Effects of butyrate on depressive symptoms and affect in depression - a pilot randomized controlled trial

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Ethical review	Approved WMO
Status	Pending
Health condition type	Mood disorders and disturbances NEC
Study type	Interventional

Summary

ID

NL-OMON57116

Source
ToetsingOnline

Brief title
Oral butyrate in depression (BUTY study)

Condition

- Mood disorders and disturbances NEC

Synonym
depression, depressive disorder

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: brain-gut axis, butyrate, depressive disorder, major

Outcome measures

Primary outcome

The primary outcomes are the feasibility (i.e., recruitment rates, participant retention and completion, protocol adherence, success of blinding strategies) and acceptability (intake of study supplement, study participation satisfaction).

Secondary outcome

Secondary outcomes are changes in depressive symptomatology, using the HDRS-17 and the Quick Inventory of Depressive Symptomatology (QIDS), changes in anhedonia using the Temporal Experience of Pleasure Scale (TEPS) and changes in positive (PA) and negative affect (NA), and affective patterns (e.g., affect fluctuation, affect dynamics) using experience sampling methodology (ESM). Other outcomes include gastrointestinal symptoms, dietary intake, faecal microbiome composition, plasma and faecal metabolites (e.g., SCFAs), inflammatory markers in blood and intestinal permeability in blood and faeces, and a biological marker of stress (e.g., hair cortisol).

Study description

Background summary

Major depressive disorder (MDD) is a serious mental health issue associated with poor mental and physical health. A large proportion of MDD patients does not respond successfully to pharmacological and/or psychological treatments and continue to suffer from symptoms. Hence, the need for alternative treatment for

MDD remains. As the aetiology and pathophysiology of depression may be influenced by intestinal dysbiosis, studies have been investigating the therapeutic effects of compounds that target the intestinal environment. Administration of probiotics and synbiotics have shown promise in reducing depressive symptoms, yet less is known about the effects of administering metabolites that are widely produced by resident microbes. One promising metabolite is butyrate, a short-chain fatty acid (SCFA) that is thought to influence depressive behaviour via the microbiota-gut-brain axis (MGBA). The gut microbiome of MDD patients consists of less butyrate-producing bacteria and administration of butyrate in rodent models of depression has been shown to reduce depressive-like behaviours. Yet, it is unknown whether butyrate has antidepressant effects in MDD patients. Butyrate is a food supplement and its safety as an orally-ingested supplement has been established in previous clinical trials, including trials performed at the Amsterdam UMC. To the best of our knowledge, effects of oral butyrate supplementation has not been investigated in psychiatric population.

Study objective

The primary objectives are to study the feasibility and acceptability of an 8-week daily oral supplementation with tributyrin (4 g/day) - the triglyceride form of butyric acid - on top of treatment as usual (TAU) in adults (18 up to 65 years) with mild-to-severe MDD. Secondary objectives are to obtain estimations of therapeutic efficacy of tributyrin supplementation regarding depressive symptoms and affect. Other objectives are to obtain insights into butyrate*s potential mechanisms of influencing depressive symptoms by assessing measures associated with the MGBA.

Study design

Pilot Study. Double-blind randomized placebo-controlled, parallel design.

Intervention

Both interventions will be provided on top of participant*s TAU. The intervention group will receive oral supplementation twice daily with 2 grams of tributyrin (Taubiotic®), totalling to 4 grams of tributyrin a day during an intervention period of 8 weeks (TAU + tributyrin). The control group will receive oral supplementation with a daily equal volume of sunflower oil as a placebo (TAU + placebo).

Study burden and risks

Patients will visit the Amsterdam UMC - location AMC 5 times: at screening (V1; week -2; circa 70 minutes), baseline (V2; week 0; circa 105 minutes), mid-trial (V3; week 4, circa 65 minutes), at the end of the trial (V4; week 8, circa 65

minutes), and at the 6 months follow-up (V5; week 24; circa 75 minutes). Before each visit - with the exception V1 - patients will be asked to fast overnight, collect faecal samples at home and fill in a nutritional diary. During visits, patients will undergo interviews and will fill in questionnaires, scalp hair will be collected, and fasting blood will be drawn. The maximum amount of blood that will be drawn over 4 study visits is 82 mL per patient. Using a mobile application, patients will report how they are feeling on 16 affect items five times a day, five days a week starting two weeks prior to the intervention period and during the intervention period (i.e., week -2 to week 8). Tributyrin is a food supplement. Patients could experience side effects of the tributyrin supplementation, however, previous trials with tributyrin capsules and sodium butyrate capsules have reported no side effects. There is no direct benefit for the volunteers, but this research might provide new insights into the pathogenesis of depression.

Contacts

Public
Amsterdam UMC

Meibergdreef 5
Amsterdam 1105AZ
NL
Scientific
Amsterdam UMC

Meibergdreef 5
Amsterdam 1105AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Aged 18 up to 65 years;
2. The participant understands the study and is capable of providing written informed consent;
3. Having sufficient knowledge of the Dutch language;
4. Having a clinical diagnosis of MDD, as confirmed with The Structured Clinical Interview for the DSM-5 (SCID-5);
5. Having a depression severity of mild or higher, as reflected by a score >= 14 on the HDRS-17;
6. Receiving treatment with antidepressant medication, starting at least four weeks prior to study inclusion;
7. Daily access to a mobile phone with iOs or Android software;
8. Having a weight ranging from normal to overweight, measured as having a BMI between 18.5 and 27.5 kg/m2

Exclusion criteria

1. Antibiotics usage within three months before inclusion;
2. Current treatment with neuromodulation, such as deep brain stimulation, repetitive transcranial magnetic stimulation
3. Having a severe disease of the digestive tract, such as celiac disease, Crohn*s disease, active ulcerative colitis or short bowel syndrome;
4. Any psychotic disorder;
5. Acute, severe suicidal tendencies;
6. Allergy or intolerance to sunflower oil;
7. Allergy or intolerance to bovine gelatine, or unwillingness to consume soft gel capsules made of bovine gelatine;

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2024
Enrollment:	24
Type:	Anticipated

Ethics review

Approved WMO Date:	12-11-2024
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-02-2025
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL85124.018.24