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Repetitive Transcranial Magnetic Stimulation Treatment for Depressive Disorders

A Practical Guide

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Preface

Depression is widely recognised as a common and significant problem that has a major impact on patients, their families, the health-care system and society in general. It is also widely recognised that the treatments available to date for depression have been insufficient to meet the needs of a considerable percentage of patients with this problem.

In this context, repetitive transcranial magnetic stimulation (rTMS) has been developed as a further treatment option. Considerable research efforts, undertaken by academic psychiatrists around the world for over 15 years, have clearly established the therapeutic efficacy of this treatment. Although considerable questions still need to be addressed in regard to the mechanism of action of rTMS and how best it should be applied, it clearly is able to substantially relieve depression for many patients who undergo this therapy.

In recent years, rTMS has progressively been approved for use in the treatment of depression in a substantial number of countries, and its use in clinical practice is now dramatically escalating. Clinicians throughout Europe, the USA, Canada and a number of other countries are increasingly utilising rTMS treatment in clinical practice across a variety of settings. However, only limited resources are currently available to support the widespread clinical utilisation of rTMS. There is a large and substantive academic literature exploring the use of this treatment, but this is not necessarily accessible in a timely manner to busy clinicians wishing to offer rTMS, or who, when using this treatment, are faced with new clinical problems.

This book is designed to address this gap. We aim to provide an accessible guide for clinicians in the use of rTMS treatment in clinical practice. The book aims to both summarise the scientific literature supporting the questions addressed, but also to provide succinct, accessible and clinically relevant information. The initial chapters provide background to aid the reader in understanding the science underpinning the use of rTMS treatment. We then consider in some depth specific aspects to do with the application of rTMS treatment of depression, including the safety of treatment and its potential side effects. We then describe both the evidence base for its use in the treatment of depression and the clinical considerations relevant to the selection of treatment parameters and identification of appropriate patients. In the final chapters, we address practical issues in treatment provision in the application of rTMS in other disorders.

This book is primarily written for clinicians who are considering providing rTMS treatment in clinical practice, or who are already doing so. However, we hope it will also provide a useful primer for researchers considering undertaking academic study in this area. As is illustrated in the pages of this book, considerable questions still need to be addressed as regards the optimisation of rTMS treatment in clinical practice. We are hopeful that academic exploration of this therapy will continue to address this important area.

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1.1 Introduction

Transcranial magnetic stimulation (TMS) is a unique experimental tool that allows researchers to non-invasively stimulate and study the cortex in healthy and diseased states [1] (Fig. 1.1). It has been used both as an investigational tool to measure a variety of cortical phenomena including cortical inhibition and plasticity [2, 3], as a probe to explore cognitive mechanisms [4] and as a treatment tool in illnesses such as depression and schizophrenia [5, 6]. This chapter will review the physical principles of TMS and repetitive transcranial magnetic stimulation (rTMS) and the neuronal structures activated by the techniques.

1.2 Overview of TMS Technology

In 1831 Michael Faraday demonstrated that a current was induced in a secondary circuit when it was brought in close proximity to the primary circuit in which a time-varying current was flowing. Here, a changing electrical field produces a changing magnetic field that, consistent with Faraday's law, causes current to flow in a nearby conducting material. With TMS, electrical charge is stored in capacitors. Periodic discharge of this stored energy from the capacitors and through a conducting coil produces a time-varying electrical field. This electrical field produces a transient magnetic field that will cause current to flow in an appropriately located secondary conducting material, such as neurons. If this current induced in the brain is of sufficient strength, it will produce depolarisation of the conducting neural tissue located just under the coil.

As described, electrical fields that are applied to neurons can excite these cells. The electrical field will produce a current in the intracellular and extracellular space. This causes cell membranes to become depolarised. An action potential is initiated when this depolarisation is of significant magnitude. Electrical fields experience resistance because of scalp and skull and other intermediary tissue. Magnetic fields,

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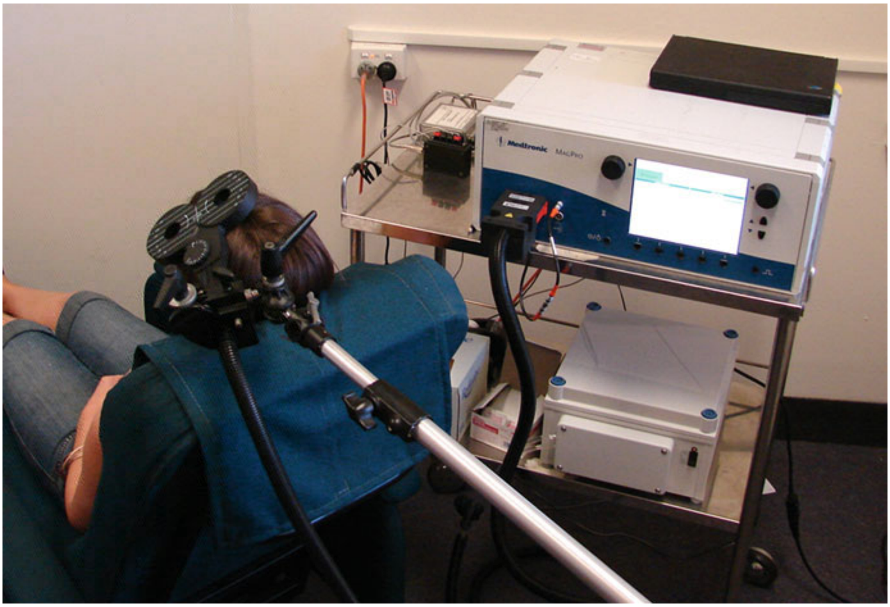

Fig. 1.1 A figure-of-8 Magstim coil held over the head in a custom-built stand. Electromyography (EMG) electrodes are placed to record muscle activity induced by stimulation of the motor cortex

by contrast, experience absolutely no resistance from the above-mentioned structures. The magnetic field strength, however, is significantly reduced in relationship to the distance between the stimulation target and the magnetic source. The circuit involved in TMS includes a capacitor, a thyristor switch and a coil. Charge and discharge of the capacitor are coordinated by the thyristor switch which acts as a gate for conduction of the electrical field through the coil. The field that is subsequently produced is either monophasic or biphasic. This difference depends on the properties of the circuit that is used.

Commercially available stimulators produce two pulse types: a biphasic pulse or a monophasic pulse. A biphasic pulse is sinusoidal and is generally of shorter duration than a monophasic pulse, which involves a rapid rise from zero, followed by a slow decay back to zero. In commercially available stimulators, several types of coils are typically used. These include circular and figure-of-eight-shaped coils. In general, figure-of-eight-shaped coils produce a stronger more focused magnetic field with better spatial resolution of activation compared to circular coils [7]. In contrast, circular coils tend to produce larger and deeper fields. This may be preferred when the neuroanatomic target is not precise. Iron-core coils are advantageous in that they tend to require less power to produce strong magnetic fields and, as a corollary, generate less heat [8]. By contrast, more traditional round or figure-of-eight copper coils generate significant heat that increases as more pulses are delivered. Two methods are used to dissipate this heat. Air can be used to effectively dissipate heat and many commercially available stimulators are indeed air-cooled.

One drawback to air cooling is the loud noise of the air compressor. Liquid cooling can also be used. In this method the liquid helps dissipate the heat by surrounding the coil, allowing for rapid heat exchange from the copper wiring to the liquid which is contiguous but not in direct contact with the coil. The H-coil is a much newer type of coil with multiple coil windings developed to generate greater depth of penetration. For example, whilst conventional figure-of-eight coils lose 50 % of their magnetic field strength when the target is more than 2 cm from the stimulator, the H-coil is able to generate sufficient field strength at 6 cm [9]. This may be advantageous given the role of deeper cortical structures (e.g. the dorsal anterior cingulate and subgenual cingulate) in the pathophysiology of depression.

By and large, in small figure-of-eight-shaped coils, neurons are activated in a cortical area of approximately 2–3 cm^2 and to a depth of approximately 2 cm [10]. In most studies, figure-of-eight coils are held over the cortex flat and at about 45° from the midline position, perpendicular to the central sulcus. This induces a current from posterior to anterior direction, perpendicular to descending pyramidal neurons and parallel to interneurons, which modulate pyramidal cell firing [11]. It is the orientation between the coil and underlying neural tissue that allows researchers to selectively activate different groups of neurons providing useful information regarding neuronal inhibition, excitation and connectivity.

1.3 Overview of Repetitive TMS (rTMS) Technology

Repetitive transcranial magnetic stimulation (rTMS) involves stimulation of the cortex by a train of magnetic pulses at frequencies between 1 and 50 Hz, in contrast to single-pulse TMS in which the frequency of stimulation is <1 Hz [12]. Higher frequencies can be achieved because the bipolar stimulus, as opposed to a unipolar stimulus, is shorter and requires less energy to produce neuronal excitability. Thus, capacitors can charge and discharge rapidly, thereby achieving high stimulation rates. It is the ability to achieve such high stimulation rates that has made rTMS a valuable tool in investigation and treatment of many neuropsychiatric disorders.

Repetitive TMS can either activate or inhibit cortical activity, depending on stimulation frequency [13]. Low-frequency (~1 Hz) stimulation for a period of approximately 15 min induces a transient inhibition, or a decrease in activity, of the cortex [14]. The mechanisms behind such inhibition is unclear, although there are similarities to long-term depression, a cellular experimental phenomena where repeated low-frequency stimulation reduces activity in individual synapses [14]. In contrast, stimulation at frequencies above 1 Hz has been shown to induce increased cortical activation [15]. The mechanisms by which such activation occurs are also unclear, although some authors suggest that it may be due to a transient increase in the efficacy of excitatory synapses [16]. It has also been argued that the orientation between the coil and underlying neural tissue that allows researchers to selectively activate different groups of neurons may be key to understanding the principles mediating its therapeutic efficacy. That is, by virtue of the fact that TMS activates neurons transsynaptically [17] (i.e. activation of interneurons), neuronal stimulation can selectively activate or inhibit the cortex.