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 Units: Subjects			
Adults (18-64 years)	48	48	
Gender categorical 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