INFORMATION SHEET

Title of Research Project:

INTERMITTENT THETA-BURST STIMULATION FOR MAJOR DEPRESSION: AN INTENSITY-RESPONSE STUDY

You are invited to participate in a clinical trial conducted by the Principal Investigator Dr. Georg S. Kranz, who is a staff member of the Department of Rehabilitation Sciences, The Hong Kong Polytechnic University. The clinical trial has been approved by the Human Subjects Ethics Subcommittee (HSESC) and the Clinical Research Ethics Sub-Committee (CRESC) of the Hong Kong Polytechnic University (Reference Numbers: HSEARS20221101008), as well as the ethics committees of all participating centers.

Participation in this clinical trial is completely voluntary. You can withdraw from this clinical trial at any time without giving reasons and without any disadvantages in your medical care. If you decide to take part, you will be given a copy of this information sheet and your signed consent form. We will also promptly inform you, should there be any new information related to this clinical trial and its procedures that may affect your willingness of continuous participation.

What is the aim of this clinical trial?
The aim of this clinical trial is to investigate a new stimulation treatment for major depression called intermittent Theta-burst stimulation (iTBS). Specifically, we want to compare three different stimulation intensities to see which treatment intensity has the greatest antidepressant effect. To this end, we will evaluate your depressive symptoms before treatment start, during, as well as after four weeks of daily stimulation treatments.

What is the course of the clinical trial?
After signing the informed consent form, you will be included in our clinical trial, which consists of four weeks of daily stimulation treatment using iTBS (five days per week). The eligibility for your participation was already determined during a screening telephone interview and during the medical consultation with the prescribing physician. This clinical trial will include 246 depressed patients. Each patient will be randomly assigned to one of three groups, each group receiving their treatment with a different stimulation intensity. You, as well as your doctor who evaluates your symptoms will not know to which group you belong.

Treatments will be delivered at the Department of Rehabilitation Sciences at the Hong Kong Polytechnic University. In some cases, treatments may also take place in the clinical center or hospital of your attending physician. The location where you receive treatment lies in the discretion of your attending physician.
Upon arrival, we will perform a psychiatric assessment and prepare for the experiment. Before the first treatment, we need to make some measurements of your head in order to stimulate over exactly the correct position. We also need to determine the individual stimulation parameters for you, which necessitates some preparation. Your treatment will start on the same day or a few days after the first screening visit (during which you receive this information and consent form). You will receive treatment once daily, five days per week (Monday to Friday), for four consecutive weeks. Each stimulation treatment lasts only for around three minutes. You should have already received an information sheet about the treatment from your prescribing physician. We will evaluate your mood as well as any side effects or inconveniences after each treatment. After the last treatment,

we will perform a psychiatric assessment again to determine how well you responded to the treatment.

What is intermittent theta-burst stimulation (iTBS)?
iTBS is a form of repetitive transcranial magnetic brain stimulation (rTMS). rTMS, as well as iTBS are used to treat psychiatric disorders, especially major depression. A stimulator provides a very short current which induces a magnetic field in a coil. If the coil is placed above the head, the magnetic field will go through the skull, enter the brain, and elicit an electric current in the brain below the coil. This current affects the activity of the brain by changing the electrical charge of the membrane of brain cells.

iTBS is a promising new form of non-invasive brain stimulation and has recently been approved as treatment for major depression by the U.S. Food and Drug Administration (FDA). There are also alternative forms of brain stimulation that have been proven to be effective in major depression. These include standard rTMS protocols or electroconvulsive therapy (ECT). rTMS and ECT have advantages and disadvantages compared to iTBS. However, your attending physician decided that a course of iTBS treatment would be the best option for you at the moment.

Are there any risks, inconveniences, or side effects?
iTBS is very safe with almost no side-effects. iTBS has been used as a treatment in thousands of patients world-wide so far. Patients receiving this kind of brain stimulation may experience slight local twitches and pricking of the skin underneath the coil. Few patients may also feel dizziness during the stimulation. Even fewer patients may experience headache during or after the stimulation. Another source of inconvenience may be the knocking noise that is associated with the stimulation.

What is the relevance and potential benefit of this clinical trial?
We hope that our clinical trial will help to optimize iTBS treatment for depression. By participating in this clinical trial and undergoing the treatment, you may directly benefit from this clinical trial. In the long-term, your participation will help other patients with major depression in the future.

Responsibilities of study participants
Your responsibilities as a participant in this clinical trial include the following: a) come to all of your trial visits and treatments as scheduled, b) provide accurate information about your medical history and current conditions, c) provide accurate information about any health problems, even if you do not think they are important, d) follow instructions as given by the researchers and your attending physician, e) do not change any of your medications without checking with your attending physician. Information_Consent_iTBS_for_MDD_v2_24.2.2022 3

Allocation of data and premature withdrawal of the clinical trial:
All information related to you will remain confidential and will be identifiable by codes only known to the researcher. You have every right to withdraw from the clinical trial before or during the trial without penalty of any kind. However, it may also be possible that the researchers decide to withdraw your participation in the clinical trial without obtaining prior consent from you. Reasons can be a) you do not meet the requirements for further participation in the clinical trial; b) the researchers or your attending physician has the impression that further participation in this clinical trial is not in your interest.

Compensation and costs related to clinical trial participation:
There are no treatment costs that need to be borne by study participants. You will receive financial

compensation of HK$100 for your expenditure of time and traveling expenses related to the participation in this clinical trial.

More information about the study:
If you would like to obtain more information about this study, please contact Dr. Georg Kranz (tel. no.: 2766-4838 / email: georg.kranz@polyu.edu.hk).

If you have any complaints about the conduct of this research study, please do not hesitate to contact Miss Cherrie Mok, Secretary of the Human Subjects Ethics Sub-Committee of The Hong Kong Polytechnic University in writing (c/o Research Office of the University) stating clearly the responsible person and department of this study as well as the HSESC Reference Number.

Thank you for your interest in participating in this study.

Dr. Georg Kranz
Principal Investigator

CONSENT TO PARTICIPATE IN RESEARCH

Title of Research Project:

INTERMITTENT THETA-BURST STIMULATION FOR MAJOR DEPRESSION: AN INTENSITY-RESPONSE STUDY

I _____ hereby consent to participate in the captioned research conducted

by _____.

I understand that information obtained from this research may be used in future research and published. However, my right to privacy will be retained, i.e. my personal details will not be revealed. Only certain designated parties and regulatory authorities such as the Clinical Research Ethics Committees of the participating centers will have the permission to access my personal data to ensure accuracy of study data acquisition.

The procedure as set out in the attached information sheet has been fully explained. I understand the benefit and risks involved. My participation in the clinical trial is voluntary.

I acknowledge that I have the right to question any part of the procedure and can withdraw at any time without penalty of any kind.

Name of participant _____

Signature of participant_____

Name of researcher_____

Signature of researcher_____

Date_____

受試者諮詢函

研究計畫標題
間歇性節律重複脈衝刺激治療抑鬱症：一項強度效應研究

您被受邀參與由香港理工大學康復科學系Georg S. Kranz 博士主持的臨床實驗研究。此臨床實驗已經獲得香港理工大學人類倫理學分委員會（HSESC）及香港理工大學臨床研究倫理分委（CRESC）(參考編號:HSEARS20221101008)，以及其它合作中心倫理委員會的批准。

參與該臨床試驗是完全自願的。您可以隨時退出該臨床試驗，而無需給出原因。這也不會對您的醫療造成任何不利影響。如果您決定參加，將獲得此資訊表和已簽署的同意書。如果有任何與該臨床試驗及其過程有關的新資訊可能影響您持續參與的意願，我們也會及時通知您。

該臨床試驗的目的是什麼？
這項臨床試驗的目的是研究一種新的治療抑鬱症的經顱磁刺激療法，稱為間歇性節律重複脈衝刺激（iTBS）。 具體而言，我們想比較三種不同的刺激強度，以查看哪種治療強度具有最大的抗抑鬱作用。 為此，我們將在治療之前，治療期間以及四個星期的治療之後對您的抑鬱症狀進行評估。

此臨床試驗的過程是什麼？
簽署知情同意書後，您將被納入我們的臨床試驗。在試驗期間，我們將對您進行為期四周，一週五天，一天一次的iTBS 治療。處方醫師在經過篩查電話採訪和醫療問詢採訪之後已經確定您的實驗參與資格。該臨床試驗將一共納入246 名抑鬱症患者。每個患者將被隨機分配到三個治療組中的一組，三組治療的刺激強度各不相同。您以及評估您症狀的醫療人員將不知道您會被分配到哪個組。

治療將在香港理工大學康復科學系進行。在某些情況下，治療也可能您主治醫師的臨床中心或醫院進行。您的主治醫生將會決定您在哪裡接受治療。

您到達治療地點之後，我們首先將進行精神健康狀況的評估和實驗的一些準備工作。在您第一次治療之前，我們需要對您的頭部進行一些測量，以保證精確刺激正確的位置。我們還需要為您確定個性化的刺激參數，這也需要進行一些準備。您的治療將在初次篩查到訪的同一天或之後的幾天內（在此期間您會收到此受試者諮詢函和知青同意書）正式開始。您的治療一共將持續四周，每週五天（星期一至星期五），每天一次。每次治療僅持續約三分鐘。您應該已經從處方醫生那裡收到了有關治療的資訊表。每次治療後，我們都會評估您的情緒狀況以及有無不良反應或不便之處。在最後一次治療後，我們將當場再次進行精神健康狀態的評估，以確定您的治療效果。

什麼是間歇性節律重複脈衝刺激（iTBS）？
iTBS 是重複性經顱磁刺激（rTMS）的一種。 rTMS 和iTBS 兩者都已用於治療精神疾病，尤其是抑鬱症。刺激器提供非常短的電流，該電流在線圈中引起磁場。如果將線圈靠近頭部，引起的磁場將穿過顱骨，進入大腦，並在線圈下方的大腦中引發電流。該電流通過改變腦細胞膜的電荷來影響大腦的活動。

iTBS 是一種有潛質的新型無創性腦刺激，最近已被美國食品藥品監督管理局（FDA）批准用於治療抑鬱症。也有其他形式的腦部刺激比如標準的rTMS 或電驚厥療法（ECT）已被證明對抑鬱症有效。但是與iTBS 相比，rTMS 和ECT 具有不足之處。因此，您的主治醫生認為目前用iTBS 進行治療將是您的最佳選擇。

是否有任何風險，不便或副作用？

iTBS 非常安全，幾乎沒有副作用。迄今為止，iTBS 已用於治療全球成千上萬的患者。接受這種大腦刺激的患者可能會出現輕微的局部肌肉抽動及線圈下皮膚的刺激感。少數患者在刺激過程中也會感到頭暈。更少數的一部分患者會在刺激期間或之後感到頭痛。此外，刺激產生的噪音可能會引發不適。

該臨床試驗的相關性和潛在益處是什麼？

我們希望我們的臨床試驗將有助於改善iTBS 對抑鬱症的治療。通過參加該臨床試驗並接受治療，您可以直接從該臨床試驗中減輕抑鬱症狀。從長遠來看，您的參與也將幫助其他抑鬱症患者。

研究參與者的責任

您作為本臨床試驗參與者的責任包括：a）按計劃進行所有的臨床拜訪和治療，b）提供有關您的病史和當前狀況的準確資訊，c）提供有關任何健康問題的準確資訊，即使您認為它們不重要，d）按照研究人員和主治醫生的指示進行操作，e）未經您的主治醫生允許，請勿更改任何藥物。

處理實驗資料和臨床試驗的提前退出

與您有關的所有資料都將被保密，並且只能通過研究人員已知的代碼來識別。您有權在臨床試驗之前或期間退出臨床試驗，而不會受到任何形式的處罰。但是，研究人員也有可能在未事先徵得您同意的情況下決定讓您退出此臨床試驗。原因可能是：a）您不符合進一步參加臨床試驗的要求； b）研究人員或您的主治醫生認為進一步參與該臨床試驗對您無益。

參與臨床試驗相關的補償和費用

此實驗的參與者無需支付任何治療費用。您參加這項臨床試驗而花費的時間和交通費，我們將給予您一百港元的經濟補助。

有關研究的更多資訊

如果您想獲得有關這項研究的更多資訊，請聯繫Georg Kranz 博士（電話：2766-4838 /電子郵件：georg.kranz@polyu.edu.hk）。

如果您對本研究的進行有任何投訴，請立即書面聯繫香港理工大學人類倫理學小組委員會秘書莫小姐（大學研究室主任）並清楚闡述研究的負責人和部門，以及HSESC 參考編號。

感謝您參與本研究。
研究負責人
Georg Kranz 博士

參與研究知情同意書

研究項目標題

間歇性節律重複脈衝刺激治療抑鬱症：一項強度效應研究

本人_____同意參與由_____開展的上述研究。

本人知悉此研究所得的資料可能被用作日後的研究及發表，但本人的私隱權利將得以保留，即本人的個人資料不會被公開。只有特定機構比如研究機構所在的臨床研究倫理委員會中心的人員才有權獲得我的個人資料來確保資料收取過程的準確性。

研究人員已向本人清楚解釋列在所附資料卡上的研究程式，本人明瞭當中涉及的利益及風險；本人自願參與此臨床實驗研究。

本人知悉本人有權就實驗過程的任何部分提出疑問，並有權隨時退出實驗而不受任何懲處。

參與者姓名 _____

參與者簽署 _____

研究人員姓名 _____

研究人員簽署 _____

日期 _____