# Immunological response to Hepatitis B vaccination in obsessive compulsive disorder patients receiving high doses of serotonin reuptake inhibitors

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The main objective of this study is to1) Determine the immunological response to hepatitis B vaccination in OCD patients that are treated with 60 mg/d paroxetine and2) Compare this response to the immunological response to hepatitis B vaccination in...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Immune disorders NEC |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON38586

**Source**
ToetsingOnline

**Brief title**
Hepatitis B vaccination in SRI-treated OCD patients

### Condition

- Immune disorders NEC
- Anxiety disorders and symptoms

**Synonym**
drug-induced immunosuppression

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Academisch Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** hepatitis B vaccination, obsessive-compulsive disorder, paroxetine, serotonin reuptake inhibitors

## Outcome measures

### Primary outcome

Primary research variables are

1) antibody titers to hepatitis B virus (anti-HBs) and

2) the cellular (T-cell) response to soluble hepatitis B antigen (HBsAg). The

number of cytokine-producing cells (IFNy, TNFa and IL2) will be determined, as

well as the HBsAg-specific T-cell proliferation.

### Secondary outcome

not applicable

# Study description

### Background summary

Serotonin reuptake inhibitors (SRI*s) such as paroxetine and venlafaxine are commonly prescribed drugs in the treatment of psychiatric disorders. The main indications for these drugs are major depression and anxiety disorders such as obsessive compulsive disorder (OCD). Although the adverse effect profile of SRI*s is well known, there is some concern about the impact of these drugs on immunity. Both in vitro and in vivo evidence shows that SRI*s have a negative effect on cellular immune responses. For instance, SRI*s supress in vitro mitogen-induced lymphocyte proliferation and induce apoptosis in activated lymphocytes.1 Also, in vivo administration of SRI*s can impair mitogen-induced lymphocyte proliferation both in animals2 and in humans3. Impairment of the immunological suppression of herpes simplex virus in patients treated with SRI*s has also been reported.4

OCD is a psychiatric condition characterized by intrusive, unwanted and recurrent thoughts (obsessions) and/or repetitive ritualistic behaviors (compulsions). The most widely prescribed drugs for OCD are SRI*s, and the condition generally requires treatment with doses 2-3 times higher than the doses administered for major depression. Whereas paroxetine is usually dosed at 20 mg/d for depression, OCD patients often receive doses up to 60 mg/d. Thus, these patients are in relatively high risk to encounter immunological disturbances due to SRI-treatment.

Although immune parameters such as cytokine production, NK-cell activity and peripheral blood cell counts in OCD patients do not seem to be altered by paroxetine or venlafaxine in the absence of an immunological stimulus5, it is possible that SRI*s may supress the efficient mounting of an immune response when an immunological challenge, such as vaccination, is present. In animal studies, a suppression of the activated immune system by SRI*s has already been described in several models of auto-immune diseases6-9.

In this study, we aim to assess the immunological response to hepatitis B vaccination in OCD patients that are treated with high doses of SRI*s (60 mg/d paroxetine). Hepatitis B vaccination has only been added to the national vaccination programme in the Netherlands starting from 1 August 2011. Therefore, the majority of the adult Dutch population did not receive vaccination to hepatitis B during childhood. Although the patients that will be included in this study are not at elevated risk for hepatitis B infection, vaccination in these patients is considered favourable given the recent changes in hepatitis B vaccination policy.

The immunological response in SRI-treated OCD patients will be compared to the one in OCD patients not taking any medication. Healthy controls are not considered a suitable reference since the immune function in healthy controls might differ from the immune function in OCD patients. Indeed, alterations in cytokine levels and NK cell activity have been reported in OCD patients.10

The results of this study might have important implications for both psychiatric and immunological fields of medicine. Indeed, if SRI*s interfere with the efficient mounting of an immune response to hepatitis B vaccination and potentially other vaccines, adequate measures should be taken when vaccinating patients treated with (high doses of) SRI*s. Follow-up of serological parameters and cellular immune responses after vaccination would then become indispensable and adjustment of vaccine doses or temporary discontinuation of SRI-therapy should be considered.

## Study objective

The main objective of this study is to
1) Determine the immunological response to hepatitis B vaccination in OCD patients that are treated with 60 mg/d paroxetine and

2) Compare this response to the immunological response to hepatitis B vaccination in non-treated control OCD patients.

## Study design

This study is an open, parallel group pilot study consisting of two groups of patients: the first group consists of ten OCD patients treated with 60 mg/d paroxetine. The second group consists of ten OCD patients that are not treated with SRI*s. Healthy controls are not considered a suitable reference since the immune function in healthy controls might differ from the immune function in OCD patients. Thus, the underlying condition might bias the results if comparison was made to healthy controls. No changes in pharmacological treatment will be introduced during this study. OCD patients that are being treated with 60 mg/d paroxetine and meet the inclusion criteria will be asked to participate in the study and will be assigned to group 1 after written informed consent has been obtained. OCD patients not currently taking any serotonergic medication that meet the inclusion criteria and give informed consent will be assigned to group 2.

Many factors affecting the immunological response after hepatitis B vaccination have been described.11 The most important amongst them are age, sex and body mass index (BMI). Since the present study is aiming to estimate the difference in immunological response between OCD patients treated with 60 mg/d paroxetine and non-treated control OCD patients in a very small cohort, these confounding factors will be taken in consideration as much as possible at the time of inclusion. Very narrow inclusion criteria will be used, in order to exclude the possibility that these factors are influencing the immunological response to hepatitis B vaccination.

A full vaccination with Hepatitis B vaccine (Engerix-B) will be performed in all patients, i.e. three doses at months 0, 1 and 6. The immunological response will be determined at three timepoints: prior to administration of the first dose (month 0), prior to administration of the second dose (month 1) and 1 month after administration of the third dose (month 7). 33 ml of venous blood will be taken at each timepoint.

Patients will be recruited from the department of psychiatry, AMC. Patients that were previously treated at the department of psychiatry, AMC will be invited for participation in the study by letters.

## Intervention

A full vaccination with Hepatitis B vaccine (Engerix-B) will be performed in all patients, i.e. three doses at months 0, 1 and 6. The immunological response will be determined at three timepoints: prior to administration of the first dose (month 0), prior to administration of the second dose (month 1) and 1

month after administration of the third dose (month 7). 33 ml of venous blood will be taken at each timepoint.

**Study burden and risks**

Participation in this study brings only a limited potential risk to the patients. A registered vaccine will be administered, and blood samples (33 ml) will be taken at three timepoints. In total, four consultations are planned for each patient. These consultations will be scheduled as much as possible simultaneously with the consultations that patients undergo as part of their regular treatment, so that the burden for the patient in relation to invested time and transport costs is kept low.

# Contacts

**Public**
Universiteit Gent (België)

Meibergdreef 5
Amsterdam 1105 AZ
NL
**Scientific**
Universiteit Gent (België)

Meibergdreef 5
Amsterdam 1105 AZ
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

Primary diagnosis: obsessive compulsive disorder according to DSM-IV criteria based on a psychiatric interview
Age: 18-40 years old
Female
Body mass index (BMI) < 25
Treated with 60 mg/d paroxetine (group 1) or not taking any serotonergic medication (group 2)
Written informed consent
Dutch or English speaking and able to answer the study questions
Capable to make his or her own choice without coercion

## Exclusion criteria

Previous hepatitis B vaccination or hepatitis B infection
Suffering from auto-immune disease such as rheumatoid arthritis, lupus erythematosus etc.
A weakened immune system, due to conditions such as HIV
Kidney and/or liver diseases
The use of immunosuppressive medication such as corticosteroids, methotrexate, cyclosporine

# Study design

## Design

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| Study phase: | 4 |
| Study type: | Interventional |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |

**Primary purpose:** Treatment

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 13-11-2014 |
| Enrollment: | 20 |

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|---|---|
| Type: | Actual |

### Medical products/devices used

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| Product type: | Medicine |
| Brand name: | Engerix-B |

## Ethics review

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| Approved WMO Date: | 12-09-2013 |
| Application type: | First submission |
| 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 |
|---|---|
| EudraCT | EUCTR2013-001806-27-NL |
| CCMO | NL44776.018.13 |