Understanding gut feelings: Probiotics and cognition

No registrations found.

Ethical review   Positive opinion
Status   Recruiting
Health condition type   -
Study type   Interventional

Summary

ID

NL-OMON28892

Source
NTR

Health condition

Mood effects
Intestinal barrier functioning
Inflammatory activity
HPA activity
Amino acid metabolism
Cognitive reactivity
Positive re-biasing of attention
Affect recognition
Reward-learning

Sponsors and support

Primary sponsor: University of Amsterdam, Department of Psychology
Source(s) of monetary or material Support: Amsterdam Brain and Cognition (ABC)

Intervention

Outcome measures

Primary outcome

The main parameter is beneficial effects on mood, which will be assessed using the following validated questionnaires:

Beck's Anxiety Inventory

The Beck Anxiety Inventory (BAI) (Beck et al., 1988) is a 21-item self-report questionnaire with high internal consistency (á = .90; Beck and Steer, 1993), which assesses the existence and severity of anxiety symptoms. A validated Dutch translation will be used (Bouman, 1994). Participants are presented with items describing common symptoms of anxiety (such as numbness and tingling, sweating not due to heat, and fear of the worst happening) and asked to rate, on a 4-point Likert scale (0, not at all, 1, mildly, 2, moderately, 3, severely), how much they have been bothered by each symptom over the past week. This instrument will be used for research and not for clinical assessment.

Center for Epidemiologic studies depression scale (CESD; Bouma et al., 1995)

For this questionnaire (á = .79 - á = .92, see Bouma et al., 1995), participants are asked to answer 20 statements with regard to how applicable these are to them ranging from 0 (never) to 3 (always). The 20 items in CESD scale measure symptoms of depression in 4 different groups: somatic-retarded activity, depressed affect, positive affect, and interpersonal affect. This instrument will be used for research and not for clinical assessment.

Leiden Index of Depression Sensitivity –revised (van der Does & Williams, 2003)

This scale has 34 items rated on a 5-point likert scale (á = .92; Solis et al., 2016) that assess the extent to which dysfunctional thought patterns activated when an individual experiences mild dysphoria (i.e. cognitive reactivity). The LEIDS-r has a total score, and six subscales assessing cognitive reactivity related to aggression (á = .80), hopelessness/suicidality (á = .83), acceptance/coping (á = .64), control/perfectionism (á = .66), risk aversion (á = .81), and rumination (á = .82; Solis et al., 2016).

Rumination Response Scale (RRS; Nolen-Hoeksema & Morrow, 1991)

The Dutch version of the RRS (á = .92, Raes et al., 2009) contains 22 items for which participants are asked to rate, on a scale from 1 (never) to 5 (almost always), how often they think or do something when they are sad or down. Besides a total score, this questionnaire provides two subscores with regard to brooding (maladaptive rumination, related to depression) and reflection (adaptive rumination, effective problem solving).

Positive and Negative Affect Scale (PANAS)

The PANAS (á = .90, Watson et al., 1988b) is a validated questionnaire that consists of two 10-item mood scales (i.e. 20 in total) and was developed to provide brief measures of positive and negative affect. Respondents are asked to rate the extent to which they have experienced each particular emotion within a specified time period, with reference to a 5-point scale. The scale points are: 1 'very slightly or not at all', 2 'a little', 3 'moderately', 4 'quite a bit' and 5 'very much'.

Secondary outcome

Interpersonal Reactivity Index (IRI; Davis, 1980)

The IRI is an empathy questionnaire (stable, trait-level) containing 28-items answered on a 5-point Likert scale ranging from "Does not describe me well" to "Describes me very well". The measure has 4 subscales, each made up of 7 different items. These subscales are (taken directly from Davis, 1983): Perspective Taking – the tendency to spontaneously adopt the psychological point of view of others Fantasy – taps respondents' tendencies to transpose themselves imaginatively into the feelings and actions of fictitious characters in books, movies, and plays Empathic Concern – assesses "other-oriented" feelings of sympathy and concern for unfortunate others Personal Distress – measures "self-oriented" feelings of personal anxiety and unease in tense interpersonal settings. These scores will not be used for clinical assessment.

Adapted O-Span

Individual working memory (emotional) operation span scores will be determined using the OSPAN (operation word span) task adapted from Turner and Engle (1989; see Unsworth et al., 2005). This task requires participants to solve simple mathematical operations while remembering words for later recall. Participants are presented with an operation–word pair and required to read the operation aloud, say 'yes' or 'no' to indicate whether the given answer is correct or incorrect, and then report the to-be-remembered word aloud. Sixty operation-word combinations will be presented in a total of 15 trials: 3 trials of each combination of calculation-word combinations (2-6). The OSPAN score can vary between 0 and 60.

Facial morphing task

This computerized task allows to assess an individual's ability to recognize facial expressions, which is thought to reflect vulnerability to depression (Harmer et al., 2009). The task presents male and female morphed facial expressions. There are 6 basic facial expressions (i.e. happiness, anger, fear, sadness, disgust, and surprise) that are presented morphed (emotional intensity: 10,20,30,40,50,60, 70,80, 90, 100%): Participants have to respond

using labeled keys to indicate which of the six basic emotions was presented. Dependent variables are percentage accurate responses and mean latencies of the six basic facial expressions (Kemmis et al., 2007). This instrument will not be used for clinical assessment.

Reading the Mind in the Eyes Task (RMET;(Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001)

The RMET is an adult test of theory of mind ability and is a measure of social cognition. The task involves inferring the mental state of a person just from the information in photographs of a person's eye region. The choice is always between four mental state terms, some of which are "basic" (such as happy, sad, angry, or afraid), and others of which are more "complex" (such as reflective, arrogant etc.). Every participant rates 36 mental stages. This instrument will not be used for clinical assessment.

Monetary reward-learning task (Berridge & Kringelbach, 2013)

In order to assess differences in wanting (motivation), liking (reward), and reinforcement learning, participants will be asked to perform a computerized task that allows differentiation between these mechanisms. Participants will be presented with and asked to make choices on the basis of (predictive) stimuli (e.g. the symbol '&' leading to reward and the symbol '*' not leading to reward) that can lead to gains or losses, allowing for the measurement of approach-related behaviour in the context of reward and reinforcement learning effects, as well as self-reported (hedonic) reactions to reward receipt or loss aversion.

Blood samples (gut permeability, inflammatory markers, bacterial translocation, metabolic markers)
3 tubes of blood (EDTA, 6ml each) will be taken at the first and second session, in order to assess gut permeability, inflammatory markers, bacterial translocation, metabolic markers, and HPA axis activity (i.e. IL-6, IL10, CRP, LPS, LPS-binding protein, plasma biogenic amines, CRH). More specifically, with regard to the assessment of biogenic amines: to evaluate whether, as proposed by animal studies, the intake of multispecies probiotics affects amino acid and biogenic amine metabolism in health human adults and thereby affects cognition and well-being, metabolomics profiling using the biogenic amine platform will be applied. Blood samples will be frozen immediately at -86 degrees C until analyses for pharmacokinetic assessments. Blood sample analyses will not be used for clinical assessment.

Salivary samples (HPA and adrenergic activity)

In order to evaluate activity of stress response systems (i.e. cortisol and alpha-amylase),

repeated saliva samples will be collected throughout the day using the 'spitting method' (Navazesh, 1993); participants will be requested to rinse the mouth with water, after which unstimulated saliva will be collected for 10 min in polypropylene cups kept on ice. Salivary analyses will not be used for clinical assessment.

Stress testing

The Socially evaluated cold pressure test (SECPT; Schwabe, Haddad, & Schachinger, 2008) will be used to measure participants' affective and physiological reactions to mild acute stress (tested by salivary cortisol and alpha-amylase samples, heart rate and blood pressure).

Study description

Background summary

Human studies provided support that manipulation of the 'microbiota-gut-brain axis' through the intake of probiotic food supplements has the potential to (positively) influence mood and cognition, possibly even reducing symptoms depression or cognitive associated risk factors in otherwise healthy non- depressed individuals. These findings are in line with the recommendation of the World Health Organization (2012) regarding the need for preventive strategies for depression. A major limitation of the human literature on probiotic supplementation, however, is that it has remained elusive by which mechanisms probiotics may yield their beneficial effects. While a number of mechanisms have been proposed on the basis of animal research, these have received little to no scrutiny in humans. Thus, in addition to establishing effects of probiotic supplementation on mood and cognition, translating these animal findings to humans is a second aim of the current study. Here the focus is on inflammatory/immune, metabolic/metabolomic, and autonomic nervous system pathways. Effects on fecal microbiome will be studied as well. By focusing on healthy, non-diagnosed individuals, the findings may gain insight in the a possible preventive role of the microbiome and probiotics in mental disorders.

Study design

Primary outcomes pre- vs post-intervention

Intervention

Multispecies probiotic vs placebo (carrier)

Contacts

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Eligibility criteria

Inclusion criteria

- Healthy adult participants

- aged 18-75 years

- Females taking hormonal contraceptives; with the exception of females post-menopause.

- Willingness to travel to the laboratory site, perform tasks and fill out questionnaires and adhere to the study intervention.

- Fluency in Dutch language

- written informed consent before inclusion

Exclusion criteria

- Implementing or planning major changes in diet; e.g. attending a weight-loss program or changing to a vegetarian or vegan diet, or initiating new food supplements (including pro- or pre-biotics).

- Current or past cardiac- (including high blood pressure), inflammatory- or auto-Immune-, gastrointestinal-, hepatic-, renal-, neurological- or psychiatric disorders or diseases, based on self-reported medical diagnosis and medication use.

- excessive alcohol intake, defined as drinking more than 21 glasses of alcohol per week;

- history of drug abuse or addiction;

- Not using hormonal contraceptives (with the exception of post-menopause females)

- Antibiotic use 3 months prior to the study

- age below 18 or above 75.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	22-10-2017
Enrollment:	150
Type:	Anticipated

Ethics review

Positive opinion

Date:	01-03-2018
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 46368
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL7063
NTR-old	NTR7301
CCMO	NL62568.018.17
OMON	NL-OMON46368

Study results