Light upon seasonality

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CHAPTER 1

Introduction
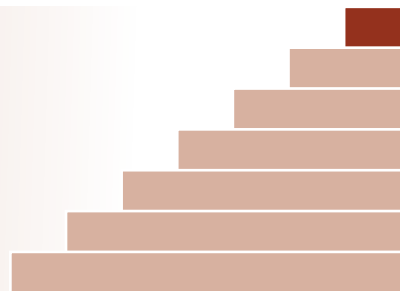
Preface

Seasonal rhythms are evident throughout nature. All humans have a varying degree of awareness of seasonal changes and are directly or indirectly affected by these changes. Based on their experiences, humans have acquired collective wisdom about the periodicity in nature and have adapted to the seasonal changes in their agricultural and economic activities as well as in the organisation of their social life.

In the present era, the biological mechanisms of circadian and seasonal rhythms in plants, animals and humans are subject to a growing body of scientific research. The earth's rotation around its axis leads to the day-night cycle. This cycle affects all life on earth and has a strong influence on human and animal physiology and behaviour[1]. For example, physiological rhythms depending on the time of day can be observed in the human sleep-wake cycle and related fluctuations of body temperature and blood plasma cortisol levels. Researchers have found circadian clocks, regulating day-night rhythms in most body tissues. These so-called "peripheral clocks" are synchronised by the "central" or "master clock" located in the hypothalamic suprachiasmatic nucleus. This central clock contains neurons that generate circadian rhythms and is influenced by environmental circadian cues like the transition from night to daytime.

A year is typically divided into seasons, with each season having its own characteristic amount of daylight, weather conditions and ecology, depending on the global position of the region[2]. The earth's orbit around the sun and its axial tilt relative to the ecliptic plane lead to an increased and decreased exposure to sunlight which is most pronounced in the polar and subpolar regions[3]. Spring, summer, autumn and winter are the common seasons in temperate and subpolar regions. Depending on the hemisphere (Northern or Southern) these seasons occur in different months of the year (e.g. winter in December, January and February in the Northern Hemisphere, and in June, July and August in the Southern Hemisphere). Tropical regions usually have two seasons: the wet season and the dry season[4].

As in all areas of human life, there are both widespread beliefs as well as scientifically-based discussions about the impact of the seasons on human well-being and illness. The doctrine that seasonal changes influence human health goes back to ancient Chinese, Indian and Greek cultures. The Hippocratic Collection describes medical theories about the influence of the weather and the seasons on the four body humors (in particular phlegm and bile) and, closely related, on the elementary qualities of hot/cold and moist/dry[5]. In this context, mental problems like melancholia are also reported[6]. However, in "Epidemics I and II" of the Hippocratic Collection, the authors seemed primarily interested in the prognostic effect of weather conditions, and hence in the relationship between the weather in one season and the occurrence of diseases in a subsequent season[5]. The seasonal impact is well-established and recognised in somatic diseases, especially infectious diseases such as influenza and some allergies[7-10]. In the general population, the seasonal impact on the mental well-being of humans and seasonal changes in mood and behaviour are considered common and are thought to cause complaints and even illnesses[11].

In this thesis, we try to answer to what extent mood, anxiety and behaviour of respondents in the general population and different patient groups are affected by the seasons.

* derived from Latin "circa" and "dies", meaning "about a day"

The burden on society of depressive and anxiety disorders

Epidemiological population studies show that mental problems are a significant health problem with an important impact on health service use and cost[12,13]. In a review of the economic impact of mental illness, Doran and Kinchin underline the significant burden mental illness places on all facets of society[14]. In their review, they conclude that mental illness results in a higher likelihood of dropping out of school, a lower probability of gaining full-time employment and reduced quality of life[14]. Based on Canadian research, they report that the total economic cost associated with mental illness will increase six-fold over the next 30 years. In 2017 mental health cost amounted to 6.9% (6.7 billion euros) of total health care in the Netherlands[12].

The loss in health and functioning at the population level can be quantified by multiplying the prevalence of the disorders with the average disability level associated with them, to give estimates of Years Lived with Disability (YLD). In 2017 the United Nations World Health Organization (WHO) published a report titled "Depression and Other Common Mental Disorders" based on the set of Global Health Estimates for 2015[15]. In this report, data on common mental disorders refer to two main diagnostic categories: depressive and anxiety disorders. Depressive disorders include two main subcategories: major depressive disorders and dysthymia. Anxiety disorders refer to generalized anxiety disorder, panic disorder, phobias, social anxiety disorder, obsessive-compulsive disorder and post-traumatic stress disorder. The most important reason to report on these conditions as a group is that they often occur sequentially in the same patient and show high comorbidity rates with more severe symptoms, higher levels of disability, and longer duration in patients suffering from both conditions simultaneously[16].

The WHO estimates that at a specific point in time (point prevalence), 4.4% of the global population will suffer from depressive disorders and 3.6% from anxiety disorders[15]. Depressive and anxiety disorders are more common among females (5.1% and 4.6%, respectively) than among males (3.6% and 2.6%, respectively). Globally, depressive disorders are the most significant contributors to non-fatal health loss (7.5% of all YLD), with anxiety disorders ranking as the sixth contributor to non-fatal health loss. Suicide, which can be the outcome of severe depression, accounts for 1.5% of all deaths worldwide. In all age groups, suicide is among the top-20 leading causes of death. In young people (15-29 years), it is the second leading cause of death.

In 2015 the WHO estimated the point prevalence of depressive disorders in the Netherlands at 4.7%, with a disease burden of 7.1% of total YLD[15]. The estimated prevalence of anxiety disorders was 6.4%, with a disease burden of 5.3% of total YLD.

The Dutch psychiatric epidemiological population studies NEMESIS-1 and 2 (Netherlands Mental Health Survey and Incidence Study) provide data on the prevalence, incidence, course and consequences of mental disorders, and for the Dutch population study the trends in mental disorders and health service use[13,17]. The lifetime prevalence of mood disorders was 20.1% and of anxiety disorders 19.6%, meaning that 1 out of 5 people suffer from a depressive or anxiety disorder at least once in their life. The 12-month

incidence for these disorders was 6.1% and 10.1% respectively, meaning that over the previous year, 1 out of 16 and 1 out of 10 suffered from depressive or anxiety disorder. In the period between 1997 and 2009 (NEMESIS-1 and NEMESIS-2), the 12-month incidence of mental disorders did not change significantly.

Depressive and anxiety disorders in DSM-IV and DSM-5

The American Psychiatric Association's "Diagnostic and Statistical Manual of Mental Disorders" (DSM) is a categorical classification system of mental disorders with associated criteria designed to facilitate a common language and reliable diagnoses for clinical practice and research in the field of psychiatry[18,19]. Since the publication of DSM-III a mental disorder has been defined as: "a syndrome characterized by clinically significant disturbance in an individual's cognition, emotion regulation, or behaviour that reflects a dysfunction in the psychological, biological or developmental processes underlying mental functioning." DSM builds diagnostic criteria on the description and aggregation of symptoms, severity and course of the condition. It defines subtypes and specifiers. Specifiers (such as seasonality in depressive disorders) are not intended to be mutually exclusive or exhaustive, and as a consequence, more than one specifier can apply to a DSM classification.

In the current fifth edition of DSM depressive disorders in adults include major depressive disorder, persistent depressive disorder (dysthymia), premenstrual dysphoric disorder, substance/medication-induced depressive disorder, depressive disorder due to another medical condition, other specified depressive disorder and unspecified depressive disorder. The core symptoms of the depressive disorder are the presence of a sad, empty or irritable mood, or the loss of pleasure in almost all activities. A depressive disorder is diagnosed when these symptoms are accompanied by cognitive and somatic changes affecting the capacity to function in everyday life. The timing and duration of the condition, as well as its presumed aetiology, differ among depressive disorders. The diagnostic code for major depressive disorder is based on whether this is a single or recurrent episode, current severity, presence of psychotic features and remission status. Specifiers for depressive disorders include: with anxious distress, with mixed (manic or hypomanic) features, with melancholic features, with atypical features, with psychotic features (mood-congruent and mood-incongruent), with catatonia, with peripartum onset, with seasonal pattern (in recurrent major depressive disorder), in partial or full remission and with a level of severity designated as mild, moderate or severe. In the course of bipolar disorders depressive episodes may also occur. In DSM-5 bipolar disorders are classified as a distinct category.

Anxiety disorders in adults in DSM-5 include specific phobia, social phobia, panic disorder, agoraphobia, generalized anxiety disorder, substance/medication-induced anxiety disorder, anxiety disorder due to a medical condition, other specified anxiety disorder or unspecified anxiety disorder[18,19]. Anxiety disorders are characterised by excessive fear and anxiety with related behavioural disturbances. Fear is defined as an emotional response to a real or perceived threat. The anticipation of a future threat is called anxiety.

Anxiety disorders differ in the types of situations or objects inducing anxiety or fear with the associated cognitions and avoidance behaviour.

In contrast to DSM-IV, in DSM-5, obsessive-compulsive and related disorders and trauma- and stressor-related disorders are in a separate category from anxiety disorders.

Defining seasonality in mood and anxiety disorders

Studies on seasonal variations in the prevalence of different types of mental disorder in the general population show different 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 disorder[20,21]. 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[22-26]. Most studies focus on the seasonal recurrence of depressive episodes. Prevalence rates of mood (affective) disorders with a seasonal pattern range from 1% to as much as 12%, depending on the diagnostic criteria used[27].

Seasonal affective disorder and subsyndromal seasonal affective disorder

The majority of research on seasonality focuses either on the general population or on a highly selected patient population consisting of patients suffering from a seasonal affective disorder. In the literature, the seasonal recurrence of depressive episodes has been designated as "seasonal affective disorder" and "subsyndromal seasonal affective disorder" for milder forms. Rosenthal and Kasper developed the Seasonal Pattern Assessment Questionnaire (SPAQ), and derived diagnostic criteria for these sub-types of depression[28,29]. A Dutch general population study of 5356 randomly selected subjects using the Seasonal Pattern Assessment Questionnaire reported a one-year prevalence of 3% for winter seasonal affective disorder and 8.5% for subsyndromal seasonal affective disorder[30].

In DSM-IV and DSM-5 seasonality is defined with the specifier "with seasonal pattern", which applies to recurrent major depressive disorder and bipolar disorder. The most important feature is a regular temporal relationship between the onset of major depressive episodes and a particular time of year (e.g. autumn or winter)[18,19]. Full remissions must also occur at a specific time of year (e.g. the depressive episodes disappear in spring). For bipolar disorder, this also applies to manic and hypomanic episodes. Other features are that in the last two years two major depressive episodes demonstrating the seasonal relationship must have occurred. Further, no non-seasonal major depressive episodes may have occurred during that same period. Over the individual's lifetime, the seasonal depressive episodes must substantially outnumber the non-seasonal major depressive episodes. Finally, an apparent effect of seasonally-related psychosocial stressors must be absent (e.g. being unemployed every winter). Symptoms often accompanying major depressive episodes with a seasonal pattern are noticeable lack of energy, hypersomnia, overeating and weight gain.

Recurrent major depressive disorder with a seasonal pattern has repeatedly been associated with the specifier of atypical features, which can be contrasted to melancholic features[31,32]. The core element of the atypical features specifier is mood reactivity (mood brightens in response to positive events) and it has to be accompanied by two or more of the following: significant weight gain or increase in appetite, hypersomnia, leaden paralysis (heavy feeling in arms or legs), and a pattern of interpersonal rejection sensitivity resulting in social or occupational impairment. The melancholic features specifier includes loss of pleasure in (almost) all activities or non-response to normally pleasant stimuli. They have to be accompanied by three or more of the following: a mood characterised by despair, moroseness or emptiness, a worse mood in the morning, early morning awakening, psychomotor agitation or retardation, significant weight loss or loss of appetite, inappropriate feelings of guilt.

Aim of this thesis

The overall objective of this thesis is to explore the association between the seasons and the affective states of respondents in samples of the general population, primary care, and specialised mental health care. In these groups, we have investigated to what extent anxiety, mood and behaviour are affected by the seasons.

The cohort studies used in this thesis

This thesis builds on data from the Netherlands Study of Depression and Anxiety (NESDA) and the internet-based study HowNutsAreTheDutch (HND)[16,33]. NESDA is an ongoing multi-site naturalistic longitudinal cohort study of 2,981 adults (18-65 years), aimed at describing the long-term course and consequences of depressive and anxiety disorders. The NESDA sample is stratified for setting: community, primary care and specialised mental health care. HND (Dutch: HoeGekIsNL) is a national internet-based crowdsourcing study designed to investigate the associations and dynamic interactions between mental strengths and vulnerabilities, both between and within respondents, in a sample from the Dutch general population[33]. In this project, individuals were invited to visit the website www.hownutsarethedutch.com and to give a self-assessment on several domains of mental health.

Outline of this thesis

In **chapter 2**, we determine whether seasonal variation exists in the severity and type of depressive and anxiety symptoms in general and in patients with a depressive or anxiety disorder. More specifically, we look for answers to the following questions: (1) Does a seasonal pattern exist in the severity of depressive and anxiety symptoms in patients visiting their general practitioner for any reason? (2) Does a seasonal pattern exist in the type (i.e. atypical or melancholic) and severity of depressive symptoms and anxiety symptoms in patients with a current depressive and/or anxiety disorder and healthy controls?

In **chapter 3** we examine potential differences in the seasonality of symptoms between patients with

a lifetime diagnosis of a depressive and/or anxiety disorder and healthy controls by administering the Seasonal Pattern Assessment Questionnaire (SPAQ), a self-rating screening instrument measuring variation in mood and behaviour retrospectively on a monthly basis.

In **chapter 4** we compare the clinical, demographic and personality characteristics of patients with a seasonal affective disorder (SAD), according to the SPAQ, with patients suffering from non-seasonal affective disorders (non-SADs) and healthy controls (HC). Prior to this, the prevalence of SAD and sub-SAD among the patients has been assessed, and it has been recorded to what diagnostic groups according to the DSM criteria they belong. We then zoom in on patients with SAD and patients with a lifetime of depressive disorder or a lifetime of comorbid anxiety and depressive disorder. Their clinical characteristics and the seasonal distribution of the scores on a depression questionnaire and two anxiety questionnaires have been compared. Finally, the seasonal distribution of depressive episodes in patients with and without SAD has been compared.

In **chapter 5**, it is noted that most studies only measure negative affect (complaints), but not positive affect. The research question is formulated of whether the seasons equally influence positive and negative affect. This is analysed in two separate groups: a group of respondents who have completed the questionnaires once and a group of respondents who have completed the questionnaires twice. Finally, a test is performed of whether the personality trait of neuroticism moderates the relation between the seasons and positive and negative affect.

In **chapter 6**, we summarise general conclusions and discuss the strengths and limitations of our studies. Additionally, we make some remarks on clinical consequences derived from our studies and finish with recommendations for further research.

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