# Clinical trial results:
# Effects of modafinil, caffeine and methylphenidate on functional brain activity and cognitive performance in healthy subjects: a randomized, placebo-controlled, double-blind fMRI study.

## Summary

| | |
|---|---|
| EudraCT number | 2012-003882-17 |
| Trial protocol | DE |
| Global end of trial date | 31 March 2014 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 03 April 2022 |
| First version publication date | 03 April 2022 |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | MKM |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02071615 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | Charité - Universitätsmedizin Berlin |
| Sponsor organisation address | Hindenburgdamm 30, Berlin, Germany, 12203 |
| Public contact | Dr. Dimitris Repantis, Klinik und Hochschulambulanz für Psychiatrie und Psychotherapie, Charitè-Universitätsmedizin, CBF, dimitris.repantis@charite.de |
| Scientific contact | Dr. Dimitris Repantis, Klinik und Hochschulambulanz für Psychiatrie und Psychotherapie, Charitè-Universitätsmedizin, CBF, dimitris.repantis@charite.de |

Notes:

### Paediatric regulatory details

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 31 March 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 March 2014 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 March 2014 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Resting state parameters from functional magnetic resonance imaging (fMRI).

Protection of trial subjects:

Safety: Blood pressure, heart rate, measures of subjective well-being (Visual Analogue Mood Scales, VAMS), adverse events (AE), serious adverse events (SAE), serious adverse reactions (SAR)

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 01 May 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Germany: 48 |
| Worldwide total number of subjects | 48 |
| EEA total number of subjects | 48 |

Notes:

### Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 48 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study was conducted at one study centers at Charité -Klinik für Psychiatrie und Psychotherapie- between August, 8th 2013 and March, 30 2014.

### Pre-assignment

Screening details:

right-handedness, healthy, male volunteers between 18-35th ages. Exclusion criteria: smokers or ex-smokers for less than 5 years, regular coffeine consumption> 4 cups per day, subjects with irregular circadian rhythm (eg shift workers), MR contraindications or other somatic illnesses or psychiatric disorders

### Period 1

| | |
|---|---|
| Period 1 title | overal trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Methylphanidate + Placebo |

Arm description:

Methylphenidate: single dose, 20 mg Methylphenidat Hexal®.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Methylphenidate |
| Investigational medicinal product code | 19262-68-1 |
| Other name | DEXMETHYLPHENIDATE HYDROCHLORIDE |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

subject received single dose 20mg Methylphenidate

| | |
|---|---|
| **Arm title** | Modafinil + Placebo |

Arm description:

Modafinil: single dose, 200 mg Vigil®

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Modafinil |
| Investigational medicinal product code | 68693-11-8 |
| Other name | |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

subject received single dose 200mg Modafinil

| | |
|---|---|
| **Arm title** | Coffeine + Placebo |

Arm description:

Coffeine: single dose, 200 mg Coffeinum®

| | |
|---|---|
| Arm type | Experimental |

| | |
|---|---|
| Investigational medicinal product name | Coffeine |
| Investigational medicinal product code | 58-08-2 |
| Other name | ANHYDROUS CAFFEINE |
| Pharmaceutical forms | Capsule |
| Routes of administration | Oral use |

Dosage and administration details:

subject received single dose 200mg Coffeine

| **Number of subjects in period 1** | Methylphanidate + Placebo | Modafinil + Placebo | Coffeine + Placebo |
|---|---|---|---|
| Started | 16 | 16 | 16 |
| Completed | 16 | 16 | 16 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | overal trial |

Reporting group description: -

| Reporting group values | overal trial | Total | |
|---|---|---|---|
| Number of subjects | 48 | 48 | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 48 | 48 | |
| Gender categorical<br>Units: Subjects | | | |
| Male | 48 | 48 | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Methylphanidate + Placebo |
| Reporting group description: Methylphenidate: single dose, 20 mg Methylphenidat Hexal®. | |

| | |
|---|---|
| Reporting group title | Modafinil + Placebo |
| Reporting group description: Modafinil: single dose, 200 mg Vigil® | |

| | |
|---|---|
| Reporting group title | Coffeine + Placebo |
| Reporting group description: Coffeine: single dose, 200 mg Coffeinum® | |

### Primary: functional connectivity (FC)

| | |
|---|---|
| End point title | functional connectivity (FC) |
| End point description: | |

| | |
|---|---|
| End point type | Primary |
| End point timeframe: 90 min | |

| End point values | Methylphanidate + Placebo | Modafinil + Placebo | Coffeine + Placebo | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 16 | 16 | 16 | |
| Units: Connectivity | | | | |
| number (not applicable) | 16 | 16 | 16 | |

### Statistical analyses

| Statistical analysis title | functional connectivity |
|---|---|
| Comparison groups | Methylphanidate + Placebo v Modafinil + Placebo v Coffeine + Placebo |
| Number of subjects included in analysis | 48 |
| Analysis specification | Pre-specified |
| Analysis type | other |
| P-value | ≤ 0.05 |
| Method | General Linear Model |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Day of assessment | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | own system |
| Dictionary version | 1 |

| Reporting groups | |
|---|---|
| Reporting group title | Methylphanidate + Placebo |
| Reporting group description: - | |
| Reporting group title | Modafin.+Placebo |
| Reporting group description: - | |
| Reporting group title | Coffein+Placebo |
| Reporting group description: - | |

| Serious adverse events | Methylphanidate + Placebo | Modafin.+Placebo | Coffein+Placebo |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 16 (0.00%) | 0 / 16 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Methylphanidate + Placebo | Modafin.+Placebo | Coffein+Placebo |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 2 / 16 (12.50%) | 3 / 16 (18.75%) |
| Nervous system disorders | | | |
| Headage | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 16 (6.25%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 1 | 1 |
| Psychiatric disorders | | | |
| sleep-onset insomnia | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 2 / 16 (12.50%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| sleep-maintenance insomnia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 16 (0.00%) | 0 / 16 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Restlessness | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 16 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 1 | 0 | 1 |
| Tiredness | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 16 (0.00%) | 1 / 16 (6.25%) |
| occurrences (all) | 0 | 0 | 1 |
| Renal and urinary disorders | | | |
| increased diuresis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 16 (0.00%) | 2 / 16 (12.50%) |
| occurrences (all) | 0 | 0 | 2 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/33201262