

# 1

## An Introduction to Schizophrenia

Hugo A. Jørgensen and Erik Johnsen

**Abstract.** The present chapter is a condensed introduction to schizophrenia as a severe mental illness. The condition is placed both in a historical and in an updated diagnostic context with regards to the characteristic symptoms and clinical features. The common belief that the occurrence of schizophrenia is the same around the world is challenged by an overt variation in reported incidence and prevalence. Environmental and genetic risk factors are briefly discussed and examples of their interaction given. The changes in brain structure and function are discussed in relation to psychosocial strain and stress and in relation to the stress-vulnerability model considered to be an integrative way of understanding the premises for the functional outcome.

**Keywords:** schizophrenia, symptoms, epidemiology, risk factors, neuropathology

Schizophrenia (literally: splitting of the mind) is a clinical syndrome with severe psychopathology within several domains including cognition, emotion, and behavior. For more than a hundred years, divergent concepts have been discussed. Today, schizophrenia is classified descriptively according to criteria outlined by either the World Health Organization (1992) or the American Psychiatric Association (1994). The two systems have developed to be quite similar (see Table 1a and Table 1b) but there are some differences.

ICD-10 emphasizes the character of the symptoms and DSM-IV gives weight to course and functional impairment. The present concept(s) of schizophrenia delineates a group of patients that is heterogeneous with respect to the extent of psychopathology, impairment of function and ability to manage a role in society. Some will suffer from one episode and be able to manage their lives after recovery, others will have several relapses with autonomous function in between, but the majority will need treatment and support more or less continuously for the rest of their lives.

The main clinical features consist of delusions, hallucinations, and thought disturbances, often called positive symptoms; and lack of drive, slowness, paucity of speech, blunted emotional responses, and social withdrawal, often called negative

# 2

## Schizophrenia: What Do We Know from Neuroimaging Research?

Maurits van den Noort and Peggy Bosch

**Abstract.** Nowadays, several neuroimaging techniques are available for the assessment of human brain function. The application of these techniques in schizophrenia research has facilitated the investigation of critical questions regarding disturbances of higher brain function and provides an opportunity to attempt to elucidate the pathophysiological basis of the disorder (Honey & Bullmore, 2002). This chapter summarizes the main neuroimaging findings in the field of schizophrenia. Although it can be concluded that the development of neuroimaging techniques has provided the technological advance necessary to examine schizophrenia, the scientific challenge for future research will be to incorporate these techniques appropriately through good experimental design.

**Keywords:** schizophrenia, ERP, PET, SPECT, (f)MRI

### Introduction

Clinicians and researchers have long believed that there is something fundamentally abnormal about the working of the brain in people with schizophrenia (Zakzanis, Poulin, Hansen, & Jolic, 2000). As a result of rapid technological development in recent years, several functional imaging techniques are now available for the *in vivo* assessment of human brain function (García-Alloza & Bacskaï, 2004). The application of a particular imaging technique is determined by the researcher's clinical question, and there are several advantages and disadvantages to each of the techniques available, which must be taken into account (Honey & Bullmore, 2002). We will now briefly discuss the main neuroimaging techniques that are used in schizophrenia research.

# 3

## The Pharmacotherapy of Schizophrenia: Past, Present, and Possible Future

Bart A. Ellenbroek

**Abstract.** Although the first description of schizophrenia as a disease (or a group of diseases) by Eugen Bleuler was made in the beginning of the last century, the etiology and neuropathology still largely remain a mystery. Nonetheless, mostly serendipitously, we now have a large armature of pharmacological tools to treat the symptoms of this devastating disorder. These so-called antipsychotic drugs are often subdivided into classical and atypical antipsychotics on the basis of their potential to induce extrapyramidal side effects, but recent studies have questioned this distinction and the drugs are now often referred to as first generation and second generation antipsychotics. These drugs preferentially reduce the positive symptoms of schizophrenia, such as hallucinations and delusions, but have little or no effect on the negative and cognitive symptoms, with the possible exception of clozapine. Although the blockade of dopamine receptors (especially the D<sub>2</sub> receptors) certainly plays a crucial role in the therapeutic effects of antipsychotic drugs, the finding that patients resistant to one antipsychotic often respond to another indicates that other, as yet unknown, neurotransmitter receptors are also involved. The lack of efficacy of the current antipsychotic drugs on negative and cognitive symptoms has led to a multitude of strategies to develop novel, more efficacious drugs. The next decade will show the success or failure of these strategies as more and more drugs without a dopaminergic component will be evaluated in large clinical studies.

**Keywords:** schizophrenia, pharmacotherapy, antipsychotic drugs, cognitive symptoms, positive symptoms

### Introduction

Schizophrenia, or more accurately the group of the schizophrenias, was first described by Eugen Bleuler at the beginning of the last century. Bleuler described a disease that was already recognized by Emil Kraepelin at the end of the 19th cen-

# 4

## Treatment of Patients with Schizophrenia in Practice: Emphasizing Early Warning Symptoms

Dick J. Brouwer, Annita Bosveld, Ineke van der Lans, and Dzelal Dani

**Abstract.** Some people experiencing an episode of mental illness may fully recover and never have any further episodes. However, a large number of people will experience another or a number of episodes during their lifetime. Mostly, these patients receive pharmacotherapy and some other kind of additional therapy. An important aspect of preventing relapse has proven to be the work on early warning symptoms. Identifying early warning signs as quickly as possible means that positive action can be taken and help can come early to minimize or prevent the impact of a relapse. Early intervention has been shown to reduce the severity of symptoms, shorten the duration of relapse, and reduce the likelihood of further episodes. This chapter describes a “standard” treatment for patients with schizophrenia, with an emphasis on early warning symptoms for schizophrenia and its importance for prevention and treatment. Moreover, attention will be given to “Hearing Voices,” a project that incorporates a method to improve the way patients handle the voices that they hear.

**Keywords:** schizophrenia, early warning symptoms, relapses, questionnaires, prevention

### Introduction

Some people who experience an episode of mental illness may fully recover and never have any further episodes. However, a large number of people will experience another or a number of episodes of mental illness during their lifetime. These renewed episodes are commonly known as relapses. A relapse is the worsening or return of specific symptoms of the illness. Depending on the severity of the relapse, the person may require hospitalization, changes in medication, and further monitoring and community support. It is important to note that the ex-

# 5

## A Cross-Cultural Approach to the Diagnosis and Management of Schizophrenia

Leila Kozak, Lorin D. Boynton, Arushi Sinha, and Jacob Bentley

**Abstract.** Cultural variation in the definition of “normal” behavior and the expression of mental illness has been recognized in the existing research literature. In Western cultures, our prevalent paradigm in science and medicine is based on the premise that mind and body are separate entities. Such a paradigm influences the diagnosis and treatment of schizophrenia. Psychiatrists need to pay attention to cross-cultural issues and be aware of the cultural context in order to establish appropriate diagnosis and treatment, while at the same time they need to expand and challenge their own notions of mental health and mental illness. There is a rapidly growing trend in medicine toward the integration of complementary therapies as an adjuvant to standard-of-care treatment. It is expected that such a trend will also become evident in modern psychiatry, in which complementary therapies such as acupuncture may offer a valid tool for the co-management of schizophrenic symptoms. It is expected that the growing field of cultural psychiatry will be a fertile ground from which a new field of psychiatry, “integrative psychiatry,” may develop and flourish.

**Keywords:** schizophrenia, cross-cultural issues in mental health, integrative medicine, integrative psychiatry, medical anthropology

### “Normal” Behavior and the Expression of Mental Illness Around the World

Cultural variation in the definition of “normal” behavior and the expression of mental illness has been recognized in the existing research literature. Modern cross-cultural psychiatry refers to the way culture influences mental illness, either by shaping pathology (pathoplasticity) or causing pathology (pathogenesis) (Kulhara & Chakrabarti, 2001). In Western cultures, the prevalent paradigm in

# 6

## What is Sleep and What Can Go Wrong with Sleep?

Anton M.L. Coenen

**Abstract.** An overview on the topic of sleep is presented. Three putative functions of sleep are highlighted: the restorative hypothesis (deep sleep seems involved in body restoration), the adaptive hypothesis (sleep is supposed to make the animal inactive and quiet at times when it is dangerous to move around), and the information processing hypothesis (sleep might play a role in memory consolidation). The structure of sleep, with its main characteristics, is mentioned and detailed information is given about REM sleep: the “dream sleep.” Sleep is a circadian rhythm, coupled to darkness and body temperature. The length of the nightly sleep and cognition during sleep are discussed. Poor sleep and sleep disorders are frequently occurring phenomena and the cause of psychophysiological insomnia is indicated. Snoring and the relation to sleeping postures are reviewed, as well as sleep apnea. A description is given of continuous positive airway pressure (CPAP), an efficient treatment for sleep apnea. Also, sleep disorders like narcolepsy and restless legs are mentioned. Finally, the impaired sleep of patients with schizophrenia is emphasized, while the presumed analogous nature of schizophrenia and REM sleep closes this review.

**Keywords:** deep sleep, REM sleep, sleep functions, sleep disorders, insomnia, snoring, narcolepsy, sleep of patients with schizophrenia

### Prologue

Good sleep is of vital importance. Sleep prepares us for a properly fit and energetic start to a new day. During sleep, a physical recovery process takes place and crucial body regeneration occurs, for which the growth hormone (somatotropine) is mainly responsible. This hormone is directly coupled to sleep and ensures that the body is “refreshed” during the night. In children, this growth hormone propagates growth; in adults it is involved in the bodily regeneration process by promoting protein synthesis. This reconstructive process occurs during the early

# 7

## Sleep of Patients with Schizophrenia On and Off Melatonin Treatment: Contradictions and Hypothesis

Vadim S. Rotenberg

**Abstract.** Positive symptoms in schizophrenia decrease the requirement for REM sleep and reduce its pressure, while negative symptoms increase the need for REM sleep. This need cannot be satisfied because REM sleep in schizophrenia is functionally insufficient. This insufficiency may relate to the decreased melatonin level. Melatonin treatment restores REM-sleep functional efficiency in patients with different mental disorders, probably also in schizophrenia. There are some signs that melatonin inhibits brain dopamine systems that are active in wakefulness and that stimulate the dopamine system responsible for REM sleep-dreams sufficiency.

**Keywords:** schizophrenia, REM, melatonin, treatment

### Sleep Disorders in Schizophrenia

In this chapter I will discuss only those sleep variables that are important for the understanding of melatonin treatment outcome.

According to many investigations (Keshavan et al., 1998; Yang & Winkelman, 2006; and the previous chapter), schizophrenia is characterized by a decrease in the percentage of slow-wave sleep (SWS). Keshavan et al. (1998) emphasized that reduced delta-counts in the first non-rapid eye movement (non-REM) sleep period, reduced delta-wave accumulation in continuous non-REM minutes, and reduced delta-power suggests that a delta-sleep deficit may be related to the primary pathophysiology of illness. Unlike REM sleep alteration (see later), delta-sleep deficits are persistent. In patients with schizophrenia sleep deprivation does not cause the increase of SWS in the subsequent night sleep, which is a typical “rebound effect” seen in healthy persons (Luby & Kaldwell, 1967).

# 8

## An Introduction to Traditional Chinese Medicine

LiPing Han

**Abstract.** In this chapter, I am going to introduce the key concepts of Traditional Chinese Medicine (TCM), and delineate its fundamental differences to Western medicine. TCM as a whole has developed over thousands of years. It contains both the theoretical knowledge and practical skills for treating illness, preventing disease and preserving a state of optimal health. To understand TCM, we have to first understand its conception of the physical world and the processes of nature; this is described by the theories of yin and yang, the five element theory, and its relationship to human beings. Next we explore the inner workings of the human physiology from a TCM perspective; from the existence and relationship between the functional activities and organic substances which compose our physiological being, to the characteristics and interrelationships of the different functional systems which exist as the Zang Fu organs. Please note that TCM theory is very distinct from our Western conventional science in some of its terminology and conceptual basis. The terms used in this chapter are based purely from a TCM translation and the names of such descriptions such as organ systems and energy flow should not be confused with the literal Western definitions that share the same terminology.

**Keywords:** TCM, yin, yang, five element theory, Zang Fu organs

### What is Traditional Chinese Medicine?

Traditional Chinese Medicine (TCM) can be visualized as three main components: basic theory, clinical medicine, and preventative medicine. Basic theory can be described as the conceptual background of TCM. It consists of the theoretical knowledge distilled from the academic ideas, opinions, and practices of some of the great doctors, scholars, and practitioners over thousands of years. These conceptualizations, such as the theories of yin and yang, five element, and qi, provide the theoretical foundations and guiding principles of TCM practice.



# 9

## The Philosophy Behind Traditional Chinese Medicine

Stan Switala

**Abstract.** This chapter first examines how Traditional Chinese Medicine (TCM) is viewed by the Western world and how the acronym TCM can have different meanings for different groups of people. Then we look at the history of TCM and discuss it in relation to the influence that Western civilization within China could have had on it. Further discussion examines how the distorted perspective that would be introduced to the Western world, at a time when Western medicine was making great advances into the molecular mechanisms of disease, would indeed make TCM look primitive, as it already had done to other early forms of traditional medicine. Finally there is some discussion of modern findings in quantum physics and consciousness, and how various authors have compared these to the integrated philosophy of TCM, where mental, emotional, lifestyle, and dietary factors all combine to influence health.

**Keywords:** philosophy, traditional Chinese medicine, quantum physics, consciousness, lifestyle

### Introduction

There is a lot of controversy about the philosophy, theory, and practice of Chinese medicine. Modern Western medicine has its own criteria for both thinking about and investigating other forms of knowledge. Research shows that acupuncture treatment is effective for some conditions, and that classical treatment is more effective than formula treatment. Some of the mechanisms of acupuncture have been established as a result of modern research, e.g., endorphin release and pain-gate theory. Some explanations of acupuncture activity have been established resulting in the abandonment – even ridicule – of Chinese theory and the philosophy upon which the theory is based. There is a suggestion by some authors that Chinese theory and its related philosophy are primitive and based solely on superstition. I hope to investigate these suggestions to determine what part of this

# 10

## Acupuncture Modalities, Methodology, and Key Problems for Western Scientific Research

Peggy Bosch, Brigitte Ausfeld, and Maurits van den Noort

**Abstract.** Several acupuncture techniques are now available, varying from manual acupuncture, acupuncture combined with moxibustion, electro-acupuncture (with or without needles), to laser-acupuncture. This chapter describes the different acupuncture modalities presently used in Western society in acupuncture research and practice. Moreover, the key methodological problems of acupuncture research in general – seen from a Western scientific point of view – are discussed. By simplifying some theories slightly, we make the backgrounds of acupuncture treatment and research more understandable. However, as stated in the previous chapter: There is more to it! For more detailed information, inevitable for a true understanding of acupuncture, we refer to the literature mentioned in this book. Finally, we conclude that consensus building among experts is necessary for a more accurate assessment of acupuncture.

**Keywords:** acupuncture modalities, methodology, control groups, placebo needle, sham acupuncture

### Manual Acupuncture Based on Traditional Chinese Medicine Principals

Acupuncture can be described as a technique of Traditional Chinese Medicine (TCM). It is a technique for unblocking qi by inserting needles at particular points on the body to balance the opposing forces of yin and yang (for a more detailed description see Chapter 8 and Chapter 9). Qi is an energy said to permeate all things; it is believed to flow through the body along 12 main pathways called meridians, of which there is one for each inner organ (Gallbladder, Liver,

# 11

## The Search for the Mechanism Behind Acupuncture: Research with Neuroimaging

Peggy Bosch and Maurits van den Noort

**Abstract.** In a search for the mechanism (or mechanisms) behind acupuncture from a Western point of view, we discuss neuroimaging results on acupuncture. The discovery of how acupuncture works, and how to create a solid explanation in Western scientific terms that can be verified by Western tests, has been a major quest in recent years. Finding such an explanation would create greater understanding and might possibly even stop the ridicule mentioned in Chapter 9. In the published literature so far, many results on subthemes within acupuncture were found. For example, some results indicate that acupuncture might be point-specific (e.g., Yan et al., 2005; Zhang, Jin, Luo, Zhang, Zeng, & Han, 2004), whereas others indicate that this is not the case (e.g., Campbell, 2006). Although more research is necessary on most issues, results and conclusions that can be drawn so far will be discussed. In this chapter we mostly aim to give a broad overview on what has been done in Western research to date.

**Keywords:** acupuncture, neuroimaging, limbic system, control group, point-specificity

### Introduction

Although acupuncture has been studied for a long time, the mechanism behind it remains an intriguing mystery (from a Western point of view). The discovery of how acupuncture works, and how to create a solid explanation in Western scientific terms that can be verified by Western tests, has been a major quest in recent years. Finding this explanation would create more understanding in Western society. Moreover, the abandonment and even ridicule discussed in Chapter 9 might be stopped and acupuncture might take its rightful place in modern medicine. In this quest for the mechanism behind acupuncture, some researchers

# 12

## Acupuncture and the Dopaminergic System

Sabina Lim, Seung Youn, and Chihyoung Son

**Abstract.** For decades, experimental approaches and clinical experience have suggested that a dysregulation in the dopaminergic system plays an important role within the pathophysiology of schizophrenia. But the evidence for an acupuncture-related dopaminergic mechanism in the treatment of schizophrenia is presently insufficient to inform clinicians and people with schizophrenia of its effects. This chapter aims to better our understanding of the role of the dopaminergic system in the dysregulation of schizophrenia and to explain the good results that have been found in acupuncture research on schizophrenia and sleep (insomnia). Furthermore, we would like to make the connection between acupuncture, schizophrenia, sleep, and dopamine through the Yin Heel Vessel (yīn qiāo mài) and the Yang Heel Vessel (yáng qiāo mài) that are assumed to be connected with insomnia.

**Keywords:** acupuncture, dopamine, schizophrenia, sleep, insomnia, Yin Heel Vessel, Yang Heel Vessel

### Introduction

Schizophrenia is a chronic disease of the central nervous system (CNS) characterized by disturbances of cognition and perception. The clinical manifestations are divided into positive symptoms like delusions, hallucinations, and thought disorganization; and negative symptoms such as lack of drive and lack of motivation with social withdrawal. The successful treatment with dopamine antagonists suggests a crucial role of the neurotransmitter dopamine in the pathophysiology of schizophrenia (see also Chapter 3). It was suggested that at least the positive symptomatology of the disease is related to an excess of dopaminergic transmission in the CNS.

In the meridian system, qi circulates through the 12 main meridians and the Yang Heel Vessel (yáng qiāo mài) during the daytime, and it circulates through

# 13

## Acupuncture and Sleep: Can Acupuncture Be Used in the Treatment of Insomnia and Schizophrenia?

Peggy Bosch, Anton M.L. Coenen, Bart A. Ellenbroek,  
and Maurits van den Noort

**Abstract.** This chapter provides a theoretical background on the effect acupuncture has on sleep and why it may be uniquely beneficial in the treatment of sleep disorders like insomnia (Flaws & Lake, 2001; Peterson, 2002). Acupuncture can be used alone or combined with (non)pharmacological interventions since no negative interactions have ever been found. We discuss the treatment effects on patients with sleep disorders as well as on patients with schizophrenia and sleep disorders in particular. Acupuncture increases melatonin levels, and as a result sleep is improved, something that is beneficial in patients with schizophrenia (Bosch & Van den Noort, 2006; Shamir et al., 2000). In addition, reports have shown that acupuncture has a positive effect on the overall condition in patients with schizophrenia (Dey, 1999; Kane & Di Scipio, 1979). However, more research is definitely needed because there are serious methodological limitations with these acupuncture studies on schizophrenia (Beecroft & Rampes, 1997).

**Keywords:** acupuncture, sleep, insomnia, schizophrenia, methodological limitations

### Introduction

Insomnia is defined as difficulty initiating or maintaining sleep with impaired daytime functioning attributed to poor sleep (for a more detailed description of insomnia and other sleep disorders see Chapter 6). It is one of the most common complaints brought to a physician's practice (Everitt, Avorn, & Baker, 1990). Although prevalence estimates of insomnia vary depending on the definitions and criteria used, epidemiologic studies indicate that approximately 30% to 35% of

# 14

## Traditional Chinese Medicine and Psychological Disorders

Yifan Yang

**Abstract.** Different mental disorders are often seen in the practice of Traditional Chinese Medicine (TCM). According to the theory of TCM, the mind and body are closely linked, and emotions are considered as the causative factors or triggers of many mental disorders. For mild and common cases of mental disorders, acupuncture and Chinese herbal medicine bring significant results in treatment. Together with meditation, diet, and lifestyle advice, they provide new possibilities for relieving the suffering of patients alongside present routine treatment. In this chapter, the understanding of mental disorders in TCM is briefly introduced with comments on the value of its treatment methods in daily practice. Moreover, some common symptoms in mental disorders and the treatment of these with acupuncture are discussed. These are meant as examples to familiarize the reader with the TCM perspective, they are not meant as standard treatments.

**Keywords:** Traditional Chinese Medicine, acupuncture, qi, five internal organs system, mental disorders

Mental disorders are often seen in the practice of general practitioners as well as the practice of alternative medicine. According to the theory of Traditional Chinese Medicine (TCM), the mind and body are closely linked, and emotions are considered as the causative factors or triggers of mental disorders. Many mental disorders can be treated by acupuncture and Chinese herbal medicine by strengthening and harmonizing the internal organs. Statements on the mind and its features, its disorders and methods of treatment can be found in the classical texts of Chinese medicine dating back 2000 years (Gao, 1982; He & Tan, 1998).

# 15

## Acupuncture and Moxibustion as Treatments for Schizophrenia and Sleep Disturbances

Qinzhong Ding, Junying Yan, and Yixiong Ma

**Abstract.** The traditional medicine of China, referred to below as Traditional Chinese Medicine (TCM), classifies mental diseases in four categories: withdrawal, mania, epilepsy, and feeble-mindedness. When we discuss individual patients, no matter how much difference there may be between the names of Western and Chinese classifications of mental diseases, the subject of the discussion – the patient – is still the same. So whether we say “potato” or “spud” (or if we use the Chinese words “malingshu” and “tudou”), we are still talking about the same thing. There are many reasons why we have differences in our classifications, but the main source of these differences is most likely historical and cultural (see also Chen, 2002). While Chinese medicine has an ancient source and more than 2000 years of history, modern medicine has but a little more than 100 years. With such a huge historical gap, it would seem logical that we would discuss the same thing in different ways. Yet these differences should not impede the communication between East and West, especially in scientific exchanges.

**Keywords:** Traditional Chinese Medicine, acupuncture, electro-acupuncture, qi, mental disorders

### Introduction

If we compare the classifications from Traditional Chinese Medicine (TCM) with those of modern psychiatry, we can find commonalities. For example, in TCM schizophrenia (F20 in ICD-10, World Health Organization, 2007; 295 in DSM-IV, American Psychiatric Association, 1994) is primarily categorized as withdrawal, with some involvement of mania and feeble-mindedness. More specifically, withdrawal includes schizophrenia’s positive symptoms (such as hallucinations, delusions, mental disturbances, and hostility), its negative symptoms (lack of

# 16

## Acupuncture in the Treatment of Schizophrenia: A Case Study

Patricia Ronan, Neil Quinton, and Dominic Harbinson

**Abstract.** The acupuncture treatment of a patient diagnosed with schizophrenia is outlined. The treatment, which extended over 20 weekly sessions, yielded very obvious benefits including cessation of psychotic symptoms, improved digestion and sleep, lessening of anxiety, and increased socialization. Positive lifestyle changes were instigated by the patient during the course of treatment and were seen to support treatment effects. Salient points about the realities of giving acupuncture treatment to a person with schizophrenia in the UK context are discussed, and the commonalities and differences between psychiatry and acupuncture are explored.

**Keywords:** acupuncture, schizophrenia, anxiety, Traditional Chinese Medicine (TCM), sleep

### Introduction

In the UK, there are only a few acupuncturists who specialize in mental health, and those who do tend to focus on depression and addictions rather than schizophrenia. The likely reason is that there is a little more evidence in these areas and it is less obvious that acupuncture might work for schizophrenia. It is also the case that patients with schizophrenia come for treatment of conditions not necessarily connected with this diagnosis. Here, we outline such a case, in which the patient came for treatment of anxiety and physical discomforts, without letting it be known that he was actually suffering from schizophrenia or asking for treatment for these symptoms. The patient made great improvements over the course of treatment. A surprising result was the disappearance of his psychotic symptoms after only a few treatments.