Hamilton Health Sciences

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Hamilton Integrated Research Ethics Board (HIREB)
293 Wellington St. N., Suite 102, Hamilton, ON L8L 8E7
Telephone: 905-521-2100, Ext. 42013
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May 6, 2015

PROJECT NUMBER: **15-049**

PROJECT TITLE: A 12-week randomized controlled trial of probiotic treatment (Lactobacillus helveticus R0052 and Bifidobacteriumlongum R0175) versus placebo in adult Obsessive Compulsive Disorder.

PRINCIPAL INVESTIGATOR: **Dr. Michael Van Ameringen**

This will acknowledge receipt of your letter dated February 17, 2015 which enclosed revised copies of the Information/Consent Form, Protocol, Health Canada Notice of Authorization and the Application Form for the above-named study. These issues were raised by the Hamilton Integrated Research Ethics Board at their meeting held on January 20, 2015. Based on this additional information, we wish to advise your study has been given ***final*** approval from the full HIREB.

The following documents have been approved on both ethical and scientific grounds:

- The submission
- Clinical Study Protocol version 2 dated January 26, 2015
- Information/Consent Form version 2 dated January 26, 2015
- Recruitment Posters (2)
- Kijiji and Twitter Online Advertisements
- Questionnaires: Yale-Brown Obsessive Compulsive Scale (Y-BOCS); Obsessive Compulsive Inventory – Revised (OCI-R); Montgomery-Asberg Depression Scale (MADRS); Dutch Dimensional Obsessive Compulsive Scale (DDOCS) English version; Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form (Q-LES-Q-SF); Sheehan Disability Inventory (SDI); DASS 21; Short-Form Leeds Dyspepsia Questionnaire (SF-LDQ); Rome III Criteria – IBS Module; Gastrointestinal Symptom Rating Scale (GSRS) and Food Frequency Questionnaire (EPIC-FFQ)
- Investigator's Brochure for Probio'Stick

The following documents have been acknowledged:

- Health Canada Notice of Authorization dated May 1, 2015; Control # 181961
- Clinical Trial Registration # NCT02334644

Please note attached you will find the Information/Consent Form and the Recruitment Posters with the HIREB approval affixed; all consent forms/posters used in this study must be copies of the attached materials.

REB #: 15-049 Van Ameringen

We are pleased to issue final approval for the above-named study for a period of 12 months from the date of the HIREB meeting on January 20, 2015. Continuation beyond that date will require further review and renewal of HIREB approval. Any changes or revisions to the original submission must be submitted on an HIREB amendment form for review and approval by the Hamilton Integrated Research Ethics Board.

PLEASE QUOTE THE ABOVE-REFERENCE PROJECT NUMBER ON
ALL FUTURE CORRESPONDENCE

Sincerely,

S. Salama

Suzette Salama, PhD.
Chair, Hamilton Integrated Research Ethics Board

McMaster University
Health Sciences

MacAnxiety Research Centre Hamilton Health Sciences

Hamilton Health Sciences – McMaster University

STUDY INFORMATION SHEET - MAIN CONSENT FORM

Title of Study: A 12-week randomized controlled trial of probiotic treatment (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) vs placebo in adult Obsessive Compulsive Disorder

Locally Responsible Investigator and Principal Investigator, Department/Hospital/ Institution:
Dr. Michael Van Ameringen; Department of Psychiatry and Behavioural Neurosciences, McMaster University, MacAnxiety Research Centre, Hamilton Health Sciences

Co-Investigator(s): Dr. Keren Grosman Kaplan; Department of Psychiatry and Behavioural Neurosciences, McMaster University
Ms. Jasmine Turna, MiNDS Program, Department of Psychiatry and Behavioural Neurosciences, McMaster University
Dr. Rebecca Anglin; Department of Psychiatry and Behavioural Neurosciences, McMaster University
Dr. Michael Surette; Department of Medicine, McMaster University

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You are being invited to take part in a research study of probiotic treatment (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) for treating obsessive-compulsive disorder (OCD).

The following paragraphs explain this study and your role in it, if you decide to participate. Please read this carefully and feel free to ask any questions. Participation in this study is entirely voluntary. You will receive a signed copy of this consent form for your records.

This study is being funded by the Academic Health Science Centre's AFP Innovation Fund.

WHY IS THIS RESEARCH BEING DONE?

You are being asked to participate in this research study because you have obsessive-compulsive disorder (OCD). You understand that OCD is defined by recurrent obsessions or compulsions which are usually time consuming or cause marked distress or significant impairment. Obsessions are persistent ideas, thoughts, impulses or images that are experienced as intrusive and inappropriate and cause marked anxiety or distress. The most common obsessions are repeated thoughts about contamination, repeated doubts, a need to have things in a particular order, aggressive or horrific impulses and sexual imagery. Compulsions are repetitive behaviours such as hand washing, ordering, checking or mental acts, such as praying, counting, and repeating words silently. The goal of these compulsions is to prevent or reduce anxiety or distress.

The normal human gut is home to millions of bacteria and it is believed that changes in these bacteria can lead to disease. Currently, changes in these bacteria have been seen in a number of illnesses including ulcerative colitis, inflammatory bowel disease, autism, celiac disease and obesity. More recently, researchers have looked at the relationship between the gut and brain and its possible contribution to psychiatric illness, including anxiety and mood disorders.

Probiotics are products which come in various forms such as capsules and powders and can often be found in foods like yoghurt. Probiotics are actually live microorganisms which directly affect gut bacteria, and can have health benefits when taken in adequate doses. There is early research which suggests that a change in gut bacteria with the use of probiotics may help decrease stress-induced physical and psychological symptoms associated with anxiety and depression.

WHAT IS THE PURPOSE OF THIS STUDY?

The main purpose of this study is to examine whether the probiotic treatment, Lactobacillus helveticus R0052 and Bifidobacterium longum R0175 may be beneficial for adults who have OCD. We are also investigating the potential relationship between the bacteria found in the gut OCD.

WHAT WILL MY RESPONSIBILITIES BE IF I TAKE PART IN THE STUDY?

Should you consent to participate, you will be asked to attend an interview with a member of our research staff. During this interview, the researcher will ask you a variety of questions regarding your current symptoms. This will take approximately 90 minutes. Following this interview you will be given some self-report questionnaires to complete which should take an additional 30 minutes. Once you have completed these questionnaires, you will also be asked to provide a sample of your blood which will be tested for levels of "biomarkers" which have been found to be associated with anxiety and possibly OCD. Biomarkers are biological molecules, found in blood, other body fluids, or tissues, that are a sign of a normal or abnormal process or of a condition or disease. You will also be asked to provide a urine sample at this visit. Finally, you will also be provided with a stool collection kit and detailed instructions on how to collect the sample. The stool sample will need to be sent to the MacAnxiety Research Centre within 4 hours of defecation. Participants will be asked to contact a local taxi service within this time frame and will arrange to have the stool samples sent to the MacAnxiety Research Centre. The costs of the taxi service will be covered by the Research Centre.

Over the 12-week double-blind treatment you will receive a probiotic formula or placebo (an inactive substance which looks like the investigational probiotic but has no medical value).

The probiotic formula and placebo will be provided to you in a sachet, containing powder, which dissolves quickly in the mouth. It can be taken without water and at any time during the day. You will be asked to take two sachets per day during or after breakfast.

If you agree to take part in this study, you will have a 50/50 chance (like the flip of a coin) that you will receive either the probiotic formula or a placebo formula which looks exactly the same as the probiotic. Since the study is double-blind, neither you, nor the study doctor, will know whether you are getting the probiotic or the placebo. This is because knowing which treatment is given to you may influence you and study doctors when reporting benefits and side effects of the treatment. It is also well known that up to one-third of patients may improve after taking a placebo as if it was an active medication.

You will be asked to return to the research centre for an additional 4 study visits, these visits will occur once every 3 weeks. Each visit will last about 1 hour.

During each visit, you will be assessed by a member of our research staff and the study doctor, who will ask you about your symptoms, and if you are experiencing any side effects. Some questionnaires (concerning your OCD symptoms, mood and diet) will also be completed at each visit.

Six weeks after you have started taking the study treatment, a member of the research team will contact you via telephone to check-in with you and to evaluate changes in your OCD symptoms. You will also

be asked to provide a stool sample after this phone call and must arrange for the taxi service to deliver it to the Research Centre, just like the first sample, at no personal expense to you.

At visit 4 (week 12), you will be assessed by the study doctor as described above. You will also be asked to provide a third stool sample. The stool collection kit will be provided prior to this visit and the instructions on how to collect the sample will be reviewed with you in detail. At this visit, you will also be asked to provide a urine sample and have a blood sample drawn.

All study personnel have a responsibility to be truthful, complete and accurate in explaining this study to you and answering any questions you may have about the study. You also have a responsibility to be truthful, complete, and accurate when answering questions for this study with the study staff.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Blood collection: Risks associated with drawing blood from your arm include some discomfort and/or bruising. Fainting, infection, excess bleeding, or clotting are also possible, but unlikely. The risk of such events is less than 1%. At visit 1 and visit 4 approximately 2 teaspoons of blood will be drawn.

Stool sample collection: There is no additional risk to you than that posed by having a regular bowel movement.

Although rare, some people who consume probiotics may experience slight gastrointestinal discomfort. Symptoms include the possibility of: gas/bloating, diarrhea, and/or abdominal discomfort.

HOW MANY PEOPLE WILL BE IN THIS STUDY?

A total of 64 people will participate in this study.

WHAT ARE THE POSSIBLE BENEFITS FOR ME AND/OR FOR SOCIETY?

You and other people may receive the benefits of any medical research. Such benefits include the possibility that your condition may improve and your participation may help future patients. There is no guarantee that you will receive any medical benefits from participating in this study.

IF I DO NOT WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

Your participation in this study is completely voluntary. Refusal to participate or withdraw from the study will involve no penalty or loss of benefits to which you are entitled. If you decide you do not want to take part in this study, this will not in any way affect your current or future care. OCD can be treated with anti-depressant medications such as fluvoxamine, fluoxetine, paroxetine, sertraline, escitalopram and clomipramine and/or psychotherapy in form of cognitive behavioural therapy.

WHAT INFORMATION WILL BE KEPT PRIVATE?

If you agree to take part in the research, all personal medical data collected during the study will be **strictly confidential**. It will be used only for the purpose of the research during your participation in this study; the study researcher will collect information such as your initials, date of birth, gender (sex), and data about your diet and your health. The information will be stored and processed with electronic data processing systems and will be kept for the duration of the investigation. In the study's database, you will only be referred to by a code number and initials. Only your study doctor will be able to link the code number to your name and he/she will keep this information, your data and your medical records

for 25 years. The data will be kept in a secure location at the MacAnxiety Research Centre, McMaster University, and it will only be accessed by those clinic staff involved in the study.

By signing this consent I give my consent to the collection, use and disclosure of my health information as described above.

A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*.

CAN PARTICIPATION IN THE STUDY END EARLY?

Your participation in this study is entirely voluntary; you have the right to withdraw from the study at any time. If you decide to be withdrawn from the study this will not affect your future medical care in any way. The study doctor may withdraw you from the study if he/she feels that it is in your best interest. If you want to discontinue in the study you can discuss alternate treatment options with the study doctor.

WILL I BE PAID TO PARTICIPATE IN THIS STUDY?

You will not be paid for participating in the study. However, the probiotic formula will be given to you free of charge and taxi fares associated with sample delivery will be covered.

WHAT HAPPENS IF I HAVE A RESEARCH-RELATED INJURY?

In case of an injury or illness suffered by your participation in this study, you will be examined by your physician and the appropriate medical care will be given. For subjects treated in accordance with the protocol all necessary medical costs not covered by your government health plan (if applicable) or your private medical insurance (if any) will be covered. In the event of a study-related injury, please contact the research centre. By signing this form, you are not giving up your legal rights, nor releasing the study doctors from their legal and professional obligations

IF I HAVE ANY QUESTIONS OR PROBLEMS, WHOM CAN I CALL?

If you have any further questions about the study or did not understand any of the technical language, you should ask the study team before you sign this Informed Consent form. If you would like more time to think about your decision to participate, you should not sign this Informed Consent Form and tell the study team. You will be given a copy of this Informed Consent Form and may ask for additional information regarding this study, at any time during the study, from the study team.

If you have questions concerning side effects or regarding the conduct of this study or in case of study-related injury, you should contact the study doctor Dr. Van Ameringen at (905) 921-7644.

In case of an emergency, please contact Dr. Van Ameringen at (905) 921-7644 *OR* go to the nearest hospital emergency department.

This study has been reviewed by the Hamilton Integrated Research Ethics Board (HIREB). The HIREB is responsible for ensuring that participants are informed of the risks associated with the research, and that participants are free to decide if participation is right for them. If you have any questions about your rights as a research participant, please call the Office of the Chair, Hamilton Integrated Research Ethics Board at 905.521.2100 x 42013.

CONSENT STATEMENT

SIGNATURE of RESEARCH PARTICIPANT

I have read the preceding information thoroughly. I have had the opportunity to ask questions and all of my questions have been answered to my satisfaction. I have been informed of the risks, benefits and alternatives to participation in this study, including the right not to participate and the right to withdraw without compromising my medical care. I know that I may ask now, or in the future, any question I have about the study or the research procedures. I understand that I will receive a signed copy of this form.

I have been assured that records relating to my care and me will be kept confidential and that no information will be released or printed that would disclose personal identity without my permission unless required by law. I consent to the review of my medical records (which will contain my name) by the research team at the MacAnxiety Research Centre, the Hamilton Integrated Research Ethics Board, Health Canada, the FDA and other regulatory authorities where the study drug may be considered for approval for the purposes as described in this Consent Form.

By signing this form I voluntarily consent to participate in this research study and have not waived any of my legal rights. I acknowledge that I will receive a copy of this signed consent form.

_____
Name of Participant

_____ _____
Signature of Participant Date (dd/mmm/yyyy)

Consent form administered and explained in person by:

_____
Name and title

_____ _____
Signature Date (dd/mmm/yyyy)

SIGNATURE OF INVESTIGATOR:

In my judgment, the participant is voluntarily and knowingly giving informed consent and possesses the legal capacity to give informed consent to participate in this research study.

_____
Name of Investigator (printed)

_____ _____
Signature of Investigator Date(dd/mmm/yyyy)

Need help with your

OBSESSIVE COMPULSIVE DISORDER?

We are currently recruiting adults (ages 18-65) for a study using a natural health supplement to treat individuals with OCD

The study will involve:

A COMPREHENSIVE ASSESSMENT TO DETERMINE ELIGIBILITY

PROVIDE BIOLOGICAL SAMPLES, BEFORE & AFTER TREATMENT

If interested, pleae contact Diana:
905 921 7644
diana@macanxiety.com

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