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Light upon seasonality

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CHAPTER 6

General Discussion

Objective of this Thesis

This thesis started with the observation that seasonal rhythms are evident all over nature. Humans have adapted to seasonal changes in agriculture, economic activities and social life. The impact of the seasons on human health can be recognized in somatic illnesses, especially infectious diseases and some allergic conditions. It is widely believed that the weather and the seasons have an impact on human mental well-being[1-3]. Publications on the subjects of chronobiology, psychology, and psychiatry support the concept of seasonal changes of mood and behaviour[4]. We do not yet, however, fully understand to what extent seasonal changes cause changes in mood and behaviour and what mechanisms play a role in this process. The main question of this thesis is to what extent seasons influence positive and negative affect in humans. To answer this question, we analysed data from samples of the general population, in patient-oriented settings in primary care and specialised mental healthcare. In this thesis, the interviews and assessments of the questionnaires were performed within the four seasons: spring (March 21–June 20), summer (June 21–September 20), autumn (September 21–December 20), and winter (December 21–March 20).

In the current chapter, we will present our findings by answering the research questions formulated in the introduction of this thesis. This general discussion includes the relevance of these findings from a theoretical and clinical point of view. We will discuss the limitations and strengths of the study design followed by recommendations for future research.

Seasonality of Depressive and Anxiety Symptoms (Study 1)

In Chapter 2, we described our first study, which took place in the context of the Netherlands Study of Depression and Anxiety (NESDA)[5]. In this study, we determined whether there is seasonal variation in the severity and type of depressive and anxiety symptoms in a primary care population and in patients with a depressive or anxiety disorder. More specifically, we wanted to find the answers to three questions:

(1) Is there a seasonal pattern in the severity of depressive and anxiety symptoms in patients who visit their general practitioner for whatever reason? In order to answer this first question, we used the screening questionnaire for affective disorders of 5,549 primary-care patients, who visited their general practitioner for whatever reason, not primarily for mental problems. We analysed the data in a multilevel model and found that the severity of depressive and anxiety symptoms showed no seasonal pattern.

(2) Is there a seasonal pattern in the severity of depressive or anxiety symptoms in patients with a depressive disorder, an anxiety disorder, or a comorbid depressive and anxiety disorder in the previous month, and healthy controls? In order to answer this second question, we analysed data of 1,090 patients who participated in the baseline assessment of NESDA. We used the Composite International Diagnostic Interview (CIDI) to establish diagnoses according to DSM-IV criteria. We found a small rise of depressive symptoms in winter in healthy controls and patients with an anxiety disorder, but not in patients with a major depression, nor in patients with a major depression and an anxiety disorder. We were unable to demonstrate a seasonal effect for anxiety symptoms as measured with the Beck Anxiety Inventory (BAI).

We found a small gender-related seasonal effect for symptoms of fear and avoidance as measured with the Fear Questionnaire (FQ), with women having more complaints in summer and autumn. We found that patients with a depressive disorder in the previous month scored lower on depressive symptoms and anxiety symptoms as measured with the self-rated version of the Inventory of Depressive Symptoms (IDS-SR) and the BAI in winter compared to summer.

(3) Is there a seasonal pattern in the type of depressive symptoms inside these groups and are there any differences between the groups? We were unable to demonstrate a distinctive seasonal pattern in the type of depressive symptoms (i.e. atypical or melancholic symptoms).

The main findings of this study can be summarised as follows: In a primary-care population, visiting their GP for whatever reason, no seasonal pattern in the severity of depressive and anxiety symptoms was found. In a clinical outpatient population, we found a small rise of depressive symptoms in winter for healthy controls and patients with an anxiety disorder, but not for patients with a major depression or patients with a major depression and a comorbid anxiety disorder. Statistically all analyses showed only small effects sizes or no effect at all for the seasons.

The major strengths of this study were its large sample size and its diagnostic procedures based on standardised structured interviews. A limitation was the lack of specific instruments determining whether the previous course of illness had a seasonal pattern. In order to address this limitation, we applied the Seasonal Pattern Assessment Questionnaire (SPAQ) and reported on the matter of previous seasonal patterns in our second and third study.

Self-attributed Seasonality (Study 2)

In our second study, we used the Seasonal Pattern Assessment Questionnaire (SPAQ) to examine the seasonality of symptoms in 2,168 NESDA patients with a lifetime diagnosis of depressive and anxiety disorders and healthy controls[6]. The SPAQ is a self-rating screening instrument that retrospectively measures variation in mood and behaviour on a monthly basis. The SPAQ assesses fluctuations in mood, energy, sleep duration, appetite, weight, and social activity. A composite measure can be calculated from its items: the Global Seasonality Score.

All groups of patients and healthy controls reported a seasonal variation in mood and behaviour. Subjects reported feeling worst in a particular month of the year, mostly in the winter months, in ascending order: healthy controls (29.9%), patients with a lifetime diagnosis of an anxiety disorder (49.4%), patients with a depressive disorder (54.9%), and patients with a depressive disorder with a comorbid anxiety disorder (65%). The Global Seasonality Score showed a similar picture on the item of feeling worst in a particular month with the lowest scores for healthy controls followed by patients with a lifetime diagnosis of an anxiety disorder, with a depressive disorder, and with a depressive and a comorbid anxiety disorder. The season in which the questionnaires were completed significantly influenced the Global Seasonality Score in this study. This score was lowest for patients who completed

the questionnaire in summer and highest for those who did so in winter, with average scores in spring and autumn.

We can summarise the main findings of this study as follows: all patients report seasonal worsening of mood and behaviour based on recall. Patients who completed the questionnaires in the winter months and patients with more severe pathology were more likely to report seasonality of mood and behaviour. As in our first study, the major strengths of this study were its large sample size and diagnostic procedures based on standardised structured interviews. A major limitation was the possible bias of having measured symptoms on the basis of long-term memory. In order to address this limitation, we conducted our third study, in which we measured seasonal differences in existing symptoms in patients with and without self-reported sensitivity to seasonal changes.

Affective Disorders With and Without Seasonality: A Comparison (Study 3)

In our third study, we compared the clinical, demographic and personality characteristics of NESDA patients with a seasonal affective disorder to patients suffering from non-seasonal affective disorders and healthy controls[7]. In addition to the diagnostic categories from the previous studies, we included patients who had developed a bipolar disorder between the first and second measurements of NESDA. We used the criteria developed by Kasper regarding the SPAQ to identify patients suffering from a seasonal affective disorder and sub-syndromal seasonal affective disorder[8]. More specifically, we sought answers to the following questions:

(1) What is the prevalence of seasonal affective disorder and sub-syndromal affective disorder in our sample? The prevalence of seasonal affective disorder in our sample was 4.6%, that of sub-syndromal-affective disorder 6.8%. The prevalence of seasonal affective disorder in the group of patients suffering from a depressive disorder in the previous month was 12.7%. For sub-syndromal-affective disorder this was 11.3%.

(2) What are the clinical characteristics of patients with seasonal affective disorder and sub-syndromal affective disorder compared to patients with an affective disorder and no seasonal affective disorder? Patients in the seasonal affective disorder group were younger, less frequently employed, were more likely to have a low income, and scored higher on the neuroticism scale than patients with a lifetime depressive disorder without a seasonal affective disorder. Patients suffering from seasonal affective disorder presented a severe clinical picture and scored high in terms of psychopathology in the previous year and month. Patients in the sub-seasonal affective disorder group were younger than patients in the seasonal affective disorder group.

(3) Is there a difference in the seasonal distribution of depressive and anxiety symptoms between patients with a lifetime depressive disorder or a lifetime comorbid anxiety and depressive disorder and patients with a seasonal affective disorder? The scores for depressive symptoms and anxiety symptoms did not vary with the seasons: not for patients with a lifetime depressive disorder or a lifetime comorbid anxiety

and depressive disorder nor for patients with a seasonal affective disorder. Patients with seasonal affective disorder scored high on the depressive and anxiety symptoms, as did patients with a bipolar disorder and patients with a lifetime depressive disorder and a comorbid anxiety disorder. Patients with a seasonal affective disorder more frequently suffered from melancholic symptoms than from atypical symptoms during a depressive episode.

(4) Is there a difference in the seasonal distribution of depressive episodes in the previous month in patients with and without seasonal affective disorder? We found no difference between these groups.

We can summarise the main findings of this study as follows: Patients with a seasonal affective disorder scored high in terms of psychopathology in the previous year. The severity of depressive and anxiety symptoms in the depressive episode in the previous month was the same for patients with or without a seasonal affective disorder. Patients with seasonal affective disorder did not suffer more frequently from depressive episodes in autumn and winter than patients without a seasonal affective disorder.

As in our first and second studies, the major strengths of this study were its large sample size and its diagnostic procedures based on standardised structured interviews. A limitation of this study is the lack of repeated measures. We aimed to overcome this limitation in our fourth study, using data from a crowdsourcing study, HowNutsAreTheDutch.

Seasonality of Positive Affect (Study 4)

In our fourth study, we stated that in most studies, only complaints (symptoms), but not positive affect of individuals are measured. In the current study, we determined if positive and negative affect showed the same seasonal pattern. For this goal, we used the data from HowNutsAreTheDutch (HoeGekIsNL), a national crowdsourcing study designed to investigate multiple continuous mental-health dimensions in a sample from the general population. We used the Positive and Negative Affect Schedule (PANAS) and the QIDS-SR to measure affect and depressive symptoms. The 60-item NEO-Five-Factor Inventory was used to measure the neuroticism domain.

First, we selected a group of 5,282 respondents who completed the questionnaires once. We found that on this population level, respondents scored higher on positive affect in spring compared to the other seasons, lower on negative affect in spring compared to autumn and lower on QIDS depressive symptoms in spring compared to the other seasons. The same pattern was visible in the separate 'seasonality-related' questions of the QIDS (with the exception of weight change and increased appetite): respondents felt less sad, slept less, had more energy, in general had more interest in spring compared to the other seasons, mainly autumn and winter.

Second, we selected a subgroup of 503 respondents who filled in the questionnaires twice. We found no within-subject seasonal differences in the scores of positive and negative affect in this group of respondents, not for respondents who filled out the questionnaires in different seasons, nor for respondents who filled out the questionnaires in the same season.

On the basis of the results of our previous studies, we also tested whether neuroticism was a moderator variable in the relation between the seasons and positive and negative affect variables. In the group of respondents who completed the questionnaires once, we found that the personality factor of neuroticism moderated the effect of the seasons in the three outcome variables (positive affect, negative affect, and depressive symptoms). More specifically, only the group of respondents classified as high-neurotic showed higher scores on the positive affect and lower on depressive symptoms in spring compared to autumn and winter. Neuroticism did not moderate within-subject seasonal differences in the group of respondents with repeated measures. All effect sizes were small or very small.

We can summarise the main findings of this study as follows: On a population level, the seasons influence positive affect in a similar way to negative affect and depressive symptoms. Spring seems to be the best season, with respondents reporting higher positive affect and lower negative affect compared to the other seasons. However, effect sizes are small, and the seasonal differences are found only in high-neurotic respondents, not in low-neurotic respondents. There were no seasonal differences in scores on positive and negative affect for respondents who completed the questionnaires twice.

Limitations and Strengths

The most important limitations of this thesis are the cross-sectional design of the first three studies, and as a consequence, the absence of longitudinal measurements within the same individual for all four seasons. Seasonal variation in mood and behaviour as well as in clinical symptoms and syndromes are longitudinal and cyclic phenomena by nature. Thus, multiple, seasonally repeated, measures during a long-term follow-up period (years) within individuals are more suitable for assessing the course of seasonal mood variation and winter depression than cross-sectional methods. Another limitation is that the diagnosis of seasonal affective disorder (winter-type) in the second and third studies relied on the assessment of the SPAQ and not on the more restrictive DSM-IV criteria of a recurrent depressive disorder with a seasonal pattern. The DSM specifier requires full remissions at a specific time of year, whereas the SPAQ asks for differences in symptom levels between the seasons. The SPAQ is known to be a useful screening instrument for seasonal affective disorder (SAD), but tends to overestimate the prevalence of SAD[9,10]. The SPAQ is also vulnerable to recall bias because it is a self-report questionnaire[11-14]. As we conclude from our studies, erroneous cognitive attribution of symptoms to the seasons may have attributed to the effect of recall bias. Another limitation is that in the NESDA studies, the naturalistic design may have masked treatment effects of the depressive and anxiety disorders. Finally, selection bias may be present because data were not primarily collected to answer the research questions of the studies.

Strengths of the studies were the large sample sizes and the diagnostic procedures based on standardised structured interviews (NESDA) and validated instruments (NESDA and HND). Other strengths were the inclusion of patients with a varying severity of psychopathology in the first three studies (NESDA), and the use of population data with repeated measures in the fourth study (HND)[15,16].

General Discussion

Summary of Findings

Our first study showed that seasonal differences in severity or type of depressive and anxiety symptoms were absent or small in effect size in a primary-care population and patient populations with a major depressive disorder and anxiety disorders. In our second study, we found an increasing percentage of self-attributed seasonality of depressive symptoms depending on the severity of patients' psychopathology. In our third study, we found that patients with seasonal affective disorder scored high in terms of psychopathology in the previous year, just as patients with a lifetime of bipolar disorder and patients with a lifetime of comorbid anxiety and depressive disorder. Patients suffering from a seasonal affective disorder also scored high on neuroticism. Remarkably, the seasonal distribution of major depressive episodes was not different for patients with or without seasonal affective disorder. In our fourth study, we found that spring is the best season with higher scores on positive affect, and lower scores on negative affect compared to the other seasons. These seasonal differences were only seen in high-neurotic respondents, not in low-neurotic respondents, and effect sizes were small. There were no seasonal differences in scores on positive and negative affect for respondents who completed the questionnaires twice. The most critical limitations were the absence of a longitudinal study design with multiple (seasonal) measurements of mood, behaviour, and personality within individuals, and the use of the SPAQ instead of DSM-IV criteria for diagnosing seasonal affective disorder.

Seasonality in Somatic Diseases

Many acute infectious diseases, such as influenza and hepatitis A, show a typical window of occurrence, which may vary depending on geographic location and differ from other diseases in the same area[17]. This seasonality is easily recognized by the public and may even lead to a designation like "flu season", but the mechanisms underlying the seasonality of infectious disease are not fully understood[18]. Martinez describes broad categories of seasonal drivers among which are environmental factors (e.g. vector seasonality, seasonal climate), host behaviour (e.g. seasonal behaviour and contact rate), host phenology (e.g. annual cycles of migration, cycles of metabolism), and exogenous biotic factors (e.g. algal density in water). Some allergies, like hay fever show seasonality[19]. Schrijver et al. described seasonality in a large sample of Dutch paediatric patients and concluded that seasonality occurs in more than one-fifth of patients with paediatric diseases. This study demonstrated seasonality in respiratory tract infections, gastroenteritis, and asthma, but also in functional complaints (abdominal pain and headache)[20].

Seasonality in Mental Disorders

As described in Chapter 1, studies on seasonal variations in the prevalence of different types of mental disorders in the general population show diverging results. On the one hand, studies in the general population using general (semi-)structured interviews or questionnaires do not demonstrate a seasonal

pattern for different categories of mental disorders [21-23]. On the other hand, studies using more specific questionnaires or performed in specific patient populations do report seasonal differences for a variety of mental disorders, like depressive disorders, anxiety disorders, eating disorders and alcoholism[24-29]. Wirtz-Justice et al. found a prevalence of 3.4% of repeated winter major depressive episodes in a prospective cohort study in Switzerland, using comprehensive diagnostic interviews. However, the period between the 5 measurements was 20 years, and a recurrence rate of 2 was used to establish the diagnosis "repeated winter major depressive episodes"[30].

Heterogeneity of Depression

As described in Chapter 1, the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) builds diagnostic criteria on the description and aggregation of symptoms, severity, and course of the condition. It defines subtypes and specifiers (e.g. seasonality in depressive disorders). There is an ongoing debate about the premises of the depression concept of DSM-5, as its basis is atheoretical and so it lacks the conceptualisation of a disease with a defined aetiology, disease symptoms, disease course, and treatment options[31]. Depression and anxiety are often accompanied by disability, which is known to be predictive of clinical parameters like treatment outcome and recurrence, but the correlation with symptom severity is only moderate[32]. Diverging treatment results, partly ascribed to the non-specificity of major depression, have led to proposals for models of depressive sub-typing based on characteristics like observed symptom profiles, aetiology, time of onset, gender, duration of complaints and treatment response[33]. Ideally, subtypes should represent homogeneous groups of cases and represent different underlying pathophysiological processes allowing us to develop specific treatment strategies.

In the meantime, researchers are trying to unravel the underlying common factors driving psychopathology and disability[32,34-37]. Lamers et al. among others used latent class analysis in the NESDA cohort and identified three classes of depression: "severe melancholic class", "severe atypical class", and "class of moderate severity"[34,35]. Patten adopted a narrative review method and listed eight possible models on aetiology: "depressive disorders as chemical imbalances", "degenerative conditions", "toxicological syndromes", "injuries", "deficiency states" (e.g. a serotonin deficiency), "an obsolete category", "medical mysteries", and "evolutionary vestiges" (maladaptation to modern environments)[36]. Lahey et al. developed a hierarchical general factor model of psychopathology, and proposed a common general factor and specific internalizing and externalising factors underlying psychopathology[37].

Seasonal Affective Disorder

Seasonal Affective Disorder, winter-type (SAD), commonly named winter depression, is one of the proposed subtypes of depression with a specific aetiology as well as a specific treatment strategy[33,38]. The validity of the concept of whether SAD is a distinct depressive subtype or a seasonality trait of patients with fluctuating minor and major depression remains a matter of debate[23,30,33,39-46].

Treatment of Seasonal Affective Disorder

Light therapy is the therapy of choice for seasonal affective disorder and is recommended in the Dutch guideline for depression[9,47]. Light therapy is a non-pharmacological treatment exposing people to artificial light, with mode of delivery and form of light varying. Side effects of light therapy are generally mild and transient. Most commonly reported side effects are headaches, blurred vision and agitation. Relative contraindications for light therapy include certain retinal diseases and medications that increase retinal sensitivity to light. Light therapy may precipitate a hypomanic or manic episode in bipolar patients. The duration of light treatment is usually short (one or two weeks), and side effects are mild compared to most drugs.

As long ago as twenty years, more than 60 studies were published by researchers all over the world on the effectiveness of light therapy for SAD[9]. In a randomized controlled trial comparing light therapy and the antidepressant fluoxetine in SAD, Lam et al. found a response rate of 67% for both groups and concluded that there were no differences in outcome between the two conditions[48]. In a review of light therapy, Golden et al. found light therapy to be superior to control conditions[38]. However, they remark that most reports on the efficacy of light therapy are not based on rigorous study designs and that it is virtually impossible to create an acceptable placebo condition for light therapy. No Cochrane Review is as yet available on light therapy for newly diagnosed cases of SAD.

In a Cochrane Review on light therapy for non-seasonal depression (version 2010), Tuinainen et al., conclude that light therapy as an adjunctive treatment to drug therapy, sleep deprivation, or both has a slightly better outcome, but this effect was not significant[49]. They also remark that the quality of reporting in the studies is poor.

Though the Cochrane Database of Systematic Reviews does not contain a review on the validity of the diagnosis or treatment of SAD, it contains four striking updates for the preventive treatment of SAD (2019). The first review focuses on light therapy as a preventive intervention[50]. According to the authors, there is limited evidence for light therapy as a preventive treatment for people with a history of SAD. Methodological limitations and the small sample size of the only available study have precluded review author conclusions on the effects of light therapy for SAD.

The second review focuses on second-generation antidepressants for preventing SAD[51]. The authors conclude: "Available evidence indicates that bupropion XL is an effective intervention for prevention of recurrence of SAD. Nevertheless, even in a high-risk population, three out of four people will not benefit from preventive treatment with bupropion XL and will be at risk for harm. Clinicians need to discuss with patients the advantages and disadvantages of preventive antidepressant treatment and might want to consider offering other potentially efficacious interventions, which might confer a lower risk of adverse events." The third review focuses on the prescription of melatonin and agomelatine for preventing SAD[52]. The authors conclude: "Given the uncertain evidence on agomelatine and the absence of studies on melatonin, no conclusion about

efficacy and safety of agomelatine and melatonin for prevention of SAD can currently be drawn".

The fourth review focuses on psychological therapies for preventing SAD[53]. The authors conclude: "The evidence on psychological therapies to prevent the onset of a new depressive episode in people with a history of SAD is inconclusive. We identified only one study, including 46 participants focusing on one type of psychological therapy. Methodological limitations and the small sample size preclude us from drawing a conclusion on benefits and harms of mindfulness-based cognitive therapy as a preventive intervention for SAD."

In all four reviews, the authors also state: "Given that comparative evidence for the preventive options is limited, the decision for or against initiating preventive treatment of SAD and the treatment selected should be strongly based on patient preferences". This refers to the process of shared decision-making, which occurs when patient and clinician reach a formulation of the present problem, and discuss how to manage it, weighing the benefits and harms of the options, and considering the patients' values, preferences and circumstances[54,55].

Light Therapy and the Common Factors in Treatment

In physical therapies and psychotherapy alike very different interventions lead to comparable results when applied to patients with similar conditions[56]. The estimated variance attributed to common factors is at least 70%, whereas for specific interventions this is 8% at most, leaving an unexplained variance of 22%[56-58]. The common factors of therapies are: the change process (opportunity of ventilating the problem, providing a rationale), therapeutic qualities (empathic, socially-sanctioned healer), relationship elements (developing an alliance relationship), treatment structure (use of a therapy rationale, use of technique or rituals), and client characteristics (positive expectations)[56,59,60]. Theoretically, the placebo effect and the effect of the common factors coincide when the specific treatment and placebo are indistinguishable[61]. This means that the appealing theory of the biological origin of seasonal complaints, the corresponding rationale for light therapy, and the difficulties in creating a placebo condition for light therapy all favour the common factors of treatment, both for patients and clinicians who apply light therapy. These factors may explain the positive effects of light therapy experienced in clinical therapy.

Vulnerability to Seasonal Changes and Depression

In an attempt to explain the heterogeneity in the pathophysiology of seasonal affective disorder Young proposed the dual vulnerability model, in which the seasonal factor has a circadian mechanism with seasonal physi¬ological symptoms, while the depression factor is related to psychological vulnerability[40,62,63]. In this theory, the underlying biological vulnerability leads to physiological symptoms like hypersomnia, lack of energy, hyperphagia and weight gain. The depression factor is related to melancholic symptoms (weight loss, and insomnia) and psychological vulnerability. This psychological vulnerability then may interact with the biological factors in the onset and duration of winter depression[40].

The Physiology of Circadian and Seasonal Rhythms

Circadian rhythms and the genetic background of the biological clock are subject to intensive research. The scientific journal "Chronobiology International" is a journal dedicated to this topic. For seasonal affective disorder, the scientific discussion about seasonal fluctuations in physiology leans heavily on the knowledge of circadian (so far not seasonal) rhythms and the alignment of the master clock by the perception of light by the eye[4]. Researchers and clinicians have postulated the theory that the biological mechanism behind seasonal affective disorder is the seasonal variation of light (photoperiod), which causes shifts in the daily melatonin onset and offset, thereby influencing the sleep-wake cycle in vulnerable persons. The neurobiological research on seasonal changes focuses on brain serotonin and dopamine systems and the immune system[42,64-66]. However, so far, no certain biological markers have been found for seasonal affective disorder, nor are there any leads to finding of such markers.

Mood and the Weather

Research on the relationship between the actual weather and mood is a topic closely associated with research on the relationship between the seasons and mood. In one of their original studies on the PANAS Clark and Watson showed that actual weather variables were not significantly related to mood[67]. According to Clark and Watson, the relation found between reported rain and mood was due to recording bias on the part of the subjects. Denissen et al. found no effect of weather parameters (e.g. temperature, wind, sunlight, photoperiod) on positive affect and only a small effect of weather parameters on negative affect[3]. Denissen et al. concluded that their study goes against the commonly held conception that weather exerts a strong influence on mood. In contrast, Sarran et al. found that the variable sunshine duration, for both the current and previous week, and global radiation for the previous week, are significantly linked to SAD symptoms[68]. In a study on the relationship between mood, actual weather, and time spent outdoors, Keller et al. found a positive interaction effect between the time spent outdoors, mild weather conditions, and mood as measured with the PANAS[2].

Psychological Vulnerability in Seasonal Affective Disorder

The dual vulnerability model does not explicate what psychological process may constitute the psychological vulnerability of SAD patients, but negative automatic thoughts, rumination, negative attribution style, and dysfunctional attitudes are thought to contribute,[69].

Personality traits are relatively stable individual characteristics, expressed in mood, cognition, behaviour, and interpersonal relations. Neuroticism is one of five personality dimensions and consists of sensitivity for negative stimuli. Neuroticism and depression are related, but the direction of the relationship is complicated. Neuroticism is a vulnerability factor for developing depressive and anxiety disorders[70,71]. It predicts both first and recurrent episodes of depression, and a change in depressive state predicts a change in neuroticism[72-75]. Meesters also discussed that the seasons may influence the scores on neuroticism scales in patients with SAD[75].

In our third study, we found that patients with SAD scored higher on neuroticism than patients with a lifetime depressive disorder[7]. Other studies describe that SAD patients score higher on neuroticism than persons from the general population but lower than non-seasonal depressed patients[74,76]. Linjegaerde et al. found the personality dimensions to be poor predictors of improvement after light therapy but saw a tendency that patients rating themselves high on the personality inventory, are the ones that experience and report the greatest improvement after light therapy[74,76]. Bagby et al. found no differences on neuroticism between SAD patients and non-seasonally depressed patients, measured during the acute depressive episode, but found higher scores on the openness dimension for SAD patients. They concluded that SAD patients may be a subgroup of depressed patients who are more imaginative, more emotionally sensitive and likely to entertain unconventional ideas[77].

The Attraction of the Concept of Seasonal Affective Disorder

There is still a debate going on about the validity of the diagnosis of SAD as a subtype of depression[23,30,33,39-46]. Arguments against the concept are: (1) Seasonality of depressive symptoms in patient populations is inconclusive and, if present, probably due to multiple causes[7,29]. (2) In longitudinal research, the majority of patients show a non-seasonal pattern of depressive episodes[4,78]. (3) There are no specific biological markers for the condition. (4) It is not possible to distinguish the specific treatment effect of light therapy (a specific form of therapy) from the common factors, because there is no placebo condition for light therapy.

Arguments in favour of the concept are: (1) Depressive disorders are recurrent. (2) If we explicitly assess seasonality of complaints, a substantial part of the general population attributes their complaints to the change of the seasons. (3) Underlying the concept of SAD is an appealing biological theory which corresponds with the collective experience of the change of the seasons. (4) Preventive therapy in the following year, which ideally starts before a major depressive episode has developed, usually follows the treatment of initially diagnosed SAD.

Seasonality of Symptoms, Mainly a Psychological Phenomenon?

We found that patients with more severe psychopathology more frequently reported seasonality of symptoms[6]. Furthermore, we found that patients in the SAD group scored high on psychopathology throughout the year but also high on the neuroticism scale[7]. It is quite possible that patients, who score high on neuroticism and have high levels of psychopathology, attribute their symptoms and unhappiness to the seasons to a greater extent than individuals with less severe complaints. The tendency to report SAD symptoms co-varies with the tendency to attribute mood fluctuations to factors beyond the individual's control, as was shown for respondents who score high on neuroticism and openness[77,79]. Rohan showed that a psychological intervention like cognitive behavioural therapy was comparably effective to light therapy in an acute episode of depression in SAD but superior to light therapy in two winters following

light therapy[80]. Thus, the psychological mechanism of cognitive attribution may play a prominent role in the attribution of complaints to the seasons[69].

Comments on the Specifier "Seasonality" in Depressive Disorders

As described in the introductory chapter of this thesis, in DSM-IV and DSM-5 seasonality is described with the specifier "with seasonal pattern", which applies to recurrent major depressive disorder and bipolar disorder. In DSM, specifiers are not intended to be mutually exclusive, and more than one specifier may be given. According to the DSM-5 "specifiers provide an opportunity to define a homogenous subgrouping of individuals with the disorder who share certain features and convey information that is relevant for the management of the individuals' disorder"[81]. The specifier "seasonality" was introduced in DSM based on expert opinions of clinicians diagnosing patients with SAD and treating them with light therapy. However, so far, no longitudinal studies have been performed assessing the validity (and temporal stability) of this specifier. The studies in this thesis suggest that the factor neuroticism has a considerable influence on the seasonal factor.

Conclusion

This thesis shows that on a group level seasonal variation in depressive symptoms, positive and negative affect is absent or limited in effect size. These findings hold for healthy controls and for patients who suffer from a depressive disorder (with or without a comorbid anxiety disorder) but, unexpectedly, also for patients suffering from a seasonal affective disorder. Second, as the severity of psychopathology increases, significantly more patients attribute their complaints to the change of the seasons. Third, patients suffering from seasonal affective disorder score high on psychopathology and a neuroticism scale. Fourth, on a population level, seasonal variation in positive and negative affect and depressive symptoms is mainly contributable to high-neurotic persons.

Based on the literature and our studies, we infer that the psychological mechanism of cognitive attribution is an underestimated factor in the aetiology of seasonal affective disorder. Finally, we conclude that seasonal affective disorder may be a conflation of recurrent depression and neuroticism with a subjectively perceived worsening of symptoms in the winter months.

Clinical Implications

A practical implication of this thesis is that clinicians should take into account that the time of year influences the perceived feelings of well- and ill-being of their patients. For patients who present themselves with seasonal fluctuations of physical and emotional complaints, the diagnosis of depression with a seasonal component should be considered. It is essential to rule out seasonally-linked psychosocial stressors that more likely explain the pattern (e.g. seasonal unemployment or school schedule). As in all cases of patients presented with a depressive disorder, underlying somatic problems should be diagnosed

and treated accordingly. Taking into account the personality structure (including the cognitive style), and beliefs the patient holds about the cause of the depressive disorder, the process of shared decision-making can be started. Follow-up consultations without initiating specific therapy, waiting for remission of symptoms in springtime, is a possible line of conduct. If therapy is required, light therapy is recommended, given the short duration of the therapy and the relatively mild side-effects. Alternative options are bupropion medication and cognitive therapy. It is crucial to monitor the symptoms and the course of the depressive disorder and switch to alternative treatment options if the depressive complaints last.

Light therapy, the antidepressant bupropion and cognitive therapy are also recommended for preventing recurrence of depressive episodes in SAD. It is essential to bear in mind that according to recent Cochrane Reviews, evidence for preventive treatment is limited, and the treatment selected should be firmly based on shared decision-making which leaves ample opportunities for patient preferences[50-53]. As argued in the discussion section, the patient's perspective and preferences are part of the common factor, which influences the outcome of therapies. Finally, although scientific questions about the validity and specificity of seasonal affective disorder and light treatment exist, it is essential to realize that careful clinical diagnostic assessment (ruling out underlying somatic pathology and considering differential diagnoses), followed by administering an appropriate therapy in a clinical setting is the cornerstone of clinical practice and an essential part of the common factor as well.

Future Research

First, and very importantly, we recommend validation studies for the specifier of seasonality in DSM diagnoses for depressive and bipolar disorder. For future research on seasonality of mood and behaviour, we recommend a longitudinal repeated measures approach with measurements of symptoms and syndromal diagnoses in all seasons. We also recommend including a validated measure of personality and cognitive style. On the basis of the literature, we also recommend including the actual weather conditions and the time spent outdoors at the time the questionnaires were completed. Our hypothesis then might be that the personality factor neuroticism, cognitive style, and time spent outdoors have a more significant influence on mood and behaviour than the actual weather conditions, the seasons, and possibly even the specific effect of light therapy.

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