as signs of an illness, which may be fatal if not diagnosed immediately (Fulton, Marcus, & Merkey, 2011). They also believe that serious illnesses are highly prevalent and tend to define good health as a state of being totally symptom free (Fulton et al., 2011; Winfried Rief & Broadbent, 2007). Beliefs and schemas are activated during illness-related critical incidents or when encountering illness-related information. The activation of schemas triggers negative automatic thoughts and interacts with mechanisms that were proposed to maintain IA. Such mechanisms can be seen in the domain of cognition, i.e. selective attention, rumination, self-focus, and thinking errors; emotion, i.e. anxiety, depression and anger; physiology, i.e. increased arousal, bodily sensations and sleep disturbance; and behavior, i.e. reassurance seeking, avoidance, bodily checking, and safety strategies.

The main premises of the cognitive-behavioral model have been empirically examined, mostly during the last two decades, and there is evidence that supports some of the dimensions of the model. However, the evidence provided for each specific process is still limited and the inter-relations between the processes are not thoroughly examined. Therefore, the mechanisms involved in the development and maintenance of this symptomatology are not very clearly understood. A thorough systematic review of the literature that evaluated existing empirical evidence for the dimensions of the cognitive-behavioral model of IA is presented in the next chapter. This systematic review, which is the first systematic review on this topic, aimed to synthesize empirical evidence on how individuals with high IA process interoceptive and exteroceptive illness-related information. Such processes are suggested by the cognitive-behavioral model as mechanisms that underlie IA. It additionally focused on identifying the gaps and providing future directions for research that would extend the theoretical model and guide the development of interventions for IA symptomatology. Following this systematic literature review, this research project focused on two major areas that warranted further investigation.

Body Vigilance and Emotional Processing of Illness-related Information

The first empirical study of this project aimed to investigate the effect of attentional focus on somatic sensations, i.e. body vigilance, on emotional responses to illness imagery, and how this is modulated by IA levels. Existing evidence supports that in high IA populations, body vigilance has a detrimental effect during processing illness-related information due to the tendency of these individuals for somatosensory amplification and biased processing of interoceptive information, manifested by interoceptive inaccuracy (Barsky & Wyshak, 1990; Köteles & Simor, 2014; Krautwurst, Gerlach, & Witthöft, 2016; Martinez, Belloch, & Botella, 1999; Zincir et al., 2016). Inaccuracy in the perception of somatic sensations in healthy populations has been linked to less efficiency in selective and divided attention skills (Matthias, Schandry, Duschek, & Pollatos, 2009), difficulties in information processing and in detecting cues that predict a following threatening situation (Pollatos, Matthias, & Schandry, 2007), somatosensory amplification (Mailloux & Brener, 2002) and more false alarms in the perception of somatic sensations (Mirams, Poliakoff, Brown, & Lloyd, 2012). This suggests that hyper-vigilance towards somatic sensations increases perceptual errors in distinguishing between true and false bodily sensations and that somatic symptom reporting under stress conditions rather reflects perceptual and reporting biases (Steptoe & Vögele, 1992). It is assumed that increased focus of attention on somatic sensations influences further processing of illness-related information, and that this is linked to IA symptomatology. This is subjected to further empirical examination in this study, which examines for the first time the effect of heightened attention to somatic sensations on emotional reactions during processing of illness-related information presented via mental imagery.

Mental imagery of emotional conditions is a widely-used experimental paradigm in examining emotional information processing, especially in populations with anxiety symptomatology (Lang, 1979; Lang & McTeague, 2009). Therefore, the emotional reactions of individuals to illness imagery was used as an experimental analog of the emotional reactions to intrusive images about illness-threats. Individuals with high levels of IA have been found to present frequent intrusive images about illness and its consequences. Depending on the severity of the preoccupation with health and illness, intrusive images influence the individual's daily functioning and maintain IA in high levels through maladaptive behavioral actions taken as a response to intrusive illness imagery (Muse, McManus, Hackmann, Williams, & Williams, 2010). Emotional reactions of individuals to illness imagery may provide an insight to the function of behavioral responses to it, however, there is only limited empirical research with contradictory findings on this topic (Brownlee, Leventhal, & Balaban, 1992; Gramling, Clawson, & McDonald, 1996). The hypothesis is that high IA individuals present heightened psychophysiological reactivity, accompanied by negative affect and high somatic sensation reports, as an exaggerated response to illness-threats, including imagined ones. This is expected to be partly explained by the hypervigilance tendencies towards somatic sensations (Easterling & Leventhal, 1989; Gramling et al., 1996). Firstly, this is expected because hypervigilance enhances perception of somatic sensations that are disorder-relevant and may mimic health problems (Steptoe & Vögele, 1992), therefore, increases emotional reactivity. Secondly, it is expected because of the associations between interoceptive accuracy and emotion regulation (Kever, Pollatos, Vermeulen, & Grynberg, 2015; Oliveira & Costa, 2014), which may suggest that interoceptive inaccuracy and difficulties in regulating emotion may result in unregulated emotional reactivity, accompanied by amplified somatic sensations.

Emotional responses during illness imagery were assessed in the context of the above hypothesis using psychophysiological measures of arousal and valence, heart-rate variability as an index of emotion regulation; and subjective reports of emotional arousal, valence and somatic symptoms. Illness imagery was based on personally-relevant scenarios of individuals' worst fears about illness-threats. Responses of individuals with high, moderate and low IA levels to illness imagery were compared to their responses to generally fearful, joyful, and neutral imagery, to test their specificity to illness imagery and high IA. For a thorough investigation of emotional reactions to illness imagery, psychophysiological measurements were included as they reflect pre-cognitive emotional processing that elicits a rather automatized emotional response triggered by environmental stimuli or internal cues such as somatic sensations. Subjective emotional experience was assessed by self-reports, which involve a goal-directed processing of information due to the activation of the reflective system as they are provided with a delay from stimulus onset (Van Bockstaele et al., 2011).

Attentional Processing of Illness-related Information

The second empirical study of the project aimed to investigate biases that influence early and later-onset attentional processes involved in processing of exteroceptive illness-related information, their time-course and associations with emotional reactivity. Illness preoccupation among individuals with high IA is assumed to be supported by selective attention to evidence that confirms the presence of an illness and discounting of evidence that indicates good health

(Warwick & Salkovskis, 1990). Empirical studies support this theoretical assumption by providing evidence about an attentional interference by illness stimuli (Gropalis, Bleichhardt, Hiller, & Witthöft, 2012; Karademas, Christopoulou, Dimostheni, & Pavlu, 2008; Owens, Asmundson, Hadjistavropoulos, & Owens, 2004; Van Den Heuvel et al., 2005; Witthoft et al., 2016; Witthöft et al., 2013; Witthöft, Rist, & Bailer, 2008), facilitated attention towards illness stimuli in early stages of processing, and difficulties in either engaging, i.e. attentional avoidance, or disengaging attention, i.e. attentional maintenance from threat in high IA (Jasper & Witthöft, 2013; Kim, Kim, & Lee, 2014; Kim & Lee, 2014). However, there is contradictory evidence that does not support such associations (Jacoby, Wheaton, & Abramowitz, 2016; Lee et al., 2013; Lees, Mogg, & Bradley, 2005), while the time-course of later-onset attentional mechanisms, i.e. attentional maintenance/avoidance, warrants further investigation. In addition, existing findings present two patterns of processing illness-related information, which need to be further investigated: a vigilance pattern characterized by facilitated attention to threat and difficulty in disengaging attention from threat; and a vigilance-avoidance pattern, characterized by facilitated attention to threat but a later shift of attention away from it (Kim et al., 2014; Kim & Lee, 2014; Lee et al., 2013).

Therefore, the purpose of this second study was to examine biases in attentional processing during exposure to environmental illness-related information among individuals with high, moderate and low IA levels, in order to reach more conclusive results about their presence, nature and time-course. For this purpose, attentional biases, including facilitated attention, vigilance and attentional maintenance/avoidance, were assessed using eye-tracking during two picture viewing tasks with extended durations of stimuli presentation to allow for the continuous assessment of attentional processes. The extent to which attentional capture by illness-related stimuli is automatic and whether it can be counteracted by voluntary attentional control (Nummenmaa, Hyönä, & Calvo, 2006) was also examined. The specificity of attentional biases to illness-related information processing was tested as compared to biases in processing generally fearful and neutral information.

The investigation of the associations of attentional biases with emotional reactivity was deemed important to gain an insight on why selective attention as a mechanism for regulating emotion is linked to the development and maintenance of IA. For this purpose, the associations between attentional bias during information processing and emotional reactions were assessed by psychophysiological measurements of arousal. It is tentative that attentional processes, especially those that present later in the information processing continuum, are selected in a more strategic fashion in order to regulate the emotional reactivity elicited by threatening information (Derakshan, Eysenck, & Myers, 2007; Gross, 1998, 2001). For example, heightened emotional reactivity may trigger attentional avoidance to distract attention away and therefore reduce distress, while the opposite effect may hold for attentional maintenance. Although these are hypotheses that need to be investigated, such individual differences in emotional reactivity during processing illness-related information may explain the two distinct patterns of attentional processing described above, i.e. vigilance vs. vigilance-avoidance. In addition, emotional responses may guide more overt behavioral responses, such as healthcare seeking/avoidance, which are known to be involved in the maintenance of IA symptomatology (Kim & Lee, 2014; Lee et al., 2013; Warwick & Salkovskis, 1990). This further attests to the importance of assessing attentional bias to illness-related information in IA, while concurrently evaluating individuals' emotional responses.

The Current Research Project

In brief, the next chapter of this project is a systematic literature review on how illness-anxious individuals process interoceptive and exteroceptive health-threatening information in an effort to synthesize existing empirical evidence for the cognitive-behavioral conceptualization of IA and identify gaps in the existing literature. Following the directions for future research identified through this systematic review, two empirical studies that investigated two major research areas that were deemed important to be further investigated form the next two chapters. As described above, the first empirical study focuses on the influence of focusing attention on somatic sensations (interoceptive stimuli) on emotional reactions to illness imagery. The second study focuses on examining the nature and time-course of attentional biases on illness-related exteroceptive stimuli, and their associations to the emotional reactivity elicited by such stimuli. In both studies, the above processes are examined among groups of individuals with low, moderate and high IA levels to investigate whether the above effects are modulated by IA. The results of the systematic literature review and the two empirical studies are discussed in terms of their contribution to scientific knowledge on illness-related information processing and on the etiological and maintenance mechanisms of IA and of potential implications that may benefit psychological practice. The present research project has received ethical approval by the National Cyprus Bioethics Committee (Protocol number: ΕΕΒΚ/ΕΠ/2017/12) and approval for archiving personal data for the purpose of the research project by the Data Protection Office in Cyprus (Application number: 3.28.472).

CHAPTER 2 │ How do illness-anxious individuals process health-threatening information? A systematic review of evidence for the cognitive-behavioral model

Abstract

According to the cognitive-behavioral model, the processing of health-threatening information among illness-anxious individuals is influenced by cognitive, affective, physiological and behavioral mechanisms. **Objective.** This study is a systematic review of research that attempted to validate central tenets of the cognitive-behavioral model regarding etiological and maintenance mechanisms in illness anxiety. **Methods.** Fifty-four studies, including correlational and experimental designs, were identified through a systematic search of databases and were appraised for their quality. **Results.** Outcomes were synthesized following a qualitative thematic approach under categories of theoretically driven mechanisms derived from the cognitive-behavioral model: attention, memory and interpretation biases, somatosensory amplification, biased processing of interoceptive information, negativity bias, emotion dysregulation, and behavioral avoidance. **Conclusions.** Findings partly support the cognitive-behavioral model, but several of its hypothetical mechanisms receive only weak support due to the scarcity of relevant studies. Directions for future research are suggested based on identified gaps in the existing literature.

Keywords: Cognitive-Behavioral model; Health-threatening information; Illness anxiety; Maintenance mechanisms; Systematic review

Background

Healthcare professionals often assume that patients are accurate reporters of their somatic symptoms and rely on their subjective reports to reach a diagnosis (Bogaerts et al., 2005). However, common somatic complaints (Burton, 2003; Rief, Hessel, & Braehler, 2001) are sometimes unrelated to physical causes. When they are accompanied by excessive anxiety, repeated body checking for signs of illness, lower threshold of alarm about personal health status and seeking of medical information or reassurance, symptom reports should instead alert health professionals about the possible presence of illness anxiety (American Psychiatric Association, 2013).

Illness anxiety (IA) received scientific attention relatively recently, compared to other anxiety disorders, with much of the evidence regarding its maintenance mechanisms accumulated during the last two decades. Studies in this field are still limited in number, sometimes produce contradictory results, and do not systematically consider the inter-relations among the hypothetical maintenance mechanisms they examine. This paints a rather unclear picture of its etiology and prohibits the identification of domains where future research should focus. An attempt to describe this literature was made by Rachman (Rachman, 2012), who presented a cognitive construal of IA and concluded that incisive evaluation of the main premises of the cognitive model remains to be conducted. The present study represents the first systematic review of the literature on maintenance mechanisms derived from the cognitive-behavioral model of IA published between 1990-2016; we specifically review studies that examined cognitive, physiological, affective and behavioral mechanisms involved in how illness-anxious individuals process health-threatening information, believed to maintain the disorder.

What is Illness Anxiety?

IA is the preoccupation that someone has or will acquire a severe medical disease. It presents on a continuum (Warwick & Salkovskis, 1990), with severe IA corresponding to the clinical diagnosis of the Illness Anxiety Disorder in DSM-5 (American Psychiatric Association, 2013). Considering the somatic complaints reported, constant worry about having an illness, frequent primary healthcare visits and excessive healthcare costs (Barsky, Orav, & Bates, 2005; Burton, 2003; Grabe, Baumeister, John, Freyberger, & Völzke, 2009; Kroenke, 2003), it is not surprising that individuals with IA experience increased levels of psychological distress (Chaturvedi et al., 2006), interpersonal and work-related difficulties (Terluin, van Rhenen, Anema, & Taris, 2011), oftentimes clinical levels of depression or anxiety (Sempértegui et al., 2017) and lower quality of life (Hyphantis et al., 2009; Leonidou et al., 2016).

The Cognitive-Behavioral Conceptualization

The cognitive-behavioral model of IA (Warwick & Salkovskis, 1990, see Figure 1) suggests that acquired knowledge and past personal or vicarious experiences with health problems jointly form specific assumptions about somatic symptoms and illness that are triggered during illness-related events or when coming into contact with illness-related information. According to the model, several behavioral, affective, cognitive and physiological dimensions are critical for the development and maintenance of IA. To test these hypotheses, several empirical studies examined the role of cognitive, affective and interoceptive mechanisms and coping behaviors. This systematic review aims to synthesize existing evidence as such variables interfere with the processing of illness-related information in IA, leading to a vicious cycle that in effect maintains the disorder, as suggested by the cognitive-behavioral model. To address the full breadth of the theoretical model, the review has a broad focus, which includes all dimensions relevant to this theoretical perspective, and their interaction. A second aim of the present review is to identify gaps in the relevant literature that warrant further investigation to inform theory and pave the way for effective interventions. Because in the literature prior to the

DSM-5 edition IA is also referred to as health anxiety or hypochondriasis, the present review includes studies on those conditions as well.

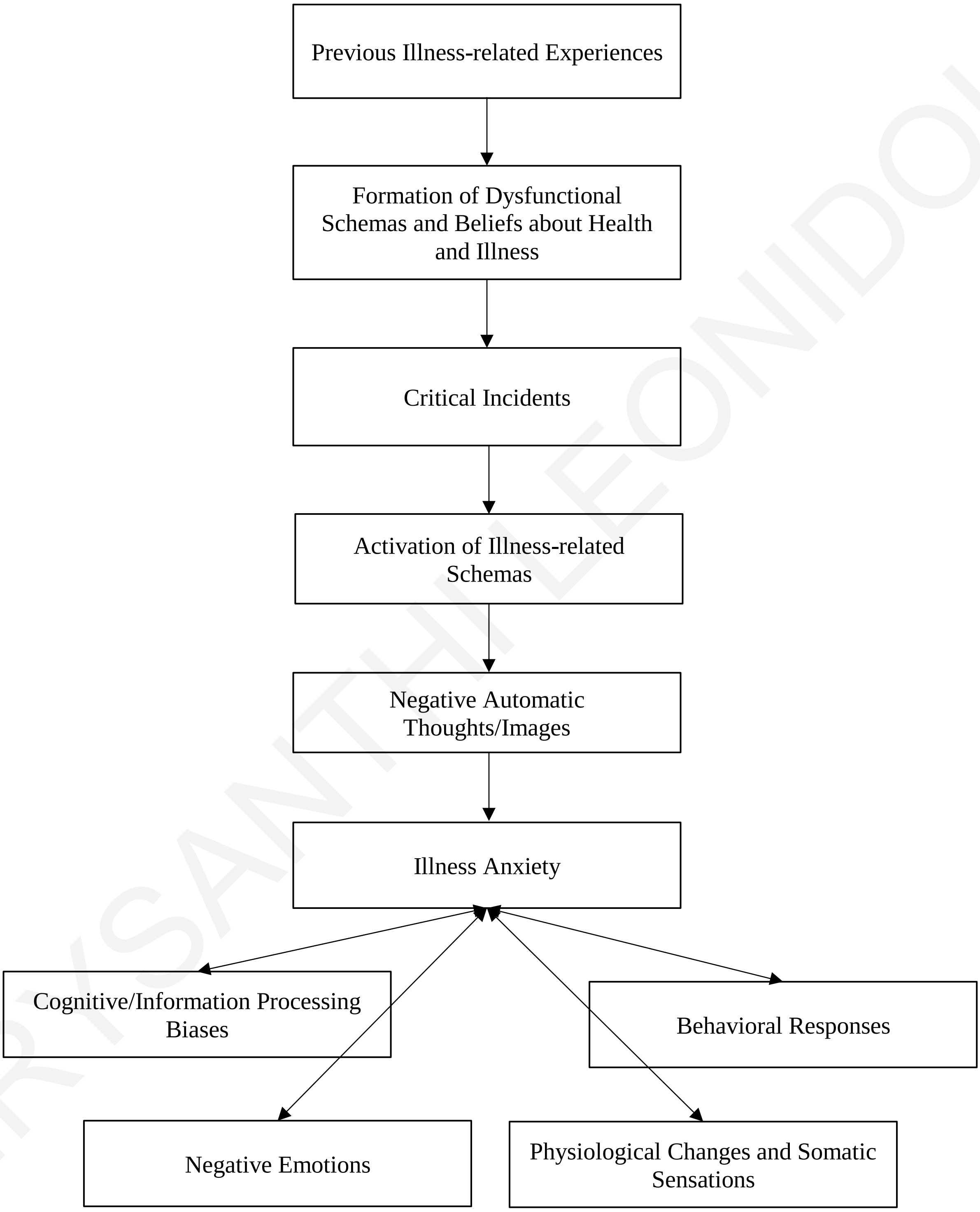

Figure 1. Representation of a simplified version of the Cognitive-Behavioral model of Illness Anxiety adapted from the original model and based on the theoretical conceptualization as presented in Warwick and Salkovskis (1990).

Method

Search Strategy

After the removal of duplicates, 88 studies were identified through search in Medline/Medline Complete, PsychINFO, PsychArticles, CINAHL Plus, and Psychology and Behavioural Sciences Collection via the EBSCOhost database and in Web of Science and EMBASE databases, in November 2016. The search terms included the words health anxiety OR hypochondriasis OR illness anxiety AND each of the keywords listed here separately: attention*, vigilan*, hypervilan*, memory bias*, percept*, interpretation, misinterpretation, attribution, misattribution, evaluation bias*, interoception, interoceptive sensitivity, somatosensory amplification, emotion regulation, emotional react*, psychophys*, coping, and avoidan*.

Selection Strategy

Following the initial search in the databases (see Figure 2 for a PRISMA-based flow chart of the search strategy (Moher, Liberati, Tetzlaff, Altman, & Group, 2009)), the results were filtered based on exclusion criteria: only peer reviewed articles were selected; with adult samples, since Illness Anxiety Disorder is an adult diagnosis; and written in the English language. The filtering strategy reduced the results to 81 articles. At this stage, titles and abstracts were examined to evaluate their relevance to the research question. Studies were selected if they were experimental or correlational; case studies, literature reviews, commentaries on published studies and intervention studies were excluded. This procedure resulted in 72 articles, published between 1990 to 2016. In the final step, the exclusion criterion was the availability of full texts, while one additional study was excluded because it examined IA-related mechanisms in relation to chronic pain specifically (Tang et al., 2007), resulting in a final count of 54 articles.

Review Strategy

Data were systematically extracted and transcribed onto standardized extraction sheets under the headings presented in Table 1. Quality appraisal of the included studies was conducted using a checklist created based on existing critical appraisal checklists (Table A1, Appendix A). The appraisal was first conducted on each individual study, and then the appraisal results were combined under categories of low/moderate/high risk for bias. Outcomes of the studies were synthesized following a qualitative thematic analysis approach.

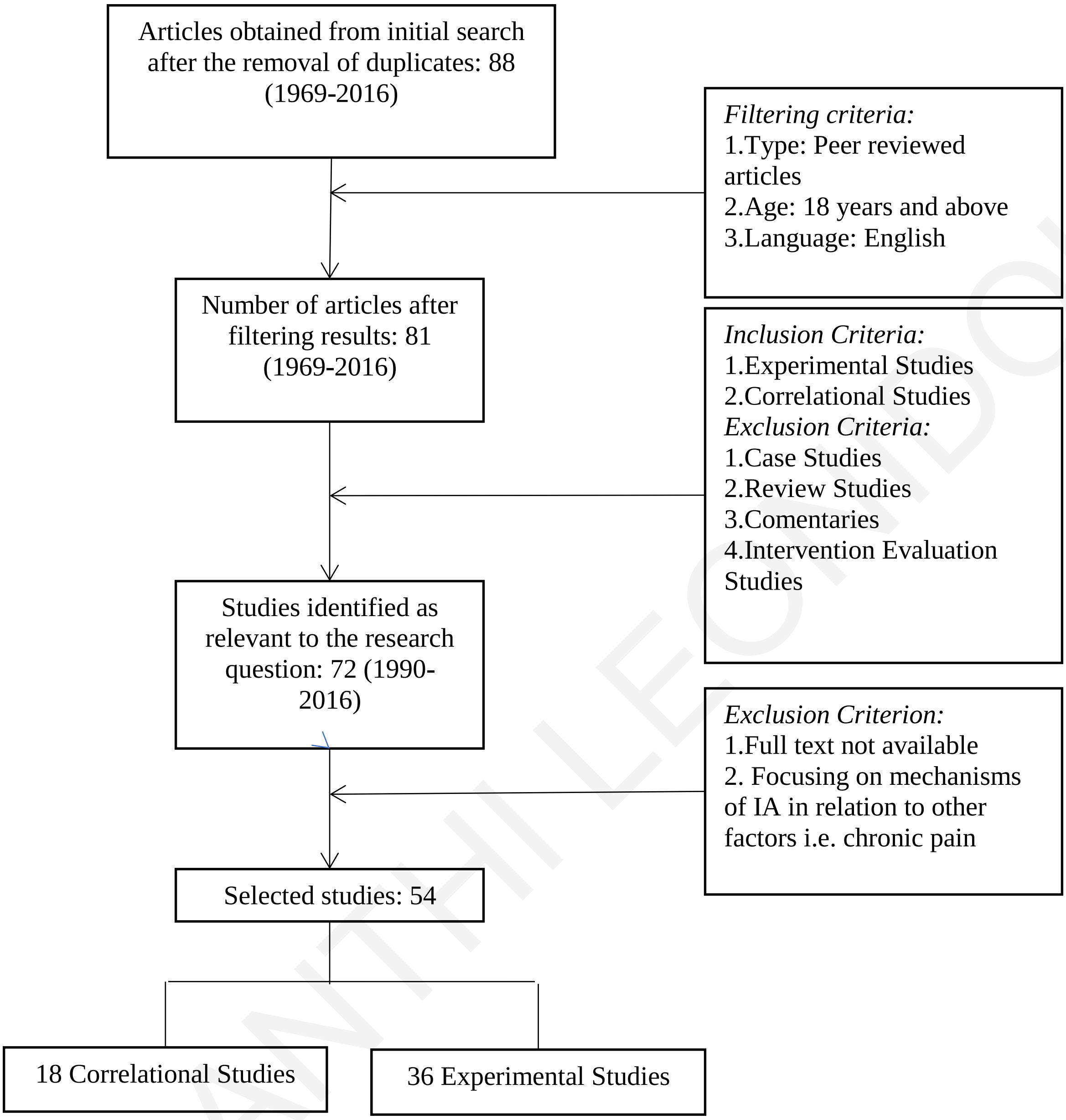

Figure 2. Flow chart of the search strategy and the inclusion/exclusion criteria in each stage.

Results

Study Characteristics

The final sample included 54 studies starting from 1990 when the first identified study on IA-related mechanisms was published. The correlational studies (*n*=18) utilized self-report scales to assess IA in association with concepts such as experiential avoidance, emotion regulation and coping, somatosensory amplification, body consciousness and vigilance, and negative affect. The experimental studies (*n*=36) utilized experimental paradigms to assess mechanisms that are proposed to underlie IA, based on the cognitive-behavioral model. Study designs and measurement methods are presented in Table 1.

Table 1. *Summary of the results by type of mechanism linked to illness anxiety*

Study	IA measure	IA definition	Sample	Design/Measures	Results
Cognitive Mechanisms					
					Attentional Biases
Gropalis et al. (2012)	MIHT	SCID-IV hypochondriasis	32 hypochondriasis patients, 27 other somatoform disorders, 25 PD, 31 controls	EST with illness, bodily complaints, panic-related and neutral words	↑to all 3 target word categories
Jacoby et al. (2016)	SHAI	Continuous	95 students	Dot-probe task with illness and neutral words presented in durations of 17ms, 500ms, and 1250ms	=to illness, general threat and neutral words in all durations
Jasper & Witthöft (2011)	MIHT, WI	Continuous	83 students	Dot-probe task with illness and neutral pictures, presented for 175ms or 500ms	↑orientation to threat at 175ms ↑difficulty to disengage from threat at 500ms
Karademas et al. (2008)	SHAI	Continuous	Study 1: 51 students, Study 2: 69 students	EST with illness and neutral words	↑to illness words
Kim & Lee (2014)	IAS	Cutoff >=55 on IAS	21 HIA-blunter group, 21 HIA-monitor group, 21 LIA-blunter group, and 21 LIA-monitor group, Median split on MBSS scales	Eye tracking, Free viewing of pairs of illness and neutral pictures presented for 6000ms	↑orientation to illness stimuli ↑difficulty to disengage from threat in the blunter group, compared to the monitorers group
Kim et al. (2014)	IAS	Upper and lower 20% on IAS	17 HIA-blunter group, 16 HIA-monitor group, 16 LIA-blunter group, and 18 LIA-monitor group, Median split on MBSS scales	Dot-probe task with illness and neutral words, presented for 1250ms	↑attentional bias for illness words ↑attentional bias in monitorers groups compared to blunters

(continued)

Lee et al. (2013)	SHAI	Continuous	56 students	Dot-probe task using pairs of illness and neutral words tailored for each participant for 500ms	=to illness words ↑difficulty to disengage from illness in health-care seekers ↑attention shifting away of illness-related pictures in health-care avoiders
Lees et al. (2005)	IAS	Upper and lower quartiles on IAS	24 HIA, 24 LIA students	Dot-probe task with illness and neutral picture and word pairs presented for 500ms and 1250ms	=for illness pictures, no bias for words
Owens et al. (2004)	IAS	Upper and lower tertiles on IAS excluding health habits scale	26 HIA, 26 MIA, 26 LIA students	EST with illness, general positive and negative words	↑to illness words
Shields & Murphy (2011)	WI, IAS	Upper and lower quartiles based on one or both measures	31 LIA, 26 HIA students	Visual Search Tasks with letters and words, RTs of correct responses	= to ill-health words compared to good-health, negative, positive and neutral words
Van Den Heuvel et al. (2005)	WI, Y-BOCS Hypochondriasis	SCID-IV hypochondriasis	13 hypochondriasis, 16 OCD outpatients, 15 PD, 19 controls	EST with congruent and incongruent color words, OCD-related, panic-related, negative words, and neutral words	↑to panic words, compared to neutral words, compared to OCD and controls, but similar with PD
Witthöft et al. (2008)	WI, SHAI	>4 on WI, >2 on the ‘‘disease phobia’’ factor of WI	54 HIA, 53 LIA students	EST with symptom, illness and neutral words	=to symptom and illness words in general, ↑emotional intrusion effect to symptom and illness words when presented first in task but not stable
Witthöft et al. (2013)	WI	Cutoff >=3 on WI	12 HIA, 12 LIA students	EST with symptom, illness and neutral words	↑to symptom words

(continued)

Witthöft et al. (2016)	WI, SHAI	SCID-IV hypochondriasis, SCIHA	88 HIA out-patients, 52 with depressive disorder, 52 healthy controls	EST with illness and neutral words	↑to illness words
					Memory bias
Ferguson et al. (2007)	WI	Continuous	60 students	Free recall task, RET of illness and non-illness words Emotional valence evaluation of words	↑for illness words, mediated by unpleasant ratings of illness words ↑speed when evaluating illness words
Gropalis et al. (2012)	MIHT	SCID-IV hypochondriasis	32 hypochondriasis patients, 27 other somatoform disorders, 25 PD, 31 controls	RET	↑for illness and neutral words
Hitchock & Matthews (1992)	IAS	Study 2: Continuous Study 3: upper and lower 10% on IAS	Study 2: 109 students Study 3: 52 LIA, 23 HIA	RET	↑for illness words
Pauli & Alpers (2002)	WI, IAS	International Diagnostic Check List-Hypochondriasis	6 hypochondriasis patients, 14 somatoform pain & hypochondriasis, 8 somatoform pain, 14 patients clinical controls	Free immediate and delayed recall of positive, negative, pain and neutral words RET	↑pain words recall ↓positive words recall =neutral and negative words recall ↑immediate recall of pain words in patients with comorbid hypochondriasis and pain disorder ↑recognition of negative and pain words (marginally significant)
Sansom-Dally et al. (2014)	SHAI	Continuous	60 students	Rumination induction/Experiential self-focus (randomly assigned), Autobiographical Memory Test, Future Imaginings Task	=autobiographical memory responses related to illness ↑illness-related future imaginings

(continued)

					(rumination induction related to more illness-related memories)
Schmidt et al. (2013)	WI	Cutoff >=5 on WI	27 HIA students, 29 Dysphoric, 28 controls	RET using illness, negative emotional, and neutral words	↑for symptom words
Witthöft et al. (2016)	WI, SHAI	SCID-IV hypochondriasis, SCIHA	88 HIA out-patients, 52 depressive disorder, 52 healthy controls	RET using illness and neutral words	↑for illness words
					Interpretation bias
Bailey & Wells (2016)	WI	Continuous	351 students	Health Scenarios Interpretation Questionnaire	↑catastrophic interpretation of scenarios (moderated by meta-cognitive beliefs)
Bailey & Wells (2016)	WI	Continuous	105 students	Health Scenarios Interpretation Questionnaire, Prospective (5 months)	↑catastrophic interpretation of scenarios in time 1 and 2 (moderated by meta-cognitive beliefs, time 1 misinterpretation did not predict time 2 IA)
Hedman et al. (2016)	HAI	SCID-IV hypochondriasis	132 HIA patients, 92 healthy controls	Exposure to pictures of individuals displaying various degrees of sickness symptoms, ratings	↓health and attractiveness ratings for healthy people ↑disgust, anxiety, perceived contagiousness and worry about health
Hitchock & Matthews (1992)	IAS	Study 2: Continuous, Study 3: Upper and lower 10% on IAS	Study 2: 109 students Study 3: 52 LIA, 23 HIA	Study 2 task: Interpretation of ambiguous sentences, Study 3 task: Interpretation of words following a sentence	↑thoughts about illness and catastrophic interpretations of bodily sensations
MacLeod et al. (1998)	IAS	Median split on IAS in the generally anxious group	16 hypochondriacs, 15 generally anxious,	Exposure to 10 common bodily sensations or	↑somatic attributions *(continued)*

			16 non-anxious (general practice)	symptoms and participants had to attribute possible causes.	
Neng & Weck (2015)	SCID-IV	SCID-IV hypochondriasis	50 hypochondriasis out-patients, 50 with a primary anxiety disorder and 50 healthy participants	Exposure to 9 common bodily sensations, participants had to attribute possible causes.	↑moderate/serious disease attributions ↓normalizing attributions
Rief et al. (1998) (Study 2)	WI	SCID-III Hypochondriasis, International Diagnostic Checklists	16 hypochondriasis patients, 46 somatization, 30 somatization and hypochondriasis, 32 clinical controls, and 101 nonclinical controls	Cognitions About Body and Health Questionnaire	↑catastrophizing interpretation of physical complaints (compared to clinical controls only)
Schmidt et al. (2013)	WI	Cutoff >=5 on WI	27 HIA, 29 Dysphoric, 28 controls	IAT with illness, negative and neutral words, latency and accuracy	↑mistakes in pairing evaluation "harmless" with specific symptoms =latencies in pairing "harmless" or "dangerous" with symptoms
Witthöft et al. (2016)	WI, SHAI	SCID-IV hypochondriasis, SCIHA	88 HIA out-patients, 52 with depressive disorder, 52 healthy controls	IAT with symptom words and dangerous/harmless as attributes	=implicit evaluations of symptom words
Physiological Mechanisms					
					Somatosensory amplification
Bailey & Wells (2016)	WI	Continuous	351 students	SSAS	↑somatosensory amplification
Bailey & Wells (2016)	WI	Continuous	105 students	SSAS, Prospective (5 months)	↑somatosensory amplification in time 1 and 2

(continued)

Barsky & Wyshak (1990)	WI	Continuous	177 medical outpatients	Somatosensory amplification questions	↑somatosensory amplification
Gramling et al. (1996)	IAS	SCID-IV Hypochondriasis	15 hypochondriasis group, 15 controls (only female)	Cold Pressor Task	↓hand temperature with longer duration ↑termination of task ↓duration in the water ↑unpleasantness ratings
Katzer et al. (2011)	WI, MIHT	Continuous	67 students	Vibrotactile Perception Task, Somatic Signal Detection Task, Ratings of confidence concerning perception of the vibrotactile stimulus	↑reports tactile sensations irrespective of whether a stimulus was presented or not
Koteles & Simor (2014)	SHAI	Continuous	180 patients in primary healthcare, 344 students	SSAS	↑somatosensory amplification in both samples
Martinez et al. (1999)	MMPI Hypochondriasis, IAS	SCID-III Hypochondriasis	17 hypochondriasis,17 PD outpatients	SSAS	=somatosensory amplification, in hypochondriasis group linked with bodily preoccupation, in panic group linked with depression
Rief et al. (1998) (Study 2)	WI	SCID-III Hypochondriasis, International Diagnostic Checklists	16 hypochondriasis, 46 somatization, 30 somatization and hypochondriasis, patients, 32 clinical controls, and 101 nonclinical controls	Cognitions About Body and Health Questionnaire	↑autonomic sensations, compared to clinical controls and comorbid somatization and hypochondriasis groups
Rodic et al. (2016)	WI	Continuous	205 students	Vibrotactile Perception Task	↓vibrotactile perception thresholds (more reports of sensations)
Zincir et al. (2014)	SHAI	Continuous	51 patients with non-cardiac chest pain	SSAS	↑somatosensory amplification in patient group with HIA

			51 healthy controls		
					Biased processing of interoceptive information
Goodwin et al. (2013)	HAI	Continuous	761 healthy adults	Private Body Consciousness Scale	↑selective attention to the body
Krautwurst et al. (2014)	WI, MIHT	Continuous	100 students	HBT NSCF task	↓heartbeat perception =ability to detect NSCF ↑false alarms in NSCF
Krautwurst et al. (2016)	WI	SCID-IV hypochondriasis	11 HIA patients, 15 healthy controls	HBT NSCF task	↑false alarms for NSCF ↑ability to detect NSCF due to comorbid anxiety =heartbeat perception
Vervaeke et al. (1999)	Groningen IAS	Continuous	113 healthy adults	Private Body Consciousness Scale	↑selective attention to the body
Wheaton et al. (2010)	SHAI	Continuous	636 students	Body Vigilance Scale	↑body vigilance
Affective mechanisms					
					Negativity bias
Goodwin et al. (2013)	HAI	Continuous	761 healthy adults	Positive and Negative Affect Schedule	↑trait negative affect
Gramling et al. (1996)	IAS	SCID-IV hypochondriasis	15 hypochondriasis group, 15 controls (only female)	Cold Pressor Task Imagery Task	↓baseline heart rate ↑heart rate during cold pressor task ↑unpleasantness ratings during the task =physiology during imagery
Jasper et al. (2015)	WI	Continuous	97 students in the experimental group, 60 in control group	Negative affect ratings after somatic symptom ratings or no somatic symptom ratings	=decline of negative affect following the symptom ratings in experimental group, stable affect in control group

Jasper & Witthöft (2013)	MIHT	Continuous	104 students	AMP with neutral, illness and no prime trials	↑unpleasantness ratings after illness primes (associations with rumination and catastrophizing)
Macatee & Cougle (2013)	SHAI	Continuous	122 students	Mirror Tracing Task, Ratings for fear, disgust, sadness, and anger, tolerance and peak reactivity indices, Distress tolerance index	↑anxiety =distress tolerance
Schreiber et al. (2014)	IAS, MIHT	SCID-IV hypochondriasis	80 hypochondriasis, 83 anxiety disorder out-patients, 90 controls	AMP with illness, symptom and neutral primes	↑negative affective reactions in illness primed trials =affective reactions in symptom trials
Witthöft et al. (2008)	WI, IAS, SHAI	>4 on WI, >2 on the ‘‘disease phobia’’ factor of WI	54 HIA, 53 LIA students	Valence and arousal ratings after EST with symptom, illness and neutral words	↑unpleasantness and arousal ratings for symptom words =unpleasantness and arousal ratings for the illness words
Witthöft et al. (2016)	WI, SHAI	SCID-IV hypochondriasis, SCIHA	88 out-patients with IA & 52 patients with depressive disorder, 52 healthy controls	Self-Assessment Manikin for valence and arousal after IAT with symptom words	↑negative evaluations of symptom words
					Emotion dysregulation
Bardeen & Fergus (2014)	WI	Continuous	482 healthy adults	ERQ, Difficulties in Emotion Regulation Scale	↑emotion regulation difficulties ↓perceived access to effective emotion regulation strategies
Doherty-Torstrick et al. (2016)	WI, MINI	SCID-IV hypochondriasis	195 patients	Avoidance scale of YBOCS-H	↑unhealthy illness-related avoidance

(continued)

Fergus (2015)	SHAI, MIHT	Continuous	Study 1: 252 healthy adults, Study 2: 371 healthy adults	Cognitive Fusion Questionnaire, Brief Experiential Avoidance Questionnaire	↑cognitive fusion, especially related to the affective and cognitive dimensions of IA ↑experiential avoidance
Gerolimatos & Edelstein (2012)	SHAI	Continuous	86 older adults & 117 students	ERQ	↑reappraisal =suppression
Gerolimatos et al. (2012)	SHAI	Continuous	86 older adults & 117 students	ERQ	=reappraisal, suppression
Görgen et al. (2014)	MIHT	Continuous	Study 1: 172 students, Study 2: 242 students	Cognitive Emotion Regulation Questionnaire, ERQ	↑rumination, catastrophizing, self-blame, other-blame, expressive suppression, reappraisal
Scutte et al. (2016)	IAS, WI	SCID-IV hypochondriasis	30 hypochondriasis, 30 PD, 30 depression patients, 30 healthy controls	Trier Illness Coping Scales, Freiburg Questionnaire on Coping with Illness	=rumination, defense against threat, and searching for information, problem analysis, cognitive avoidance =self-estimated coping abilities ↑rumination when faced with their most feared disease vs. other disease
Lautenbacher et al. (1998)	IAS	>4 cutoff on sum of Disease Phobia & Hypochondriac beliefs scales of IAS	16 HIA, 12 LIA in-patients in psychosomatic clinic	Distraction (Mental arithmetic task) vs no distraction conditions, Ratings of intensity and unpleasantness of painful and non-painful heat stimuli	=reduction of perceived intensity and unpleasantness of the painful stimuli after distraction
Wheaton et al. (2010)	SHAI	Continuous	512 LIA, 124 HIA	Acceptance & Action Questionnaire II	↑experiential avoidance

(continued)

Zincir et al. (2014)	SHAI	Continuous	51 patients with non-cardiac chest pain, 51 controls	Toronto Alexithymia Scale	↑alexithymia in patient group
Behavioral Mechanisms					
Abramowitz & Moore (2007)	MINI	MINI hypochondriasis diagnostic criteria	14 in safety behaviours group 13 in response-prevention group	Exposure to illness preoccupation triggers + Safety behaviours/Response prevention	Exposure: ↑anxiety, ↑urge for safety behaviour Safety behaviour: ↓anxiety, ↑urge for safety behaviour Response-prevention: ↓(gradual) anxiety and urge
Brady et al. (2014)	SHAI	Mean +2SD (cutoff score >25), <16 on contamination	20 HIA, 20 Contamination-fearful, 20 Non-anxious	BAT, Ratings of anxiety and disgust	↑avoidance, disgust and anxiety (compared to non-anxious, similar to contamination-fearful)
Goetz et al. (2012)	SHAI	Continuous	156 students	BAT, Ratings of disgust	↑disgust, avoidance, related to ↑health-related reassurance seeking

Note. Illness anxiety groups: HIA=High Illness Anxiety; MIA=Medium Illness Anxiety; LIA=Low Illness Anxiety.

Abbreviations of measures: WI=Whiteley Index; IAS=Illness Attitudes Scales; HAI=Health Anxiety Inventory; SHAI=Short Health Anxiety Inventory; YBOCS-H=Yale-Brown Obsessive-Compulsive Scale-Hypochondriasis; MIHT=Multidimensional Inventory of Hypochondriacal Traits; SCID=Structured Clinical Interview of DSM; MINI=Mini International Neuropsychiatric Interview; SCIHA=Structured Clinical Interview of Health Anxiety; SSAS=Somatosensory Amplification Scale; ERQ=Emotion regulation Questionnaire.

Abbreviations of experimental paradigms: AMP=Affect Misattribution Procedure; RET=Recognition Task; EST=Emotional Stroop Task; HBT=Heartbeat Tracking task; NSCF=Nonspecific Skin Conductance Fluctuations task; BAT=Behavioral Approach Tasks.

Participant Characteristics

In 30 of the 54 studies, participants were university/college students, while the samples in the rest of the studies consisted of community volunteers (*n*=5), medical outpatients (*n*=4), mental health outpatients (*n*=12) and inpatients (*n*=1). Clinical or medical samples were compared to control groups consisting of students or community volunteers with low levels of IA or clinical groups diagnosed with other somatoform or anxiety disorders but not with Illness Anxiety Disorder. In almost all studies the sample consisted of both genders, except of one study where only females were recruited. Participants were screened with well-established measures of IA and hypochondriasis (see Table 1).

Outcomes Assessed

The outcomes assessed in the included studies referred to mechanisms linked to IA, as suggested by the CBT model, which were examined either in relation to IA as a continuous variable (low-high levels), or as group differences between low and high IA. Outcome variables can be categorized as: 1. Cognitive mechanisms: attentional, memory and interpretation biases; 2. Physiological mechanisms: somatosensory amplification and biased processing of interoceptive information; 3. Affective mechanisms: negativity bias and emotion dysregulation; and 4. Behavioral mechanisms, i.e. behavioral avoidance.

Cognitive mechanisms

Attentional biases. Selective attention towards health-threatening cues, as maintenance mechanism in high IA was initially suggested by Kellner (Kellner, 1986). High IA individuals seem to selectively attend to evidence that confirms the presence of an illness, but discount evidence that indicates good health (Warwick & Salkovskis, 1990). Fourteen studies were identified that focused on assessing attentional biases in IA, using the Emotional Stroop task (EST; *n*=7), the dot-probe task (*n*=5), the Free Viewing task with eye tracking (*n*=1) and the Visual Search task (*n*=1), using illness-related pictures or words compared to neutral, generally negative and positive or disorder-specific stimuli. All seven EST studies, provided evidence for an attentional bias toward illness-related compared to neutral words in individuals with high IA or a clinical diagnosis of IAD, compared to individuals with low IA or healthy controls, respectively (Gropalis et al., 2012; Karademas et al., 2008; Owens et al., 2004; Van Den Heuvel et al., 2005; Witthoft et al., 2016; Witthöft et al., 2013, 2008). Five studies used the dot-probe paradigm, which is effective in looking into different stages of attentional processing (Cisler & Koster, 2010). One of the dot-probe studies indicated a positive association between IA and an early focus of attention at 175ms and a slower disengagement of attention from pictorial illness stimuli at 500ms exposure times (Jasper & Witthoft, 2011), while the another dot-probe study supported attentional bias at 1250ms exposure time to illness words (Kim et al., 2014). In contrast, the other three dot-probe studies showed no differences between high and low IA in early orientation of attention to and later engagement of attention from illness-related words (Jacoby et al., 2016; Lee et al., 2013; Lees et al., 2005) and pictures (Lees et al., 2005). Absence of attentional bias was also supported by the single study using a Visual Search task with words (Shields & Murphy, 2011). In contrast, findings supportive of the presence of attentional biases were corroborated by one eye tracking study that indicated an early orientation of attention towards pictorial illness stimuli and either a later difficulty in disengaging attention or a tendency to shift attention away from these stimuli (Kim & Lee, 2014).

More specifically, a difficulty in disengaging attention from illness-related words was more evident among individuals who tend to seek healthcare more often, compared to individuals who avoid healthcare (Lee et al., 2013); a difficulty to disengage attention from illness-related pictures, was specific to individuals with high IA, who were characterized as monitorers, compared to blunters[1]. In contrast, individuals who avoid healthcare were characterized by an avoidant attention bias pattern, as indicated by early disengagement from illness-related words (Lee et al., 2013), and blunters showed a tendency to shift attention away from illness-related pictures (Kim et al., 2014; Kim & Lee, 2014). This distinction between the attentional processing patterns seems to represent an heterogeneity among illness-anxious individuals, which was not evident among individuals with low IA, who showed no within-group differences in attentional processes related to dispositional coping strategies (Kim & Lee, 2014). Therefore, 10 out of 14 studies support the presence of some form of attentional bias in IA, but these biases seem to be modulated by individual differences leading to two different patterns: vigilance vs vigilance-avoidance.

Memory bias. Although memory bias is not explicitly included in the cognitive-behavioral model, it may influence other stages of cognitive processing, as it makes illness-related information more readily available. Such bias for disorder-specific information, i.e. illness-related, has been observed in the form of increased retrieval and recognition rate of illness-related words, compared to neutral words, in some studies. Memory bias was assessed in seven studies using an accuracy index and reaction time during immediate and delayed recall tasks (*n*=2) and recognition tasks (*n*=6) with illness-related, symptom or pain words, compared to neutral words as the to-be-remembered stimuli. Findings of all of the above studies showed that individuals with high, compared to low, IA recognize words related to illness, health and bodily pain faster and more accurately, while they also show better free recall for such words (Ferguson, Moghaddam, & Bibby, 2007; Gropalis et al., 2012; Hitchcock & Mathews, 1992; Pauli & Alpers, 2002; Schmidt, Witthöft, Kornadt, Rist, & Bailer, 2013; Witthoft et al., 2016).

[1] Monitorers: individuals who are vigilant for threatening information throughout the whole processing continuum. Blunters: those who initially direct their attention to threat but when threat is identified they shift attention away from it; those who fit a “vigilance-avoidance pattern” (Derakshan et al., 2007).

One additional study examined memory bias using the Autobiographical Memory Test and the Future Imaginings Task[2] (Sansom-Daly, Bryant, Cohn, & Wakefield, 2014). Although this study also showed memory bias in IA, which was specific for future-directed memory for illness-related events, compared to other themes, the autobiographical memory bias about past illness-related events was equivalent across IA levels. It should be noted that two studies that examined the valence and arousal value of the illness stimuli as mediators of memory bias, supported that the higher arousal and unpleasantness of stimuli may drive this effect (Ferguson et al., 2007; Witthoft et al., 2016), which may provide preliminary evidence for the interaction between cognitive and emotional processes in IA.

Interpretation bias. Like memory bias, interpretation bias makes illness-related information more accessible when one encounters health-threatening cues, which may maintain and increase IA by providing evidence in support of the illness preoccupation. Nine studies examined interpretation and attribution bias using the Implicit Association Task (IAT; *n*=2), asking participants to categorize illness-related, emotional and neutral words as dangerous or harmless; questionnaires or lists of words that assess attributions for health scenarios and bodily sensations (*n*=6); and a task involving evaluation of pictures showing other persons with various degrees of sickness symptoms (*n*=1). Eight of these studies supported an association between IA and the tendency to interpret illness-related information in a catastrophic manner (Bailey & Wells, 2015, 2016; Hitchcock & Mathews, 1992; Winfried Rief & Hiller, 1998) and to attribute to a greater degree bodily symptoms to somatic, moderate or severe disease rather than to normal bodily functions (MacLeod, Haynes, & Sensky, 1998; Neng & Weck, 2015). In addition, the tendency to perceive illness as more probable in high, compared to low, IA individuals seems to hold not only for themselves, but also for other, apparently healthy individuals, whom they perceive as less healthy (Hedman et al., 2016). The results were contradicted by Witthöft and colleagues (2016), who did not find group differences on the IAT and attributed their negative findings to either validity issues of the task or emotional habituation due to previous exposure of their participants to the same words. However, findings overall, except for this single study, support the presence of interpretation bias in high IA when processing illness-related information.

Physiological mechanisms

Somatosensory amplification. Biased processing is not evident merely during environmental information processing, but also during processing one's own somatic cues. According to the somatosensory amplification hypothesis for hypochondriasis (Barsky &

[2] The Autobiographical Memory Test required individuals to recall specific past events, while the Future Imaginings Task required them to imagine specific future events in response to positive, negative and somatic cue words.

Wyshak, 1990), individuals with high IA are vigilant towards somatic sensations but they misinterpret normal and innocuous sensations as signs of a medical disease. This interpretation elicits inflated emotional/physiological reactivity that amplifies somatic sensations, which in turn leads to more attention to somatic sensations and increased physiological arousal (Köteles, Szemerszky, Freyler, & Bárdos, 2011; Marcus, Gurley, Marchi, & Bauer, 2007). Eleven studies examined somatosensory amplification using questionnaires (*n*=7), the Cold Pressor (*n*=1), the Vibrotactile Perception (*n*=2), and the Somatic Signal Detection tasks (*n*=1). Six of the studies using self-report methodologies supported a link between high IA and somatosensory amplification (Bailey & Wells, 2015, 2016; Barsky & Wyshak, 1990; Köteles & Simor, 2014; Winfried Rief & Hiller, 1998; Zincir et al., 2016), while in one such study somatosensory amplification was found to be similar between hypochondriasis and panic disorder groups (Martinez et al., 1999). The experimental findings further supported the presence of somatosensory amplification among women with high IA, who rated the cold pressor task as more unpleasant and terminated easier and more quickly compared to controls (Gramling et al., 1996). In addition, high IA was associated with a lower threshold and more false alarms for feeling tactile sensations in two studies (Katzer, Oberfeld, Hiller, & Witthöft, 2011; Rodic, Meyer, Lieb, & Meinlschmidt, 2016). These findings provide supportive evidence for somatosensory amplification as a mechanism involved in biased processing of somatic information in IA.

Biased processing of interoceptive information. To understand the factors that underlie the misinterpretation of somatic sensations it is also important to look into interoception and interoceptive awareness, the “sensory-perceptual processes for events occurring inside the body, including visceral perception” (Cameron, 2002, p. 3), and representation of the ensuing physiological response (Craig, 2002). Five studies examined interoceptive awareness in relation to IA, using questionnaires (*n*=3), the Heartbeat Detection (*n*=2) and the Non-Specific Skin Conductance tasks (*n*=2). From the three questionnaire studies, self-reported body vigilance and body consciousness showed a positive association with IA, supporting that illness-anxious individuals believe that they have increased interoceptive awareness (Goodwin, Fairclough, & Poole, 2013; Vervaeke, Bouman, & Valmaggia, 1999; Wheaton, Berman, Franklin, & Abramowitz, 2010). However, experimental findings support that they show decreased interoceptive accuracy (i.e. the ability to accurately perceive bodily sensations, condition and activity). High IA was associated with more false alarms for non-specific skin conductance fluctuations, although their sensitivity to skin conductance fluctuations was similar to that of low IA participants, especially when controlling for comorbidity with anxiety disorders (Krautwurst, Gerlach, Gomille, Hiller, & Witthöft, 2014; Krautwurst et al., 2016).[3] Evidence for interoceptive sensitivity to one's own heartbeats is inconsistent: Krautwurst and colleagues (2014) showed a negative association between IA and accuracy on the heartbeat detection task, whereas the second study of the same research group (Krautwurst et al., 2016) did not found group differences, which raises the need for replication studies. In sum, questionnaire studies support an increased self-perceived interoceptive awareness in IA, derived perhaps by increased attentional bias to and accessibility of somatosensory information; however, very limited experimental data support inaccurate responses to skin conductance fluctuations (more false alarms), with the findings regarding heartbeat sensitivity warranting further investigation due to their scarcity and contradictory nature.

Affective mechanisms

Negativity bias. Since negative affect seems to influence interoceptive accuracy and its relationship with body vigilance (Bogaerts et al., 2005, 2008), and interferes with memory processes as mentioned above, the investigation of affective processes that interfere with information processing is necessary to understand the mechanisms of IA. The tendency to evaluate health-threatening cues as more intense and negative seems to contribute to the salience of these cues, which potentially makes information processing more susceptible to cognitive and interoceptive biases (Ferguson et al., 2007; Witthoft et al., 2016). Eight studies focused on affect evaluation and its link to IA: one study assessed trait negative affect with the Positive and Negative Affect Schedule, while all the other studies assessed state negative affect as a response to distressing conditions, including a cold pressor task followed by illness imagery (n=1), somatic symptom ratings (n=1), the Affect Misattribution Procedure (AMP) using symptom and illness primes (n=2), the EST with illness and symptom words (n=1), an IAT (n=1) and the Mirror Tracing task (n=1). In addition to the link between high IA and trait negative affect supported by one study (Goodwin et al., 2013), experimental findings indicated increased physiological arousal (heart-rate) during the cold pressor task, paired with increased unpleasantness ratings in the high IA group, although group differences in physiology and affect during a different task (imagery) were not significant (Gramling et al., 1996). Results of the one study using the mirror tracing task supported a positive association between state-anxiety and IA (Macatee & Cougle, 2013), while four out of five studies using illness and symptom words to induce stress, reported positive associations between unpleasantness and arousal ratings after exposure to some types of these stimuli and IA (Jasper & Witthöft, 2013; Schreiber, Neng, Heimlich, Witthöft, & Weck, 2014; Witthoft et al., 2016; Witthöft et al., 2008). These findings

[3] False alarms about skin conductance fluctuations refer to the D' parameter derived based on the signal detection theory and explains the individuals' ability to distinguish between bodily arousal and non-arousal; sensitivity to skin conductance fluctuations refers to the c parameter and it is the response criterion based on the signal detection theory (see Krautwurst, Gerlach, Gomille, Hiller, & Witthöft, 2014).

suggest that a putative mechanism associated with the cognitive characteristics of IA (including biased information processing and interoceptive inaccuracy) may be increased negative affect.

However, in the aforementioned studies, results were inconsistent with regards to the type of health-threatening information the processing of which was impaired by negative affect: associations between unpleasantness ratings and high IA were found for illness-primed trials but not for symptom-primed trials in one study (Jasper & Witthöft, 2013; Schreiber et al., 2014). To the contrary, increased negative affect was found for symptom and not for illness words during the EST and IAT paradigms in two other studies (Witthoft et al., 2016; Witthöft et al., 2008). A tentative explanation of these contradictory findings pertains to the implicit nature of primes in AMT, in contrast to explicit evaluations of health-threatening words for valence and intensity: When individuals with high IA implicitly process illness-related information they may feel more threatened due to implicit associations and beliefs they hold about illness. Instead, during explicit evaluations, illness-related information may be seen as similarly unpleasant regardless of IA levels, perhaps because both groups more consciously process their responses, producing more socially desirable answers. The opposite may apply to symptom-related information, so that regardless of IA levels, somatic symptoms are seen as unpleasant. However, when explicitly evaluating these symptoms, high IA individuals may rate them as more unpleasant, because they make more frequent illness attributions to symptoms, in contrast to more normalizing attributions in moderate or low IA (MacLeod et al., 1998; Neng & Weck, 2015). High IA individuals also tend to explicitly discuss symptoms, presenting them in a particularly negative light to receive reassurance from others (Warwick & Salkovskis, 1990).

Not all evidence concurs that negative affect plays a role in IA information processing, however. One experimental study indicated a reduction in negative affect after participants rated a list of somatic symptoms, not influenced by IA levels. The authors' interpretation was that focusing on only few somatic symptoms due to the rating task potentially helped in reducing negative affect (Jasper, Hiller, Berking, Rommel, & Witthöft, 2014). In sum, despite some contradictory results, most studies support the presence of increased negative affect after exposure to distressing and illness/symptom-related contexts in high IA, which suggests a negativity bias during evaluating the affective properties of health-threatening information.

Emotion dysregulation. In addition to the increased negative affectivity in high IA when processing health-threatening information, strategies to regulate affect are deemed to play an important role in the maintenance of IA. When encountering threatening information individuals employ strategies to regulate the elicited emotions; strategies may be adaptive or maladaptive (Gross & Thompson, 2007). Failed or maladaptive emotion regulation (e.g. amplified negative affect when one is trying to decrease it) may help to maintain anxiety about health. We identified ten studies that examined emotion regulation, including emotion-focused coping, based on questionnaire measures (*n*=9), and one study using an experimental task to investigate the effect of distraction from pain stimuli as an emotion regulation strategy, on the intensity and unpleasantness of these stimuli. Bardeen and Fergus (2014) showed a link between high IA and difficulties in emotion regulation and a reduced perceived access to effective emotion regulation strategies.

Questionnaire studies examining the predominant emotion regulation strategies relied upon by those high in IA, showed positive associations with experiential avoidance, a type of trait-like avoidant coping (Doherty-Torstrick, Walton, Barsky, & Fallon, 2016; Fergus, 2014; Wheaton, Berman, & Abramowitz, 2010); cognitive fusion, i.e. the tendency to be overly influenced by and emotionally react to the content of thoughts (Fergus, 2014); rumination, catastrophizing, expressive suppression, self-blame and other-blame (Görgen, Hiller, & Witthöft, 2014). Findings regarding reappraisal were inconsistent: two studies found that higher use of reappraisal predicted higher score in IA, although only in specific dimensions, i.e. illness likelihood (Gerolimatos & Edelstein, 2012b) and the perceptual dimension (Görgen et al., 2014), whereas Gerolimatos and Edelstein (2012a) presented negative results about the predictive value of reappraisal in IA. Schütte and colleagues (Schütte, Vocks, & Waldorf, 2016) did not find group differences in perceived coping ability and in strategies such as cognitive avoidance and rumination about non-specific illness; rumination was increased in high IA only when encountering a specific feared disease. Assessment of illness-related coping in this study, rather than general emotion regulation and coping, as in the previous studies may account for the absence of group differences in the strategies assessed. This possibility leads to the hypothesis that perhaps the way of coping with an illness (whether real or perceived) may be similar regardless of IA levels, or that IA differ only in emotion regulation strategies that aim to regulate affect in general, like experiential avoidance, which is not consistently assessed. In all, findings support a rather avoidant pattern of processing affect, which, based on the experimental study of Lautenbacher and colleagues (Lautenbacher, Pauli, Zaudig, & Birbaumer, 1998), may be reinforced because it reduces negative affect temporarily but may preclude interpretation of health-threatening information and innocuous somatic sensations as “harmless” and normal, thus perpetuating IA (Byrne & Ditto, 2005; Taylor, Parker, & Bagby, 1997).

Behavioral mechanisms

In addition to the cognitive and emotional responses toward health-threats, IA is also deemed by the cognitive-behavioral model to be characterized by a range of more overt coping behaviors that may serve as a maintenance mechanism by preventing the awareness of information that comes in contrast to the perceived health-threat. These behaviors are probably negatively reinforced by providing a sense of false safety (Salkovskis, 1991; Tang et al., 2007).

Only three studies examined behavioral coping mechanisms in IA maintenance. In two of the studies using the Behavioral Avoidance Tasks, illness-anxious participants showed high anxiety and disgust levels accompanied by an increased degree of behavioral avoidance during exposure to illness-related conditions (Brady & Lohr, 2014; Goetz, Lee, & Cougle, 2012). Furthermore, results from an exposure and response prevention paradigm (*n*=1) showed that exposure to personally-relevant triggers provoked anxiety and urges to repeatedly perform safety behaviors, which lasted in the long-term (Abramowitz, Deacon, & Valentiner, 2007). Taken together, these findings highlight the role of behavioral avoidance in maintaining IA, especially when triggered by emotional responses, e.g. temporary anxiety decrease, or attention manipulation. Behavioral avoidance may include avoidant and safety-seeking behaviors and may in turn trigger healthcare utilization and reassurance seeking (Olatunji, Deacon, Abramowitz, & Valentiner, 2007), maintaining IA symptomatology.

Discussion

According to the cognitive-behavioral model, health-threatening information processing is influenced by the activation of illness-related dysfunctional schemas formed during previous illness-related experiences (Warwick & Salkovskis, 1990). This systematic review aimed to synthesize existing evidence on mechanisms that interfere with information processing in IA, to examine the degree to which they support and/or further extend the cognitive-behavioral conceptualization of IA. Considering the cognitive mechanisms, findings provide evidence for a particularly sensitive and biased attentional system of illness-anxious individuals towards health-threatening information. Although these findings should be treated with caution due to some contradictory results, high IA was linked to an early focus of attention towards threat, which may explain difficulties in inhibiting unnecessary information processing; while later-onset attentional processes, like difficulty in disengaging or shifting attention away, may prevent illness-anxious individuals from adaptively dealing with health-threats and taking in disconfirming information (Derakshan et al., 2007). A few studies showed individual differences in later-onset processes, suggesting heterogeneity among IA individuals, however, further replication via experimental paradigms that allow the investigation of attentional processes along a time continuum are needed to draw firm conclusions. Studies using eye tracking methods, seem well-suited for this purpose, as other methodologies (e.g. EST, dot-probe) assess attentional processes only in specific timeframes, and seemed more likely to provide mixed results. In addition, although not consistently, methodologies using pictorial, compared to word stimuli, were more effective in triggering and capturing specific types of attentional bias in IA, and therefore should be preferred in future investigations.

Second, although memory and interpretation biases were not part of existing theoretical models, findings of this review suggest that revised conceptualizations may need to take them into account more explicitly, as the evidence shows rather consistently that they characterize information processing in high IA (Martin, Buech, Schwenk, & Rief, 2007). Illness-anxious individuals tend to interpret harmless health-related information and bodily sensations as dangerous and catastrophic and encode these biased interpretations in memory accompanied by negative emotional evaluations, making it more likely to later retrieve these interpretations and evaluations more easily (Ferguson et al., 2007). Memory and interpretation biases may therefore need to become an important addition to the conceptualization of IA.

Physiological changes and the awareness and interpretation of bodily sensations were previously proposed as a central aspect of IA (Warwick & Salkovskis, 1990), while the presumed tendency of illness-anxious individuals to amplify innocuous somatic sensations received much attention by researchers. Reviewed evidence supports a positive association between somatosensory amplification with IA, although this is mostly based on questionnaire studies. A range of experimental paradigms assessing somatic sensations' perception provided evidence about biased interoceptive and exteroceptive awareness, mainly in the direction of inaccuracy in perception, including false alarms, when they are expected to identify somatic sensations, despite their belief that they are highly aware of what is happening in their body. More replication studies and new paradigms seem to be required to investigate awareness of personally-fearful somatic sensations and to clarify the role of interoceptive inaccuracy in theoretical models of IA.

Since illness-related schemas are often developed under distressing conditions, aspects of the emotional experience are also stored and retrieved when these schemas are activated (Witthoft et al., 2016). Negative evaluation of the affective properties of health-threatening cues was found to influence information processing, although, caution should be applied in looking at the results: Many studies focused on subjective reports of valence and arousal in response to stimuli to examine this association, thus, replication studies including more objective measures of emotion, including autonomic measures of arousal and facial electromyography to measure emotional valence, will provide further evidence about automatic aspects of the emotional experience and their role in information processing. The contradictory findings on explicit vs implicit evaluation tasks (Witthoft et al., 2016) should also be considered and clarified by future studies, as they may suggest a dissociation between implicit and explicit affective responses to health-threatening stimuli.

Emotional processing of health-threatening information specifically, and emotional processing and regulation strategies in general that may influence information processing in IA, is a field still in its infancy. Although some studies were identified covering each of these topics, there is a general dearth of relevant experimental studies: Further examination will provide evidence regarding all components of the emotional response system, including actions taken to regulate emotions and the function that these serve in IA. Findings from studies on other populations who may share characteristics with IA have shown an association between low interoceptive accuracy and alexithymia (Herbert, Herbert, & Pollatos, 2011), and associations between alexithymia and psychosomatic symptoms, mediated by experiential avoidance (Panayiotou et al., 2015), which are all constructs that may deserve to be considered in models of IA, to better consider the role of affect and its effective and ineffective regulation.

An additional finding of this review is that most studies examined mechanisms that seem to underlie IA separately and only a few focused on understanding the interaction between them. Understanding of the function of cognitive biases and behavioral coping may be enhanced by examining the emotional reaction of individuals during exposure to health-threatening interoceptive and exteroceptive cues, through measuring both subjective and physiological emotional responses. In addition, future studies should include stimuli that may elicit emotions other than health-threat, primarily examined to-date, to investigate the specificity of the above processes to IA, and their relation to emotion processing in general. Additional areas to be addressed in future research may include controlling for comorbidity with other symptomatology, gender, age and presence of medical diagnoses, which did not seem to bias the current review, but which have also not been extensively considered. Replication and extension of existing results in medical and psychiatric samples with higher levels of IA and greater dysfunction and distress would also contribute to this literature. Such research endeavors may help in identifying factors and processes that mediate and moderate the relation of the above mechanisms with IA and in reaching more conclusive findings on the inter-relations between the mechanisms. In sum, this systematic review synthesized existing evidence on the mechanisms that have been linked to IA and the interactions between them, provided information that can further extend the cognitive-behavioral model of IA, while highlighting directions for future research for the better understanding, prevention and treatment of a costly and frequent condition.

CHAPTER 3 │ Illness-related imagery under the influence of attention to somatic sensations: We all respond the same, regardless of illness anxiety levels

Abstract

Illness imagery is highly distressing and has been linked to the development and maintenance of illness anxiety, especially when it is combined with processes such as hypervigilance to somatic sensations. **Objective.** This study investigated the influence of heightened attention on somatic sensations of arousal on the emotional responses during illness imagery, and the effect of illness anxiety levels. **Methods.** 101 students (81 female; 18-35 years old) with low, moderate and high levels of illness anxiety, participated in an experimental task where they had to imagine personally-relevant illness scenarios and standardized generally fearful, joyful and neutral scenarios, after they underwent an attention manipulation to focus their attention on somatic sensations or environmental stimuli. Emotional responses assessed during imagery included subjective ratings of arousal, valence and somatic sensations, and psychophysiological measures of heart-rate, heart-rate variability, skin conductance level, and facial electromyography. **Results.** Findings showed increased reports of emotional arousal, negative affect and somatic symptoms, accompanied by negative emotion expressions but a hypo-arousal physiological response pattern during illness imagery after focusing on somatic sensations, irrespective of illness anxiety levels. **Conclusion.** Under these conditions, the observed emotional response to illness imagery in combination with maladaptive behavioral responses may increase the risk for developing and perpetuating illness anxiety. More mindful and non-judgmental approaches to illness imagery and the experienced somatic sensations may reduce this risk.

Keywords: *Illness imagery; Illness anxiety; Interoceptive attention; Emotional responses, Psychophysiological responses.*

Background

Illness anxiety (IA) is characterized by preoccupation with having or acquiring a severe medical disease that persists despite appropriate medical reassurance (Rachman, 2012). Severe IA, accompanied by significant levels of distress and impairment in functioning, is diagnosed as Illness Anxiety Disorder (American Psychiatric Association, 2013). In addition to the suffering of the individual (Chaturvedi et al., 2006; Sempértegui et al., 2017; Terluin et al., 2011), IA is also costly in terms of medical service utilization (Burton, 2003; Grabe et al., 2009; Kroenke, 2003). This makes research on understanding the etiological and maintenance mechanisms of IA a priority.

The cognitive-behavioral conceptualization supports that IA is developed through dysfunctional schemas about illness, formed during previous personal and vicarious illness-related emotionally-laden events (Warwick & Salkovskis, 1990). According to the bio-informational theory of emotion, emotional events are encoded in associative networks in memory, which include stimulus representations, meaning and response representations (Cuthbert et al., 2003; Lang, Levin, Miller, & Kozak, 1983; Lang & McTeague, 2009; Vrana & Lang, 1990; Weerts & Lang, 1978). Emotionally-laden illness-threats (Leventhal, Diefenbach, & Leventhal, 1992) are also stored in such networks, which are activated when one is exposed to any sensory cue related to the specific event, e.g. when illness-anxious individuals confront illness-threats coming from bodily and environmental sources. When the network is activated, emotional events are retrieved, which may explain why during periods of high distress, illness-anxious individuals tend to frequently report images about getting a medical diagnosis, suffering with a severe illness, death and the consequences on significant others (Muse et al., 2010; Wells & Hackmann, 1993). Illness-related images are thought to be intrusive and spontaneous in response to a cue rather than voluntary and deliberate (Berntsen, 2010; Mace, 2007). Retrieval of such images influences processing of illness-related information in a way that is suggested to increase and maintain IA (Muse et al., 2010; Warwick & Salkovskis, 1990), although the mechanism through which this happens remains to be investigated, which is the aim of this study.

During aversive mental imagery, activation of the associative network includes activation of the defensive-motivational physiological system and negative expressive behaviors (Cuthbert et al., 2003; Lang et al., 1983; Lang & McTeague, 2009; Vrana & Lang, 1990; Weerts & Lang, 1978). Existing research documents two distinct response patterns to threat-related imagery associated with specific categories of anxiety symptomatology: The first pattern involves increased psychophysiological reactivity accompanied by high distress reports. The second pattern involves a hypo-arousal physiological response, despite high distress reports; explained by the high vs. low associative strength, respectively, between threatening cue and response representations (Cuthbert et al., 2003; Lang & McTeague, 2009; Panayiotou, Karekla, Georgiou, Constantinou, & Paraskeva-Siamata, 2017). Although the role of emotional responses to imagery has been extensively examined in other categories of psychological symptomatology in an effort to provide tailored interventions to individuals' needs, in IA, it has received only limited attention.

The only relevant evidence is derived from two studies that tested the hypothesis that individuals who present IA symptoms respond to illness imagery with heightened physiological reactivity. Both were based on the theoretical assumption that increased psychophysiology in illness-anxious individuals is derived from the effortful evaluation of and, possibly, misinterpretation of the somatic sensations elicited by illness imagery as medical symptoms. Findings of Brownlee and colleagues (1992) supported this hypothesis by showing increased physiological reactivity (heart-rate) during illness imagery among individuals with hypochondriacal traits and body vigilance, compared to frequent healthcare users and controls. In contrast, Gramling and colleagues (1996) found no differences in physiological reactivity (heart-rate and neck electromyography) during illness imagery. The limited and contradictory nature of the findings invites further investigation to reach conclusions about the role of emotional responses to illness imagery in the maintenance of IA.

In line with the hypothesis for heightened physiological reactivity, the reactions of illness-anxious individuals to illness-threats, including imagined ones, have been assumed to be justified by their heightened attention to somatic sensations (Easterling & Leventhal, 1989). This hypervigilance enhances perception of somatic sensations that are disorder-relevant and may mimic health problems (Steptoe & Vögele, 1992). Despite this increased attention, however, somatic sensation reports by illness-anxious individuals are not highly accurate. They are instead influenced by interoceptive inaccuracy, the inability to accurately perceive and report on somatic sensations, and by somatosensory amplification, the tendency to amplify somatic sensations instead of interpreting them as the outcome of normal physiological functioning (Köteles & Simor, 2014; Köteles et al., 2011; Krautwurst et al., 2014, 2016; Marcus et al., 2007; Martinez et al., 1999). Since perception of visceral activity is a key component of emotional experience (Damasio, 1994, 1999; James, 1984; Schachter & Singer, 1962), it can be assumed that emotional reactions to illness imagery in IA are not in response to the distressing content of such imagery but may also be influenced by misperceived somatic cues, which are experienced as threatening. To our knowledge, this hypothesis has not been tested yet.

In addition, individuals high in IA may perceive emotional reactivity itself as somatic symptomatology linked to illness. This further increases physiological arousal and results in amplified somatic sensations, which may lead to graver symptom interpretations. This vicious cycle is supported by evidence from studies on healthy individuals, which showed a decline in accuracy in somatic sensation perception under conditions that elicit stress (Fairclough & Goodwin, 2007), negative emotions (Werner, Mannhart, Reyes Del Paso, & Duschek, 2014) and somatic symptoms (Bogaerts et al., 2008; Mirams, Poliakoff, Brown, & Lloyd, 2012). Whereas, interoceptive accuracy shows positive associations with subjective and objective measures (heart-rate variability) of emotion regulation (Kever et al., 2015; Oliveira & Costa, 2014), it can be expected that emotion *dys*regulation would be associated with biased perception of somatic sensations possibly because of increased and unregulated arousal. Under the above conditions, automatized and schema-driven processing precludes a more controlled processing of somatic sensations and may result in their misinterpretation as signs of illness. In turn this may lead to behavioral responses to intrusive images of illness-threats aiming to reduce distress, such as body checking, reassurance and healthcare seeking, and rumination (Muse et al., 2010). This further highlights the necessity to investigate the emotional responses to illness imagery especially during focusing attention on somatic sensations, as it may be the mechanism that underlies the association between illness imagery and IA.

Current Study

Based on the assumption that increased attention to somatic sensations, even if inaccurate, may be a critical part of the disorder's maintenance mechanism, this study aimed to examine the influence of attentional focus on somatic sensations on emotional responses during illness imagery, and whether this is modulated by IA levels. We used an experimental manipulation to increase participants' attentional focus on either interoceptive information or innocuous environmental information, as a control condition. We then examined whether the attention manipulation influenced emotional responses during mental imagery of personally-relevant illness scenarios vs. standardized generally fearful, joyful, and neutral scenarios, and if it affected responses differently depending on level of IA. Limited empirical findings suggest that increased physiological arousal during illness-related or stress-inducing periods should be expected in high IA (Brownlee et al., 1992; Gramling et al., 1996), and also biased processing of somatic sensations following increased interoceptive attention (Mirams et al., 2012) and higher unpleasantness ratings after exposure to illness-related information (Jasper et al., 2014; Schreiber et al., 2014). Therefore, we expected increased subjective and physiological arousal (heart-rate and skin conductance) during illness imagery after the interoceptive focus, compared to the exteroceptive focus condition. We also expected more negative valence, as indicated by self-reports, increased corrugator and decreased zygomatic activity, and more somatic sensation reports. These emotional responses were expected to be more profound during illness imagery, compared to the other imagery conditions, especially in the high IA group, compared to the moderate and low IA groups.

Considering that emotion dysregulation may play a role in emotional responses to illness imagery due to biased perception of somatic sensations, we further examined group differences in resting-state heart-rate variability as a measure of autonomic regulation. Resting-state heart-rate variability was found to be associated with emotion regulation ability (Williams et al., 2015) and has not been previously examined in relation to IA. Based on evidence from the anxiety disorders literature (Chalmers, Quintana, Abbott, & Kemp, 2014), we expected lower resting-state heart-rate variability in the high compared to low and moderate IA groups. In addition, we hypothesized that physiological responses to imagery (heart-rate and skin conductance) may be influenced by an effort of individuals to regulate emotion that would be reflected on parasympathetic activity; hence, we statistically controlled for its effect as a covariate in analyses.

Methods

Participants

Participants were 101 students (81 female; 18-35 years old) receiving course credit for their participation. Exclusion criteria included age below 18 or above 35 and presence of vision or hearing disability that would prevent individuals from participating in the experiment. Participants were screened through an online questionnaire. Those who provided consent to be contacted for the experimental phase were invited to the laboratory. All interested participants were invited irrespective of IA levels until data were collected for half of the sample; after this point, participants were invited more selectively based on extreme low or high scores on IA, to increase the range of IA scores in the sample. The research assistants who conducted the experiments were blind to the IA level of each participant. Participants were assigned into groups of low, medium and high IA based on the suggested clinical cut-off score of the Illness Attitudes Scales (>47) (Hedman, Ljótsson, et al., 2015) and upper and lower tertiles on the Short Health Anxiety Inventory.[4] This resulted in 30 participants per group, after eleven participants were removed based on high discordance in their IA scores between the two screening measures. Univariate ANOVAs showed significant group differences in IA levels: the high IA group reported higher levels of IA compared to the moderate and low IA groups and the low IA group reported lower levels of IA compared to the moderate IA group. Groups did not differ in age, gender and self-reported medical conditions frequency and baseline measures of interoceptive accuracy, resting-state heart-rate variability and baseline physiological reactivity (see Table 2).

Experimental Design

The experiment was a mixed 3x4x2 design with group (low, moderate and high IA) as the between-subjects variable and imagery condition (illness, fearful, joyful, neutral) and attention manipulation (interoceptive or exteroceptive focus) as the within-subject variables. Participants completed 16 trials each consisting of a resting phase, an attention manipulation phase and an imagery phase. The design included an equal number and equally distributed presentations of the four imagery conditions and the attention manipulation task in two counterbalanced orders.

[4] The low IA group had scores below the clinical cut-off in IAS and scored in the lower tertile on SHAI (<9), the high IA group scored above the clinical cut-off in IAS and in the upper tertile on the SHAI (>14), and the moderate IA group scored either below or above but close to the clinical cut-off in IAS and in the middle tertile on the SHAI.

Table 2. *Characteristics of the groups based on illness anxiety level*

	Low IA (*n*=30)	Moderate IA (*n*=30)	High IA (*n*=30)			
	N	*N*	*N*	χ^2	*df*	*p*
Gender				2.92	2	>.050
Male	8	7	3			
Female	22	23	27			
Medical condition						
No	28	24	24	2.71	2	>.050
Yes	2	6	6			
	M (SD)	*M (SD)*	*M (SD)*	*F*	*df*	*p*
Age	21.60 (3.86)	21.47 (3.83)	21.68 (3.69)	0.03	2,87	>.050
Baseline Interoceptive Accuracy	61.78 (19.62)	60.47 (17.77)	63.79 (21.03)	0.22	2,87	>.050
Resting-state RMSSD	42.25 (19.48)	45.03 (18.98)	50.97 (28.27)	1.14	2,88	>.050
Baseline HR *Δ*(bpm)	84.09 (7.50)	81.45 (9.01)	81.16 (9.16)	1.00	2,86	>.050
Baseline SCL *Δ*(μS)	8.72 (4.08)	10.12 (4.01)	7.80 (3.58)	2.66	2,86	>.050
Baseline Corrugator EMG *Δ*(μV)	4.17 (1.99)	3.85 (1.31)	3.77 (3.58)	.046	2,84	>.050
Baseline Zygomatic EMG *Δ*(μV)	4.01 (2.90)	5.24 (3.56)	3.66 (2.99)	1.91	2,81	>.050
IAS total	28.67 (8.08)^{ab}	37.00 (8.80)^{ac}	61.90 (11.32)^{bc}	121.63	2,87	<.001
SHAI total	6.10 (2.51)^{ab}	12.00 (1.76)^{ac}	21.10 (5.73)^{bc}	40.33	2,87	<.001

Note. ^{abc} p<.001

Experimental stimuli

The experimental stimuli were scripts, which included personally-relevant illness scenarios and standardized fearful, joyful and neutral scenarios. The personally-relevant scenarios were created based on scene construction forms that guided participants to create scenarios of their worst illness fears (Cuthbert et al., 2003) on the basis of the bio-informational view of affective imagery (Foa & Kozak, 1986; Lang, 1979). Participants who had booked an appointment for the experiment, received via email two days before their appointment the scene construction form that they had to complete with four illness scenarios and return on the day of the experiment. Participants who forgot it, completed the form in the laboratory before all the experimental procedures. The researcher read the scripts before the experiment to make sure that participants followed the instructions and requested changes in the scripts when needed. Examples of personally-relevant illness scenarios were: *"While I am having a bath I suddenly find a lump on my breast; I am in panic and I think that I will die.", "I am studying at home when suddenly I feel a chest pain; I think that I have a heart attack and I immediately call my doctor", "I just received an AIDS diagnosis; I worry about how the others will think about me* *and about how my life will be from now on", "I wake up at the hospital severely injured after a car accident; I try to move my body parts as I fear that I am paralyzed and I will never be able to walk again."* (see Table 3 for the categories and frequency of the themes of illness scenarios).

Standardized scenarios were selected from a pool of emotional scripts, which were translated and adapted into Greek by Panayiotou (2008) and describe daily situations that are expected to elicit general fear (e.g. "*A strange man is following me through a bad area of town; Sweat pours down my face as I listen to his footsteps getting closer"*), joy (e.g. "*I jump up with excitement as my dad drives up the road with my Christmas present, a brand new car!"*) and neutral emotions (e.g. "*I lean against the wall, watching people passing by as I wait for a friend before class*.").

Table 3. *Thematic categories of the personally-relevant illness scenarios and frequency of each theme (total N of scenarios: 404)*

Theme	*N*	%
Cancer-related worries	99	24.50
Injury and disability fears	91	22.52
Non-specific illness worries	81	20.05
Intolerance-related worries	21	5.20
Worries about cardiovascular problems	16	3.96
Contamination fear	15	3.71
Worries related to damage in the central nervous system	14	3.47
Fear of medical errors	13	3.22
Worries about disorders in sensory organs	12	2.97
Psychological worries	8	1.98
Worries about gynaecological problems	7	1.73
Autoimmune diseases worries	4	0.99
Diabetes-related worries	2	0.50
Kidney failure-related worries	2	0.50
Worries about the impact of bad health habits	2	0.50
Vicarious illness and suffering worries	2	0.50
Worries about respiratory problems	1	0.25
Thyroid disorders-related worries	1	0.25
Worries about the impact of environmental pollution	1	0.25
Physical threat during generally fearful situations	1	0.25

Procedure

Upon arrival at the laboratory, participants were provided with information about the experiment and an informed consent form. The research assistants guided participants to a dimly lit room and had them to sit in an armchair in front of a T.V. screen, where instructions for all the experimental phases were presented. Electrodes for physiological recording were then attached and headphones fitted (SONY-MDR-7506). After the physiological recording checks, a 5-minute adjustment period followed for physiological recording to stabilize and the participants were familiarised with the equipment. The Heartbeat Tracking task to measure baseline interoceptive accuracy (Schandry, 1981; see below) followed and then participants were given instructions for the experiment and went through an example trial to make sure that they understood the instructions. Each experimental trial was preceded by instructions on the screen and a tone, which signalled the beginning and end of each of the three trial phases so that participants could close their eyes without having to keep their attention on the screen. The experiment was controlled using E-Prime 2.

Resting phase. The resting phase lasted 20 seconds and participants were instructed to use the "count 1" method (i.e. please clear your mind and silently repeat the word "one" to yourself) to help them relax (Benson, Greenwood, & Klemchuk, 1975).

Attention manipulation phase. Following the resting phase, the attention manipulation instructions appeared on the screen, asking the participants to either interoceptively focus their attention (IF) or to exteroceptively focus attention (EF) on environmental stimuli for periods of 25/35/45/60s. During IF, participants were asked to count their heartbeats according to the Heartbeat Tracking task of Schandry (1981). This task measures interoceptive accuracy as participants count how many heartbeats they feel over varying time intervals by concentrating on their heartbeats, without taking their pulse or attempting any other physical manipulations that might facilitate the detection of heartbeats. Electrocardiography (ECG) was monitored continuously so that the participants' reported heartbeat number was compared with the heartbeats measured by ECG. Interoceptive accuracy was calculated by taking the absolute value of the modulus of the actual value minus the estimated value, dividing this by the actual value, and multiplying by 100 to express inaccuracy as a percentage: [(actual – estimated) ÷ actual] × 100; the inverse was the measure of accuracy. Higher percentage in interoceptive accuracy was an indication that participants directed their attention to interoceptive cues, as instructed.

For the EF, a similar task to the heartbeat tracking paradigm was developed. Participants were asked to count a tone they were hearing through headphones that was repeated every 1 second in a very low volume, in a range between 40-60 decibels, for the same time intervals as in the IF and to report the number of the tones they heard. A comparison between the reported and the actual number of the tones was used to assess participants' compliance to the task.

Imagery phase. After participants noted their counted heartbeats or tones, the research assistant read through a microphone a script, drawn among the four conditions and participants were asked to memorize and imagine it during the subsequent imagery phase as vividly as possible for 30 seconds.

Measures

Screening measures

The Short Health Anxiety Inventory (Salkovskis, Rimes, Warwick, & Clark, 2002) total score was used in this study to measure participants' IA levels; in this sample, Cronbach's α=.89. It is an 18-item questionnaire that assesses the features of IA as proposed by the cognitive-behavioral model of IA (Warwick & Salkovskis, 1990). Each item consists of four statements that correspond to a 4-point Likert scale according to the level that one has a tendency or characteristic (score range: 0-54). This short version has shown comparable reliability and validity to the 64-item version, which indicated excellent psychometric properties (Hedman et al., 2015). In addition to the total score, the questionnaire provides two factors: Health Anxiety and Negative Consequences. The Greek version of the SHAI (Karademas et al., 2008) showed a good fit of the two-factor model (Leonidou & Panayiotou, 2016).

The Illness Attitudes Scales (IAS; Kellner, 1987) total score was used as an additional measure of IA. It is a 27-item scale and assesses fears, attitudes and beliefs associated with hypochondriacal concerns and abnormal illness behaviour on a 5-point Likert scale (score range: 0-108). The IAS shows very good psychometric properties (Hedman et al., 2015) and gives both a total score, and scores of nine subscales: Worry about illness, Concerns about pain, Health habits, Hypochondriacal beliefs, Fear of death, Disease phobia, Bodily preoccupations, Treatment experience, Effects of symptoms. It was translated into Greek for the purpose of this study and initial confirmatory factor analysis supported the existing factor structure and model fit (Leonidou & Panayiotou, 2017a). Cronbach's α=.85 for the total scale in this sample.

Psychophysiological measures

Psychophysiological reactivity was recorded using the BIOPAC MP150 and the AcqKnowledge Data Acquisition and Analysis Software 3.9 during all the phases of the experiment. Heart-rate reactivity (HR) as an index of emotional arousal was measured by ECG recorded at the two inner forearms and filtered by a BIOPAC ECG100C bioamplifier sampled at 1000 Hz, set to record HR between 40 and 140 beats per minute (BPM), and converted to BPM online. The Rate Detector function in AcqKnowledge set to detect peaks between 40 and 140 BPM and reject noise 5% of peak was used to count the heartbeats. The Root Mean Square of Successive Differences (RMSSD) as a resting-state heart-rate variability index was calculated based on heart-rate recording during the 5-minute adjustment period in the beginning of experiment using ARTiiFACT (Kaufmann, Sütterlin, Schulz, & Vögele, 2011). Skin conductance level (SCL) was also used as a measure of arousal, using GSR100C transducer amplifier and electrodes attached on the medial phalanx of the index and middle fingers of the non-dominant hand, sampled at 250 Hz. Facial electromyography as a measure of emotional valence was recorded at the right corrugator supercilii and zygomaticus major muscles, by attaching two electrodes in each muscle, sampled at 1000 Hz, filtered (band pass, 20Hz high frequency, 500Hz low frequency), integrated over 20 samples, and rectified.

Self-reported emotion

Following the end of each trial, participants rated the emotional valence, arousal and the vividness they experienced during imagery on a 9-point scale. They also reported any somatic sensations they had felt by selecting from a list that included sensations such as chest pain, dizziness, faintness, heart palpitations, stomach ache, backpain, pain in hands, legs or joints, headache, dyspnoea, fatigue or low energy, numbness, weakness, hot flushes or chills or any other sensation. These were chosen from the Patient Health Questionnaire (Kroenke, Spitzer, & Williams, 2001) in a way that at least one sensation per category was represented.

Data Reduction and Analysis

Raw psychophysiological data were reduced by calculating the mean of HR (BPM), SCL (μS) and corrugator and zygomatic activity (μV) during the 20-second resting phases and during the 30-second imagery phases. The SCL data of 14 participants, HR data of 4 participants, zygomatic activity data of 10 participants and corrugator activity data of 6 participants were not included in analyses due to technical problems. Outliers below or above 2.5 standard deviations to the mean were removed from the raw data. Change scores of the physiological measurements were created by subtracting mean physiology during each resting phase from each subsequent imagery phase, to control for baseline reactivity. The mean of each measurement was calculated for each experimental condition and data were examined for normal distribution and outliers using histograms and boxplots. Few extreme outliers were replaced in the corrugator and zygomatic activity variables with the highest value, calculated after the identified outliers had been removed; 2.86% of values were replaced in total.

To test the effect of experimental manipulation, repeated-measures ANOVAs were conducted on the total sample (n=101) for each psychophysiological and self-report measure separately, using attention manipulation and scenario types as the within-subjects variables. Greenhouse-Geisser corrections were applied when the assumption of sphericity was not met (see ε values in parentheses below). Repeated-measures ANOVAs for HR and SCL variables were repeated adding RMSSD to test its effect as a covariate. Planned contrasts were corrected with the Holm-Bonferroni method for multiple comparisons (Holm, 1979); corrected alpha levels applied: 1st-rank α=.016, 2nd-rank α =.025, 3rd-rank α =.050). Effects were assumed to have a large effect size if $\eta_p{}^2$>.25, medium if $\eta_p{}^2$>.09, small if $\eta_p{}^2$>.01. To test the effect of IA levels, mixed-model ANOVAs were conducted, using the same within-subjects variables as above and adding the IA groups as the between-subjects variable.

Results

Vividness of Imagery and Difficulty of the Attention Manipulation Task

The mean score on the vividness of imagery across all conditions (*M*=6.92, *SD*=1.19) shows that rather vivid imagery was achieved. Participants reported that the IF was more difficult (*M*=7.11, *SD*=2.49) than the EF (*M*=2.54, *SD*=2.00), $F(1,98)=198.34$, $p<.001$, $\eta_p^2=.67$. This was also reflected in participants' mean accuracy on the counting task, which was significantly lower during IF (*M*=69.91, *SD*=16.20), compared to EF (*M*=95.62, *SD*=4.63), $F(1,96)=231.33$, $p<.001$, $\eta_p^2=.71$.

Effects of Experimental Manipulation and Illness Anxiety

Self-reported arousal

Table 4 presents means and SDs (total sample and group scores) for outcome variables. Repeated-measures ANOVA showed a significant main effect of imagery condition on arousal reports, $F(2.44,239.38)=248.82$, $p<.001$, $\eta_p^2=.72$ ($\varepsilon=.81$). Planned contrasts showed higher arousal reports after illness imagery compared to joyful, $F(1,98)=27.42$, $p<.001$, $\eta_p^2=.22$, and neutral imagery, $F(1,98)=517.44$, $p<.001$, $\eta_p^2=.84$; arousal reported after illness imagery was, however, lower compared to fearful imagery, $F(1,98)=18.55$, $p<.001$, $\eta_p^2=.16$. The attention manipulation also had a significant main effect on arousal reports, $F(3,98)=16.79$, $p<.001$, $\eta_p^2=.15$, being higher after IF compared to EF (see Figure 3).

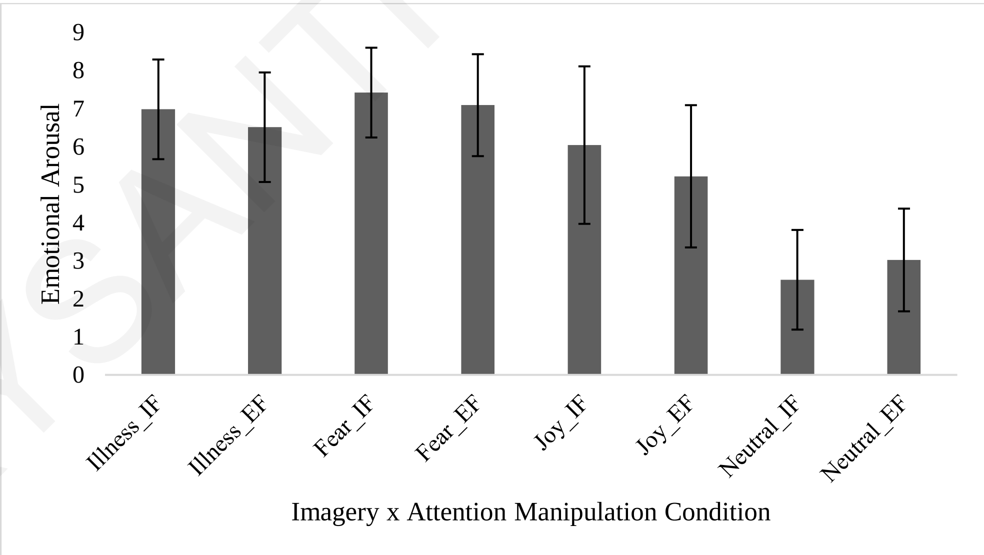

Figure 3. Self-reported emotional arousal for the total sample (1=not intense at all, 9=extremely intense emotion) during imagery.

Table 4. *Means and standard deviations (in parentheses) for self-reported and physiological measurements*

	Interoceptive Focus Task				Exteroceptive Focus Task			
	Illness	Fearful	Joyful	Neutral	Illness	Fearful	Joyful	Neutral
Arousal (1-9)[a]	6.98 (1.31)	7.42 (1.18)	6.04 (2.07)	2.50 (1.31)	6.51 (1.44)	7.09 (1.34)	5.22 (1.87)	3.02 (1.35)
High IA	7.05 (1.22)	7.43 (1.02)	6.26 (2.06)	2.97 (1.59)	6.55 (1.33)	6.69 (1.61)	5.24 (1.86)	3.36 (1.34)
Moderate IA	6.83 (1.35)	7.40 (1.36)	5.97 (2.03)	2.47 (1.27)	6.47 (1.40)	7.12 (1.16)	5.42 (1.89)	2.82 (1.53)
Low IA	6.90 (1.34)	7.26 (1.18)	6.07 (1.98)	2.00 (0.90)	6.38 (1.49)	7.10 (1.24)	5.10 (1.79)	2.79 (1.23)
Valence (1-9)[a]	1.92 (1.21)	2.30 (1.21)	8.18 (1.34)	6.84 (1.32)	2.18 (1.10)	2.45 (1.41)	8.01 (1.22)	5.76 (1.19)
High IA	1.72 (0.84)	2.07 (1.20)	7.97 (1.34)	6.83 (1.26)	2.29 (1.09)	2.55 (1.60)	7.97 (1.34)	5.71 (1.29)
Moderate IA	2.15 (1.39)	2.45 (1.23)	7.83 (1.78)	6.72 (1.38)	2.08 (0.98)	2.32 (1.09)	8.02 (1.11)	5.70 (1.24)
Low IA	2.00 (1.41)	2.50 (1.31)	8.62 (0.62)	6.84 (1.39)	2.22 (1.21)	2.57 (1.62)	8.02 (1.28)	5.83 (1.15)
Somatic Sensations (n)[a]	2.06 (1.82)	1.62 (1.60)	0.66 (0.99)	0.40 (0.72)	1.79 (1.71)	1.38 (1.48)	0.45 (0.65)	0.39 (0.72)
High IA	2.55 (2.26)	1.87 (2.08)	0.78 (1.16)	0.52 (0.96)	1.97 (2.05)	1.55 (1.98)	0.58 (0.93)	0.53 (1.00)
Moderate IA	1.73 (1.45)	1.40 (1.12)	0.68 (0.93)	0.37 (0.54)	1.68 (1.59)	1.18 (1.13)	0.42 (0.57)	0.30 (0.55)
Low IA	1.80 (1.73)	1.42 (1.56)	0.50 (0.90)	0.27 (0.58)	1.50 (1.49)	1.18 (1.22)	0.33 (0.36)	0.28 (0.50)
HR Δ(bpm)[a]	-5.79 (5.86)	-4.58 (5.73)	-5.09 (5.60)	-6.11 (6.17)	-3.58 (4.16)	-6.02 (5.43)	-6.14 (5.78)	-5.08 (5.65)
High IA	-5.16 (5.48)	-2.96 (5.68)	-4.42 (5.73)	-5.66 (5.78)	-2.22 (4.52)	-4.68 (5.96)	-5.16 (5.01)	-5.56 (5.43)
Moderate IA	-6.71 (6.36)	-4.79 (5.45)	-5.21 (5.83)	-5.50 (5.89)	-4.37 (4.13)	-7.24 (5.66)	-6.47 (6.25)	-4.23 (5.43)
Low IA	-6.40 (6.41)	-6.47 (6.11)	-6.37 (5.16)	-7.60 (7.47)	-4.38 (4.16)	-6.89 (4.73)	-7.25 (6.23)	-6.27 (6.52)
SCL Δ(μS)[a]	-0.28 (0.67)	-0.37 (0.57)	-0.30 (0.71)	-0.50 (0.71)	-0.13 (0.66)	-0.25 (0.66)	-0.31 (0.74)	-0.28 (0.56)
High IA	-0.16 (0.75)	-0.29 (0.59)	-0.20 (0.68)	-0.40 (0.74)	0.13 (0.70)	-0.28 (0.62)	-0.29 (0.63)	-0.20 (0.72)
Moderate IA	-0.24 (0.77)	-0.26 (0.59)	-0.34 (0.74)	-0.55 (0.65)	-0.16 (0.75)	-0.14 (0.81)	-0.29 (0.74)	-0.34 (0.49)
Low IA	-0.48 (0.45)	-0.51 (0.55)	-0.46 (0.62)	-0.42 (0.79)	-0.28 (0.50)	-0.30 (0.52)	-0.33 (0.89)	-0.28 (0.51)
Corrugator EMG Δ(μV)[a]	0.88 (1.88)	0.70 (1.53)	-0.55 (1.32)	0.20 (1.14)	0.55 (1.55)	0.84 (2.22)	-0.57 (1.78)	0.57 (1.51)
High IA	1.02 (1.74)	0.79 (1.32)	-0.43 (2.41)	0.34 (0.99)	0.38 (1.39)	1.11 (2.12)	-0.42 (2.41)	0.96 (1.37)
Moderate IA	0.86 (1.54)	0.44 (1.32)	-0.50 (1.15)	0.09 (1.07)	0.79 (1.41)	0.68 (2.15)	-0.21 (1.13)	0.46 (1.39)
Low IA	0.65 (1.75)	0.69 (1.79)	-0.85 (1.46)	-0.01 (1.38)	0.29 (1.67)	0.85 (2.55)	-1.09 (1.70)	0.28 (1.68)
Zygomatic EMG Δ(μV)[a]	-0.61 (2.04)	-0.02 (1.57)	1.30 (3.17)	-0.44 (1.33)	-0.04 (1.23)	-0.03 (1.42)	1.76 (3.49)	-0.29 (1.79)
High IA	-0.02 (0.95)	0.21 (1.07)	1.40 (3.15)	-0.14 (0.95)	0.35 (0.95)	0.25 (1.30)	2.26 (3.79)	0.08 (1.17)
Moderate IA	-0.47 (1.65)	-0.02 (1.75)	1.33 (3.30)	-0.44 (1.43)	-0.19 (1.26)	0.07 (1.53)	1.44 (3.07)	-0.00 (0.88)
Low IA	-1.12 (1.62)	-0.48 (1.49)	0.45 (2.68)	-0.52 (1.30)	-0.36 (1.29)	-0.37 (1.31)	1.13 (3.14)	-1.20 (2.53)

Note. [a]Means and SDs of the total sample.

The effect of each imagery condition on arousal depended on the effect of attention manipulation; this interaction was significant, $F(2.75,269.70)=16.18$, $p<.001$, $\eta_p^2=.14$ ($\varepsilon=.92$). Planned contrasts showed that for illness imagery, higher arousal was reported after IF compared to EF, while for neutral imagery, lower arousal was reported after IF compared to EF, $F(1,98)=26.56$, $p<.001$, $\eta_p^2=.21$. The contrasts between illness and fearful or joyful imagery in relation to attention manipulation were not significant, suggesting a similar effect of attention manipulation on these imagery conditions, i.e. higher arousal after IF compared to EF. Mixed-model ANOVA showed no interaction of IA group by imagery condition, $F(4.90,208.10)=0.58$, $p>.05$ ($\varepsilon=.82$); attention manipulation, $F(2,85)=1.35$, $p>.05$; and their interaction, $F(5.48,232.99)=0.65$, $p>05$ ($\varepsilon=.97$).[5]

Self-reported valence

Imagery condition had a significant main effect on self-reported valence, $F(2.07, 203.56)=681.99$, $p<.001$, $\eta_p^2=.87$, ($\varepsilon=.69$). Planned contrasts showed more negative valence reported after illness imagery compared to fearful, $F(1,98)=9.02$, $p<.01$, $\eta_p^2=.08$; and especially to joyful, $F(1,98)=1307.61$, $p<.001$, $\eta_p^2=.93$; and neutral imagery, $F(1,98)=591.54$, $p<.001$, $\eta_p^2=.86$. Attention manipulation had a main effect on valence, $F(1,98)=10.40$, $p<.01$, $\eta_p^2=.10$, with participants reporting more positive valence after IF compared to EF (see Figure 4).

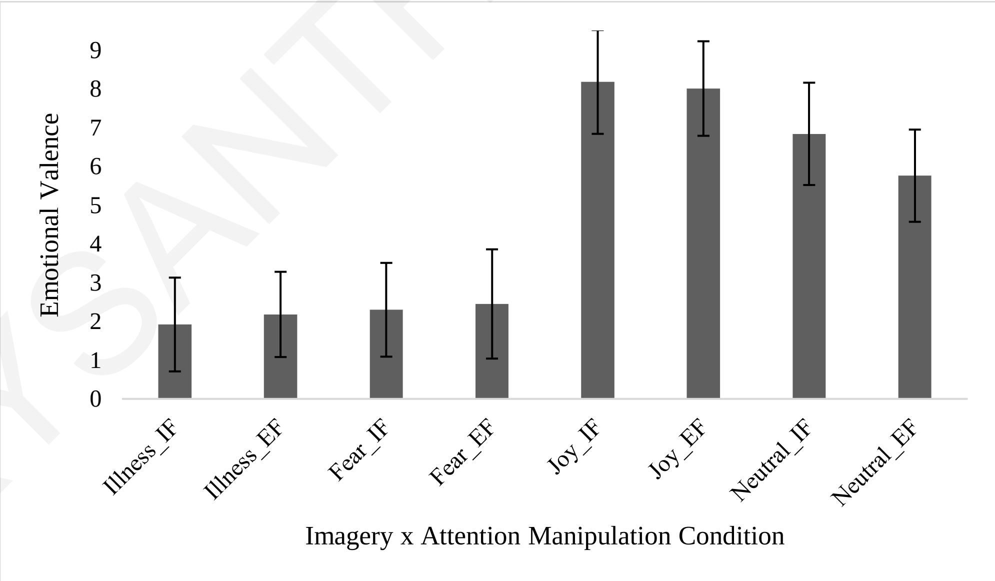

Figure 4. Self-reported emotional valence (1=extremely unpleasant, 9=extremely pleasant) during imagery for the total sample.

[5] All mixed-model ANOVAs were repeated controlling for depression, generalized anxiety, panic, agoraphobia, social anxiety and somatization symptoms, which were assessed using the Psychiatric Diagnostic Screening Questionnaire (PDSQ; Zimmerman & Mattia, 2001), and the results remained the same.

However, the interaction effect indicated that the effect of imagery condition on valence depends on the type of attention manipulation, $F(2.59,253.91)=21.43$, $p<.001$, $\eta_p^2=.18$ ($\varepsilon=.86$). Planned contrasts showed a significant difference in the interaction effect between the illness and neutral imagery, $F(1,98)=81.43$, $p<.001$, $\eta_p^2=.45$: while for illness imagery valence was slightly more negative, for neutral imagery valence was more positive after IF compared to EF. The contrasts between illness and fearful or joyful imagery in relation to attention manipulation were not significant, i.e. similar levels of valence after IF and EF in these conditions. Mixed-model ANOVA showed no interaction of group by imagery condition, $F(4.11,174.52)=0.18$, $p>.05$ ($\varepsilon=.68$); attention manipulation, $F(2,85)=1.97$, $p>.05$; and their interaction, $F(5.07,215.42)=0.19$, $p>.05$ ($\varepsilon=.85$).

Self-reported somatic sensations

In addition, imagery condition had a main effect on somatic sensation reports, $F(1.50,150.28)=78.88$, $p<.001$, $\eta_p^2=.44$ ($\varepsilon=.50$). Planned contrasts showed higher reports in the illness compared to the fearful, $F(1,100)=24.12$, $p<.001$, $\eta_p^2=.19$, joyful, $F(1,100)=88.57$, $p<.001$, $\eta_p^2=.47$) and neutral conditions, $F(1,100)=102.51$, $p<.001$, $\eta_p^2=.51$. Attention manipulation effect was also significant, $F(3,100)=20.17$, $p<.001$, $\eta_p^2=.17$, however, the interaction effect of imagery condition by attention manipulation was non-significant, $F(2.57,257.13)=2.21$, $p>.05$ ($\varepsilon=.86$), which indicates slightly more somatic sensation reports after IF in all imagery conditions (see Figure 5). Mixed-model ANOVA showed no interaction of group by imagery condition, $F(3.08,134.26)=0.48$, $p>.05$ ($\varepsilon=.51$); attention manipulation, $F(2,87)=0.73$, $p>.05$; and their interaction, $F(5.14,223.70)=0.92$, $p>.05$.

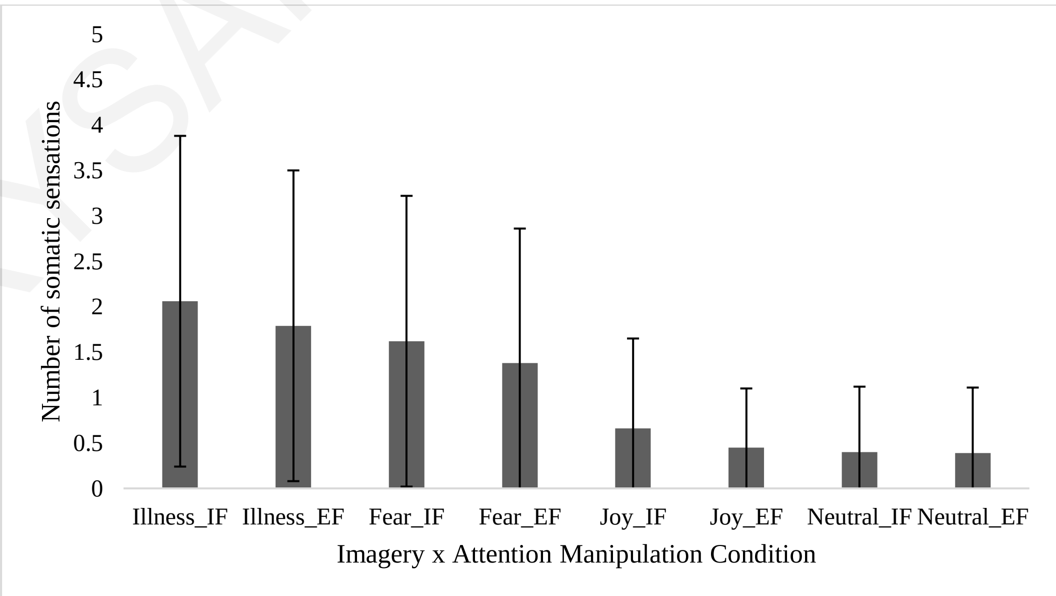

Figure 5. Self-reported somatic sensations and symptoms (number) during imagery for the total sample.

Heart-rate reactivity

Repeated-measures ANOVA using the HR change scores as the dependent variable, showed no main effects of imagerυ, $F(2.68,257.47)=1.49$, $p>.05$ ($\varepsilon=.89$) and attention manipulation, $F(1,96)=0.38$, $p>.05$. However, the interaction effect on HR during imagery was significant, $F(3,94)=8.63$, $p<.001$, $\eta_p^2=.22$. This means that the effect of imagery condition on HR is influenced by the effect of attention manipulation that preceded each imagery condition. Planned contrasts showed a significant difference in the interaction effect between illness and fearful, $F(1,96)=16.92$, $p<.001$, $\eta_p^2=.15$, and joyful, $F(1,96)=13.77$, $p<.001$, $\eta_p^2=.13$; but not neutral conditions, $F(1,96)=1.34$, $p>.05$. While the effect of IF in illness and neutral conditions is more HR deceleration from baseline (lower HR), in the fearful and joyful conditions the effect of IF is less HR deceleration (higher HR), compared to the effect of EF (see Figure 6). RMSSD ($M=45.67$, $SD=22.73$) was entered as a covariate in the model, to test whether parasympathetic activity explains the effect of the interaction between imagery and attention manipulation on HR. After the influence of the covariate has been removed, the interaction effect on HR was no longer significant $F(3,92)=2.10$, $p>.05$. Mixed-model ANOVA showed non-significant interaction of group by imagery condition, $F(5.32,220.96)=1.11$, $p>.05$ ($\varepsilon=.89$); attention manipulation, $F(2,83)=0.22$, $p>.05$; and their interaction, $F(6,164)=0.35$, $p>.05$.

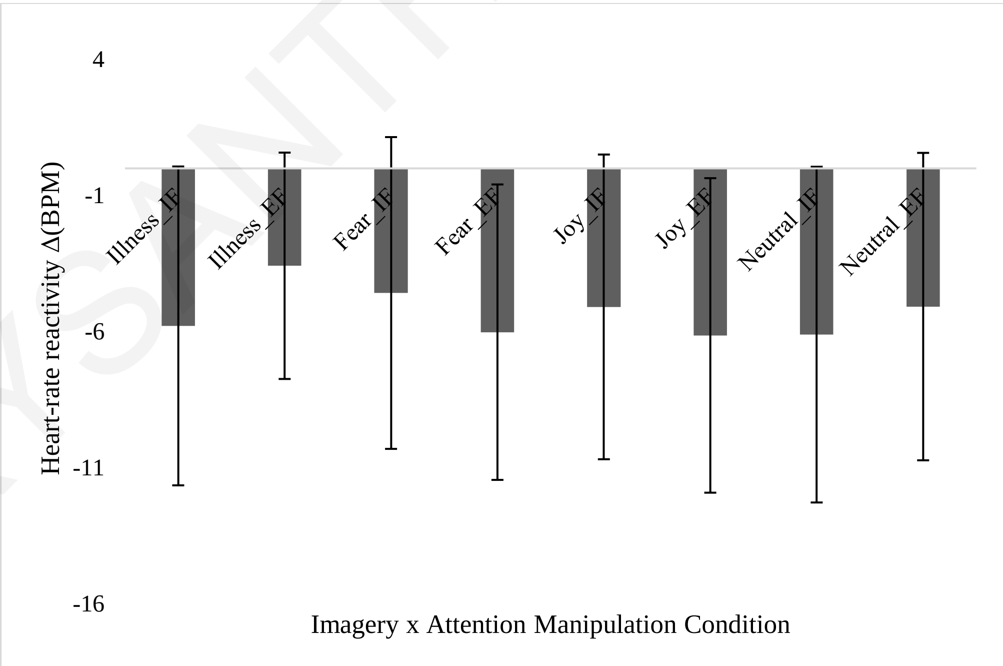

Figure 6. Heart-rate reactivity Δ(BPM) during imagery for the total sample.

Skin conductance level

The main effect of imagery condition on SCL was significant, $F(2.63,226.02)=3.75$, $p=.015$, $\eta_p^2=.04$ ($\varepsilon=.94$). Planned contrasts showed higher SCL during the illness imagery, compared to neutral; $F(1,86)=8.87$, $p<.01$, $\eta_p^2=.08$; but not compared to the fearful, $F(1,86)=3.47$, $p>.05$, and joyful imagery, $F(1,86)=3.89$, $p>.025$, which was expected due to the nature of these conditions that elicit high emotional arousal. There was also a significant main effect of attention manipulation, $F(1,86)=10.45$, $p<.01$, $\eta_p^2=.11$; as the interaction effect was not significant, $F(3,84)=1.37$, $p>.05$, the effect of attention manipulation on SCL was similar across all imagery conditions, i.e. decreased SCL after IF (see Figure 7). In a follow-up analysis, when the effect of RMSSD as a covariate was removed, the effect of imagery condition on SCL was no longer significant, $F(2.63,221.04)=0.17$, $p>.05$ ($\varepsilon=.88$); the effect of attention manipulation remained significant, $F(1,84)=5.01$, $p=.023$, $\eta_p^2=.06$. Mixed-model ANOVA showed non-significant interaction of group by imagery condition, $F(5.07,192.62)= 1.82$, $p>.05$, ($\varepsilon=.85$); attention manipulation, $F(2,80)=0.28$, $p>.05$; and their interaction, $F(6,158)=0.66$, $p>.05$.

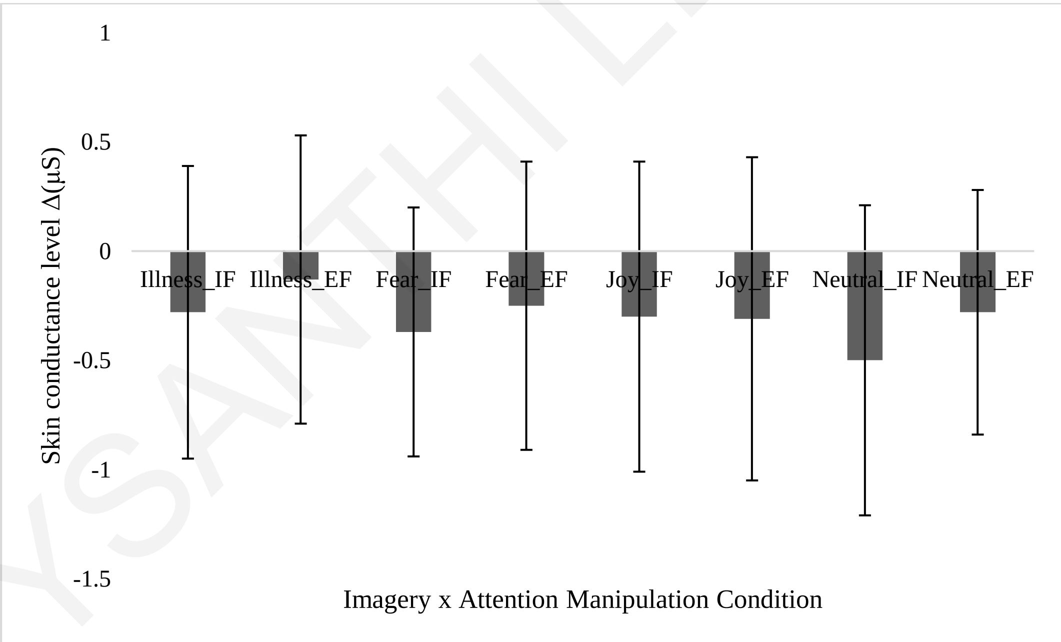

Figure 7. Skin conductance level Δ(μS) during imagery for the total sample.

Facial electromyography

In examining the effects of experimental manipulation on corrugator activity, there was a main effect of imagery condition, $F(2.52, 234.63)=27.27$, $p<.001$, $\eta_p^2=.23$ ($\varepsilon=.84$). As expected, illness imagery triggered significantly greater corrugator activity compared to joyful, $F(1,93)=45.17$, $p<.001$, $\eta_p^2=.33$; but not compared to neutral, $F(1,93)=4.99$, $p>.025$; and fearful imagery during which corrugator activity was similar, $F(1,93)=0.17$, $p>.05$. Although the main effect of attention manipulation was not significant, $F(1,93)=0.21$, $p>.05$, the interaction between imagery condition and attention manipulation was, $F(2.77,257.91)=3.41$, $p=.023$, $\eta_p^2=.04$ ($\varepsilon=.92$). Planned contrasts showed that the interaction effect was significantly different between illness and neutral, $F(1,93)=8.99$, $p<.01$, $\eta_p^2=.09$; but not fearful, $F(1,93)=3.50$, $p>.05$, and joyful imagery, $F(1,93)=1.88$, $p>.05$. IF triggers higher corrugator activity during illness imagery, but lower corrugator activity during neutral imagery, compared to EF (see Figure 8). Interaction effect of group on corrugator activity was non-significant with imagery condition, $F(5.08,203.27)=0.85$, $p>.05$ ($\varepsilon=.85$); attention manipulation, $F(2,80)=0.63$, $p>.05$; and their interaction, $F(5.38,215.22)=0.49$, $p>.05$ ($\varepsilon=.90$).

A main effect of imagery condition on zygomatic activity was also indicated, $F(1.66,144.96)=26.27$, $p<.001$, $\eta_p^2=.23$ ($\varepsilon=.56$), and as expected, planned contrasts showed a significant difference between illness and joyful imagery, $F(1,87)=33.25$, $p<.001$, $\eta_p^2=.28$, but not fearful, $F(1,87)=3.89$, $p=.052$, and neutral imagery, $F(1,87)=0.07$, $p>.05$. There was also a main effect of attention manipulation, $F(1,87)=4.85$, $p=.030$, $\eta_p^2=.05$, and the interaction effect was not significant, $F(2.63,228,37)=1.49$, $p<05$ ($\varepsilon=.88$), which indicates slightly less zygomatic activity after IF in all imagery conditions (see Figure 9). Interaction effect of group on zygomatic activity was non-significant with imagery condition, $F(3.28,122.80)=0.12$, $p>.05$ ($\varepsilon=.55$); attention manipulation, $F(2,75)=0.14$, $p>.05$; and their interaction, $F(4.72,177.12)=1.21$, $p>.05$ ($\varepsilon=.79$).[6]

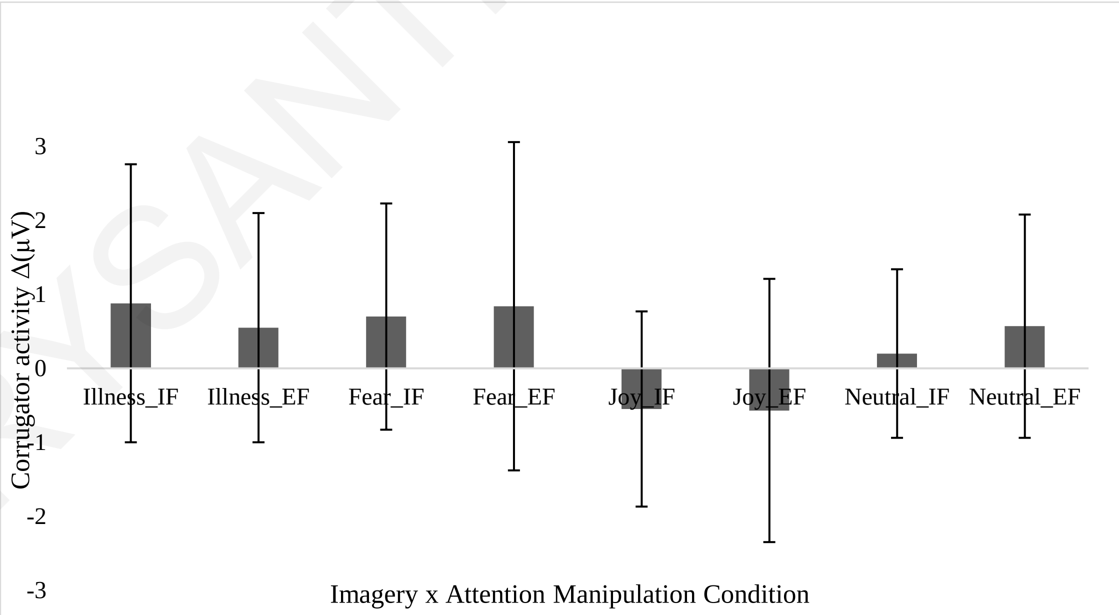

Figure 8. Corrugator activity Δ(μV) during imagery for the total sample.

[6] Due to positively skewed distributions, the analyses for the effects on facial EMG were repeated using square-root transformed variables, and based on the Greenhouse-Geisser correction for sphericity the results were similar.

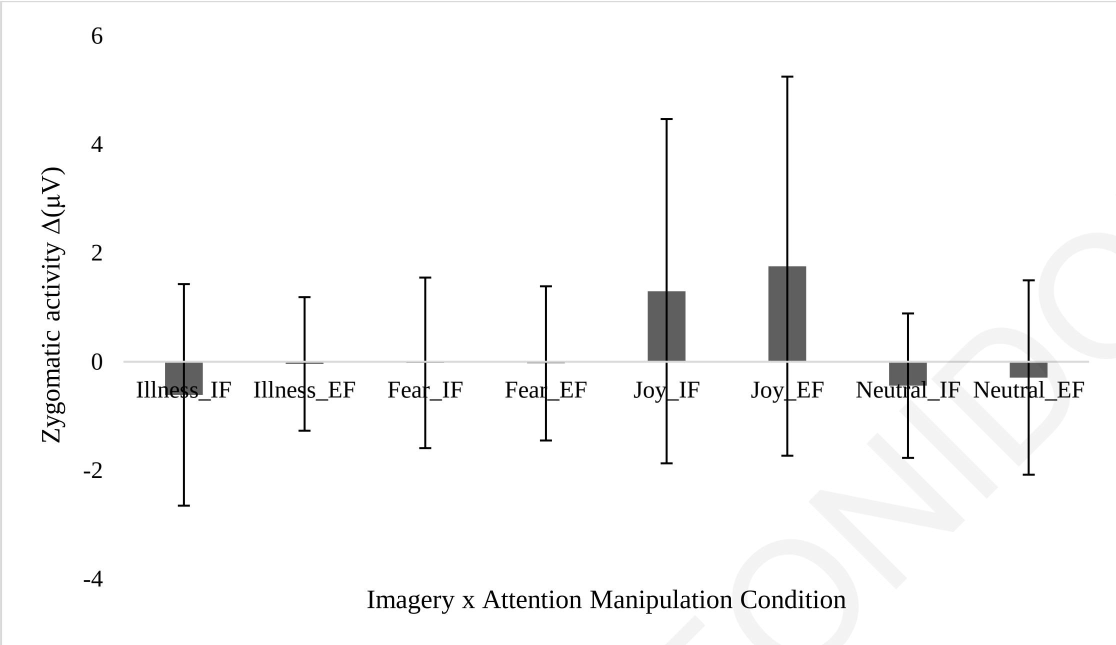

Figure 9. Zygomatic activity *Δ*(µV) during imagery for the total sample.

Discussion

The current study investigated the effect of focusing attention on somatic sensations vs. focusing attention on environmental stimuli on subjective and psychophysiological emotional responses during illness imagery and how these effects are modulated by IA levels. The overall results are consistent with the expectation that illness imagery, irrespective of attention manipulation, triggers emotional reactions evident in both self-reports and physiological reactivity. The results are in line with the study of Brownlee and colleagues (1992), who reported increased emotional arousal, negative affect and physiological reactivity (HR, SCL, respiratory rate) during illness compared to neutral imagery. In our study, the distressing and unpleasant nature of illness imagery was further supported by higher negative valence and somatic sensation reports, compared not only to neutral but also to generally fearful and joyful imagery. In addition, illness imagery was rated as more intense, and was linked to greater corrugator and less zygomatic activity, compared to joyful imagery (a highly arousing condition with a positive valence), although similarly intense compared to generally fearful imagery. SCL was similarly increased during illness, fearful and joyful imagery, as compared to neutral scenarios, suggesting that all three elicit high levels of bodily arousal.

The major novel contribution of this study are findings regarding the effect of attentional focus on somatic sensations on subjective and physiological emotional reactions to illness imagery. Interaction effects showed that some of the emotional reactions of participants depended on the type of the attention manipulation, supporting our initial hypothesis. Findings showed that in intense emotional conditions, both aversive and positive (illness, fearful and joyful imagery), prior focus on somatic sensations of arousal led to higher self-reported emotional arousal and negative valence, as compared to exteroceptive focus of attention. In contrast, in neutral imagery, when a less extreme subjective and physiological response was expected, IF was associated with decreased arousal and increased positive emotions. These results were further supported by the facial electromyography indices, i.e. corrugator activity, indicative of negative emotion, was higher during the high arousal imagery conditions, while zygomatic activity was lower in all conditions after IF. This may be thought of in the context of body scan exercises during mindfulness training usually conducted in neutral or calming environments (Weck, Neng, & Stangier, 2013). During such training participants often report low stress and positive emotions, i.e. a pleasant relaxation, however, we do not have much evidence about how people perceive emotional responses when using the same exercises in intense emotional contexts. Our findings provide preliminary evidence about higher perceived emotional arousal and negative affect in emotionally intense conditions after increasing interoceptive attentional focus.

In contrast to the high subjective arousal after IF in intense emotional conditions and contrary to our initial hypothesis, however, HR was lower (more deceleration from baseline) after IF compared to EF, during illness but also neutral scenarios; whereas in joyful and fearful scenarios HR was higher (less deceleration from baseline). HR deceleration from baseline may reflect parasympathetic activity that was more profound after focusing attention on somatic sensations during personally-relevant illness imagery and neutral imagery, which may have been perceived as an ambivalent condition by individuals. Part of the variance of HR and SCL, which was also lower after IF, was indeed explained by the RMSSD index of heart-rate variability that mostly represents parasympathetic activity of the autonomic nervous system, and potentially indicates emotion regulation related reactivity (Appelhans & Luecken, 2006). Increased parasympathetic activity was previously linked to inward attention meditation (Wu & Lo, 2008), a technique similar to the IF in this study. Another plausible explanation about the decreased HR responsiveness to illness and neutral imagery after IF may be the decreased salience of the expected emotional response in these scripts, compared to scripts for joyful and fearful imagery (Lang, 1979). In all, this may mean that attentional focus on somatic sensations of arousal triggers a hypo-arousal pattern of emotional response in conditions that may be perceived as ambivalent and potentially more generally distressing, and this may be explained by efforts to regulate emotion, i.e. more parasympathetic control influence on HR during illness and neutral compared to fearful and joyful imagery and on SCL during all imagery conditions after IF.

Moreover, the discordance between subjective and physiological (HR) indices of arousal, especially observed during illness imagery should be noted here. Although after focusing on somatic sensations participants show less HR, they perceive more subjective arousal induced by illness imagery. These findings may reflect tendencies for a ruminative or worrisome approach to the emotions and somatic sensations elicited during illness imagery, i.e. more reminiscent of the emotional responses of people with non-focal, broad negative affect and generalized anxiety rather than focal, specific fears (Cuthbert et al., 2003; Lang & McTeague, 2009; Panayiotou et al., 2017). The hypo-arousal physiological response (HR deceleration) may be therefore explained by the temporary stress reducing effect of rumination and worrying, which are, although, characterized by high reports of distress (Borkovec & Hu, 1990; Delgado et al., 2009; Fisher & Newman, 2013; Kirschner, Hilbert, Hoyer, Lueken, & Beesdo-Baum, 2016), i.e. high emotional arousal, negative affect, more somatic sensations, and negative facial expressive behavior. This discordance in emotional experience needs to be further investigated in relation to specific emotion regulation strategies to understand its function and maintenance role in IA.

Findings regarding the IA group effects did not support our hypothesis that they would modulate affective responses to illness imagery. Although the high IA group, compared to the moderate and low IA group, presented higher self-reported emotional arousal, somatic sensations and negative valence, as well as increased corrugator and lower zygomatic activity but a trend for lower HR and SCL after the IF during illness imagery, these effects did not reach statistical significance. Resting-state heart-rate variability was also in similar levels across groups indicating no differences in autonomic regulation. The absence of effects of IA levels may be attributed to two main reasons: First, although the high IA group presented relatively high levels of IA, the sample is non-clinical and therefore illness imagery may not be significantly more distressing among this sample of high IA individuals compared to the moderate and low IA groups. In addition, the IF was perceived as equally difficult and may have elicited high distress in all groups, and therefore, more somatic sensation reports irrespective of IA levels as it was found in previous studies (Mirams et al., 2012). Second, the utilization of personally-relevant illness imagery makes this condition equally distressing for all individuals. It is generally plausible that intrusive illness-related images and the evoked emotional reactions are not merely a characteristic of severe IA (Langlois, Ladouceur, Patrick, & Freeston, 2004), since people who report low or moderate IA levels also worry about their health and perceive illness-related information as threatening, compared to information that is emotionally neutral (Shields & Murphy, 2011). Although the current study provides important findings about the influence of attentional focus on somatic sensations on the emotional reactions to illness imagery among young, healthy in their majority, individuals with a range of IA levels, future studies should replicate these results in clinical samples with more severe and dysfunctional IA levels.

An additional limitation of this study may have been the focus of the IF task on heart-rate, as heart-related sensations may not be relevant or fearful to all individuals, especially in such a young age. The heartbeat tracking task provided the advantages of a previously-tested paradigm and it was easy to control in an experimental setting; its validity as a manipulation is verified by the fact that it had effects on emotional reactions during imagery. Future studies should aim to a body scan task with broader focus so that more categories of somatic sensations will be targeted. However, this study has noteworthy strengths. First, the inclusion of both subjective and objective measures of emotion made possible a thorough investigation of emotional responses to illness imagery, and has been proved essential to observe the discordance between different aspects of emotional response during illness imagery. Second, the inclusion of personally-relevant illness scenarios tailored to participants' worst illness-related fears precluded absence of effects due to irrelevance of stimuli. Personally-relevant stimuli in experimental designs examining dimensions of IA are suggested due to the variability in this population regarding the fear of specific symptoms and diseases, which may change from time to time (Newby et al., 2017). Third, inclusion of other imagery types in addition to neutral imagery provided the opportunity to test the specificity of emotional response to illness imagery compared to other intense emotional conditions.

More importantly, this study design can be thought as an experimental analog in assessing emotional reactions to intrusive illness imagery under the influence of heightened attention to somatic sensations, therefore, findings may inform the conceptualization of illness-related information processing in a range of IA levels. After focusing their attention to somatic sensations during illness imagery, individuals, irrespective of IA levels in this study, presented increased reports of emotional arousal, negative affect and somatic sensations, accompanied by negative emotion expression, but a hypo-arousal physiological response pattern. Assuming a ruminative and worrisome attitude to the experienced emotions, which reduces distress temporarily but prevents adaptive processing of the emotional experience, it is a tentative hypothesis that the persistence of such emotional responses due to frequent intrusion of illness-related images and heightened attention to somatic sensations increases and perpetuates IA over time. This emotional response pattern may also explain the reassurance and healthcare seeking behavioral responses, which further contribute to the development and maintenance of the symptomatology and which also potentially represent avoidance of experienced emotions and sensations.

Findings have implications in prevention and therapeutic interventions. Focusing on somatic sensations may increase processing of motor and visceral response aspects of the associative network, which was also supported by participants' emotional reactions in this study, and is suggested to produce greater effects on reduction of phobic behavior (Lang, 1979).

Therefore, interoceptive attentional focus techniques, e.g. a simple heartbeat tracking task, could be incorporated in therapeutic interventions for IA. Mindful body scan exercises and interoceptive exposure techniques are already being used as part of therapy for IA and in most cases have been effective in introducing a changed and more adaptive way to confront somatic sensations and intrusive images (McManus, Muse, Surawy, Hackmann, & Williams, 2015; Walker & Furer, 2008; Weck et al., 2013; Williams, McManus, Muse, & Williams, 2011). This study supports the utilization of such techniques in the controlled therapy setting as they seem to trigger processing of all aspects of emotional experience when dealing with perceived illness-threats. It is important to note, however, that emphasis should be placed on changing individuals' attitude towards somatic sensations and illness imagery to a more mindful, non-judgmental one, as self-focus may be either adaptive or maladaptive depending on the presence of ruminative and catastrophizing characteristics (Mor & Winquist, 2002; Surawy, McManus, Muse, & Williams, 2015). Such techniques may also be useful for young healthy populations, as this study's sample, with the purpose to prevent development of symptomatology in groups of individuals with high risk of IA. Similar experimental paradigms examining the effects of attentional focus on somatic sensations over time in a longitudinal design may inform the field about the effectiveness of such techniques in processing illness-threats in a more adaptive way. This study's findings extend prior knowledge about emotional reactions to illness imagery by presenting evidence for aspects of emotional experience that are influenced by heightened focus of attention on somatic sensations of arousal, an important component of the cognitive-behavioral model of IA.

CHAPTER 4 │ Attentional processing of illness-related stimuli: Biases and autonomic correlates observed irrespective of illness anxiety levels

Abstract

Attentional bias during processing of illness-related stimuli was suggested to contribute to the development and maintenance of illness anxiety. **Objective.** This study investigated the presence and time-course of components of attentional bias and their association to emotional reactivity during processing of illness-related pictorial stimuli. **Method.** 100 participants (77 female; 18-35 years old) with low, moderate and high levels of illness anxiety underwent a free viewing task with illness, generally fearful and neutral picture pairs and a cued viewing task with illness and neutral picture pairs, during both of which eye-tracking and psychophysiological measures of arousal were recorded. **Results.** Irrespective of illness anxiety levels, participants showed an orienting bias towards illness and fearful compared to neutral stimuli, and sustained vigilance to illness compared to neutral stimuli during the free viewing task. Whereas, they showed an avoidant attentional processing pattern of illness compared to neutral stimuli in the cued viewing task. More avoidance tendencies in both tasks were associated with higher subjective ratings and physiological measures (skin conductance response) of emotional arousal. **Conclusion.** Attentional bias to illness stimuli is observed irrespective of illness anxiety levels, and its specific components may be influenced by the task nature and its potential influence on perceived control over attention allocation. Associations between attentional bias components and emotional reactivity provide preliminary evidence about attention allocation as a mechanism in regulating emotion.

Keywords: *Attentional bias; Illness anxiety; Emotional reactivity; Vigilance; Avoidance; Voluntary control.*

Background

Attentional bias is the preferential allocation of attention to threatening stimuli relative to neutral stimuli (Bar-Haim, Lamy, Pergamin, Bakermans-Kranenburg, & Van Ijzendoorn, 2007; MacLeod, Mathews, & Tata, 1986; Mogg & Bradley, 1998). It is a common characteristic of individuals suffering from anxiety symptomatology (Cisler & Koster, 2010), but appears to also characterize illness anxiety (IA), the preoccupation with having or acquiring a serious medical illness, which is persistent despite appropriate medical reassurance (Rachman, 2012). Conceptualization models of IA, suggest that illness-anxious individuals are particularly sensitive and attentionally biased towards interoceptive or exteroceptive illness-related cues (Kellner, 1986; Marcus et al., 2007; Warwick & Salkovskis, 1990). Allocation of attention is typically proposed to be a mechanism of emotion regulation (Gross, 1998, 2001), so that during exposure to a perceived threat, individuals strategically focus their attention to regulate the elicited emotions. In IA, however, attention allocation seems to work in a way that contributes to the maintenance of symptomatology. This study attempts to examine the presence of specific components of attentional bias and their time-course during processing of illness-related stimuli, which are believed to be particularly threatening for individuals with high compared to lower levels of IA (Abramowitz, Olatunji, & Deacon, 2007). It is also the first study that examines the strategic attention allocation in relation to emotional reactivity elicited during stimulus exposure in IA, based on the hypothesis that attention allocation is a mechanism of emotion regulation.

During the last two decades, several studies have investigated attentional bias in IA focusing both on automatic, stimulus-driven, and on strategic attentional processes (Beck & Clark, 1997; Cisler & Koster, 2010). Studies using the Emotional Stroop task provided evidence for an attentional bias towards illness words, compared to neutral, generally negative and positive words, among individuals with high compared to low IA (Gropalis et al., 2012; Karademas et al., 2008; Owens et al., 2004; Van Den Heuvel et al., 2005; Witthoft et al., 2016; Witthöft et al., 2013, 2008). The dot-probe paradigm was also applied to examine specific components of attentional bias over time, including facilitated attention, i.e. ease of detection of threat relative to non-threat stimuli; attentional maintenance, i.e. difficulty in disengaging attention from threat relative to nonthreat stimuli; and attentional avoidance, i.e. shifting of attention away from threat relative to non-threat stimuli (Cisler & Koster, 2010). Based on dot-probe studies, IA has been linked to attentional bias to illness words at 1250ms exposure duration (Kim et al., 2014), and to an orienting bias at 175ms but a difficulty in disengaging attention from illness pictures at 500ms (Jasper & Witthoft, 2011). These findings were further supported by an eye-tracking study that indicated an early orientation of attention towards pictorial illness stimuli and either a later difficulty in disengaging attention or a tendency to shift attention away from these stimuli during the 6000ms exposure duration (Kim & Lee, 2014). However, other dot-probe studies and one study using the visual search task contradicted these findings and showed no differences between high and low IA in any attentional bias component to illness stimuli (Jacoby, Wheaton, & Abramowitz, 2016; Lee et al., 2013; Lees, Mogg, & Bradley, 2005; Shields & Murphy, 2011). In addition to the contradictory results attributed to methodological differences, the different stimulus exposure durations in the experimental paradigms perplex conclusions about the specific components of attentional bias linked to IA and their time-course. This is especially true when it comes to distinguishing between attentional mechanisms involved in maintaining IA, which take place during early vs. later, or automatic vs. strategic, attentional processing stages.

In addition to the attempt to establish the specific attentional biases characterizing IA over time, prior research also identified individual characteristics that appear to modulate them. The attentional maintenance bias was found to be more evident among individuals who tend to seek healthcare often (Lee et al., 2013); and among individuals with high IA, who were characterized with a vigilant information processing style, i.e. they are alert for and sensitive to threat-relevant information (Kim et al., 2014; Kim & Lee, 2014). Attentional avoidance, on the other hand, was more evident among individuals who avoid healthcare (Lee et al., 2013), and individuals who use an avoidant information processing style, i.e. they avoid threat-relevant information (Kim et al., 2014; Kim & Lee, 2014). This distinction between the attentional processing patterns suggests the presence of individual differences leading to two different patterns: vigilance vs. vigilance-avoidance, which may serve a different function during threat processing. Understanding this heterogeneity and the specific function of each processing pattern in regulating emotion is ultimately important in designing tailored and personalized treatment goals and treatments for people suffering from IA.

In the context of strategically using attention allocation to regulate emotion (Gross, 1998, 2001), vigilance serves the protective function to scan information for signs of threat and prevent threat if possible. The vigilance-avoidance pattern (see the vigilance-avoidance hypothesis; Derakshan, Eysenck, & Myers, 2007) on the other hand, serves a dual function. Individuals are initially vigilant for threat, however, during later processing stages, there is a more instrumental use of strategies in order to avoid the intensity and the duration of physiological arousal triggered by threat. Studies that examined the vigilance-avoidance hypothesis in the context of anxiety disorders (e.g. General Anxiety Disorder, Panic Disorder) and health complaints (Olatunji et al., 2007; Weinberg & Hajcak, 2011; Zvolensky & Forsyth, 2002) provided evidence in support of this account, which documents the presence of early hyper-vigilance to emotional stimuli but a failure to maintain attention and elaboratively process the emotion and physiological reactivity elicited by the stimuli at later stages of processing. The avoidant component of this pattern then serves to prevent exposure to and elaborative processing of the feared stimuli in a way that would have promoted habituation and modification of fear representations (Foa & Kozak, 1986; Warwick & Salkovskis, 1990).

Although the vigilance-avoidance hypothesis has been provided as a potential explanation for attentional biases in IA (Jasper & Witthoft, 2011; Kim et al., 2014; Kim & Lee, 2014), there are no studies to date examining the association between later-stage attentional biases in IA and emotional reactivity triggered by illness stimuli, which the attentional avoidance is purported to prevent. To our knowledge, this is the first study testing the vigilance vs. vigilance-avoidance hypothesis by examining emotional reactivity, measured by both psychophysiological indices and self-reports, in response to attentional allocation to illness stimuli.

Current Study

In this study we attempted to extend prior findings on attentional biases during processing of illness pictorial stimuli in high IA, compared to moderate and low IA. To address the question about the time-course of specific components of attentional bias, participants' eye movements were tracked continuously during exposure to two stimuli that competed for attentional resources at the same time; an advantage over expecting to observe specific attentional processes during fixed time intervals as in the dot-probe paradigm. Eye-tracking is considered as an appropriate measure to address the above research question (Armstrong & Olatunji, 2012; Bradley, Mogg, & Millar, 2000; Nummenmaa et al., 2006), and was used in the context of two experimental tasks: First, during a free viewing task (FVT), participants could freely view picture pairs formed with illness, generally fearful and neutral content. Second, during a cued viewing task (CVT), participants had to focus on one picture during the presentation of pairs made up of illness and neutral pictures, as indicated by a cue. In addition to initial orientation of attention and the duration of first fixation, indices of vigilance were retained from the early time intervals of 0-0.5s and 0.5-1.0s; indices for attentional maintenance and avoidance were retained from a later time interval of 1.0-6.5s after stimulus onset. This method allowed for the investigation of specific attentional bias components during specific time intervals, i.e. vigilance is expected early in the exposure duration, maintenance/avoidance are expected to be observed in later time intervals (Wieser, Pauli, Weyers, Alpers, & Mühlberger, 2009). This was an advantage over calculating attentional bias indices based on the whole exposure duration (Kim & Lee, 2014), which does not help to observe differences in attentional processes between early and later time intervals.

To examine the associations between the different attentional patterns and emotional reactivity, physiological measures of emotional arousal were recorded continuously during the two experimental tasks and associations with the indices of attentional bias were examined. The question addressed was whether emotional reactivity, subjective and physiological, is related to specific patterns of processing illness-threats when individuals can freely allocate their attention and when they are cued about where to focus their attention. Using both the FVT and the CVT helped to address the question whether biased attention allocation can be circumvented by voluntary control, as required by the CVT, to counteract the automaticity of attentional bias to illness stimuli in early and later stages of attentional processing (Nummenmaa et al., 2006). Generally fearful stimuli as compared to illness and neutral stimuli were included in the FVT to examine the specificity of attentional bias to illness, disorder-relevant stimuli in producing attentional biases in IA.

Considering existing findings from dot-probe and eye-tracking studies, which supported attentional bias in IA (Jasper & Witthoft, 2011; Kim et al., 2014; Kim & Lee, 2014), during the FVT, we expected greater probability of initial orientation of attention to illness stimuli compared to neutral stimuli of the same pair and compared to generally fearful stimuli of the same pair; and to illness stimuli that were paired with neutral stimuli compared to fearful stimuli paired with neutral stimuli, in high IA compared to moderate and low IA groups. Additionally, vigilance to illness stimuli (more dwell time and difficulty in disengaging attention) compared to neutral and fearful stimuli (in FVT) during the early stage of attentional processing (0-0.5s and 0.5-1.0s intervals) in both tasks was hypothesized to be more profound in high IA. Later-onset attentional processes, i.e. attentional maintenance to or avoidance of illness stimuli, were expected to function as strategies performed to regulate emotion, including physiological reactivity in both tasks, and subjective arousal and unpleasantness in the CVT. This was assessed by examining potential differences in dwell time on each picture type between the time intervals and by testing the associations between attentional bias indices and emotional reactivity.

Method

Sample

Participants were 100 university students (77 female; 18-35 years old) receiving course credit for their participation. Exclusion criteria included age below 18 or above 35 and presence of vision or hearing disability that would prevent them from participating in the experiment; participants who reported corrected-to-normal vision were included. Participants were screened through an online questionnaire. Those who consented to be contacted were invited to the laboratory. All interested participants were invited for the experiment irrespective of IA levels until data were collected for about half of the sample size; after this point, participants were invited more selectively based on extreme low or high scores on IA, to increase the range of IA scores in the sample. Participants were assigned into groups of low, moderate and high IA based on the suggested clinical cut-off score of the Illness Attitudes Scales (>47) (Hedman et al., 2015) and upper and lower tertiles on the Short Health Anxiety Inventory.[7] This resulted in 30 participants per group, after ten participants were removed due to the discordance in their IA scores between the two screening measures. Between groups difference on IA levels was significant: the high IA group reported higher levels of IA compared to the moderate and low IA

[7] The low IA group had scores below the clinical cut-off in IAS and scored in the lower tertile in SHAI (<8), the high IA group scored above the clinical cut-off in IAS and in the upper tertile in the SHAI (>18), and the moderate IA group scored either below or above but close to the clinical cut-off in IAS and in the middle tertile in SHAI.

groups and the low IA group reported lower levels of IA compared to the moderate IA group. Groups did not differ in age, gender and self-reported medical condition frequency, and baseline levels of physiological reactivity (see Table 5).

Table 5. *Characteristics of the groups based on illness anxiety levels*

	Low IA (*n*=30)	Moderate IA (*n*=30)	High IA (*n*=30)			
	N	*N*	*N*	χ^2	*df*	*p*
Gender						
Male	11	4	6	4.85	2	>.050
Female	19	26	24			
Medical Condition						
No	28	25	27	1.58	2	>.050
Yes	2	5	3			
	M (SD)	*M (SD)*	*M (SD)*	*F*	*df*	*p*
Age	21.87 (3.71)	21.77 (3.59)	21.78 (3.36)	0.01	2,87	>.050
Baseline HR *Δ*(bpm)	82.19 (12.42)	81.76 (11.74)	80.64 (11.58)	0.13	2,86	>.050
Baseline SCR *Δ*(μS)	13.91 (5.89)	13.27 (6.44)	15.34 (9.25)	0.51	2,72	>.050
IAS total	28.10 (8.91)[ab]	38.80 (6.26)[ac]	59.07 (9.64)[bc]	105.23	2,87	<.001
SHAI total	6.30 (2.45)[ab]	13.30 (2.77)[ac]	19.33 (5.75)[bc]	81.93	2,87	<.001
Self-reported focus of attention during the free viewing task						
Attention on illness pictures	5.20 (2.51)	5.90 (2.12)	6.30 (2.31)	1.73	2,89	>.050
Attention on violence pictures	8.83 (17.24)	6.30 (2.07)	6.17 (2.20)	0.66	2,89	>.050
Attention on neutral pictures	3.93 (2.89)	4.50 (2.10)	4.13 (2.01)	0.54	2,89	>.050
Same attention to all pictures	4.77 (2.58)	4.33 (1.99)	4.00 (1.00)	0.91	2,89	>.050
Self-reported focus of attention during the cued viewing task						
Attention on the cued picture	7.90 (1.58)	7.87 (0.68)	7.48 (1.66)	0.83	2,88	>.050
Attention on illness distractor	2.03 (1.27) [a]	3.23 (2.11)	3.76 (2.26) [a]	6.24	2,88	<.001
Attention on neutral distractor	2.23 (1.81)	2.67 (1.75)	2.24 (1.46)	0.65	2,88	>.050

Note. [abc] were significant at the *p*<.001 level.

Experimental Design

Free viewing task

The experimental design involved two separate tasks. The FVT (Figure 10) was based on a 3x6 design with group (low, moderate and high IA) as the between-subjects variable and picture type per pair (illness-neutral (I-N), illness-fearful (I-F), fearful-neutral (F-N)) as the within-subjects variable. It included 48 trials with an equal number and equally distributed presentations of the three picture pair types in 8 blocks with 6 trials each, presenting pairs of two pictures: two blocks with I-N picture pairs, two blocks with I-F pairs, two blocks with F-N pairs and two blocks included all types of pairs. Trials were randomized within block and blocks were presented in two counterbalanced orders. Each trial started with a drift correction, followed by a small fixation cross, which remained in the middle of the screen (512, 384) for 1.5s, followed by the picture pair, which remained on the screen for 6.5s. A blank screen was presented for 1.0/1.5/2.0s randomly after the end of each trial to alleviate the participants' fatigue (Armstrong & Olatunji, 2012). Participants were instructed to look at the pictures as they would look at a photograph album (Liossi, Schoth, Godwin, & Liversedge, 2014) and they were told that pupil dilation was measured during picture viewing (Buckner, Maner, & Schmidt, 2010). No further instructions were provided to prevent influencing automatized attentional processes, which was the main mechanism under investigation in this task.

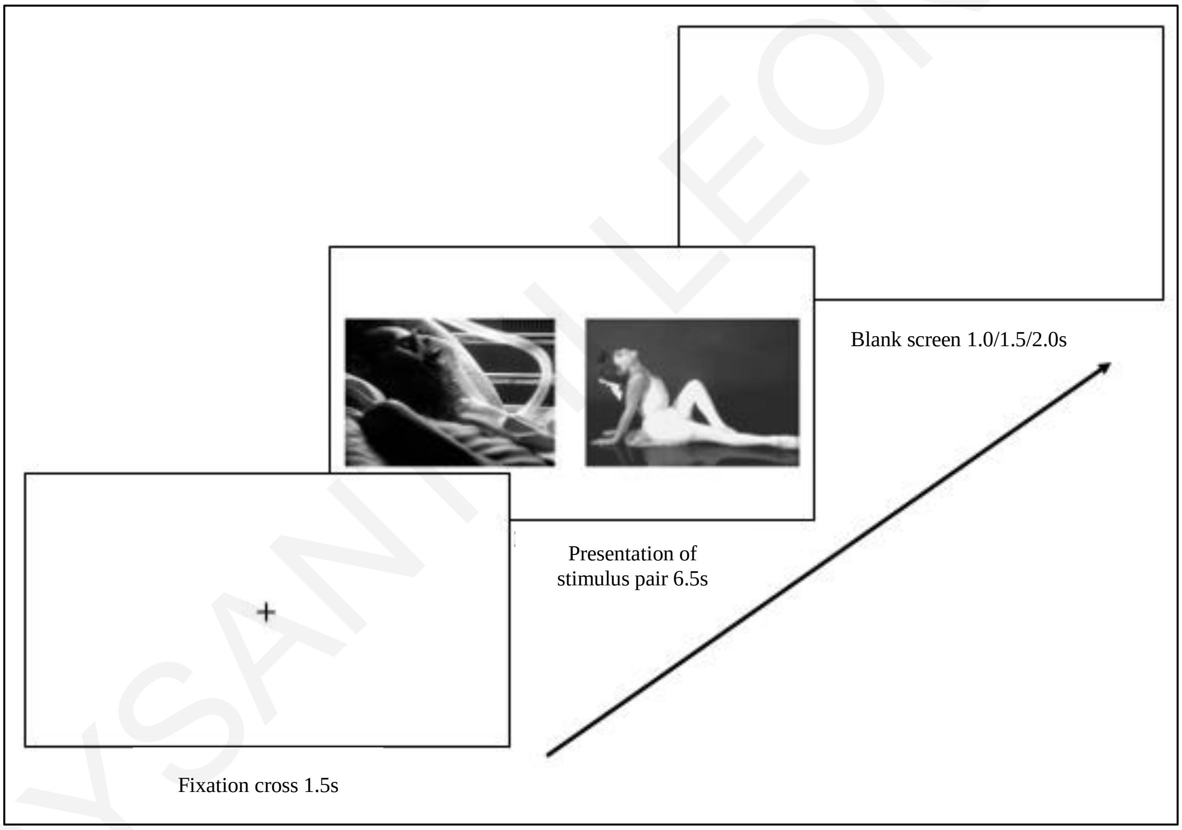

Figure 10. Example of a trial in the Free Viewing Task.

Cued viewing task

The CVT (Figure 11), was based on a 3x2 design, where picture pairs were all of the same type, i.e. illness and neutral pairs. Group (low, moderate and high IA) served as the between-subjects variable and attention manipulation (focus on illness picture vs. focus on neutral picture) served as the within-subjects variable. This task included 48 trials with an equal number and equally distributed presentation of the attention manipulation type in 4 blocks with 12 trials each presented in two counterbalanced orders. Each trial started with a drift correction, followed by a fixation cross presented in the middle of the screen for 1.5s. The cue was then presented, which was either an arrow pointing to the right on the right side of the screen (768, 384) or an arrow pointing to the left on the left side of the screen (256, 384). Participants were instructed to focus on the cue and then, when the picture pair was displayed, to attend to the picture as indicated by the cue. The cue was a fixation trigger so picture pair display was triggered if participants focused on it for 150ms. Then the picture pair was presented for 6.5s and participants had to look at the side of the screen where the cue was previously presented. A blank screen was again presented for 1.0/1.5/2.0s randomly after the end of each trial. Participants self-reported about the emotional arousal (low-high intensity) and valence (pleasantness-unpleasantness) experienced because of the attended picture on a 9-point scale following each trial. Both tasks started with two practice trials with neutral picture pairs to help familiarize participants with each task.

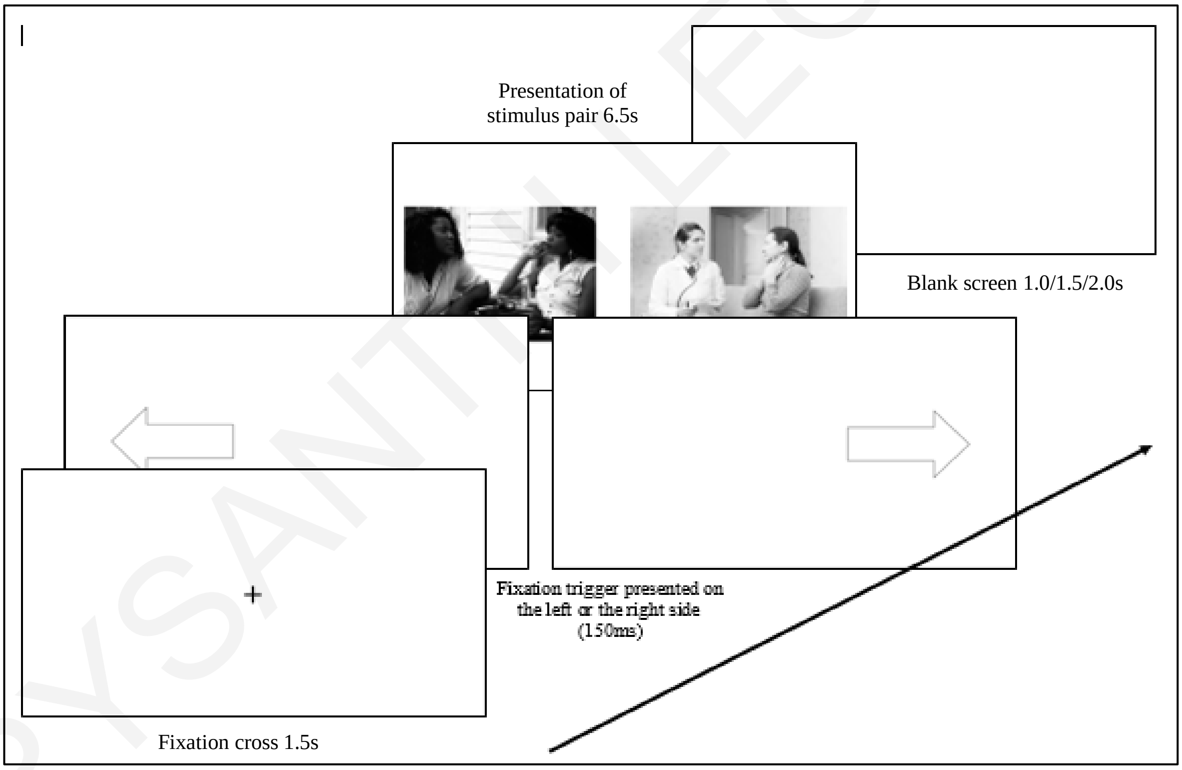

Figure 11. Example of a trial in the Cued Viewing Task.

Experimental stimuli

The experimental stimuli were pictures gathered from three resources: Fearful and neutral pictures were taken from the International Affective Picture System (IAPS; Lang, Bradley, & Cuthbert, 1997); illness pictures were taken from IAPS, the picture set used by Lees and colleagues (personal communication in October 2016; Lees et al., 2005) and the Google

Images search engine using the search terms: illness, symptoms, medical procedures.[8] Pictures were transformed into black and white and were matched in pairs based on their complexity as much as possible, i.e. how many objects were in the picture, whether there were humans or not etc. Picture dimensions were 345x245 pixels and were presented in the middle left (256, 384) and right side of the screen (768, 384) on a white background. Each type of picture was equally presented on the left or the right side of the screen within each pair to control for the tendency to scan information directing eye movements from left to right and each picture was presented only once during the experiment to prevent habituation effects.

Procedure

Following informed consent, participants underwent the Miles test (Miles, 1930) to identify their dominant eye. They were seated in a dimly lit room in front of a computer screen (BENQXL24IIT 24”, screen resolution: 1280x1024, display resolution: 1024x768), where the pictures were presented and in front of the eye-tracking equipment. The display screen was in approximately 70cm from participants’ eyes and the camera lens was about 60cm from below participants’ head. The electrodes for psychophysiological recording were attached and participants were asked to rest for five minutes to help them familiarize with the setting and for psychophysiology measures to stabilize. After the 5-minute resting period, participants placed their head on the chin-rest and the calibration procedure was carried out at least twice, before each task. The FVT and the CVT were carried out separated by another 5-minute resting period for participants to relax. The experiment was controlled using Experiment Builder (SR Research, Ottawa). Participants were encouraged to finish each task before taking a break. They could also take a break between blocks if they reported being tired. After the experiment electrodes were removed and participants answered questions about where they focused their attention during experiment on a 9-point scale (totally non-representative-totally representative) and they were debriefed.

Measures

Screening instruments

The set of screening questionnaires included: The Short Health Anxiety Inventory (Salkovskis et al., 2002) total score was used to measure participants’ IA levels (Cronbach’s α=.87). It is an 18-item questionnaire, designed to assess the features of IA as proposed by the

[8] Pictures were selected from a bigger pool after they were rated by an independent sample of 20 university students (12 female; 18-29 years old). Selected illness pictures were rated as highly related to health/illness (*M*=7.50, *SD*=1.09, range 1-9), moderately emotionally intense (*M*=5.34, *SD*=1.73), rather unpleasant (*M*=3.17, *SD*=1.15) and low in fearfulness (*M*=3.80, *SD*=1.89). Selected fearful pictures were rated as rather not related to health/illness (*M*=4.67, *SD*=2.51), emotionally intense (*M*=6.61, *SD*=2.02), unpleasant (*M*=2.46, *SD*=1.18) and moderately fearful (*M*=5.55, *SD*=2.57). Selected neutral pictures were rated as not related to health/illness (*M*=2.02, *SD*=1.31), not emotionally intense (*M*=3.18, *SD*=1.31), neither pleasant nor unpleasant (*M*=5.99, *SD*=1.15) and low in fearfulness (*M*=1.55, *SD*=0.84).

cognitive-behavioral model of IA (Warwick & Salkovskis, 1990). Each item consists of four statements that correspond to a 4-point Likert scale according to the level that one has a tendency or characteristic (score range: 0-54). This short version has shown comparable reliability and validity to the 64-item version, which has excellent psychometric properties (Hedman et al., 2015). The questionnaire provides a total IA score, and the negative consequences of IA score, as well as three factors: Illness Likelihood, Illness Severity and Body Vigilance. The Greek version of the SHAI (Karademas et al., 2008) showed a good model fit following the two-factor model (Leonidou & Panayiotou, 2016).

The Illness Attitudes Scales (IAS; Kellner, 1987) total score was used as an additional measure of IA. It is a 27-item scale and assesses fears, attitudes and beliefs associated with hypochondriacal concerns and abnormal illness behaviour on a 5-point Likert scale (score range: 0-108). The IAS shows very good psychometric properties (Hedman et al., 2015) and in addition to a total score, it gives scores of nine subscales: Worry about illness, Concerns about pain, Health habits, Hypochondriacal beliefs, Fear of death, Disease phobia, Bodily preoccupations, Treatment experience, Effects of symptoms. It was translated into Greek for the purpose of this study and initial confirmatory factor analysis supported the existing factor structure and model fit (Leonidou & Panayiotou, 2017a); Cronbach's α=.83 in this study.

Eye-tracking measurements and data reduction

Eye movements were recorded using EyeLink 1000 Plus Desktop Mount (SR Research, Ottawa), monocularly using the dominant eye (in 2 cases the non-dominant eye was used because it was better captured) at a sampling rate of 1000Hz. Calibration was done using a 9-point template so that pupil threshold was >70 and <120 and corneal reflection between 200–240. Validation of the calibration was accepted if the error rate was <.05 on average and no calibration was accepted with an error above 1. Two rectangular interest areas were drawn prior to the experiment, one for each picture per pair and the fixations within the interest areas were used to calculate scores. Fixation was defined as any fixation recorded after the first 100ms from stimulus onset and lasted ≥100ms (Wieser, Pauli, Weyers, et al., 2009). Initial orientation of attention was assessed in the FVT, by calculating the probability of first fixation on each picture type (%). First fixations for both tasks in this study were observed within the window of 0.2-1.0s from stimulus onset. Vigilance and early attentional engagement were assessed in both tasks by calculating the mean score of the percentage of time spent fixating on each picture as a function of the total time fixating on both pictures after creating interest periods of the first and second 0.5s intervals from stimulus onset. Later-stage attentional processes, i.e. attentional maintenance/avoidance, were assessed from 1s after stimulus onset to 6.5s (stimulus offset) and were calculated as percentages as above (Wieser, Pauli, Weyers, et al., 2009). Early disengagement from threat, defined as shifting attention away from threat (Cisler & Koster, 2010), was assessed by briefer first fixation durations on each picture type (Armstrong & Olatunji, 2012). There was a 0.23% of the total number of trials (1 trial missing in 2 participants, 9 trials missing in 1 participant) that was missing due to recording problems in the FVT and 0.19% (1-3 trials missing from 6 participants) in the CVT. Three participants were excluded from the CVT analyses due to >58% of missing trials. A small number of extreme outlier values (<3% for both tasks) were replaced with the minimum or maximum value per variable.

Physiological measurements and data reduction

Psychophysiological measures of emotional arousal were recorded during all phases of the experiment using BIOPAC MP150 and the AcqKnowledge Data Acquisition and Analysis Software 3.9. Heart-rate reactivity (HR) was measured by ECG recorded at the two inner forearms and filtered by a BIOPAC ECG100C bioamplifier sampled at 1000 Hz, set to record HR between 40 and 140 beats per minute (BPM), and converted to BPM online. Evoked heart-rate responses were scored by determining for each participant and each trial the maximum deceleration from baseline between 0.5-3.5s and the maximum acceleration from baseline between 3.5-6.5s after trial onset (Wieser, Pauli, Alpers, & Muhlberger, 2009). Skin conductance response (SCR) was measured by GSR100C transducer amplifier and electrodes attached on the medial phalanx of the index and middle fingers of the non-dominant hand, sampled at 250 Hz. It was scored as the largest increase in conductance between 1.0-6.5s after trial onset compared to the mean activity in a 1s pre-trial. For the FVT, SCR data for 22 participants, and for the CVT, SCR data for 20 participants, and HR data for 3 participants (who were the same participants excluded due to many missing trials during the CVT) were excluded from analyses due to technical problems. Outliers below or above 2.5 standard deviations to the mean were removed from the raw data. The mean of each measurement was calculated for each experimental condition and data were examined for normal distribution and outliers using histograms and boxplots. A small number of extreme outliers (<5% for both tasks) was replaced with the maximum or minimum value in each variable, calculated after removal of outliers.

Data Analysis

To examine picture type effects in FVT based on the presented hypotheses, repeated-measures ANOVAs were conducted for each eye-tracking variable separately, using the picture type per picture pair as the within-subjects variable. Greenhouse-Geisser corrections were applied when the assumption of sphericity was not met (see ε values in parentheses below). To examine picture type effects in CVT, repeated-measures ANOVAs were tested for each eye-tracking, psychophysiological and self-report variable separately with picture type as the within-subjects variable for target and distractor pictures separately. To examine differences in the percentage of dwell time on each picture during the exposure continuum, two repeated-measures ANOVAs were also conducted to test the interaction effect of time interval by picture type on dwell time. The above analyses on the effects of picture type and time interval were conducted including the total sample (n=100). To test the effect of IA levels, mixed-model ANOVAs were conducted, using the same within-subjects variables as above and adding the three IA groups as the between-subjects variable. Multiple comparisons were tested with Bonferroni tests and corrected with the Holm-Bonferroni method (Holm, 1979); 1st rank α value=.01, 2nd rank α=.0125, 3rd rank α=.016, 4th rank α=.025, 5th rank α=.05. Effects were assumed to have a large effect size if η_p^2>.25, medium if η_p^2>.09, small if η_p^2>.01. Correlations, followed up by regressions for the variables that showed significant correlations, were used to examine the associations between eye-tracking and physiological and subjective emotional reactivity variables.

Results

Free Viewing Task

Main effect of picture type per picture pair and interactions with illness anxiety levels

Participants reported that during the FVT, they mostly focused their attention on generally fearful pictures (M=7.00, SD=9.59) and on illness pictures (M=5.86, SD=2.35) and they focused less on neutral pictures (M=4.20, SD=2.20). IA groups did not differ in their responses (see Table 1).

Orienting bias. During the FVT (see Table 6 for means and SDs), picture type had a significant effect on the first fixation location, $F(3.21,577.92)=27.72$, $p<.001$, $\eta_p^2=.22$ (ε=.642). Post-hoc comparisons showed that the probability of the first fixation location on illness pictures of I-N pairs was higher compared to the neutral pictures of the same pairs, however, first fixations on illness pictures of I-F pairs were not significantly higher than first fixations on the fearful pictures of the same pairs. The probability of the first fixation between illness pictures of I-N pairs and fearful pictures of F-N pairs was not significantly different (ee Figure 12). When examining the interaction between picture type and IA group, the results were not significant, $F(6.35,276.09)=0.35$, $p>.05$ (ε=.64)[9].

Early engagement with threat. Picture type also had an effect on first fixation durations, $F(5,95)=3.83$, $p<.01$, $\eta_p^2=.17$, with participants fixating for longer durations on illness pictures compared to neutral pictures of I-N pairs. All other differences in first fixation durations were not significant (see Figure 13). Interaction with IA group effect was not significant for first fixation durations, $F(10,168)=0.71$, $p>.05$.

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[9]All mixed-model ANOVAs were repeated controlling for depression, generalized anxiety, panic, agoraphobia, social anxiety and somatization symptoms, which were assessed using the Psychiatric Diagnostic Screening Questionnaire (PDSQ; (Zimmerman & Mattia, 2001), and the results remained the same.

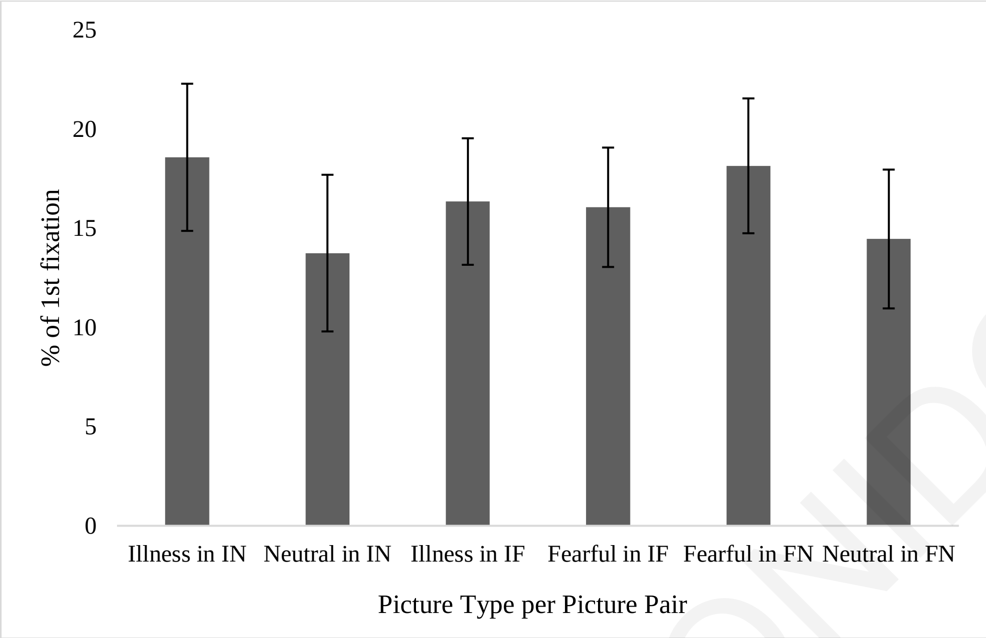

Figure 12. Early orienting bias based on the mean percentage of dwell time on each picture in the total nuber of trials for the total sample.

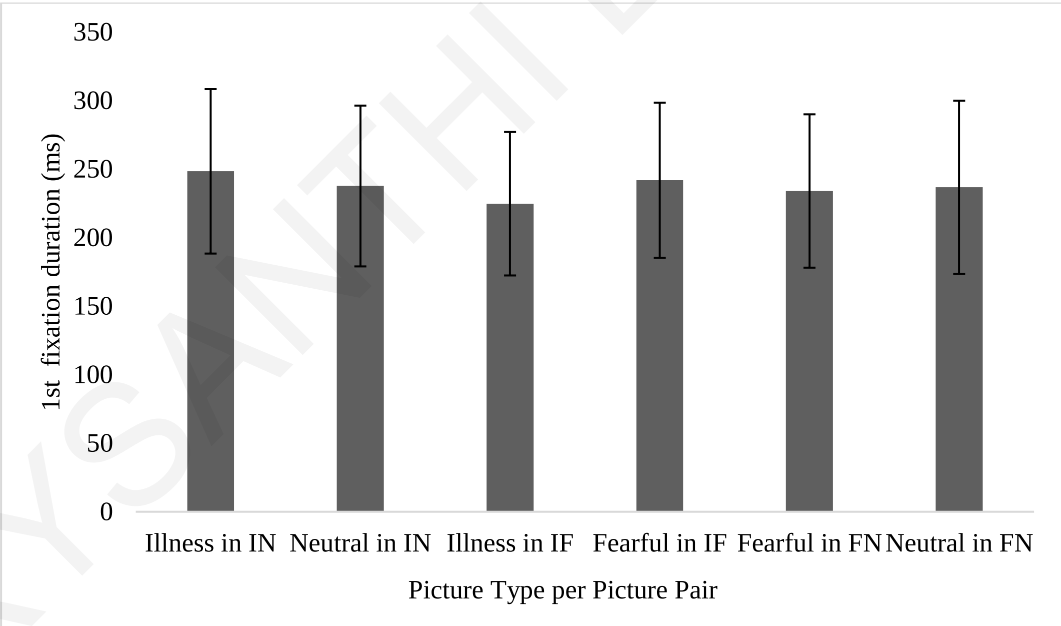

Figure 13. Early engagement of attention based on first fixation durations (ms) on each picture type for the total sample.

Vigilance. When examining the first and second 0.5s intervals from stimulus onset, picture type had a significant effect on the percentage of dwell time during the first, $F(3,97)=33.76$, $p<.001$, $\eta_p^2=.51$, and the second intervals, $F(3,97)=56.06$, $p<.001$, $\eta_p^2=.63$. Post-hoc comparisons showed that in both intervals, dwell time on illness pictures of I-N pairs and fearful pictures of F-N pairs was higher compared to the neutral pictures of the same pairs. Dwell time between illness and fearful pictures of I-F pairs and between illness pictures of I-N pairs and fearful pictures of F-N pairs was not significantly different (see Figure 14). Interaction effect with IA groups on dwell time was non-significant during the first, $F(6,172)=0.80$, $p>.05$, and the second 0.5s intervals, $F(6,172)=0.30$, $p>.05$. The interaction between picture type and time interval on percentage of dwell time was significant, $F(6,94)=13.39$, $p<.001$, $\eta_p^2=.46$. Planned contrasts showed a significant effect between the first and the second 0.5s intervals, between illness and neutral pictures of I-N pairs, $F(1,99)=16.68$, $p<.001$, $\eta_p^2=.14$; but not between illness pictures of I-N pairs and fearful pictures of F-N pairs, $F(1,99)=3.08$, $p>.05$. Dwell time on illness pictures of I-N pairs and fearful pictures of F-N pairs was increased, whereas for neutral pictures of I-N pairs it shows a reduction (see Figure 15).

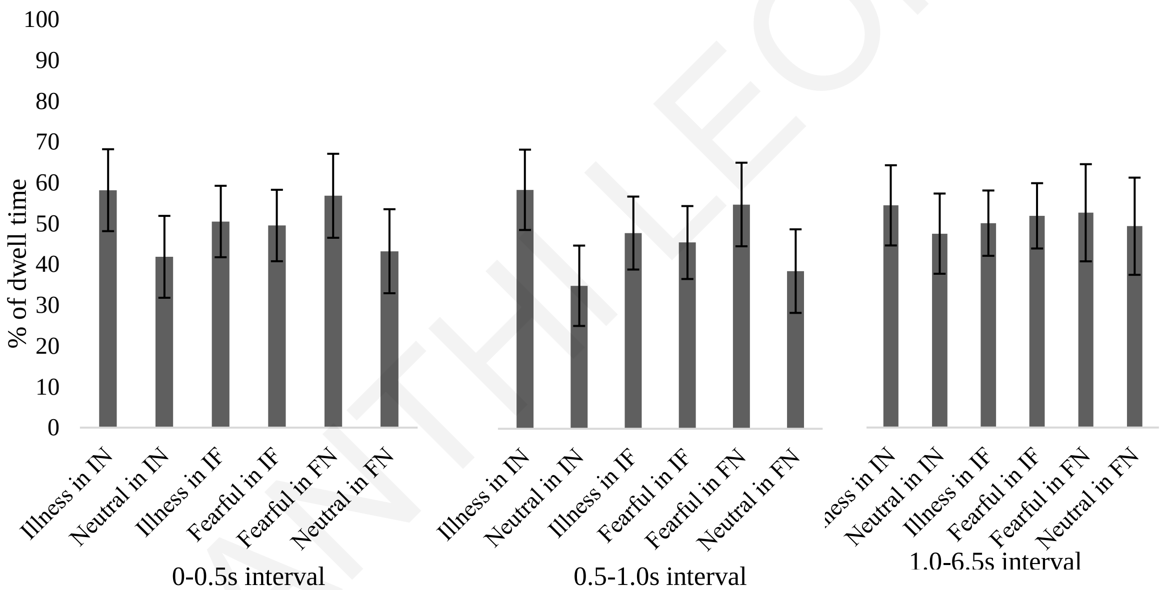

Figure 14. Percentage of dwell time on each picture type over the three time intervals for the total sample.

Attentional maintenance/avoidance. During the 1.0-6.5s interval, picture type had also a significant effect on the percentage of dwell time, $F(3,97)=5.71$, $p<.01$, $\eta_p^2=.15$. Percentage of dwell time was significantly higher on illness pictures compared to neutral pictures of I-N pairs. All other differences were not significant (see Figure 14). Planned contrasts also showed significant interaction between picture type and time interval on percentage of dwell time (see above) between the first 0.5s and the 1.0-6.5s interval, which was significantly different between illness and neutral pictures of I-N pairs, $F(1,99)=13.01$, $p<.001$, $\eta_p^2=.12$; but non-significant between illness pictures of I-N pairs and fearful pictures of F-N pairs, $F(1,99)=0.06$, $p>.05$. Dwell time on illness pictures of I-N pairs and fearful pictures of F-N pairs showed a decrease from the first 0.5s to the 1.0-6.5s interval, hence dwell time on their neutral pairs showed an increase (see Figure 15). When examining the effect of IA groups, its interaction with picture type, $F(6,172)=1.31$, $p>.05$; and with picture type by interval were not significant, $F(12,166)=0.89$, $p>.05$.

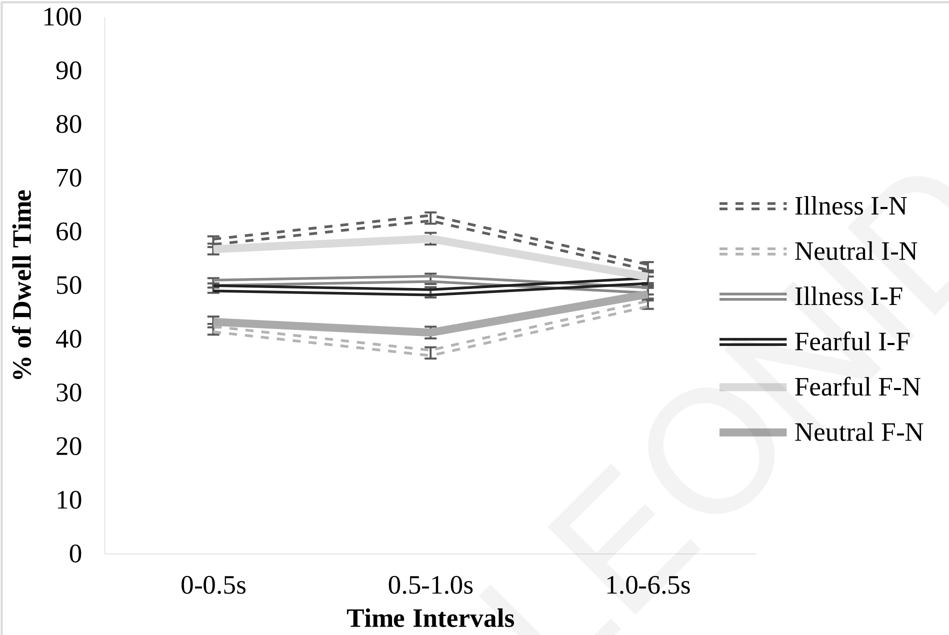

Figure 15. Interaction effect of picture type by time interval on the percentage of dwell time.

Associations between eye tracking and psychophysiological variables

During the presentation of I-N pairs, SCR was positively associated with the percentage of dwell time on neutral pictures and therefore negatively associated with the percentage of dwell time on illness pictures during the second 0.5s interval. In addition, SCR was negatively associated with the first fixation durations on illness pictures. Regression analysis further supported that briefer first fixation durations on illness pictures of I-N pairs predicted higher SCR, $\beta=-.23$, $p=.04$, whereas dwell time on illness pictures was not a significant predictor of SCR, $\beta=-.18$, $p>.05$, $F(2,77)=4.38$, $p=.04$, $R^2=.06$. During the presentation of I-F pairs, there was a significant positive correlation between the percentage of dwell time on illness pictures and therefore a negative association between percentage of dwell time on fearful pictures during the second 0.5s interval and HR acceleration. More dwell time on illness pictures of I-F pairs predicted more HR acceleration, $\beta=.20$, $p=.05$, $F(1,99)=3.98$, $p=.05$, $R^2=.04$. All other correlations were not statistically significant (see Tables B1-B3 in Appendix B).

Table 6. *Means and standard deviations (in parentheses) for eye tracking measures per picture type per picture pair, and psychophysiological measures per picture pair during the free viewing task*

	Illness in I-N pair	Neutral in I-N pair	Illness in I-F pair	Fearful in I-F pair	Fearful in F-N pair	Neutral in F-N pair
Eye tracking measures						
1st fixation location (% trials total)*	18.58 (3.71)[a]	13.75 (3.95)[a]	16.35 (3.19)	16.06 (3.01)	18.15 (3.40)[b]	14.46 (3.50)[b]
Low IA	18.75 (3.75)	13.68 (3.93)	15.97 (3.06)	16.67 (2.84)	18.13 (3.83)	14.38 (3.88)
Moderate IA	17.71 (3.27)	14.51 (3.35)	16.11 (2.38)	16.53 (3.09)	18.13 (3.20)	14.65 (2.87)
High IA	19.10 (4.21)	13.12 (4.65)	17.15 (3.66)	14.79 (2.81)	17.99 (3.48)	14.65 (3.43)
1st fixation duration (ms)*	248.42 (60.01)[a]	237.70 (58.67)[a]	224.77 (52.36)	241.90 (56.57)	234.08 (55.96)	236.75 (63.16)
Low IA	265.44 (64.58)	230.09 (66.07)	223.52 (59.84)	228.42 (52.97)	222.71 (58.76)	229.22 (66.50)
Moderate IA	257.15 (47.08)	257.82 (59.99)	239.99 (49.80)	257.44 (55.36)	251.87 (55.83)	247.06 (68.14)
High IA	240.88 (73.60)	230.74 (48.86)	214.05 (48.24)	241.67 (65.14)	227.00 (52.89)	238.29 (61.14)
Dwell time (% trial) 0-0.5s*	58.16 (10.03)[a]	41.84 (10.03)[a]	50.49 (8.75)	49.51 (8.75)	56.79 (10.29)[b]	43.21 (10.29)[b]
Low IA	59.01 (10.12)	40.99 (10.12)	49.57 (8.73)	50.43 (8.73)	56.90 (11.58)	43.10 (11.58)
Moderate IA	56.36 (8.81)	43.64 (8.81)	49.67 (8.81)	50.33 (8.81)	56.94 (10.08)	43.06 (10.08)
High IA	59.35 (10.54)	40.65 (10.54)	52.90 (8.02)	47.10 (8.02)	55.87 (9.15)	44.13 (9.15)
Dwell time (% trial) 0.5-1.0s*	62.56 (10.52)[a]	37.44 (10.52)[a]	51.24 (9.55)	48.76 (9.55)	58.72 (10.94)[b]	41.28 (10.94)[b]
Low IA	63.80 (9.48)	36.20 (9.48)	52.12 (9.74)	47.88 (9.74)	59.25 (12.28)	40.75 (12.28)
Moderate IA	61.60 (10.58)	38.40 (10.58)	50.16 (10.38)	49.84 (10.38)	58.51 (10.73)	41.49 (10.73)
High IA	63.26 (11.76)	36.74 (11.76)	51.69 (9.37)	48.31 (9.37)	57.71 (8.73)	42.29 (8.73)
Dwell time (% trial) 1.0-6.5s*	53.40 (9.64)[c]	46.60 (9.64)[c]	49.12 (7.85)	50.88 (7.85)	51.62 (11.68)	48.38 (11.68)
Low IA	53.15 (9.59)	46.85 (9.59)	46.76 (7.05)	53.24 (7.05)	50.52 (11.88)	49.48 (11.88)
Moderate IA	52.50 (9.71)	47.50 (9.71)	50.52 (7.38)	49.48 (7.38)	50.79 (12.76)	49.21 (12.76)
High IA	54.31 (9.29)	45.69 (9.29)	50.95 (8.95)	49.05 (8.95)	52.46 (10.09)	47.54 (10.09)

(continued)

Psychophysiological measures			
Maximum SCR *Δ*(μS) 1.0-6.5s*	0.15 (0.18)	0.12 (0.19)	0.14 (0.19)
Low IA	0.18 (0.20)	0.17 (0.21)	0.18 (0.24)
Moderate IA	0.15 (0.18)	0.12 (0.17)	0.13 (0.19)
High IA	0.15 (0.17)	0.08 (0.20)	0.11 (0.16)
HR Deceleration *Δ*(bpm) 0.5-3.5s*	-6.64 (3.89)	-6.33 (4.46)	-6.63 (3.85)
Low IA	-7.39 (4.46)	-7.92 (5.18)	-7.38 (4.86)
Moderate IA	-6.59 (3.64)	-6.01 (2.85)	-6.20 (3.05)
High IA	-5.88 (3.87)	-5.04 (5.17)	-6.42 (3.79)
HR Acceleration *Δ*(bpm) 3.5-6.5s*	6.24 (4.53)	6.68 (4.84)	6.43 (4.53)
Low IA	7.28 (5.73)	7.51 (5.39)	7.99 (5.61)
Moderate IA	5.11 (2.26)	5.87 (3.63)	5.81 (3.81)
High IA	6.46 (5.19)	6.05 (4.90)	6.58 (5.47)

Note. Abbreviations for picture pairs: I-N=illness-neutral; I-F=illness-fearful; F-N=fearful-neutral.
* Means and SDs of the total sample (n=100).
[a,b] Bonferroni post hoc comparisons significant at the <.001, [c] significant at the <.01.
Differences in physiological measures between picture pairs were non-significant, for SCR, $F(1.70,130.96)=2.33$, $p>.05$ ($\varepsilon=.85$); for HA Deceleration, $F(1.24,123.20)=0.47$, $p>.05$ ($\varepsilon=.62$); for HR Acceleration, $F(1.86,184.21)=1.27$, $p>.05$ ($\varepsilon=.93$).

Cued Viewing Task

Main effect of picture type and interactions with illness anxiety levels

Attention manipulation was successful during the CVT as the percentages of dwell time on target pictures were higher than 95.9% during all the examined intervals (0-0.5s, 0.5-1.0s, 1.0-6.5s). After the task, participants reported that they followed the attention manipulation instructions and focused on the target pictures (M=7.72, SD=1.42), while reports for getting distracted by illness (M=3.18, SD=2.19) and neutral distractors (M=2.49, SD=1.71) were in low levels. When testing group differences in these reports, the high IA group reported more distraction by illness distractors, compared to the low IA group (see Table 5).

Early disengagement from threat. During the CVT (see Table 7 for the means and SDs), picture type had a significant effect on first fixation duration, $F(1,96)=10.75$, $p<.01$, $\eta_p^2=.10$ (see Figure 16). In this task, first fixation durations were significantly lower on illness compared to neutral target pictures. In both neutral and illness distractors there were zero first fixations as participants were already focusing on the location of target pictures at the trial start because of the preceding cue. First fixation duration was not influenced by the interaction between picture type and IA groups, $F(2,84)=1.78$, $p>.05$.

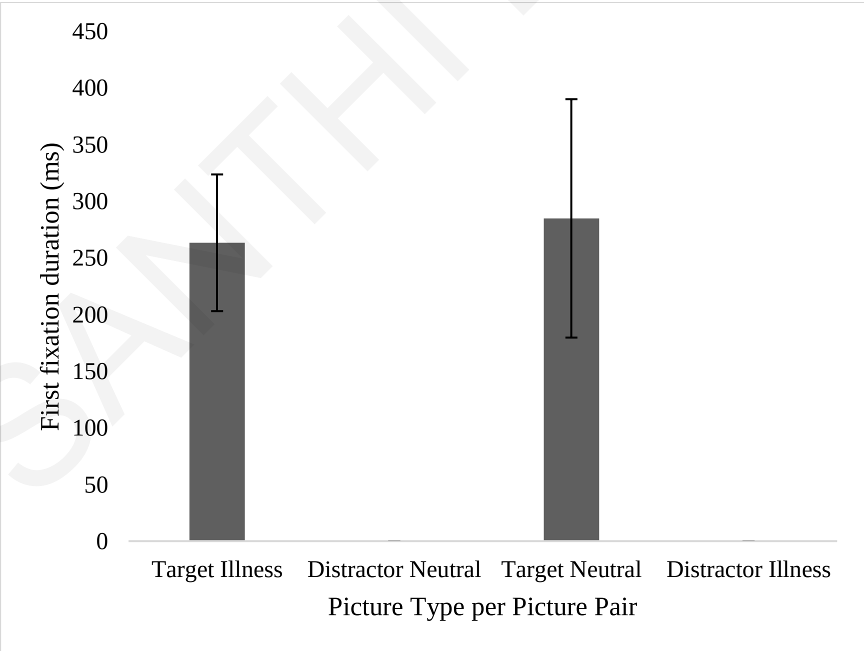

Figure 16. Early engagement of attention based on first fixation durations (ms) on each picture type for the total sample.

Vigilance. In the first 0.5s interval, effect of picture type on percentage of dwell time both among target and distractor pictures was non-significant, $F(1,96)=1.60$, $p>.05$. In the second 0.5s interval, the effect of picture type on dwell time was, however, significant,

$F(1,96)=14.25$, $p<.001$, $\eta_p^2=.13$, with participants having higher dwell time on neutral compared to the illness target pictures. The same effect was found for distractor pictures in this interval, i.e. higher dwell time on neutral compared to illness distractors (see Figure 18). IA group interaction with picture type did not influence dwell time on target and distractor pictures during the first, $F(2,84)=0.34$, $p>.05$, and the second 0.5s intervals, $F(2,84)=0.97$, $p>.05$. The interaction of picture type by time interval on the percentage of dwell time was statistically significant for target pictures, $F(1.36,130.15)=9.96$, $p<.01$, $\eta_p^2=.09$ ($\varepsilon=.68$). Planned contrasts showed a significant difference between the first and the second 0.5s intervals, $F(1,96)=13.45$, $p<.001$, $\eta_p^2=.12$. While for illness targets dwell time decreases significantly from the first to the second 0.5s interval, for neutral targets dwell time shows a more gradual decrease. Therefore, there is a similar interaction effect for distractor pictures, although in the opposite direction: dwell time on illness distractors increases more gradually, whereas dwell time on neutral distractors shows a more profound increase from the first to the second 0.5s interval (see Figure 17).

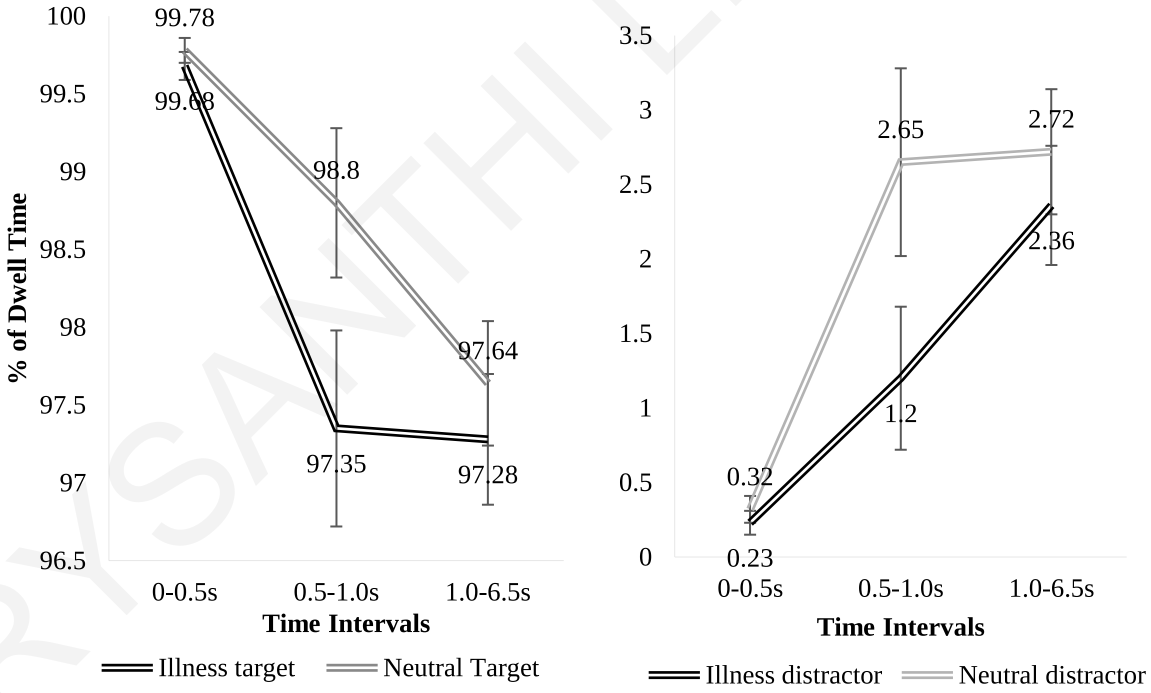

Figure 17. Interaction effect of picture type by time interval on the percentage of the dwell time for target pictures on the left and distractor pictures on the right.

Attentional maintenance/avoidance. When examining the eye movements during the 1.0-6.5s interval, the percentages of dwell time were again significantly higher for neutral compared to illness both target and distractor pictures, $F(1,96)=4.20$, $p=.04$, $\eta_p^2=.04$ (see Figure

18). Planned contrasts for the interaction effect of picture type by time interval on the percentage of dwell time (see above) showed non-significantly different interaction effect between the first 0.5s and the 1.0-6.5s intervals, $F(1,96)=2.11$, $p>.05$, which means that dwell time is similarly increasing for both target and distractor pictures irrespective of the type (see Figure 17). IA group interaction with picture type, $F(2,84)=0.66$, $p>.05$, and with picture type by interval interaction were not significant, $F(2.83,118.72)=0.94$, $p>.05$ ($\varepsilon=.71$), which means that the above effects are not depended on IA levels.

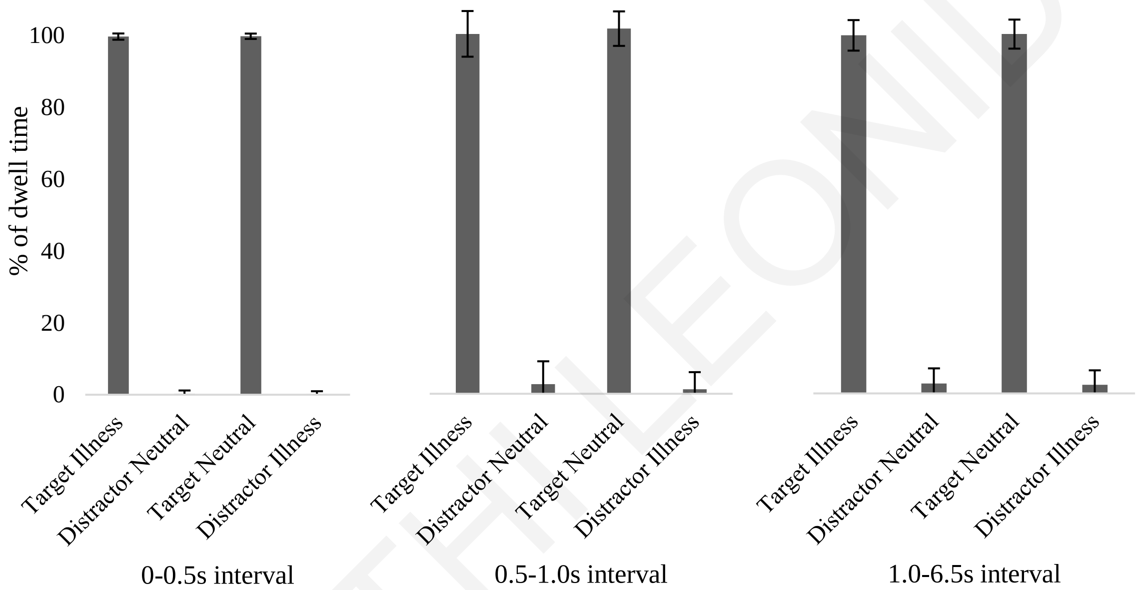

Figure 18. Percentage of dwell time on each picture type over the three time intervals for the total sample.

Subjective ratings and psychophysiological measurements. Participants rated illness compared to the neutral target pictures as more unpleasant, $F(1,96)=742.58$, $p<.001$, $\eta_p^2=.89$, and emotionally intense, $F(1,96)=496.04$, $p<.001$, $\eta_p^2=.84$. However, psychophysiological responses were similar during trials where illness picture was the target and trials where neutral picture was the target: $F(1,96)=1.00$, $p>.05$ for SCR; $F(1,96)=2.23$, $p>.05$ for HR deceleration; and $F(1,96)=0.10$, $p>.05$ for HR acceleration. IA group interaction with picture type did not influence arousal, $F(2,84)=1.35$, $p>.05$, and valence ratings of target pictures, $F(2,84)=1.11$, $p>.05$, SCR, $F(2,70)=1.17$, $p>.05$; HR acceleration, $F(2,84)=2.60$, $p>.05$, and HR deceleration, $F(2,84)=2.97$, $p>.05$.

Table 7. *Means and standard deviations (in parentheses) for eye tracking measures per picture type, psychophysiological reactivity and subjective ratings for the target pictures during the cued viewing task*

	Target Illness	Distractor Neutral	Target Neutral	Distractor Illness
Eye tracking measures				
1st fixation duration (ms)*	263.39 (60.34)	0.00 (0.00)	284.92 (105.23)	0.00 (0.00)
Low IA	261.51 (56.16)	0.00 (0.00)	280.72 (78.49)	0.00 (0.00)
Moderate IA	271.68 (66.25)	0.00 (0.00)	305.59 (125.52)	0.00 (0.00)
High IA	250.49 (40.97)	0.00 (0.00)	255.85 (44.68)	0.00 (0.00)
Dwell time (% trial) 0-0.5s *	99.69 (0.87)	0.31 (0.87)	99.78 (0.75)	0.22 (0.75)
Low IA	99.69 (0.94)	0.31 (0.94)	99.76 (0.62)	0.24 (0.62)
Moderate IA	99.74 (0.80)	0.26 (0.80)	99.94 (0.22)	0.06 (0.22)
High IA	99.50 (1.05)	0.50 (1.05)	99.53 (1.22)	0.47 (1.22)
Dwell time (% trial) 0.5-1.0s *	97.40 (6.18)	2.60 (6.18)	98.82 (4.67)	1.18 (4.67)
Low IA	97.06 (8.66)	2.94 (8.66)	98.17 (8.12)	1.83 (8.12)
Moderate IA	98.40 (3.20)	1.60 (3.20)	99.41 (1.19)	0.59 (1.19)
High IA	96.59 (5.47)	3.41 (5.47)	98.83 (2.42)	1.17 (2.42)
Dwell time (% trial) 1.0-6.5s *	97.34 (4.15)	2.66 (4.15)	97.68 (3.95)	2.32 (3.95)
Low IA	97.87 (3.82)	2.13 (3.82)	97.99 (3.80)	2.00 (3.80)
Moderate IA	97.61 (3.29)	2.39 (3.28)	98.06 (3.22)	1.94 (3.22)
High IA	96.36 (4.93)	3.64 (4.93)	97.01 (4.12)	2.99 (4.12)
Psychophysiological measures				
Maximum SCR Δ(μS) 1.0-6.5s *	-0.85 (8.74)		0.14 (0.25)	
Low IA	0.13 (0.19)		0.14 (0.24)	
Moderate IA	-3.40 (16.67)		0.20 (0.30)	
High IA	0.12 (0.24)		0.10 (0.21)	
HR Deceleration Δ(bpm) 0.5-3.5s *	-7.68 (4.78)		-8.05 (5.31)	
Low IA	-8.56 (5.31)		-9.64 (6.98)	
Moderate IA	-6.55 (3.49)		-7.02 (3.57)	

(continued)

High IA	-8.27 (5.81)	-7.79 (5.34)
HR Acceleration *Δ*(bpm) 3.5-6.5s *	6.72 (4.91)	6.65 (5.58)
Low IA	7.57 (6.07)	8.20 (7.39)
Moderate IA	6.65 (3.99)	5.97 (3.85)
High IA	6.26 (5.24)	6.06 (5.67)
Subjective ratings		
Intensity (1-9) *	6.05 (1.14)	3.26 (1.19)
Low IA	5.77 (1.07)	3.36 (1.13)
Moderate IA	6.14 (1.04)	3.26 (1.18)
High IA	6.14 (1.30)	3.33 (1.28)
Unpleasantness (1-9) *	6.60 (0.93)	3.40 (0.95)
Low IA	6.37 (0.94)	3.50 (0.86)
Moderate IA	6.68 (0.84)	3.39 (0.77)
High IA	6.68 (0.90)	3.49 (1.12)

Note. * Means and SDs of the total sample (n=97).

Associations between eye-tracking, subjective ratings and psychophysiological variables

During the CVT, a positive association was found between arousal ratings for the illness targets with the percentage of dwell time on neutral distractors, whereas there was a negative association between arousal ratings for illness targets with dwell time on illness targets during the 1.0-6.5s interval. Regression analyses supported that higher dwell time during the 1.0-6.5s on neutral distractors predicted higher subjective ratings of emotional arousal for the illness targets, β=.22, p=.03, F(1,96)=4.74, p=.03, R^2=.05. All other correlations were not significant (see Tables B4-B5 in Appendix B).

Discussion

The present study investigated the time-course of attentional bias components during processing of illness pictorial stimuli using eye-tracking during a free and a cued viewing task. It additionally examined the associations between attentional bias components and emotional reactivity, in groups of low, moderate and high IA. Overall, the results are in line with the expectation that illness-related information processing is linked to a preferential allocation of attention, although this finding was not more profound among individuals with high IA as initially hypothesized. Results can, however, inform the literature on the time-course of attentional bias components, voluntary control of attention allocation and associations with emotional reactivity during the processing of illness-threats.

Findings from the FVT supported this study's hypotheses about a vigilant pattern of processing illness stimuli when presented with neutral pairs, irrespective of IA levels. Participants presented an orienting bias to illness stimuli, a difficulty in disengaging attention from and vigilance to these stimuli during the early time intervals (0-1.0s) when presented with a neutral pair but not when presented with a generally fearful pair. The above components of attentional bias were also observed towards generally fearful stimuli when presented with a neutral pair, suggesting similar attentional biases to both illness and generally fearful stimuli.

During later stages of attentional processing (1.0-6.5s interval), there was a maintenance bias specifically observed for illness compared to neutral stimuli. Despite this finding, attentional maintenance on illness stimuli compared to neutral stimuli showed a significant decrease compared to the first interval, which may be indicative of habituation over time. Results about attentional biases to illness stimuli, which is the focus of the present study, are in line with previous evidence supporting attentional bias to illness stimuli, irrespective of IA levels (Lees et al., 2005; Shields & Murphy, 2011). In general, when freely inspecting pictures, individuals show a preferential attention allocation to illness and generally fearful, compared to neutral stimuli in early stages of processing, while in later stages, there is a specific maintenance bias on illness compared to neutral stimuli, although to a lesser extend compared to early processing stages.

Findings from the CVT also supported the presence of attentional biases, irrespective of IA levels, although in a different direction. In this case, participants showed earlier disengagement from illness and slower disengagement from neutral stimuli, despite instructions to maintain attention on target pictures for the whole exposure continuum. In addition, although in the first interval there was no effect of picture type, in the second and third intervals, time spent on neutral compared to illness targets and distractors increased. It is possible that participants after the first few trials in this task realised that only one picture in each pair was illness-related/threatening while the other was neutral/non-threatening. Therefore, maintaining attention, potentially strategically, on neutral target pictures for longer may have been less effortful and stressful for participants, compared to keeping attention on illness target pictures, as their threatening content may have made participants more susceptible to neutral distractors. Although in general there was more distraction over time, possibly explained by being curious for the other picture or getting bored with staring at one picture, the rapid increase of dwell time on neutral distractors compared to a more gradual increase of time on illness distractors supports the above conclusion.

Taken together, findings show that individuals exhibited a more vigilant mode of attentional processing of illness stimuli, when they were given control over attention allocation (FVT). In previous studies, this pattern was more profound among individuals who are generally vigilant when confronting threatening information and among frequent healthcare seekers (Kim et al., 2014; Kim & Lee, 2014; Lee et al., 2013). In contrast, individuals exhibited a more protective mode of attentional processing, also characterized by a voluntary avoidance tendency, that would minimize cognitive processing of illness-threat when exposure to stimuli was externally controlled (CVT). Such a pattern was previously observed among individuals who tend to cognitively avoid threatening information and rarely seek healthcare (Kim & Lee, 2014; Lee et al., 2013). The voluntary avoidance finding is also in line with a study that used a similar experimental paradigm to examine voluntary attentional control (Nummenmaa et al., 2006). It is a tentative explanation that perceived control of attention allocation influences the strategic use of attentional processes when confronting illness-threats. Perceived control was indeed assumed to influence attentional bias to illness stimuli in IA as it is suggested to increase/decrease vulnerability to threat (Lecci & Cohen, 2007); this remains to be further investigated in future studies.

The limited observed associations between attentional bias components and physiological reactivity, despite initial expectations, are also interesting to discuss. During the FVT, shifting attention away from illness stimuli earlier than shifting attention away from neutral stimuli after initial fixations, and more dwell time on neutral compared to illness stimuli during the second 0.5s interval was associated with higher SCR. During the CVT, illness compared to neutral target pictures were rated as more emotionally arousing and unpleasant, however they did not elicit greater physiological arousal. Arousal ratings were the only emotional reactivity variable linked to attention allocation; higher arousal ratings of illness target pictures were linked to getting more easily ‘distracted’ by neutral distractors, potentially as a strategy used to avoid threat/distress. These results, although very limited, partly support the hypothesis that high subjective and physiological arousal during exposure to illness stimuli is associated with avoidance tendencies, possibly aiming to regulate emotional reactivity. Future studies should further test this hypothesis by examining the causality in this relationship and the effect of attentional processes on emotional reactivity in the long-term after exposure to stimulus.

High IA individuals in this study believed that they were distracted more by illness pictures when these served as distractors in the CVT. In addition, their mean scores on attentional bias components showed a non-significant trend for more vigilance and maintenance of attention on illness stimuli in the FVT, and more avoidance tendencies of illness stimuli in the CVT. However, the overall results support that illness stimuli are perceived as threatening irrespective of IA levels and are in line with previous research that has demonstrated mixed (Lee et al., 2013; Lees et al., 2005) and null findings (Jacoby et al., 2016). This finding can gain theoretical support from the premise that there is a predisposition to attend to stimuli perceived as threatening within the environment as it is impossible to attend to all parts of a visual scene at the same time (Gerritsen, Frischen, Blake, Smilek, & Eastwood, 2008; Kahneman & Triesman, 1984; LeDoux, 1995). Illness-related information may be perceived as threatening by all individuals, especially when it competes emotionally neutral/non-threatening information.

Other possible explanations for the absence of IA effects should be also discussed. First, the absence of associations between attentional bias and IA was previously attributed to the nomothetic, and not idiographic, selection of stimuli to be illness-related/threatening for the sample on average (Jacoby et al., 2016). However, stimuli used in this study in their majority represented generic illness-related scenes, not tight to a specific health problem, e.g. pictures representing visits to the doctor or medical procedures. In addition, previous studies that used personally-relevant stimuli did not support associations between IA and attentional bias (Lee et al., 2013), whereas studies that used nomothetically selected stimuli supported such associations (Jasper & Witthoft, 2011; Kim et al., 2014; Kim & Lee, 2014). In fact, it is not that the experimental manipulation effects were not observed at all in this study, since attentional biases were observed in the total sample, it is that IA did not influence the experimental manipulation.

This leads to two other possible explanations. Although the high IA group in our sample had high IA levels compared to the other groups, mean scores showed less severity compared to other study samples (Kim & Lee, 2014). It is supported by existing literature that in non-severe IA levels stimuli as those used in this study may not activate illness schemata, which are expected to be part of high strength associative networks and readily available in pathological IA (Williams, Watts, MacLeod, & Mathews, 1997). It is suggested that when examining attentional bias in analog samples, inclusion of experimentally induced illness-related concerns in the laboratory is important (Jacoby et al., 2016); it seems that attentional biases are more likely to occur under state anxiety conditions (Lecci & Cohen, 2007, 2002; Quigley, Nelson, Carriere, Smilek, & Purdon, 2012). State anxiety may be also increased by increasing interoceptive attention especially in individuals with high IA who are fearful towards somatic sensations; this can be tested in future investigations. The third explanation concerns the utilization of IA measures that are not relevant to attentional bias. Previous studies with mixed findings about attentional bias in IA, observed associations between specific subscales of IA measures, or other measures relevant to this category of symptomatology, concerning either the somatic dimension, e.g. anxiety sensitivity, body vigilance, or the behavioral aspects, e.g. healthcare and information seeking and avoidance behaviors. In contrast, associations with cognitive aspects of IA, including measures such as the SHAI, were not supported (Lecci & Cohen, 2002; Lee et al., 2013; Lees et al., 2005). A follow-up study should be carried out focusing on the association of components of attentional bias with specific dimensions of IA using empirically founded subscales, rather than focusing on the severity of IA symptomatology.

Limitations that are specific for this study design include, first, the fixation trigger during the CVT to cue attentional focus on one picture per pair that proved to be very controlled, therefore, it did not allow for early-onset attentional bias. However, the purpose of this design was to preclude inspection of both pictures before focusing on the target one and was successful (in contrast to Nummenmaa et al., 2006); automatic orientation of attention was already examined in the FVT. This also yielded important findings about the abilities of individuals to control their attention allocation in early processing stages when cued appropriately. A second concern comes with physiological measures. It is plausible that physiological reactivity was influenced by the presence of both stimuli in each pair, and not clearly by focusing more on one stimulus. The design of the experimental tasks in this study only allowed for testing associations between attentional bias indices and physiological reactions, which was also limited by the small sample size for such analyses.

Several strengths of this study's design add to the importance of findings. Investigation of specific time intervals for specific components of attentional bias is a major advantage as it made possible the differentiation between early and later onset attentional biases and changes over time in processing patterns that provide evidence for a vigilance vs. vigilance-avoidance processing pattern. A second advantage is the inclusion of two different tasks that reflected a controlled by participants allocation of attention and an externally (experimentally) controlled allocation of attention. This allowed for the observation of distinct attentional processing patterns influenced by the task, which may provide another explanation for contradictory results in the research field of attentional bias in IA. In addition, the inclusion of generally fearful stimuli in the FVT proved to be useful as we could observe that in our sample attentional bias in early processing stages was similar between illness and fearful stimuli, whereas in later stages it was specific for illness stimuli. This may also be relevant in high IA populations, especially in the case of comorbidity with other anxiety symptomatology; hence generally fearful stimuli should be included in studies examining attentional bias in IA. Finally, the very limited and preliminary findings obtained here regarding emotional reactivity suggest that the inclusion of subjective and physiological measures of emotion in future studies is useful in examining the function of attentional bias as mechanism in regulating emotional reactivity.

More importantly, this study has several practical implications. Participants in our study, who were young and relatively healthy adults, presented attentional biases to illness stimuli, and to generally fearful stimuli for some of the components, irrespective of IA levels, in contrast to previous research that find such biases in samples with pathological IA. This raises the concern that instead of being a consequence of IA, such processing patterns may predispose healthy young participants to such symptoms. Having such biases may prevent the individual from realizing that their perception of the threat is exaggerated (In-Albon, Kossowsky, & Schneider, 2010) and by processing the threat in an elaborative way that would modify threat representations (Foa & Kozak, 1986). Such processing patterns may increase the risk for IA, therefore, interventions that will prevent development of such symptomatology may be helpful. Attentional Bias Modification (ABM) training received some attention as a therapeutic intervention in the research field of IA, however, results are still limited and contradictory (Lee, Goetz, Turkel, & Siwiec, 2015; Papageorgiou & Wells, 1998). Recent literature reviews suggest several modifications aiming to optimize ABM training procedures (MacLeod & Grafton, 2016; Mogg & Bradley, 2018). This study's findings may be also useful for the optimization of the ABM training, mostly with regards to perceived control over attention allocation as it seems to play a role in attentional processing of illness stimuli. It should be, therefore, taken into consideration when deciding on the specific targeted attentional processes during the ABM training and may be also used as a manipulation to increase the variance of the conditions under which individuals are trained on both in samples with pathological IA and in populations with high risk in developing IA symptomatology. The present study extends existing literature on the time-course of attentional bias components, voluntary control of attention allocation and associations with emotional reactivity during the processing of illness-threats and it can inform future experimental and intervention studies in the relevant research field.

CHAPTER 5 | General Discussion and Conclusions

Illness-related information processing has been suggested to play an important role in the mechanism that underlies the development and maintenance of IA (Marcus et al., 2007; Rachman, 2012; Warwick & Salkovskis, 1990). This is further supported by the systematic literature review conducted in the context of the present research project, which synthesized empirical evidence on how individuals with high IA process interoceptive and exteroceptive health-threatening information based on the main premises of the cognitive-behavioral model (Warwick & Salkovskis, 1990). A major assumption in the conceptualization model of IA is that selective attention to both interoceptive and exteroceptive illness-related cues influences individuals' responses to such cues in a way that increases and maintains IA (Warwick & Salkovskis, 1990). This assumption is supported by limited, and oftentimes contradictory, evidence. In addition, there is even scarcer research on the evaluation of individuals' emotional responses to illness-related cues and their interaction with selective attention processes. These gaps in the literature on the model of IA invite further investigation, therefore, this was the purpose of the present research project.

More specifically, the first empirical study in this research project examined the role of attentional focus on somatic sensations on the emotional reactions of individuals to illness imagery. The second empirical study examined the time-course and nature of attentional biases towards pictorial illness-related stimuli and their associations with emotional reactivity triggered by the stimuli. The effect of IA levels was examined in both studies. In general, findings from these studies, which will be discussed below, highlight the interactions between cognitive and affective aspects of processing of interoceptive and exteroceptive illness-related cues, although such interactions were observed irrespective of IA levels. It is tentative that the non-pathological levels of IA in samples of young, healthy in their majority adults, may explain the null results about the effects of IA, which contradict existing findings on the link between IA and illness imagery (Brownlee et al., 1992) and attentional biases (Jasper & Witthoft, 2011; Kim & Lee, 2014). Although participants in the high IA groups in both empirical studies reported higher levels of IA compared to the levels of IA found in previous studies with student populations based on the SHAI (Salkovskis et al., 2002; Witthöft et al., 2008), and only slightly lower levels of IA based on the IAS compared to clinical populations (Hedman et al., 2015); levels of IA were not as high as in clinical populations suffering with pathological IA. It is also possible that the categorization of participants in three groups, including a moderate IA group, may have masked differences in the variables under study between extreme groups of low and high IA levels that were, however, observed in previous studies (e.g. Kim & Lee, 2014). In general, the total score of the measures used, which focus on assessing the severity of IA and not the scores on specific dimensions, may have not been successful in identifying higher scores in some of the dimensions of IA that may be specifically related to the variables investigated in the empirical studies here. Despite the unexpected null results about the effect of IA levels, findings have major contributions to theory and clinical practice in the related research field.

Systematic Literature Review Findings

The literature review, which was the first on this topic that followed a systematic and rigorous methodology, was successful in evaluating the empirical evidence available about the main premises of the cognitive-behavioral conceptualization model of IA (Warwick & Salkovskis, 1990) and in identifying gaps that provided directions for future research. Findings of the review suggest that most studies examining selective attention and attentional biases in IA supported such associations (Jasper & Witthoft, 2011; Karademas, 2009; Kim et al., 2014; Kim & Lee, 2014). However, there are some contradictory results (Jacoby et al., 2016; Shields & Murphy, 2011) attributed to methodological differences in the study designs, while the nature and the time-course of specific components of attentional bias invite further investigation with methodologies that allow for such explication, e.g. eye-tracking. In addition, findings suggest the inclusion of memory and interpretation biases more explicitly in the conceptualization model of IA, since there is adequate supportive evidence about such associations (Ferguson et al., 2007; Hitchcock & Mathews, 1992; Neng & Weck, 2015; Pauli & Alpers, 2002). When it comes to the physiological and emotional dimensions of the IA conceptualization, it is evident that the few supportive findings of the model (Jasper et al., 2014; Köteles & Simor, 2014; Krautwurst et al., 2016; Schreiber et al., 2014) highlight the need for replication and new experimental studies. Such studies should examine the biased processing of interoceptive information and clarify its role in IA development and maintenance. Further research is also warranted in emotional processing of illness-related information, emotion regulation aspects, and their interaction with interoceptive processes by extending the evaluation of emotional reactions to illness-related cues to include both objective, i.e. physiological, and subjective measures of emotion. More importantly, the findings highlight the importance of the investigation of the inter-relations between the different dimensions of the cognitive-behavioral model. Such inter-relations may provide an insight in the function of the mechanisms and their link to IA development and maintenance.

Illness Imagery under the Influence of Attention on Somatic Sensations

Following the suggestions of the systematic literature review for more experimental studies on emotional processing of illness-related information and its interactions with interoceptive processes, the first empirical study examined the influence of heightened attention on somatic sensations on emotional reactions during illness imagery. Findings show that illness imagery triggers emotional reactions evident in subjective and physiological aspects of emotion, irrespective of IA levels. Supporting and extending the results of the few existing studies (Brownlee et al., 1992; Gramling et al., 1996), illness imagery, irrespective of attention manipulation, elicited greater emotional arousal and more negative valence based on self-reports and physiological indices, compared to imagery of neutral scripts, and, for some emotional reaction variables, compared to joyful and generally fearful conditions.

The major contribution of this study pertains to findings regarding the effect of attentional focus on somatic sensations. Following focusing on somatic sensations and during imagery of illness, generally fearful and joyful scenarios reports of emotional arousal and negative valence were higher, as compared to the effect of exteroceptive focus of attention. In contrast, neutral imagery after focusing on somatic sensations elicited less arousal and more positive emotions. Facial electromyography indices supported the above results about illness imagery showing more corrugator and less zygomatic activity. Reports of somatic sensations were higher after interoceptive focus of attention in all imagery conditions. However, a hypo-arousal physiological response was observed after focus on somatic sensations during the illness and neutral imagery (lower HR, lower SCL) and the joyful and fearful imagery (lower SCL), partly explained by heart-rate variability as an indication of greater parasympathetic activity, possibly related to efforts for emotion regulation. The discordance between subjective and physiological arousal, manifested by high reports of emotional arousal, negative emotions and somatic sensations, but a hypo-arousal physiological response, is assumed to be related to a worrisome, ruminative attitude towards somatic sensations and illness imagery aiming to reduce distress, as was supported in previous studies (Borkovec & Hu, 1990; Delgado et al., 2009; Fisher & Newman, 2013; Kirschner et al., 2016).

This study was designed based on widely-used experimental paradigms for mental imagery (Constantinou, Panayiotou, & Theodorou, 2014; Cuthbert et al., 2003; Panayiotou et al., 2017; Vrana & Lang, 1990) and interoceptive accuracy, i.e. the heart-beat tracking task (Schandry, 1981). Its strengths also include the utilization of both subjective and physiological measurements of emotion, the inclusion of personally-relevant scripts of individuals' worst fears for illness-threats and other standardized scripts of emotional conditions in addition to neutral imagery, which made this investigation more rigorous. Considering the above, this study's findings extend prior knowledge about emotional reactions to illness imagery by presenting evidence for more aspects of emotional experience that are influenced, including somatic sensation reports and facial electromyography. It also provides evidence about the specificity of some aspects of emotional experience to illness imagery compared to imagery of other intense emotional conditions. More importantly, this study is the first to inform existing literature for the effect of focusing attention to somatic sensations and its interaction with illness imagery, both important components of the cognitive-behavioral model of IA. Although hypervigilance to somatic sensations was assumed to play a role during illness imagery in IA, this is the first study that uses an attention manipulation to test this hypothesis, even though results do not support its specific link to IA.

Attentional Biases and Associations to Emotional Reactivity

Findings of the systematic literature review also identified a gap in the literature on attentional biases in IA, which guided the focus of the second empirical study in this project. This study supports prior findings that processing of illness-related pictorial stimuli is susceptible to attentional biases, although this is evident irrespective of IA levels (Lees et al., 2005; Shields & Murphy, 2011). Despite this unexpected finding, which may be explained by the predisposition to attend threatening stimuli in our environment due to the limited capacity of attentional resources in humans (Gerritsen et al., 2008; Kahneman & Triesman, 1984; LeDoux, 1995), this study can significantly inform theory and practice regarding the nature and time-course of attentional biases to illness stimuli, and their associations with emotional reactivity. During the free viewing of picture pairs, the processing pattern was characterized by an orienting bias and vigilance during early processing stages towards illness and generally-fearful relative to neutral stimuli, whereas in illness-fearful pairs there was no bias in allocation of attention on the two stimuli. In the same task, a maintenance bias was observed during later stages of processing specifically for the illness compared to the neutral stimuli. However, during the cued viewing of pictures, the attentional processing pattern was mostly characterized by avoidance of illness compared to neutral target stimuli, while participants were distracted more by the neutral compared to the illness distractor stimuli; and by apparently voluntary avoidance of illness stimuli in both early and later stages of processing. These findings may reflect the different levels of control (Lecci & Cohen, 2007) over allocation of attention potentially perceived by participants during the two tasks. This suggests that more control may reduce perceived vulnerability, hence, individuals focus their attention for longer durations on illness stimuli. Less control may increase vulnerability which, therefore, triggers more fearful and avoidance tendencies. The very limited and preliminary findings of this study regarding the link between attentional bias components and subjective and physiological emotional reactivity, show an association between increased emotional arousal and tendencies to avoid illness stimuli.

This study provides findings based on the free viewing task, that were in line with previous studies indicating attentional bias to illness stimuli, irrespective of IA (Lees et al., 2005; Shields & Murphy, 2011), and generally support the vigilance hypothesis. However, it also provides evidence about avoidance tendencies, which partly support the vigilance-avoidance hypothesis (Derakshan et al., 2007); vigilance was not assessed due to the design of the cued viewing task. A noteworthy observation is that the two attentional processing patterns were exhibited by the same participants, and it is the task nature that seems to have influenced the pattern of attentional processing. The inclusion of the two tasks proved to be important as it allowed for the above observation. In addition, this study was designed in a way that made feasible the investigation of specific components of attentional bias during specific time intervals, utilizing eye-tracking to measure allocation of attention continuously to two competing stimuli, including generally fearful in addition to neutral stimuli as comparison conditions. The inclusion of physiological measurements is also a strength of this study as it provided preliminary findings about associations between attentional bias components and emotional reactivity based on the hypothesis that attention allocation is an emotion regulation mechanism.

Future Research Directions

Both empirical studies extend existing literature in two major components of the conceptualization model of IA. Despite the importance of their contribution, limitations of the designs and new questions that have been raised through the investigations provide directions for future research. First, the inclusion of samples of young, healthy in their majority, adults has been proved useful in examining the mechanisms that were proposed to be involved in the development and maintenance of IA in a wide range of IA levels. This made possible the observation of findings about the effects of attentional processing of interoceptive and exteroceptive illness-related information and associations with emotional responses to such information, irrespective of IA levels. However, it is important that both study designs will be replicated in samples with pathological levels of IA and in medical populations, who present higher levels of IA compared to the general population, to replicate the above findings in these samples. It is assumed that individuals with severe IA have associative networks in memory about illness-threats, which are more easily activated due to the high associative strength between cue and response representations (Williams et al., 1997). Therefore, such networks may influence illness-related information processing in this population. Moreover, the comorbidity of IA with other categories of psychological symptomatology, should receive more attention in future studies. It is possible that the presence of psychological symptoms related to other anxiety disorders or depression may have influenced the results in a way that have masked differences between groups of high, moderate and low IA. Such symptomatology may also contribute to the perceived emotional intensity and negativity of illness-related information. In addition, the investigation of the link between specific dimensions of IA, using empirically supported subscales, rather than the total severity score of IA (Jacoby et al., 2016), may be useful when testing the influence of IA in experimental investigations which focus on specific dimensions of IA. This warrants investigation in follow-up studies.

Considering the first study more specifically, it is suggested that future investigations should replicate findings about the effect of heightened attentional focus on somatic sensations, by the utilization of other interoceptive focus tasks, that involve a broader range of somatic sensations, in addition to heart-rate. This is suggested because heart-rate sensations may not be relevant and fearful to all individuals due to the variability in this population regarding the fear of specific symptoms and diseases, which may change from time to time (Newby et al., 2017). Furthermore, it is suggested that future studies may use a longitudinal design to examine the long-term effects of interoceptive focus of attention if such a technique is used as part of an intervention for the prevention of development of IA symptomatology. Another question that has been raised based on the findings of this study is related to the emotion regulation strategies that potentially underlie the discordance observed between subjective and physiological arousal, especially during illness imagery. Follow-up studies should focus specifically on examining the link of this discordance in emotional experience to rumination, that was assumed to be related to a hypo-arousal physiological response in previous investigations (Borkovec & Hu, 1990; Fisher & Newman, 2013; Kirschner et al., 2016). In addition, experiential avoidance, a dispositional trait representing an avoidant way of coping with internal experiences, which was linked to IA (Wheaton, Berman, & Abramowitz, 2010), should be also examined in relation to the discordance in emotional experience as such associations have been observed in previous studies (Leonidou & Panayiotou, 2017b; Sloan, 2004).

Considering the second study, three main directions for future research are noteworthy. First, a promising addition in the experimental design is the inclusion of manipulations that increase state IA, as such manipulations have been previously successful in triggering more profound attentional biases (Lecci & Cohen, 2007, 2002). It is additionally suggested that an attention manipulation that would increase interoceptive focus of attention, as the one used in the first study of this project, may also increase state IA, and may provide further information about the combined effects of hypervigilance to somatic sensations and attentional bias to environmental illness-related information. In the case that such a manipulation is applied, personal relevance of the conditions used to elicit state anxiety should be taken into consideration. Secondly, the inclusion of physiological recording as a measure of emotional reactivity seems to be promising in terms of understanding the function of attentional biases in regulating emotion. However, future designs may find other ways to control for emotional reactivity that may be explained by methodological issues such as the inclusion of two stimuli. For example, designs that will assess emotional reactivity during single stimulus display in addition to the two-stimuli display may be thought; while greater sample sizes are needed to increase the statistical power. Third, considering the potential role of perceived by individuals control over attention allocation, future studies should aim to further assess this variable by including measures that assess locus of control. It has been previously suggested that the tendency to avoid health-related information, compared to vigilance for such information, may be used as a strategy to avoid mental discomfort or because of perceived powerlessness and low self-efficacy in a situation due to external locus of control (Byrne, 2008; Case, Andrews, Johnson, & Allard, 2005). These variables should be assessed in designs that investigate attentional biases to health-related stimuli in IA as they may explain the presence of different attentional processing patterns. In addition to the gaps identified by the systematic literature review, the above directions should be considered in future studies examining dimensions of the conceptualization model of IA.

Clinical Implications

The findings may also contribute to the clinical practice in populations who exhibit high risk in developing IA symptomatology. It is plausible that individuals with high risk in developing IA are more vulnerable when biased processing patterns of illness-related information are persistent. Although the link of these processing patterns to IA has not been supported in this research project, findings show that heightened attention to somatic sensations interacts with illness imagery in a way that influences emotional reactivity. In addition, attentional bias to illness-related images, involving vigilance and avoidance tendencies was preliminary linked to emotional responses. This means that selective and biased attention during processing of interoceptive and exteroceptive health-threatening stimuli and the context where it happens, i.e. high or low perceived control, other stimuli types in the same context, as well as its function in regulating emotional reactivity should be included in the assessment and conceptualization of IA symptomatology.

Findings may have implications about techniques used as part of psychological interventions targeting either prevention or treatment of IA symptoms. Considering the results of the first study, interoceptive attentional focus techniques, e.g. a simple heartbeat tracking task or other mindfulness body scan exercises and interoceptive exposure techniques (McManus et al., 2015; Walker & Furer, 2008; Weck et al., 2013; Williams et al., 2011), could be incorporated in such interventions. These techniques are suggested to trigger processing of all aspects of emotional experience when dealing with perceived illness-threats and to produce greater effects on reduction of phobic behavior (Lang, 1979). Emphasis should be placed on changing individuals' attitude towards somatic sensations and illness imagery to a more mindful, non-judgmental one, aiming to prevent or reduce maladaptive ruminative and catastrophizing approaches to such internal experiences (Mor & Winquist, 2002; Surawy et al., 2015).

Considering the results of the second study, Attentional Bias Modification training, which received some attention in the research field of IA (Lee, Goetz, Turkel, & Siwiec, 2015; Papageorgiou & Wells, 1998), may use evidence from this study for its optimization with regards to control over attention allocation. Findings show that perceived control may play a role in attentional processing of illness stimuli. Therefore, it may be taken into consideration when deciding on the specific target attentional processes during the training and may be also used as a manipulation during training to increase the variance of the conditions under which individuals are trained on. In general, training individuals in strategies that will help them be more open, with a non-judgmental and mindful attitude during processing illness-related information is an important addition to interventions targeting IA symptoms, including Attentional Bias Modification training.

Conclusions

The present research project highlights the importance of understanding the role of processing interoceptive and exteroceptive illness-related information, especially when it is influenced by biases. This is supported by the systematic literature review presented in Chapter 2 and its findings that were further extended by the two empirical studies presented in Chapters 3 and 4. Null findings about the link of such processes with increased levels of IA, show that the effects of these processes characterize illness-related information processing, irrespective of IA levels in a sample of young, relatively healthy, adults. This potentially reflects the threatening nature of illness-related information, which attracts more attentional focus compared to non-threatening information; although there are additional possible explanations discussed above. Since the conceptualization model of IA and existing empirical evidence support the effect of such processes in the development and maintenance of IA, the presence of such processing patterns in young adults, especially when in high risk of developing IA, may be targeted in prevention programs.

This project addressed gaps in the literature by systematically reviewing existing empirical evidence on the dimensions of the cognitive-behavioral model. Building on the identified gaps, it addressed specific research questions on the interaction between cognitive and affective aspects of processing interoceptive and exteroceptive illness-related cues. Although such interactions were observed irrespective of IA levels, findings have novel contributions to theory and clinical practice in the related research field, and invite future investigations to further address specific research questions.

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APPENDICES

Appendix A

Table A 1. *Quality appraisal checklist*

RESEARCH QUESTION
clearly stated procedure and IVs identified outcome variables indicated target population and setting specified
SELECTION OF PARTICIPANTS
free from bias inclusion/exclusion criteria and sufficient evidence criteria applied equally in all study groups health, demographics, and other characteristics of subjects described subjects representative sample of the relevant population
COMPARABLE STUDY GROUPS
method of assigning the subjects to the groups described and unbiased/randomization identified distribution of demographics and disease factors equal across groups comparable on important confounding factors/taken into consideration in analysis if diagnostic test was there an independent blind comparison with an appropriate reference standard
METHOD FOR HANDLING WITHDRAWALS
described number and characteristics response rate
PROCEDURE
clearly described
OUTCOMES
clearly defined measurements valid and reliable Relevant confounding variables measured
STATISTICAL ANALYSIS
adequately described results reported appropriately correct statistical tests assumptions of tests not violated levels of significance and confidence intervals reported controlling for confounding factors
CONCLUSIONS
discussion of findings biases and limitations discussed
CONFLICT OF INTEREST
no bias due to funding

Note. As some of the studies were correlational, characteristics in this checklist that were not relevant to correlational research were not accounted for during the quality assessment in this review.

Table A 2. *Quality appraisal results*

Study	Risk of Bias High	Risk of Bias Medium	Risk of Bias Low	Comments on missing information
Correlational studies				
Bailey & Wells (2016a)			+	Assumptions of statistical tests
Bailey & Wells (2016b)			+	Conflict of interest information not available
Bardeen & Fergus (2014)		+		Confounding factors not measured/controlled for, Conflict of interest information not available
Barsky & Wyshak (1990)			+	Assumptions of statistical tests, Conflict of interest information not available
Doherty-Torstrick et al. (2016)			+	Assumptions of statistical tests
Fergus (2015)			+	Conflict of interest information not available
Gerolimatos & Edelstein (2012)			+	
Gerolimatos et al. (2012)			+	Conflict of interest information not available
Goodwin et al. (2013)			+	Assumptions of statistical tests
Görgen et al. (2014)			+	Assumptions of statistical tests, Conflict of interest information not available
Martinez et al. (1999)		+		Assumptions of statistical tests, Biases and limitations not discussed, Conflict of interest not available
Koteles & Simor (2014)			+	Assumptions of statistical tests
Rief et al. (1998, study 2)			+	Assumptions of statistical tests, Conflict of interest information not available
Scutte et al. (2016)			+	Assumptions of statistical tests
Vervaeke et al. (1999)			+	Conflict of interest information not available
Wheaton et al. (2010)			+	Assumptions of statistical tests, Conflict of interest information not available
Wheaton et al. (2010)			+	Conflict of interest information not available
Zincir et al. (2014)			+	
Experimental studies				
Abramowitz & Moore (2007)			+	Assumptions of statistical tests, Conflict of interest information not available
Brady et al. (2014)			+	Conflict of interest information not available
Ferguson et al. (2007)			+	Assumptions of statistical tests, Conflict of interest information not available
Goetz et al. (2012)			+	Assumptions of statistical tests, Conflict of interest information not available
Gramling et al. (1996)			+	Assumptions of statistical tests
Gropalis et al. (2012)		+		Confounding factors not measured/controlled for, Assumptions of statistical tests, Conflict of interest information not available
Hedman et al. (2016)			+	Assumptions of statistical tests, Conflict of interest information not available

(continued)

Hitchock & Matthews (1992)		+	Assumptions of statistical tests, Conflict of interest information not available
Jacoby et al. (2016)	+		Confounding factors not measured/controlled for
Jasper & Witthöft (2011)	+		Confounding factors not measured/controlled for, Assumptions of statistical tests, Conflict of interest information not available
Jasper & Witthöft (2013)		+	Conflict of interest information not available
Jasper et al. (2015)		+	Assumptions of statistical tests, Conflict of interest information not available
Karademas et al. (2008)		+	Assumptions of statistical tests, Conflict of interest information not available
Katzer et al. (2011)		+	Conflict of interest information not available
Kaur et al. (2011)		+	Assumptions of statistical tests, Conflict of interest information not available
Kim & Lee (2014)		+	Assumptions of statistical tests
Kim et al. (2014)		+	Assumptions of statistical tests, Conflict of interest information not available
Krautwurst et al. (2014)		+	Assumptions of statistical tests
Krautwurst et al. (2016)		+	Assumptions of statistical tests
Lautenbacher et al. (1998)		+	Assumptions of statistical tests, Conflict of interest information not available
Lee et al. (2013)		+	
Lees et al. (2005)		+	Assumptions of statistical tests, Conflict of interest information not available
Macatee & Cougle (2013)		+	Conflict of interest information not available
MacLeod et al. (1998)		+	Assumptions of statistical tests, Conflict of interest information not available
Neng & Weck (2015)		+	Assumptions of statistical tests, Conflict of interest information not available
Owens et al. (2004)		+	Assumptions of statistical tests
Pauli & Alpers (2002)		+	Assumptions of statistical tests
Rodic et al. (2016)		+	
Sansom-Dally et al. (2014)		+	Assumptions of statistical tests, Conflict of interest information not available
Schmidt et al. (2013)		+	Assumptions of statistical tests
Schreiber et al. (2014)		+	
Shields et al. (2011)		+	Assumptions of statistical tests
Van Den Heuvel et al. (2005)		+	Assumptions of statistical tests
Witthöft et al. (2008)		+	Assumptions of statistical tests, Conflict of interest information not available
Witthöft et al. (2013)		+	Assumptions of statistical tests
Witthöft et al. (2016)		+	Assumptions of statistical tests

Appendix B

Table B1. *Correlations between eye tracking and physiological measures during I-N pairs in the free viewing task*

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Maximum SCR Δ(μS)	-	-.335**	.286*	-.091	.091	-.225*	.225*	-.042	.042	-.099	.099	-.233*	-.111
2. HR Deceleration Δ(bpm)			-.761**	-.013	.013	.090	-.090	.107	-.107	.017	-.096	.121	.070
3. HR Acceleration Δ(bpm)				-.012	.012	-.123	.123	-.134	.134	-.043	.160	-.127	-.039
4.Dwell time on H 0-0.5s					-1.000**	.451**	-.451**	.102	-.102	.796**	-.844**	-.047	-.085
5.Dwell time on N 0-0.5s						-.451**	.451**	-.102	.102	-.796**	.844**	.047	.085
6.Dwell time on H 0.5-1.0s							-1.000**	.328**	-.328**	.387**	-.486**	.124	-.069
7.Dwell time on N 0.5-1.0s								-.328**	.328**	-.387**	.486**	-.124	.069
8.Dwell time on H 1.0-6.5s									-1.000**	.119	-.104	-.083	-.043
9.Dwell time on N 1.0-6.5s										-.119	.104	.083	.043
10.1st fixation location on H											-.713**	.092	.020
11.1st fixation location on N												.005	.054
12.1st fixation duration on H													.469**
13.1st fixation duration on N													-

Note. ** <.01 level; * < .05.

Table B 2. *Correlations between eye tracking and physiological measures during I-F pairs in the free viewing task*

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Maximum SCR *Δ*(μS)	-	-.060	.266*	-.040	.040	-.061	.061	-.077	.077	.062	.074	-.029	.049
2. HR Deceleration *Δ*(bpm)			-.377**	-.027	.027	.054	-.054	.107	-.107	.001	.103	-.121	.072
3. HR Acceleration *Δ*(bpm)				.070	-.070	.198*	-.198*	.022	-.022	.075	-.126	.034	.016
4.Dwell time on H 0-0.5s					-1.000**	.444**	-.444**	-.142	.142	.772**	-.804**	.114	.190
5.Dwell time on F 0-0.5s						-.444**	.444**	.142	-.142	-.772**	.804**	-.114	-.190
6.Dwell time on H 0.5-1.0s							-1.000**	-.129	.129	.421**	-.341**	.084	-.110
7.Dwell time on F 0.5-1.0s								.129	-.129	-.421**	.341**	-.084	.110
8.Dwell time on H 1.0-6.5s									-1.000**	-.109	.076	-.104	.063
9.Dwell time on F 1.0-6.5s										.109	-.076	.104	-.063
10.1st fixation location on H											-.749**	.174	.149
11.1st fixation location on F												.035	-.119
12.1st fixation duration on H													.327**
13.1st fixation duration on F													-

Note. ** <.01 level; * < .05.

Table B 3. *Correlations between eye tracking and physiological measures during F-N pairs in the free viewing task*

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Maximum SCR Δ(μS)	-	-.196	.175	-.098	.098	-.021	.021	-.015	.015	.049	-.101	.044	-.109
2. HR Deceleration Δ(bpm)			-.679**	.021	-.021	.039	-.039	-.122	.122	.003	-.008	-.027	.141
3. HR Acceleration Δ(bpm)				.032	-.032	-.002	.002	.096	-.096	-.062	.089	-.032	-.141
4.Dwell time on F 0-0.5s					-1.000**	.528**	-.528**	-.027	.027	-.879**	.782**	-.196	.063
5.Dwell time on N 0-0.5s						-.528**	.528**	.027	-.027	.879**	-.782**	.196	-.063
6.Dwell time on F 0.5-1.0s							-1.000**	.208*	-.208*	-.460**	.407**	-.072	.135
7.Dwell time on N 0.5-1.0s								-.208*	.208*	.460**	-.407**	.072	-.135
8.Dwell time on F 1.0-6.5s									-1.000**	.050	-.068	.086	.001
9.Dwell time on N 1.0-6.5s										-.050	.068	-.086	-.001
10.1st fixation location on F											-.800**	.161	-.054
11.1st fixation location on N												-.186	.077
12.1st fixation duration on F													.512**
13.1st fixation duration on N													-

Note. ** <.01 level; * < .05.

Table B 4. *Correlations between eye tracking and physiological measures during trials with illness targets in the cued viewing task*

	1	2	3	4	5	6	7	8	9	10	11	12
1. Maximum SCR *Δ*(μS)	-	-.116	.038	-.041	.041	-.042	.042	.032	-.032	.072	-.060	-.052
2. HR Deceleration *Δ*(bpm)			-.744**	-.077	.077	-.065	.065	.007	-.007	.051	.052	.127
3. HR Acceleration *Δ*(bpm)				.038	-.038	.040	-.040	-.143	.143	-.010	-.067	-.093
4.Dwell time on I target 0-0.5s					-1.000**	.324**	-.324**	.288**	-.288**	.077	.013	.026
5.Dwell time on N distractor 0-0.5s						-.324**	.324**	-.288**	.288**	-.077	-.013	-.026
6.Dwell time on I target 0.5-1.0s							-1.000**	.525**	-.525**	.089	-.096	-.022
7.Dwell time on N distractor 0.5-1.0s								-.525**	.525**	-.089	.096	.022
8.Dwell time on I target 1.0-6.5s									-1.000**	.046	-.218*	-.122
9.Dwell time on N distractor 1.0-6.5s										-.046	.218	.122
10.1st fixation duration on I target											-.231*	-.248*
11.Self-reported Arousal for I target												.848**
12.Self-reported Valence for I target												-

Note. ** <.01 level; * < .05.

Table B 5.*Correlations between eye tracking and physiological measures during trials with neutral targets in the cued viewing task*

	1	2	3	4	5	6	7	8	9	10	11	12
1. Maximum SCR *Δ*(μS)	-	-.137	.232*	.002	-.002	.040	-.040	.060	-.060	-.087	-.045	-.027
2. HR Deceleration *Δ*(bpm)			-.828**	-.111	.111	-.077	.077	.100	-.100	.099	.062	.026
3. HR Acceleration *Δ*(bpm)				.058	-.058	.007	-.007	-.175	.175	-.058	-.004	-.022
4.Dwell time on N target 0-500ms					-1.000**	.485**	-.485**	.347**	-.347**	.104	-.162	-.138
5.Dwell time on I distractor 0-500ms						-.485**	.485**	-.347**	.347**	-.104	.162	.138
6.Dwell time on N target 500-1000ms							-1.000**	.225*	-.225*	.035	-.068	-.049
7.Dwell time on I distractor 500-1000ms								-.225*	.225*	-.035	.068	.049
8.Dwell time on N target 1000-6500ms									-1.000**	.069	-.074	-.055
9.Dwell time on I distractor 1000-6500ms										-.069	.074	.055
10.1st fixation duration on N target											-.102	-.150
11.Self-reported Arousal for N target												.870**
12.Self-reported Valence for N target												-

Note. ** <.01 level; * < .05.