Mental functioning, brain Tryptophan availability and affect; the role of the immune system

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Gastrointestinal inflammatory conditions
Study type	Observational invasive

Summary

ID

NL-OMON55728

Source
ToetsingOnline

Brief title
Mental functioning; the role of the immune system

Condition

- Gastrointestinal inflammatory conditions
- Mood disorders and disturbances NEC

Synonym
inflammatory bowel disease, irritable bowel syndrome

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Affect, kynurenine, Mentale prestatie, Serotonin, Tryptophan degradation

Outcome measures

Primary outcome

The main study parameter consists of variations in plasma TRP/LNAA ratio

(indicator of brain TRP availability).

Secondary outcome

Secondary parameters are pre-post changes in physiological indices of stress

and/ or negative affectivity (cortisol), inflammatory reactivity and indicators

of subjective stress/ negative affectivity (mood, negative attention bias).

Study description

Background summary

Everyone is confronted with stressful life events. Stressors, however, do not affect everyone similarly. Whether stress has a detrimental effect on health and affect is, among other factors, dependent on the individual degree of stress resilience. Various neurobiological systems were found to mediate stress tolerance, most importantly the mutually interacting brain serotonergic (5-HT) system and Hypothalamic-pituitary adrenal axis (HPA) - commonly recognized as the neuroendocrine stress adaptation system. Exposure to acute severe or long-term persistent stress can induce abnormalities in both systems, leading to exaggerated adaptive responsiveness to future stressors and hence increased stress vulnerability. Indeed, mounting evidence indicates that persistent stress can impair serotonergic neurotransmission and HPA-related stress hormone regulation.

Recently, however, it was hypothesized that sensitization of the stress response may have a pro-inflammatory root as well. Activation of the immune system - more specifically the release of immune signaling molecules caused by systemic infection/inflammation or chronic mental stress - may additionally increase stress sensitivity by negatively affecting 5-HT synthesis and/or neurotransmission and HPA-axis regulation.

In the current project, we aim to investigate the likeliness of this proposition. We will examine whether chronic immune activation affects the neuroendocrine (HPA) stress adaptation system and therefore mental- emotional stress resilience.
By including the role of the immune system in the current biological-psychological model of stress resilience, we may develop a better understanding of individual differences in stress sensitivity and related affective illness.

Study objective

The primary objective of the study is to explore whether immune activation potentiates stress vulnerability by increasing serotonin dysfunction (lower tryptophan ratio*s). This objective is based on the hypotheses that pro-inflammatory cytokines induce a shift in tryptophan metabolism, thereby hypothetically resulting in reduced 5-HT synthesis and diminished regulatory control over the HPA axis.

Secondary objectives focus on group differences (patients with an inflammatory disease versus healthy controls) with respect to objective stress response, inflammatory response and affective response in the face of acute stressors.

Since it is increasingly recognized that stress induces an inflammatory response as well (irrespective of the presence of an inflammatory disease/infection/tissue damage), which may facilitate inflammation-induced-TRP degradation and HPA dysregulation even further, chronic stress will be included as an additional primer of stress sensitivity.

Study design

In a repeated measure between subjects design, patients with systemic gastrointestinal complains and healthy controls are monitored for both brain tryptophan availability (prior to acute stress exposure), objective/ subjective stress before and after acute stress exposure. This study uses a 2 (gastrointestinal complains, controls) x 2 (high/low stress) x 2 (before/ after stress exposure) study design.

Study burden and risks

Participants will visit the research lab only once for a total time of 3 h. A standardized, quick and non-invasive, laboratory stress protocol will be applied to elicit autonomic and glucocorticoid stress responses. The stress task lasts solely 15 minutes (5 minutes preparation time, 10 minutes acute stress). Any risks associated with 10 minutes acute stress induction can be considered negligible and the burden minimal. Prior and post stress induction, participants will perform two short behavioural tasks (negative affective priming). In addition, participants will complete a computerized mood

questionnaire four times (after arrival, pre-post stress, post-recovery) and a life stress questionnaire. In addition, a total of six serial saliva samples will be drawn for cortisol and cytokine assessments and one blood sample to measure TRP/LNAA ratio*s. Participants will receive ¤75,- compensation for participation in the experiment. In the event of early termination, participants will be compensated pro rata.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Officially diagnosed gastrointestinal disease: IBD or IBS (no inclusion criterion for control group)
- Aged between 18- 60 years
- Normal BMI (18.5- 25)

- Willing and able to give written informed consent
- Good understanding of the Dutch language
The control group will be matched as closely as possible with the patient group on gender and age

Exclusion criteria

- Indications of acute or chronic disease or psychiatric disorder (other than a chronic gastrointestinal disease) at study entry
- Symptoms of a cold / fever / the flu at study entry
- Use of medication, apart from contraceptives- especially medications that affect the dependent variable
- Pregnancy in the last 6 months / breastfeeding
- Known excessive alcohol or drugs use (>15 week)
- Smoking

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2019
Enrollment:	68
Type:	Actual

Ethics review

Approved WMO Date:	31-12-2018
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL65900.068.18