Clinical trial results:
STUDY OF ATTENTION AND IMPULSIVITY IN HEALTHY HUMAN VOLUNTEERS

Summary

EudraCT number	2018-003271-35
Trial protocol	DK
Global end of trial date	18 December 2019

Results information

Result version number	v1 (current)
This version publication date	25 September 2021
First version publication date	25 September 2021

Trial information

Trial identification

Sponsor protocol code	KU-AIM-01-2018

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	University of Copenhagen
Sponsor organisation address	Øster Farimagsgade 2A, Copenhagen, Denmark, 1353
Public contact	Jon Lansner, University of Copenhagen, 45 61668876, jl@psy.ku.dk
Scientific contact	Jon Lansner , University of Copenhagen, 45 61668876, jl@psy.ku.dk

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	15 December 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 December 2019
Global end of trial reached?	Yes
Global end of trial date	18 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to investigate in young, healthy participants whether and to what degree single doses of methylphenidate, atomoxetine, amphetamine, and modafinil:
a) enhance the TVA visual speed (C) and Visual Short Term Memory (VSTM) storage capacity (K) parameters,
b) produce a reduction on commission and omission errors, and improvements in d', reaction times and correct responses on the Conners CPT, and
c) whether objectively measured changes in visual perceptual speed are associated with changes in subjective alertness and pleasantness of the task.

Protection of trial subjects:

Participants will have no history of psychiatric, neurological or cardiovascular illness, no history of drug addiction. No pregnant or breastfeeding woman will be included. A pregnancy test will be done during the interview to avoid the inclusion of pregnant women. Women will be asked to follow any of the next contraception measures that have been considered acceptable by the CTFG. Subjects who are lactose intolerant or show any allergies to the excipients/active ingredients used in the administered drugs will not be included. Participants will have had no recreational use of psychostimulants in the last 3 months. Subject with a body mass index smaller than 18 or larger than 30 will be excluded for pharmacological safety and efficacy concerns.
Risk of side-effects is minimized by screening for psychiatric conditions using the MINI interview, by performing an electrocardiogram, and by measuring the blood pressure before and after the intervention. A medical emergency procedure protocol provided by the Capital Region of Denmark and the continuous presence of a doctor will ensure the most efficient handling of any unexpected side effects. The level of Investigational Medicinal Product (IMP) accountability undertaken should decrease the risk of treatment mishandling and ensure that adequate treatment is provided to the participants. The extent of drug accountability documentation has been considered adequate to ensure the integrity of the trial data and the safety of the participants.
There is no risk associated to the cognitive testing used for this study, although it may be accompanied by slight fatigue. Participants will not be allowed to drive/ride after testing. Subject may get monetary compensation for their use of public transportation. Skilled and experience professionals will be responsible for blood sampling, thus minimizing any potential discomfort.
After drug administration, a light meal will be provided to decrease potential nausea.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 February 2019
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	Denmark: 104
Worldwide total number of subjects	104
EEA total number of subjects	104

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)	104
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment will happen in the Copenhagen area using online advertisement and posters in study halls.

Pre-assignment

Screening details:

Screening is conducted via interviews, tests and questionnaires prior to testing

Pre-assignment period milestones

Number of subjects started	104
Number of subjects completed	99

Pre-assignment subject non-completion reasons

Reason: Number of subjects	History of psychiatric illness: 1
Reason: Number of subjects	Cardiovascular condition: 3
Reason: Number of subjects	major vision impairment: 1

Period 1

Period 1 title	AIM-C (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

To ensure that the administrator of the task does not know which treatment is given to each participant, electronic documents containing such information will be stored separately from the administration schema. This will be part of the randomization and blinding of treatments/participants. A collaboration with professionals from H. Lundbeck A/S has been established to optimize and ensure the quality of this process.

Arms

Are arms mutually exclusive?	Yes
Arm title	AIM-C Part A

Arm description:

Part A will be conducted on a different sample than Part B. The pharmacological tools to be used in this second study will be methylphenidate and atomoxetine. The general design for Part A is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for methylphenidate and atomoxetine (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Arm type	Experimental
Investigational medicinal product name	Methylphenidate
Investigational medicinal product code	N06BA04
Other name	Ritalin, Concerta
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Methylphenidate 20mg (2x10mg). Vendor: Alternova. Package Name: Methylphenidat “Alternova”,

tabletter
Methylphenidate 40mg (2x20mg). Vendor: Alternova. Package Name: Methylphenidat “Alternova”, tabletter
To ensure the placebo and drugs match the same sensory specifications over-encapsulation will be chosen as a blinding method. The process of over-encapsulation, together with the purchase of drugs, will be done in in collaboration with Capital Region Pharmacy.

Investigational medicinal product name	Atomoxetine
Investigational medicinal product code	N06BA09
Other name	Strattera, (R)-N-Methyl-3-phenyl-3-(o-tolyloxy)propan-1-amine
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Atomoxetine 40mg (1x40mg). Vendor: Actavis. Package name: Atomoxetin “Actavis” hårde kapsler
Atomoxetine 60mg (1x60mg). Vendor: Actavis. Package name: Atomoxetin “Actavis” hårde kapsler
To ensure the placebo and drugs match the same sensory specifications over-encapsulation will be chosen as a blinding method. The process of over-encapsulation, together with the purchase of drugs, will be done in in collaboration with Capital Region Pharmacy.

Arm title	AIM-C Part B

Arm description:

Part B will be conducted on a different sample. The pharmacological tools to be used in this second study will be dexamphetamine and modafinil. The general design for Part B is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for dexamphetamine and modafinil (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Arm type	Experimental
Investigational medicinal product name	Modafinil
Investigational medicinal product code	N06BA07
Other name	Provigil, Alertec, Modavigil, CRL-40476, Diphenylmethylsulfinylacetamide
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Modafinil 200 mg (2x100 mg), Vendor: Orion Corporation. Package name: Modafinil “Orion”, tabletter
Modafinil 400 mg (2x200 mg), Vendor: Orion Corporation. Package name: Modafinil “Orion”, tabletter
To ensure the placebo and drugs match the same sensory specifications over-encapsulation will be chosen as a blinding method. The process of over-encapsulation, together with the purchase of drugs, will be done in in collaboration with Capital Region Pharmacy.

Investigational medicinal product name	Dexamphetamine
Investigational medicinal product code	N06BA02
Other name	Dexedrine, DextroStat, Metamina, Attentin, Zenzedi, ProCentra, Amfexa, D-Amphetamine
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dexamphetamine 10mg (1x10mg), Vendor: Orifarm A7S. Package name: Attentin, tabletter (Orifarm A/S)
Dexamphetamine 10mg, (1x20mg) Vendor: Orifarm A7S. Package name: Attentin, tabletter (Orifarm A/S)
To ensure the placebo and drugs match the same sensory specifications over-encapsulation will be chosen as a blinding method. This is a common and effective solution to blinding solid oral formulations . The process of over-encapsulation, together with the purchase of drugs, will be done in in collaboration with Capital Region Pharmacy

Number of subjects in period 1[1]	AIM-C Part A	AIM-C Part B
Started	44	55
Attended visit 1	34	48
Completed	29	37
Not completed	15	18
Illness >2 weeks	2	3
Logistical reasons	6	-
Did not obtain contact lenses	1	-
Side-effects of the drugs	1	-
Inclusion criteria no longer met	2	-
Side-effects of the treatment	-	3
Personal or logistic reasons	-	9
No response after contact	3	3

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: 104 subjects attended the screening visit during the pre-assignment period, however 5 subjects did not meet the criteria for inclusion, and thus only 99 were enrolled in the study, as described. This creates a confusion in this registration system, as the 104 are counted as part of the baseline period, when in fact only 99 were included.

Baseline characteristics

Reporting groups	
Reporting group title	AIM-C
Reporting group description: -	

Reporting group values	AIM-C	Total	
Number of subjects	99	99	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	99	99	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	24.19		
standard deviation	± 2.79	-	
Gender categorical Units: Subjects			
Female	67	67	
Male	32	32	
ASRS - Adult Self-Report Scale questionnaire			
Number of marks in the darkly shaded boxes in the first 6 questions, indicating potential adult ADHD. Kessler, R. C., Adler, L. A., Gruber, M. J., Sarawate, C. A., Spencer, T., & Van Brunt, D. L. (2007). Validity of the World Health Organization Adult ADHD SelfReport Scale (ASRS) Screener in a representative sample of health plan members. International journal of methods in psychiatric research, 16(2), 52-65.			
Units: Part A score (0-6)			
arithmetic mean	1.48		
standard deviation	± 1.42	-	

Subject analysis sets	
Subject analysis set title	Part A - Attended first visit
Subject analysis set type	Full analysis
Subject analysis set description: Only subjects that had attended atleast one visit was included in the analysis.	
Subject analysis set title	Part B - Attended first visit
Subject analysis set type	Full analysis
Subject analysis set description: Participants in Part B	

Subject analysis set title	Part A - Placebo
Subject analysis set type	Full analysis
Subject analysis set description: The placebo condition for participants in Part A	
Subject analysis set title	Part A - MPH20
Subject analysis set type	Full analysis
Subject analysis set description: The methylphenidate 20mg condition for participants in Part A	
Subject analysis set title	Part A - MPH40
Subject analysis set type	Full analysis
Subject analysis set description: The methylphenidate 40mg condition for participants in Part A	
Subject analysis set title	Part A - ATX40
Subject analysis set type	Full analysis
Subject analysis set description: The atomoxetine 40mg condition for participants in Part A	
Subject analysis set title	Part A - ATX60
Subject analysis set type	Full analysis
Subject analysis set description: The atomoxetine 60mg condition for participants in Part A	
Subject analysis set title	Part B - AMPH10
Subject analysis set type	Full analysis
Subject analysis set description: The dexamphetamine 10mg condition for participants in Part B	
Subject analysis set title	Part B - AMPH20
Subject analysis set type	Full analysis
Subject analysis set description: The dexamphetamine 20mg condition for participants in Part B	
Subject analysis set title	Part B - MOD200
Subject analysis set type	Full analysis
Subject analysis set description: The modafinil 200mg condition for participants in Part B	
Subject analysis set title	Part B - MOD400
Subject analysis set type	Full analysis
Subject analysis set description: The modafinil 400mg condition for participants in Part B	
Subject analysis set title	Part B - Placebo
Subject analysis set type	Full analysis
Subject analysis set description: The placebo condition for participants in Part B	

Reporting group values	Part A - Attended first visit	Part B - Attended first visit	Part A - Placebo
Number of subjects	34	48	32
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years)			

Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over	34	48	32
Age continuous Units: years arithmetic mean standard deviation	24.24 ± 2.73	23.94 ± 2.36	 ±
Gender categorical Units: Subjects			
Female Male	26 8	30 18	
ASRS - Adult Self-Report Scale questionnaire			
Number of marks in the darkly shaded boxes in the first 6 questions, indicating potential adult ADHD. Kessler, R. C., Adler, L. A., Gruber, M. J., Sarawate, C. A., Spencer, T., & Van Brunt, D. L. (2007). Validity of the World Health Organization Adult ADHD SelfReport Scale (ASRS) Screener in a representative sample of health plan members. International journal of methods in psychiatric research, 16(2), 52-65.			
Units: Part A score (0-6) arithmetic mean standard deviation	 1.56 ± 1.46	 1.43 ± 1.43	 ±

Reporting group values	Part A - MPH20	Part A - MPH40	Part A - ATX40
Number of subjects	32	30	30
Age categorical Units: Subjects			
In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over	 32	 30	 30
Age continuous Units: years arithmetic mean standard deviation	 ±	 ±	 ±
Gender categorical Units: Subjects			
Female Male			
ASRS - Adult Self-Report Scale questionnaire			
Number of marks in the darkly shaded boxes in the first 6 questions, indicating potential adult ADHD. Kessler, R. C., Adler, L. A., Gruber, M. J., Sarawate, C. A., Spencer, T., & Van Brunt, D. L. (2007). Validity of the World Health Organization Adult ADHD SelfReport Scale (ASRS) Screener in a representative sample of health plan members. International journal of methods in psychiatric research, 16(2), 52-65.			

Units: Part A score (0-6)			
arithmetic mean			
standard deviation	±	±	±

Reporting group values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20
Number of subjects	30	41	41
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	30	41	41
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	±
Gender categorical			
Units: Subjects			
Female			
Male			
ASRS - Adult Self-Report Scale questionnaire			
Number of marks in the darkly shaded boxes in the first 6 questions, indicating potential adult ADHD. Kessler, R. C., Adler, L. A., Gruber, M. J., Sarawate, C. A., Spencer, T., & Van Brunt, D. L. (2007). Validity of the World Health Organization Adult ADHD SelfReport Scale (ASRS) Screener in a representative sample of health plan members. International journal of methods in psychiatric research, 16(2), 52-65.			
Units: Part A score (0-6)			
arithmetic mean			
standard deviation	±	±	±

Reporting group values	Part B - MOD200	Part B - MOD400	Part B - Placebo
Number of subjects	43	44	44
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)	43	44	44
From 65-84 years			
85 years and over			

Age continuous Units: years arithmetic mean standard deviation	± 	± 	±
Gender categorical Units: Subjects			
Female Male			
ASRS - Adult Self-Report Scale questionnaire			
Number of marks in the darkly shaded boxes in the first 6 questions, indicating potential adult ADHD. Kessler, R. C., Adler, L. A., Gruber, M. J., Sarawate, C. A., Spencer, T., & Van Brunt, D. L. (2007). Validity of the World Health Organization Adult ADHD SelfReport Scale (ASRS) Screener in a representative sample of health plan members. International journal of methods in psychiatric research, 16(2), 52-65.			
Units: Part A score (0-6) arithmetic mean standard deviation	± 	± 	±

End points reporting groups

Reporting group title	AIM-C Part A

Reporting group description:

Part A will be conducted on a different sample than Part B. The pharmacological tools to be used in this second study will be methylphenidate and atomoxetine. The general design for Part A is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for methylphenidate and atomoxetine (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Reporting group title	AIM-C Part B

Reporting group description:

Part B will be conducted on a different sample. The pharmacological tools to be used in this second study will be dexamphetamine and modafinil. The general design for Part B is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for dexamphetamine and modafinil (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Subject analysis set title	Part A - Attended first visit
Subject analysis set type	Full analysis

Subject analysis set description:

Only subjects that had attended atleast one visit was included in the analysis.

Subject analysis set title	Part B - Attended first visit
Subject analysis set type	Full analysis

Subject analysis set description:

Participants in Part B

Subject analysis set title	Part A - Placebo
Subject analysis set type	Full analysis

Subject analysis set description:

The placebo condition for participants in Part A

Subject analysis set title	Part A - MPH20
Subject analysis set type	Full analysis

Subject analysis set description:

The methylphenidate 20mg condition for participants in Part A

Subject analysis set title	Part A - MPH40
Subject analysis set type	Full analysis

Subject analysis set description:

The methylphenidate 40mg condition for participants in Part A

Subject analysis set title	Part A - ATX40
Subject analysis set type	Full analysis

Subject analysis set description:

The atomoxetine 40mg condition for participants in Part A

Subject analysis set title	Part A - ATX60
Subject analysis set type	Full analysis

Subject analysis set description:

The atomoxetine 60mg condition for participants in Part A

Subject analysis set title	Part B - AMPH10
Subject analysis set type	Full analysis
Subject analysis set description:	
The dexamphetamine 10mg condition for participants in Part B	
Subject analysis set title	Part B - AMPH20
Subject analysis set type	Full analysis
Subject analysis set description:	
The dexamphetamine 20mg condition for participants in Part B	
Subject analysis set title	Part B - MOD200
Subject analysis set type	Full analysis
Subject analysis set description:	
The modafinil 200mg condition for participants in Part B	
Subject analysis set title	Part B - MOD400
Subject analysis set type	Full analysis
Subject analysis set description:	
The modafinil 400mg condition for participants in Part B	
Subject analysis set title	Part B - Placebo
Subject analysis set type	Full analysis
Subject analysis set description:	
The placebo condition for participants in Part B	

Primary: d-prime CPT

End point title	d-prime CPT
End point description:	
d-prime of the CPT task	
End point type	Primary
End point timeframe:	
Effects of MPH and ATX on the CPT were tested 125 minutes after ingestion of drug or placebo. Effects of AMPH and MOD on the CPT were tested 155 minutes after ingestion of drug or placebo.	

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[1]	32[2]	30[3]	30[4]
Units: standard deviation				
arithmetic mean (standard error)	-3.24 (± 0.91)	-3.53 (± 0.59)	-3.42 (± 0.66)	-3.19 (± 0.9)

Notes:

[1] - The placebo condition for participants in Part A

[2] - This was a cross over design

[3] - This was a crossover design

[4] - This was a crossover design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[5]	41[6]	41[7]	43[8]
Units: standard deviation				
arithmetic mean (standard error)	-3.18 (± 0.73)	-3.50 (± 0.74)	-3.65 (± 0.65)	-3.45 (± 0.67)

Notes:
[5] - This was a crossover design
[6] - This was a crossover design
[7] - This was a crossover design
[8] - This was a crossover design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[9]	44[10]		
Units: standard deviation				
arithmetic mean (standard error)	-3.51 (± 0.58)	-3.22 (± 0.62)		

Notes:
[9] - This was a crossover design
[10] - This was a crossover design

Statistical analyses

Statistical analysis title	d-prime: Placebo - MPH20

Statistical analysis description:
Difference between Placebo and MPH20

Evaluated via a linear mixed-effects model:

[d-prime + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.01
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	-0.07
Variability estimate	Standard error of the mean
Dispersion value	0.1

Statistical analysis title	d-prime: Placebo - MPH40

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[d-prime + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH40

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.44
upper limit	-0.03
Variability estimate	Standard error of the mean
Dispersion value	0.1

Statistical analysis title	d-prime: Placebo - ATX40

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[d-prime + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.55
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.27
Variability estimate	Standard error of the mean
Dispersion value	0.1

Statistical analysis title	d-prime: Placebo - ATX60

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[d-prime + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX60

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.49
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.28
Variability estimate	Standard error of the mean
Dispersion value	0.1

Statistical analysis title	d-prime: Placebo - AMPH10

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[d-prime + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - AMPH10 v Part B - Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.44
upper limit	-0.1
Variability estimate	Standard error of the mean
Dispersion value	0.09

Statistical analysis title	d-prime: Placebo - AMPH20

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[d-prime + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH20

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	-0.24
Variability estimate	Standard error of the mean
Dispersion value	0.09

Statistical analysis title	d-prime: Placebo - MOD200

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[d-prime + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.016
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	-0.04
Variability estimate	Standard error of the mean
Dispersion value	0.08

Statistical analysis title	d-prime: Placebo - MOD400

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[d-prime + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD400

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.44
upper limit	-0.11
Variability estimate	Standard error of the mean
Dispersion value	0.08

Primary: C - CPT

End point title	C - CPT

End point description:

Decision criterion for the CPT

End point type	Primary

End point timeframe:

Effects of MPH and ATX on the CPT were tested 125 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the CPT were tested 155 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[11]	32[12]	30[13]	30[14]
Units: standard deviation				
arithmetic mean (standard error)	-0.86 (± 0.32)	-0.91 (± 0.21)	-0.87 (± 0.29)	-0.85 (± 0.37)

Notes:

[11] - This was performed in a crossover design

[12] - This was performed in a crossover design

[13] - This was performed in a crossover design

[14] - This was performed in a crossover design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[15]	41[16]	41[17]	43[18]
Units: standard deviation				
arithmetic mean (standard error)	-0.84 (± 0.34)	-0.96 (± 0.24)	-0.92 (± 0.21)	-0.92 (± 0.22)

Notes:

[15] - This was performed in a crossover design

[16] - This was performed in a crossover design

[17] - This was performed in a crossover design

[18] - This was performed in a crossover design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[19]	44[20]		
Units: standard deviation				
arithmetic mean (standard error)	-0.95 (± 0.2)	-0.94 (± 0.25)		

Notes:

[19] - This was performed in a crossover design

[20] - This was performed in a crossover design

Statistical analyses

Statistical analysis title	C-CPT: Placebo - MPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.34
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.153
upper limit	0.053
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	C-CPT: Placebo - MPH40

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.87
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.097
upper limit	0.115
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	C-CPT: Placebo - ATX40

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.79
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.119
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	d-prime: Placebo - ATX60

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.74
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.088
upper limit	0.123
Variability estimate	Standard error of the mean
Dispersion value	0.05

Statistical analysis title	C-CPT: Placebo - AMPH10

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH10
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.056
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.082
upper limit	0.044
Variability estimate	Standard error of the mean
Dispersion value	0.03

Statistical analysis title	C-CPT: Placebo - AMPH20

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.63
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.048
upper limit	0.078
Variability estimate	Standard error of the mean
Dispersion value	0.03

Statistical analysis title	C-CPT: Placebo - MOD200

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.58
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.045
upper limit	0.079
Variability estimate	Standard error of the mean
Dispersion value	0.03

Statistical analysis title	C-CPT: Placebo - MOD400

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - MOD400 v Part B - Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.74
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.071
upper limit	0.051
Variability estimate	Standard error of the mean
Dispersion value	0.03

Primary: HRT - CPT

End point title	HRT - CPT

End point description:

Hit Reaction Time in the Continuous Performance Task

End point type	Primary

End point timeframe:

Effects of MPH and ATX on the CPT were tested 125 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the CPT were tested 155 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[21]	32[22]	30[23]	30[24]
Units: milliseconds				
arithmetic mean (standard error)	353.90 (± 50.21)	338.43 (± 38.57)	342.95 (± 40.98)	354.71 (± 51.52)

Notes:

[21] - This was performed in a cross-over design

[22] - This was performed in a cross-over design

[23] - This was performed in a cross-over design

[24] - This was performed in a cross-over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[25]	41[26]	41[27]	43[28]
Units: milliseconds				
arithmetic mean (standard error)	357.43 (± 56.65)	328.47 (± 32.65)	333.48 (± 34.34)	332.9 (± 33.49)

Notes:

[25] - This was performed in a cross-over design

[26] - This was performed in a cross-over design

[27] - This was performed in a cross-over design

[28] - This was performed in a cross-over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[29]	44[30]		

Units: milliseconds				
arithmetic mean (standard error)	327.97 (± 31.12)	338.03 (± 37.51)		

Notes:

[29] - This was performed in a cross-over design

[30] - This was performed in a cross-over design

Statistical analyses

Statistical analysis title	HRT-CPT: Placebo - MPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[HRT + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-15.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.929
upper limit	-7.357
Variability estimate	Standard error of the mean
Dispersion value	4.19

Statistical analysis title	HRT-CPT: Placebo - MPH40

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[HRT + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-10.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.106
upper limit	-2.043

Variability estimate	Standard error of the mean
Dispersion value	4.32

Statistical analysis title	HRT-CPT: Placebo - ATX40

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[HRT + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.94
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.804
upper limit	8.142
Variability estimate	Standard error of the mean
Dispersion value	4.29

Statistical analysis title	HRT-CPT: Placebo - ATX60

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[HRT + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - ATX60 v Part A - Placebo
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.72
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.56
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.959
upper limit	10.084
Variability estimate	Standard error of the mean
Dispersion value	4.31

Statistical analysis title	HRT-CPT: Placebo - AMPH10

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[HRT + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH10
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-10.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.302
upper limit	-4.987
Variability estimate	Standard error of the mean
Dispersion value	2.62

Statistical analysis title	HRT-CPT: Placebo - AMPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[HRT + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.002
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-8.37
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.523
upper limit	-3.207
Variability estimate	Standard error of the mean
Dispersion value	2.61

Statistical analysis title	HRT-CPT: Placebo - MOD200

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[HRT + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.01
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-6.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.69
upper limit	-1.547
Variability estimate	Standard error of the mean
Dispersion value	2.57

Statistical analysis title	HRT-CPT: Placebo - MOD400

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[HRT + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD400
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-12.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-17.542
upper limit	-7.515
Variability estimate	Standard error of the mean
Dispersion value	2.54

Primary: HRT.SD - CPT

End point title	HRT.SD - CPT

End point description:

The standard deviation of the Hit Reaction Time in the Continuous Performance Task

End point type	Primary

End point timeframe:

Effects of MPH and ATX on the CPT were tested 125 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the CPT were tested 155 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[31]	32[32]	30[33]	30[34]
Units: milliseconds				
arithmetic mean (standard error)	0.2 (± 0.06)	0.17 (± 0.04)	0.17 (± 0.03)	0.2 (± 0.06)

Notes:

[31] - Conducted in a cross-over design

[32] - Conducted in a cross-over design

[33] - Conducted in a cross-over design

[34] - Conducted in a cross-over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[35]	41[36]	41[37]	43[38]
Units: milliseconds				
arithmetic mean (standard error)	0.2 (± 0.05)	0.18 (± 0.05)	0.17 (± 0.04)	0.18 (± 0.04)

Notes:

[35] - Conducted in a cross-over design

[36] - Conducted in a cross-over design

[37] - Conducted in a cross-over design

[38] - Conducted in a cross-over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[39]	44[40]		
Units: milliseconds				
arithmetic mean (standard error)	0.17 (± 0.03)	0.2 (± 0.05)		

Notes:

[39] - Conducted in a cross-over design

[40] - Conducted in a cross-over design

Statistical analyses

Statistical analysis title	HRT.SD - CPT: Placebo - MPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[HRT.SD + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH20

Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.044
upper limit	-0.018
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	HRT.SD - CPT: Placebo - MPH40

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[HRT.SD + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	-0.023
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	HRT.SD - CPT: Placebo - ATX40

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[HRT.SD + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX40

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.64
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.016
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	HRT.SD - CPT: Placebo - ATX60

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[HRT.SD + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.56
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.017
upper limit	0.009
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	HRT.SD - CPT: Placebo - AMPH10

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[HRT.SD + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH10

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	-0.01
Variability estimate	Standard error of the mean
Dispersion value	0.005

Statistical analysis title	HRT.SD - CPT: Placebo - AMPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[HRT.SD + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.042
upper limit	-0.022
Variability estimate	Standard error of the mean
Dispersion value	0.005

Statistical analysis title	HRT.SD - CPT: Placebo - MOD200

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[HRT.SD + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD200

Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.005
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.024
upper limit	-0.004
Variability estimate	Standard error of the mean
Dispersion value	0.005

Statistical analysis title	HRT.SD - CPT: Placebo - MOD400

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[HRT.SD + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD400
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.035
upper limit	-0.016
Variability estimate	Standard error of the mean
Dispersion value	0.005

Primary: VAR - CPT

End point title	VAR - CPT

End point description:

Variability in hit reaction time between sub-blocks of the continuous performance test.

End point type	Primary

End point timeframe:

Effects of MPH and ATX on the CPT were tested 125 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the CPT were tested 155 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[41]	32[42]	30[43]	30[44]
Units: milliseconds				
arithmetic mean (standard error)	0.05 (± 0.02)	0.04 (± 0.01)	0.04 (± 0.01)	0.05 (± 0.02)

Notes:

[41] - Conducted wit a cross-over design

[42] - Conducted wit a cross-over design

[43] - Conducted wit a cross-over design

[44] - Conducted wit a cross-over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[45]	41[46]	41[47]	43[48]
Units: milliseconds				
arithmetic mean (standard error)	0.05 (± 0.02)	0.05 (± 0.03)	0.04 (± 0.02)	0.05 (± 0.02)

Notes:

[45] - Conducted wit a cross-over design

[46] - Conducted wit a cross-over design

[47] - Conducted with a cross-over design

[48] - Conducted with a cross-over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[49]	44[50]		
Units: milliseconds				
arithmetic mean (standard error)	0.04 (± 0.01)	0.05 (± 0.02)		

Notes:

[49] - Conducted with a cross-over design

[50] - Conducted with a cross-over design

Statistical analyses

Statistical analysis title	VAR - CPT: MPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[VAR + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.07
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.014
upper limit	0.001
Variability estimate	Standard error of the mean
Dispersion value	0

Statistical analysis title	CAR - CPT: MPH40

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[VAR + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.016
upper limit	-0.001
Variability estimate	Standard error of the mean
Dispersion value	0

Statistical analysis title	VAR - CPT: ATX40

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[VAR + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.69
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.006
upper limit	0.009

Variability estimate	Standard error of the mean
Dispersion value	0

Statistical analysis title	VAR - CPT: ATX60

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[VAR + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.003
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.005
upper limit	0.01
Variability estimate	Standard error of the mean
Dispersion value	0

Statistical analysis title	VAR - CPT: AMPH10

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[VAR + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH10
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.07
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.005
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.011
upper limit	0
Variability estimate	Standard error of the mean
Dispersion value	0.003

Statistical analysis title	VAR - CPT: AMPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[VAR + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.011
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.017
upper limit	-0.005
Variability estimate	Standard error of the mean
Dispersion value	0.003

Statistical analysis title	VAR - CPT: MOD200

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[VAR + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.03
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.006
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.012
upper limit	-0.001
Variability estimate	Standard error of the mean
Dispersion value	0.003

Statistical analysis title	VAR - CPT: MOD400

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[VAR + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD400

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.012
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.017
upper limit	-0.005
Variability estimate	Standard error of the mean
Dispersion value	0.003

Primary: BLKCH - CPT

End point title	BLKCH - CPT

End point description:

Variations in hit reaction time between blocks in the continuous performance task

End point type	Primary

End point timeframe:

Effects of MPH and ATX on the CPT were tested 125 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the CPT were tested 155 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[51]	32[52]	30[53]	30[54]
Units: milliseconds				
arithmetic mean (standard error)	0.006 (± 0.004)	0.001 (± 0.003)	0.01 (± 0.002)	0.013 (± 0.004)

Notes:

[51] - Conducted using a cross-over design

[52] - Conducted using a cross-over design

[53] - Conducted using a cross-over design

[54] - Conducted using a cross-over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[55]	41[56]	41[57]	43[58]
Units: milliseconds				
arithmetic mean (standard error)	0.014 (± 0.004)	0.002 (± 0.002)	0.005 (± 0.001)	0.002 (± 0.002)

Notes:

[55] - Conducted using a cross-over design

[56] - Conducted using a cross-over design
[57] - Conducted using a cross-over design
[58] - Conducted using a cross-over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[59]	44[60]		
Units: milliseconds				
arithmetic mean (standard error)	0.009 (± 0.002)	0.0043 (± 0.002)		

Notes:
[59] - Conducted using a cross-over design
[60] - Conducted using a cross-over design

Statistical analyses

Statistical analysis title	BLKCH - CPT: MPH20

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[BLKCH + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.17
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.012
upper limit	0.002
Variability estimate	Standard error of the mean
Dispersion value	0

Statistical analysis title	BLKCH - CPT: MPH40

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[BLKCH + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH40

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.25
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.003
upper limit	0.012
Variability estimate	Standard error of the mean
Dispersion value	0

Statistical analysis title	BLKCH - CPT: ATX40

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[BLKCH + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.001
upper limit	0.014
Variability estimate	Standard error of the mean
Dispersion value	0

Statistical analysis title	BLKCH - CPT: ATX60

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[BLKCH + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX60

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.08
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.001
upper limit	0.014
Variability estimate	Standard error of the mean
Dispersion value	0

Statistical analysis title	BLKCH - CPT: AMPH10

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[BLKCH + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - AMPH10 v Part B - Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.27
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.002
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.007
upper limit	0.002
Variability estimate	Standard error of the mean
Dispersion value	0.002

Statistical analysis title	BLKCH - CPT: AMPH20

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[BLKCH + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH20

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.91
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.0003
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.004
upper limit	0.005
Variability estimate	Standard error of the mean
Dispersion value	0.002

Statistical analysis title	BLKCH - CPT: MOD200

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[BLKCH + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.24
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.003
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.007
upper limit	0.002
Variability estimate	Standard error of the mean
Dispersion value	0.002

Statistical analysis title	BLKCH - CPT: MOD400

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[BLKCH + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - MOD400 v Part B - Placebo

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.047
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.004
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.008
Variability estimate	Standard error of the mean
Dispersion value	0.002

Primary: ISI - CPT

End point title	ISI - CPT

End point description:

Variability in hit reaction time between different inter-stimulus interval conditions in the continuous performance task

End point type	Primary

End point timeframe:

Effects of MPH and ATX on the CPT were tested 125 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the CPT were tested 155 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[61]	32[62]	30[63]	30[64]
Units: milliseconds				
arithmetic mean (standard error)	0.057 (± 0.006)	0.048 (± 0.004)	0.041 (± 0.004)	0.049 (± 0.005)

Notes:

[61] - This was conducted using a cross over design

[62] - This was conducted using a cross over design

[63] - This was conducted using a cross over design

[64] - This was conducted using a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[65]	41[66]	41[67]	43[68]
Units: milliseconds				
arithmetic mean (standard error)	0.049 (± 0.004)	0.043 (± 0.003)	0.041 (± 0.003)	0.052 (± 0.004)

Notes:
[65] - This was conducted using a cross over design
[66] - This was conducted using a cross over design
[67] - This was conducted using a cross over design
[68] - This was conducted using a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[69]	44[70]		
Units: milliseconds				
arithmetic mean (standard error)	0.046 (± 0.004)	0.051 (± 0.005)		

Notes:
[69] - This was conducted using a cross over design
[70] - This was conducted using a cross over design

Statistical analyses

Statistical analysis title	ISI - CPT: MPH20

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[ISI + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.018
upper limit	-0.002
Variability estimate	Standard error of the mean
Dispersion value	0

Statistical analysis title	ISI - CPT: MPH40

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[ISI + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH40

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	-0.007
Variability estimate	Standard error of the mean
Dispersion value	0

Statistical analysis title	ISI - CPT: ATX40

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[ISI + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.16
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.002
Variability estimate	Standard error of the mean
Dispersion value	0

Statistical analysis title	ISI - CPT: ATX60

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[ISI + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX60

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.096
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.016
upper limit	0.001
Variability estimate	Standard error of the mean
Dispersion value	0

Statistical analysis title	ISI - CPT: AMPH10

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[ISI + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH10
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.009
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.008
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.015
upper limit	-0.002
Variability estimate	Standard error of the mean
Dispersion value	0.003

Statistical analysis title	ISI - CPT: AMPH20

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[ISI + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - AMPH20 v Part B - Placebo

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.017
upper limit	-0.005
Variability estimate	Standard error of the mean
Dispersion value	0.003

Statistical analysis title	ISI - CPT: MOD200

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[ISI + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - MOD200 v Part B - Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.41
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.003
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.003
upper limit	0.008
Variability estimate	Standard error of the mean
Dispersion value	0.003

Statistical analysis title	ISI - CPT: MOD400

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[ISI + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - MOD400 v Part B - Placebo

Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.005
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.01
upper limit	0.001
Variability estimate	Standard error of the mean
Dispersion value	0.003

Primary: K - TVA

End point title	K - TVA

End point description:

Maximal number of letters contained in Visual Short Term Memory

End point type	Primary

End point timeframe:

Effects of MPH and ATX on the TVA were tested 90 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the TVA were tested 120 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[71]	32[72]	30[73]	30[74]
Units: Letters				
arithmetic mean (standard error)	3.36 (± 0.64)	3.31 (± 0.54)	3.42 (± 0.55)	3.30 (± 0.66)

Notes:

[71] - Conducted in a cross over design

[72] - Conducted in a cross over design

[73] - Conducted in a cross over design

[74] - Conducted in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[75]	41[76]	41[77]	43[78]
Units: Letters				
arithmetic mean (standard error)	3.24 (± 0.57)	3.68 (± 0.59)	3.71 (± 0.68)	3.61 (± 0.62)

Notes:

[75] - Conducted in a cross over design

[76] - Conducted in a cross over design

[77] - Conducted in a cross over design

[78] - Conducted in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[79]	44[80]		
Units: Letters				
arithmetic mean (standard error)	3.66 (± 0.62)	3.66 (± 0.63)		

Notes:

[79] - Conducted in a cross over design

[80] - Conducted in a cross over design

Statistical analyses

Statistical analysis title	K - TVA: MPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[K + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.45
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.154
upper limit	0.068
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	K - TVA: MPH40

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[K + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.12
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.09

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.233
upper limit	0.204
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	K - TVA: ATX40

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[K + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.25
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.181
upper limit	0.047
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	K - TVA: ATX60

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[K + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.05
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.231
upper limit	-0.002
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	K - TVA: AMPH10

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[K + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH10
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.59
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.147
upper limit	0.083
Variability estimate	Standard error of the mean
Dispersion value	0.07

Statistical analysis title	K - TVA: AMPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[K + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.33
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.06

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.058
upper limit	0.171
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	K - TVA: MOD200

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[K + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.33
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.168
upper limit	0.057
Variability estimate	Standard error of the mean
Dispersion value	0.06

Statistical analysis title	K - TVA: MOD400

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[K + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - MOD400 v Part B - Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.96
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.002

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.108
upper limit	0.114
Variability estimate	Standard error of the mean
Dispersion value	0.006

Primary: t0 - TVA

End point title	t0 - TVA

End point description:

The shortest exposure duration in which the participant can report atleast one letter

End point type	Primary

End point timeframe:

Effects of MPH and ATX on the TVA were tested 90 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the TVA were tested 120 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[81]	32[82]	30[83]	30[84]
Units: milliseconds				
arithmetic mean (standard error)	17.421 (± 1.776)	16.572 (± 1.719)	15.076 (± 1.479)	17.046 (± 1.874)

Notes:

[81] - This was conducted in a cross over design

[82] - This was conducted in a cross over design

[83] - This was conducted in a cross over design

[84] - This was conducted in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[85]	41[86]	41[87]	43[88]
Units: milliseconds				
arithmetic mean (standard error)	18.328 (± 1.763)	15.307 (± 1.652)	16.777 (± 1.809)	17.014 (± 1.854)

Notes:

[85] - This was conducted in a cross over design

[86] - This was conducted in a cross over design

[87] - This was conducted in a cross over design

[88] - This was conducted in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[89]	44[90]		
Units: milliseconds				

arithmetic mean (standard error)	16.698 (± 1.581)	14.854 (± 1.15)		

Notes:

[89] - This was conducted in a cross over design

[90] - This was conducted in a cross over design

Statistical analyses

Statistical analysis title	t0 - TVA: MPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[t0 + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - MPH20 v Part A - Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.995
upper limit	1.467
Variability estimate	Standard error of the mean
Dispersion value	1.13

Statistical analysis title	t0 - TVA: MPH40

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[t0 + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.07
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.392
upper limit	0.151

Variability estimate	Standard error of the mean
Dispersion value	1.15

Statistical analysis title	t0 - TVA: ATX40

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[t0 + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.95
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.359
upper limit	2.205
Variability estimate	Standard error of the mean
Dispersion value	1.15

Statistical analysis title	t0 - TVA: ATX60

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[t0 + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.27
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.023
upper limit	3.569
Variability estimate	Standard error of the mean
Dispersion value	1.16

Statistical analysis title	t0 - TVA: AMPH10

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[t0 + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - AMPH10 v Part B - Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.66
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.501
upper limit	2.372
Variability estimate	Standard error of the mean
Dispersion value	0.98

Statistical analysis title	t0 - TVA: AMPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[t0 + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.18
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.612
upper limit	3.252
Variability estimate	Standard error of the mean
Dispersion value	0.98

Statistical analysis title	t0 - TVA: MOD200

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[t0 + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - MOD200 v Part B - Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.15
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.507
upper limit	3.294
Variability estimate	Standard error of the mean
Dispersion value	0.96

Statistical analysis title	t0 - TVA: MOD400

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[t0 + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - MOD400 v Part B - Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.042
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.066
upper limit	3.795
Variability estimate	Standard error of the mean
Dispersion value	0.95

Primary: C - TVA

End point title	C - TVA

End point description:

Visual Processing Speed in the Theory of VIsual Attention Test

End point type	Primary

End point timeframe:

Effects of MPH and ATX on the TVA were tested 90 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the TVA were tested 120 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[91]	32[92]	30[93]	30[94]
Units: letters pr second				
arithmetic mean (standard error)	76.12 (± 31.95)	84.32 (± 32.56)	83.87 (± 31.97)	80.85 (± 27.50)

Notes:

[91] - This was conducted in a cross over design

[92] - This was conducted in a cross over design

[93] - This was conducted in a cross over design

[94] - This was conducted in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[95]	41[96]	41[97]	43[98]
Units: letters pr second				
arithmetic mean (standard error)	85.20 (± 28.31)	125.33 (± 146.86)	118.11 (± 155.35)	105.72 (± 90.75)

Notes:

[95] - This was conducted in a cross over design

[96] - This was conducted in a cross over design

[97] - This was conducted in a cross over design

[98] - This was conducted in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[99]	44[100]		
Units: letters pr second				
arithmetic mean (standard error)	90 (± 40.37)	92.64 (± 52.02)		

Notes:

[99] - This was conducted in a cross over design

[100] - This was conducted in a cross over design

Statistical analyses

Statistical analysis title	C- TVA: MPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - MPH20 v Part A - Placebo

Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.11
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	7.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.796
upper limit	16.589
Variability estimate	Standard error of the mean
Dispersion value	4.65

Statistical analysis title	C - TVA: MPH40

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.07
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	8.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.677
upper limit	18.005
Variability estimate	Standard error of the mean
Dispersion value	4.73

Statistical analysis title	C- -TVA: ATX40

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX40

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.41
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	3.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.456
upper limit	13.331
Variability estimate	Standard error of the mean
Dispersion value	4.75

Statistical analysis title	C - TVA: ATX60

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.06
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	9.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.312
upper limit	18.567
Variability estimate	Standard error of the mean
Dispersion value	4.78

Statistical analysis title	C - TVA: AMPH10

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH10

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	15.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.443
upper limit	23.732
Variability estimate	Standard error of the mean
Dispersion value	4.38

Statistical analysis title	C - TVA: AMPH20

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.013
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	10.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.331
upper limit	19.588
Variability estimate	Standard error of the mean
Dispersion value	4.38

Statistical analysis title	C - TVA: MOD200

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD200

Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.056
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	8.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.232
upper limit	16.744
Variability estimate	Standard error of the mean
Dispersion value	4.3

Statistical analysis title	C - TVA: MOD400

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[C + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - MOD400 v Part B - Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.17
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	5.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	14.159
Variability estimate	Standard error of the mean
Dispersion value	4.22

Primary: Alpha - TVA

End point title	Alpha - TVA

End point description:

The ratio of reports of targets over distractors

End point type	Primary

End point timeframe:

Effects of MPH and ATX on the TVA were tested 90 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the TVA were tested 120 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[101]	32[102]	30[103]	30[104]
Units: ratio				
arithmetic mean (standard error)	0.14 (± 0.14)	0.13 (± 0.12)	0.13 (± 0.13)	0.13 (± 0.12)

Notes:

[101] - This was conducted in a cross over design

[102] - This was conducted in a cross over design

[103] - This was conducted in a cross over design

[104] - This was conducted in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[105]	41[106]	41[107]	43[108]
Units: ratio				
arithmetic mean (standard error)	0.15 (± 0.14)	0.11 (± 0.15)	0.13 (± 0.21)	0.11 (± 0.20)

Notes:

[105] - This was conducted in a cross over design

[106] - This was conducted in a cross over design

[107] - This was conducted in a cross over design

[108] - This was conducted in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[109]	44[110]		
Units: ratio				
arithmetic mean (standard error)	0.13 (± 0.31)	0.15 (± 0.34)		

Notes:

[109] - This was conducted in a cross over design

[110] - This was conducted in a cross over design

Statistical analyses

Statistical analysis title	Alpha - TVA: MPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[Alpha + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.87
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.043
upper limit	0.036
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Alpha - TVA: MPH40

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[Alpha + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.89
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.043
upper limit	0.037
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Alpha - TVA: ATX40

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[Alpha + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.87
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.043
upper limit	0.037
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Alpha - TVA: ATX60

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[Alpha + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.81
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.036
upper limit	0.045
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Alpha - TVA: AMPH10

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[Alpha + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH10
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.53
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0633
upper limit	0.032
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Alpha - TVA: AMPH20

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[Alpha + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - AMPH20 v Part B - Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.15
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.082
upper limit	0.013
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Alpha - TVA: MOD200

Statistical analysis description:
Evaluated via a linear mixed-effects model:

[Alpha + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - MOD200 v Part B - Placebo
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.035
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.097
upper limit	-0.003
Variability estimate	Standard error of the mean
Dispersion value	0.02

Statistical analysis title	Alpha - TVA: MOD400

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[Alpha + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - MOD400 v Part B - Placebo
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.31
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.069
upper limit	0.022
Variability estimate	Standard error of the mean
Dispersion value	0.02

Secondary: w-index - TVA

End point title	w-index - TVA

End point description:

The w-index of the TVA provides the ratio between targets reported in the left or right visual hemisphere

End point type	Secondary

End point timeframe:

Effects of MPH and ATX on the TVA were tested 90 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the TVA were tested 120 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[111]	32[112]	30[113]	30[114]
Units: ratio				
arithmetic mean (standard error)	0.512 (± 0.021)	0.519 (± 0.022)	0.0495 (± 0.019)	0.514 (± 0.019)

Notes:

[111] - The study was conducted in a cross over design

[112] - The study was conducted in a cross over design

[113] - The study was conducted in a cross over design

[114] - The study was conducted in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[115]	41[116]	41[117]	43[118]
Units: ratio				
arithmetic mean (standard error)	0.529 (± 0.021)	0.496 (± 0.019)	0.494 (± 0.018)	0.503 (± 0.019)

Notes:

[115] - The study was conducted in a cross over design

[116] - The study was conducted in a cross over design

[117] - The study was conducted in a cross over design

[118] - The study was conducted in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[119]	44[120]		
Units: ratio				
arithmetic mean (standard error)	0.499 (± 0.015)	0.500 (± 0.017)		

Notes:

[119] - The study was conducted in a cross over design

[120] - The study was conducted in a cross over design

Statistical analyses

Statistical analysis title	w-index - TVA: MPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[w-index + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.56
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.01

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.016
upper limit	0.029
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	w-index - TVA: MPH40

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[w-index + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.26
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.037
upper limit	0.009
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	w-index - TVA: ATX40

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[w-index + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.78
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.027
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	w-index - TVA: ATX60

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[w-index + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.08
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.003
upper limit	0.045
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	w-index - TVA: AMPH10

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[w-index + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH10
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.64
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.005

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.025
upper limit	0.015
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	w-index - TVA: AMPH20

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[w-index + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.61
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.026
upper limit	0.015
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	w-index - TVA: MOD200

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[w-index + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.85
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.002

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.018
upper limit	0.022
Variability estimate	Standard error of the mean
Dispersion value	0.01

Statistical analysis title	w-index - TVA: MOD400

Statistical analysis description:

Evaluated via a linear mixed-effects model:

[w-index + Visit + Sex + Baseline + Drug + (1 I SubjectId]

Comparison groups	Part B - Placebo v Part B - MOD400
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.46
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.027
upper limit	0.012
Variability estimate	Standard error of the mean
Dispersion value	0.01

Secondary: VAS-A0 - Alertness

End point title	VAS-A0 - Alertness

End point description:

Visual Analogue Scale - Alertness version

End point type	Secondary

End point timeframe:

Administered at the time of drug intake

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[121]	32[122]	30[123]	30[124]
Units: percentage points				
arithmetic mean (standard deviation)	53.76 (± 16.2)	57.07 (± 15.1)	50.52 (± 17.2)	54.10 (± 17.5)

Notes:
[121] - Conducted in a cross over design
[122] - Conducted in a cross over design
[123] - Conducted in a cross over design
[124] - Conducted in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[125]	41[126]	41[127]	43[128]
Units: percentage points				
arithmetic mean (standard deviation)	51.76 (± 17.8)	46.43 (± 15.9)	47.92 (± 19.3)	48.35 (± 18.3)

Notes:
[125] - Conducted in a cross over design
[126] - Conducted in a cross over design
[127] - Conducted in a cross over design
[128] - Conducted in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[129]	44[130]		
Units: percentage points				
arithmetic mean (standard deviation)	49.73 (± 19.3)	47.0 (± 21.2)		

Notes:
[129] - Conducted in a cross over design
[130] - Conducted in a cross over design

Statistical analyses

Statistical analysis title	VAS-A0: MPH20

Statistical analysis description:
Repeated Measures Anova

Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.92
Method	ANOVA
Parameter estimate	Mean difference (final values)

Statistical analysis title	VAS-A0: MPH40
Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.12
Method	ANOVA

Statistical analysis title	VAS-A0: ATX40
Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.53
Method	ANOVA

Statistical analysis title	VAS-A0: ATX60
Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.23
Method	ANOVA

Statistical analysis title	VAS-A0: AMPH10
Comparison groups	Part B - AMPH10 v Part B - Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.89
Method	ANOVA

Statistical analysis title	VAS-A0: AMPH20
Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.79
Method	ANOVA

Statistical analysis title	VAS-A0: MOD200
Comparison groups	Part B - Placebo v Part B - MOD200

Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.69
Method	ANOVA

Statistical analysis title	VAS-A0: MOD400
Comparison groups	Part B - Placebo v Part B - MOD400
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.44
Method	ANOVA

Secondary: VAS-A1 - Alertness

End point title	VAS-A1 - Alertness

End point description:

End point type	Secondary

End point timeframe:

Effects of MPH and ATX on the VAS-A1 were tested 90 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the VAS-A1 were tested 120 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[131]	32[132]	30[133]	30[134]
Units: percentage points				
arithmetic mean (standard deviation)	49.48 (± 18.6)	64.79 (± 24.3)	73.45 (± 20.6)	49.69 (± 22.7)

Notes:

[131] - This was conducted in a cross over design

[132] - This was conducted in a cross over design

[133] - This was conducted in a cross over design

[134] - This was conducted in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[135]	41[136]	41[137]	43[138]
Units: percentage points				
arithmetic mean (standard deviation)	36.17 (± 19.9)	64.30 (± 22.0)	77.14 (± 22.9)	56.22 (± 20.2)

Notes:
[135] - This was conducted in a cross over design
[136] - This was conducted in a cross over design
[137] - This was conducted in a cross over design
[138] - This was conducted in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[139]	44[140]		
Units: percentage points				
arithmetic mean (standard deviation)	67.76 (± 17.6)	48.47 (± 22.7)		

Notes:
[139] - This was conducted in a cross over design
[140] - This was conducted in a cross over design

Statistical analyses

Statistical analysis title	VAS-A1: MPH20
Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.004
Method	ANOVA

Statistical analysis title	VAS-A1: MPH40
Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	VAS-A1: ATX40
Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.97
Method	ANOVA

Statistical analysis title	VAS-A1: ATX60
Comparison groups	Part A - Placebo v Part A - ATX60

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.015
Method	ANOVA

Statistical analysis title	VAS-A1: AMPH10
Comparison groups	Part B - AMPH10 v Part B - Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.002
Method	ANOVA

Statistical analysis title	VAS-A1: AMPH20
Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	VAS-A1: MOD200
Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.12
Method	ANOVA

Statistical analysis title	VAS-A1: MOD400
Comparison groups	Part B - Placebo v Part B - MOD400
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.001
Method	ANOVA

Secondary: VAS-A2 - Alertness

End point title	VAS-A2 - Alertness

End point description:

End point type	Secondary

End point timeframe:

Effects of MPH and ATX on the VAS-A2 were tested 125 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the VAS-A2 were tested 145 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[141]	32[142]	30[143]	30[144]
Units: Percentage Points				
arithmetic mean (standard deviation)	37.28 (± 23.2)	66.14 (± 19.0)	76.07 (± 18.9)	37.10 (± 26.24)

Notes:

[141] - This was performed in a cross over design

[142] - This was performed in a cross over design

[143] - This was performed in a cross over design

[144] - This was performed in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[145]	41[146]	41[147]	43[148]
Units: Percentage Points				
arithmetic mean (standard deviation)	31.14 (± 20.7)	62.16 (± 21.9)	73.46 (± 21.3)	51.19 (± 22.6)

Notes:

[145] - This was performed in a cross over design

[146] - This was performed in a cross over design

[147] - This was performed in a cross over design

[148] - This was performed in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[149]	44[150]		
Units: Percentage Points				
arithmetic mean (standard deviation)	60.24 (± 16.3)	33.32 (± 22.8)		

Notes:

[149] - This was performed in a cross over design

[150] - This was performed in a cross over design

Statistical analyses

No statistical analyses for this end point

Secondary: VAS-P - Pleasurability

End point title	VAS-P - Pleasurability

End point description:

Visual Analogue Scale - Pleasurability: "How pleasureable was the cognitive test session?"

End point type	Secondary

End point timeframe:

Effects of MPH and ATX on the VAS-P were tested 125 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the VAS-P were tested 145 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[151]	32[152]	30[153]	30[154]
Units: Percentage Points				
arithmetic mean (standard deviation)	34.21 (± 20.8)	59.34 (± 23.3)	65.17 (± 25.0)	33.62 (± 23.9)

Notes:

[151] - Conducted in a cross over design

[152] - Conducted in a cross over design

[153] - Conducted in a cross over design

[154] - Conducted in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[155]	41[156]	41[157]	43[158]
Units: Percentage Points				
arithmetic mean (standard deviation)	31.21 (± 20.6)	48.7 (± 24.8)	55.9 (± 30.5)	39.2 (± 24.9)

Notes:

[155] - Conducted in a cross over design

[156] - Conducted in a cross over design

[157] - Conducted in a cross over design

[158] - Conducted in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[159]	44[160]		
Units: Percentage Points				
arithmetic mean (standard deviation)	47.5 (± 22.8)	26.6 (± 22.3)		

Notes:

[159] - Conducted in a cross over design

[160] - Conducted in a cross over design

Statistical analyses

Statistical analysis title	VAS-P: MPH20
Comparison groups	Part A - Placebo v Part A - MPH20

Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	VAS-P: MPH40
Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	VAS-P: ATX40
Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.88
Method	ANOVA

Statistical analysis title	VAS-P: ATX60
Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.46
Method	ANOVA

Statistical analysis title	VAS-P: AMPH10
Comparison groups	Part B - Placebo v Part B - AMPH10
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	VAS-P: AMPH20
Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	VAS-P: MOD200
Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	VAS-P: MOD400
Comparison groups	Part B - Placebo v Part B - MOD400
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Secondary: HR - CPT - Heart Rate

End point title	HR - CPT - Heart Rate

End point description:

End point type	Secondary

End point timeframe:

Heart Rate while performing the CPT test.
Effects of MPH and ATX on the CPT were tested 125 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the CPT were tested 155 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[161]	32[162]	30[163]	30[164]
Units: Beats pr minute				
arithmetic mean (standard deviation)	69 (± 8.47)	79 (± 13.38)	82 (± 15.92)	77 (± 12.56)

Notes:
[161] - Conducted in a cross over design
[162] - Conducted in a cross over design
[163] - Conducted in a cross over design
[164] - Conducted in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[165]	41[166]	41[167]	43[168]
Units: Beats pr minute				
arithmetic mean (standard deviation)	76 (± 13.66)	81 (± 13.27)	84 (± 13.90)	80 (± 13.93)

Notes:
[165] - Conducted in a cross over design
[166] - Conducted in a cross over design
[167] - Conducted in a cross over design
[168] - Conducted in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[169]	44[170]		
Units: Beats pr minute				
arithmetic mean (standard deviation)	84 (± 12.28)	71 (± 11.14)		

Notes:
[169] - Conducted in a cross over design
[170] - Conducted in a cross over design

Statistical analyses

Statistical analysis title	HR - CPT: MPH20
Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HR - CPT: MPH40
Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HR - CPT: ATX40
Comparison groups	Part A - Placebo v Part A - ATX40

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HR - CPT: ATX60
Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.001
Method	ANOVA

Statistical analysis title	HR - CPT: AMPH10
Comparison groups	Part B - Placebo v Part B - AMPH10
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HR - CPT: AMPH20
Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HR - CPT: MOD200
Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HR - CPT: MOD400
Comparison groups	Part B - Placebo v Part B - MOD400
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Secondary: HRV-CPT - RMSSQ

End point title	HRV-CPT - RMSSQ

End point description:

End point type	Secondary

End point timeframe:

Heart Rate Variability - The root mean square of the standard deviation during the CPT test.
Effects of MPH and ATX on the CPT were tested 125 minutes after drug or placebo.
Effects of AMPH and MOD on the CPT were tested 155 minutes after drug or placeb

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[171]	32[172]	30[173]	30[174]
Units: beats pr minute				
arithmetic mean (standard deviation)	53 (± 23.01)	41 (± 17.94)	40 (± 21.63)	38 (± 15.66)

Notes:

[171] - Conducted in a cross over design

[172] - Conducted in a cross over design

[173] - Conducted in a cross over design

[174] - Conducted in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[175]	41[176]	41[177]	43[178]
Units: beats pr minute				
arithmetic mean (standard deviation)	41 (± 20.19)	40 (± 24.73)	36 (± 18.01)	42 (± 24.68)

Notes:

[175] - Conducted in a cross over design

[176] - Conducted in a cross over design

[177] - Conducted in a cross over design

[178] - Conducted in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[179]	44[180]		
Units: beats pr minute				
arithmetic mean (standard deviation)	37 (± 18.78)	51 (± 22.41)		

Notes:
[179] - Conducted in a cross over design
[180] - Conducted in a cross over design

Statistical analyses

Statistical analysis title	HRV-CPT: MPH20
Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.002
Method	ANOVA

Statistical analysis title	HRV-CPT: MPH40
Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.004
Method	ANOVA

Statistical analysis title	HRV-CPT: ATX40
Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HRV-CPT: ATX60
Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.008
Method	ANOVA

Statistical analysis title	HRV-CPT: AMPH10

Comparison groups	Part B - AMPH10 v Part B - Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.009
Method	ANOVA

Statistical analysis title	HRV-CPT: AMPH20
Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HRV-CPT: MOD200
Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.016
Method	ANOVA

Statistical analysis title	HRV-CPT: MOD400
Comparison groups	Part B - Placebo v Part B - MOD400
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Secondary: HR - TVA - Heart Rate

End point title	HR - TVA - Heart Rate

End point description:

Heart Rate during the TVA test

End point type	Secondary

End point timeframe:

Data was collected during the TVA test
Effects of MPH and ATX on the TVA were tested 90 minutes after ingestion of drug or placebo.
Effects of AMPH and MOD on the TVA were tested 120 minutes after ingestion of drug or placebo.

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[181]	32[182]	30[183]	30[184]
Units: beats pr minute				
arithmetic mean (standard deviation)	73 (± 9.23)	82 (± 11.51)	85 (± 15.82)	81 (± 14.17)

Notes:

[181] - This was conducted in a cross over design

[182] - This was conducted in a cross over design

[183] - This was conducted in a cross over design

[184] - This was conducted in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[185]	41[186]	41[187]	43[188]
Units: beats pr minute				
arithmetic mean (standard deviation)	81 (± 15.11)	86 (± 13.83)	86 (± 13.87)	85 (± 12.73)

Notes:

[185] - This was conducted in a cross over design

[186] - This was conducted in a cross over design

[187] - This was conducted in a cross over design

[188] - This was conducted in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[189]	44[190]		
Units: beats pr minute				
arithmetic mean (standard deviation)	89 (± 14.55)	75 (± 12.29)		

Notes:

[189] - This was conducted in a cross over design

[190] - This was conducted in a cross over design

Statistical analyses

Statistical analysis title	HR - TVA: MPH20
Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HR - TVA: MPH40
Comparison groups	Part A - Placebo v Part A - MPH40

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HR - TVA: ATX40
Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HR - TVA: ATX60
Comparison groups	Part A - Placebo v Part A - ATX60
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.002
Method	ANOVA

Statistical analysis title	HR - TVA: AMPH10
Comparison groups	Part B - AMPH10 v Part B - Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HR - TVA: AMPH20
Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HR - TVA: MOD200
Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Statistical analysis title	HR - TVA: MOD400
Comparison groups	Part B - Placebo v Part B - MOD400
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Secondary: HRV - TVA - RMSSQ

End point title	HRV - TVA - RMSSQ

End point description:

End point type	Secondary

End point timeframe:

The root mean square of the standard deviation of heart rate during the TVA test.
Effects of MPH and ATX on the TVA were tested 90 minutes after drug or placebo.
Effects of AMPH and MOD on the TVA were tested 120 minutes after drug or placebo

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	32[191]	32[192]	30[193]	30[194]
Units: beats pr minute				
arithmetic mean (standard deviation)	40 (± 19.67)	32 (± 14.47)	30 (± 18.44)	33 (± 17.43)

Notes:

[191] - Conducted in a cross over design

[192] - Conducted in a cross over design

[193] - Conducted in a cross over design

[194] - Conducted in a cross over design

End point values	Part A - ATX60	Part B - AMPH10	Part B - AMPH20	Part B - MOD200
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30[195]	41[196]	41[197]	43[198]
Units: beats pr minute				
arithmetic mean (standard deviation)	32 (± 18.21)	30 (± 18.53)	33 (± 18.76)	32 (± 15.68)

Notes:
[195] - Conducted in a cross over design
[196] - Conducted in a cross over design
[197] - Conducted in a cross over design
[198] - Conducted in a cross over design

End point values	Part B - MOD400	Part B - Placebo		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	44[199]	44[200]		
Units: beats pr minute				
arithmetic mean (standard deviation)	29 (± 17.14)	41 (± 21.92)		

Notes:
[199] - Conducted in a cross over design
[200] - Conducted in a cross over design

Statistical analyses

Statistical analysis title	HRV - TVA: MPH20
Comparison groups	Part A - Placebo v Part A - MPH20
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.02
Method	ANOVA

Statistical analysis title	HRV - TVA: MPH40
Comparison groups	Part A - Placebo v Part A - MPH40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.008
Method	ANOVA

Statistical analysis title	HRV - TVA: ATX40
Comparison groups	Part A - Placebo v Part A - ATX40
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.65
Method	ANOVA

Statistical analysis title	HRV - TVA: ATX60
Comparison groups	Part A - Placebo v Part A - ATX60

Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.14
Method	ANOVA

Statistical analysis title	HRV - TVA: AMPH10
Comparison groups	Part B - AMPH10 v Part B - Placebo
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.009
Method	ANOVA

Statistical analysis title	HRV - TVA: AMPH20
Comparison groups	Part B - Placebo v Part B - AMPH20
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.009
Method	ANOVA

Statistical analysis title	HRV - TVA: MOD200
Comparison groups	Part B - Placebo v Part B - MOD200
Number of subjects included in analysis	87
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.004
Method	ANOVA

Statistical analysis title	Copy of HRV - TVA: MOD400
Comparison groups	Part B - Placebo v Part B - MOD400
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	< 0.001
Method	ANOVA

Post-hoc: MPH plasma concentration (mg /kg)

End point title	MPH plasma concentration (mg /kg)

End point description:

End point type	Post-hoc

End point timeframe:

Blood samples were drawn upon completion of each test session

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	35	35
Units: mg / kg				
number (not applicable)	0.0	0.001	0.018	0.0

End point values	Part A - ATX60			
Subject group type	Subject analysis set			
Number of subjects analysed	35			
Units: mg / kg				
number (not applicable)	0.0			

Statistical analyses

No statistical analyses for this end point

Post-hoc: MPH plasma concentration (ng / L)

End point title	MPH plasma concentration (ng / L)

End point description:

End point type	Post-hoc

End point timeframe:

Blood samples were drawn upon completion of each test session

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	35	35
Units: ng / L				
number (not applicable)	0.0	9.238	17.692	0.0

End point values	Part A - ATX60			
Subject group type	Subject analysis set			
Number of subjects analysed	35			
Units: ng / L				
number (not applicable)	0.0			

Statistical analyses

No statistical analyses for this end point

Post-hoc: ATX plasma concentration (mg / kg)

End point title	ATX plasma concentration (mg / kg)

End point description:

End point type	Post-hoc

End point timeframe:

Blood samples were drawn upon completion of each test session

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	35	35
Units: mg / kg				
number (not applicable)	0.0	0.0	0.0	0.253

End point values	Part A - ATX60			
Subject group type	Subject analysis set			
Number of subjects analysed	35			
Units: mg / kg				
number (not applicable)	0.364			

Statistical analyses

No statistical analyses for this end point

Post-hoc: ATX plasma concentration (ng / L)

End point title	ATX plasma concentration (ng / L)

End point description:

End point type	Post-hoc

End point timeframe:

Blood samples were drawn upon completion of each test session

End point values	Part A - Placebo	Part A - MPH20	Part A - MPH40	Part A - ATX40
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	35	35
Units: ng / L				
number (not applicable)	0.0	0.0	0.0	248.5

End point values	Part A - ATX60			
Subject group type	Subject analysis set			
Number of subjects analysed	35			
Units: ng / L				
number (not applicable)	356.8			

Statistical analyses

No statistical analyses for this end point

Post-hoc: AMPH plasma concentration (mg / kg)

End point title	AMPH plasma concentration (mg / kg)

End point description:

End point type	Post-hoc

End point timeframe:

Blood samples were drawn upon the completion of each test session

End point values	Part B - AMPH10	Part B - AMPH20	Part B - MOD200	Part B - MOD400
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	48	48	48
Units: mg / kg				
number (not applicable)	0.024	0.049	0.0	0.0

End point values	Part B - Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	48			
Units: mg / kg				
number (not applicable)	0.0			

Statistical analyses

No statistical analyses for this end point

Post-hoc: MOD plasma concentration (mg / kg)

End point title	MOD plasma concentration (mg / kg)

End point description:

End point type	Post-hoc

End point timeframe:

Blood samples were drawn upon the completion of each test session

End point values	Part B - AMPH10	Part B - AMPH20	Part B - MOD200	Part B - MOD400
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	48	48	48	48
Units: mg / kg				
number (not applicable)	0.0	0.0	3.5	7.8

End point values	Part B - Placebo			
Subject group type	Subject analysis set			
Number of subjects analysed	48			
Units: mg / kg				
number (not applicable)	0.0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Upon completion of each test session a questionnaire was provided for each participant to fill out.

Assessment type	Systematic

Dictionary used

Dictionary name	none
Dictionary version	0

Reporting groups

Reporting group title	AIM-C Part A - Placebo

Reporting group description:

Part A will be conducted on a different sample than Part B. The pharmacological tools to be used in this second study will be methylphenidate and atomoxetine. The general design for Part A is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for methylphenidate and atomoxetine (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Reporting group title	AIM-C Part B - Placebo

Reporting group description:

Part B will be conducted on a different sample. The pharmacological tools to be used in this second study will be dexamphetamine and modafinil. The general design for Part B is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for dexamphetamine and modafinil (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Reporting group title	AIM-C Part A - MPH20

Reporting group description:

Part A will be conducted on a different sample than Part B. The pharmacological tools to be used in this second study will be methylphenidate and atomoxetine. The general design for Part A is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for methylphenidate and atomoxetine (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Reporting group title	AIM-C Part A - MPH40

Reporting group description:

Part A will be conducted on a different sample than Part B. The pharmacological tools to be used in this second study will be methylphenidate and atomoxetine. The general design for Part A is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for methylphenidate and atomoxetine (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Reporting group title	AIM-C Part A - ATX40

Reporting group description:

Part A will be conducted on a different sample than Part B. The pharmacological tools to be used in this second study will be methylphenidate and atomoxetine. The general design for Part A is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for methylphenidate and atomoxetine (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Reporting group title	AIM-C Part A - ATX60

Reporting group description:

Part A will be conducted on a different sample than Part B. The pharmacological tools to be used in this second study will be methylphenidate and atomoxetine. The general design for Part A is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for methylphenidate and atomoxetine (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Reporting group title	AIM-C Part B - AMPH10

Reporting group description:

Part B will be conducted on a different sample. The pharmacological tools to be used in this second study will be dexamphetamine and modafinil. The general design for Part B is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for dexamphetamine and modafinil (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Reporting group title	AIM-C Part B - AMPH20

Reporting group description:

Part B will be conducted on a different sample. The pharmacological tools to be used in this second study will be dexamphetamine and modafinil. The general design for Part B is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for dexamphetamine and modafinil (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Reporting group title	AIM-C Part B - MOD200

Reporting group description:

Part B will be conducted on a different sample. The pharmacological tools to be used in this second study will be dexamphetamine and modafinil. The general design for Part B is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for dexamphetamine and modafinil (low and high doses of each), and for placebo, allowing for within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Reporting group title	AIM-C Part B - MOD400

Reporting group description:

Part B will be conducted on a different sample. The pharmacological tools to be used in this second study will be dexamphetamine and modafinil. The general design for Part B is a double blind, placebo-controlled, within-subject, counter-balanced investigation. Each participant is tested in five separate sessions for dexamphetamine and modafinil (low and high doses of each), and for placebo, allowing for

within-subject comparisons. Before each experimental session, participants are given a high or a low dose of the drugs or placebo. The different doses will allow for analyses of dose-response relationships of the cognitive effects of the drugs. A diagram-balanced Latin square design will be used to achieve counterbalanced effects, so that each of the possible treatment sequences will be used. In all sessions, participants will be tested on both the Combi-TVA and the Conners CPT when the effect of the drug can be assumed to have reached its maximal level

Serious adverse events	AIM-C Part A - Placebo	AIM-C Part B - Placebo	AIM-C Part A - MPH20
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 32 (0.00%)	0 / 44 (0.00%)	0 / 32 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	AIM-C Part A - MPH40	AIM-C Part A - ATX40	AIM-C Part A - ATX60
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	0 / 30 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	AIM-C Part B - AMPH10	AIM-C Part B - AMPH20	AIM-C Part B - MOD200
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	0 / 43 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	AIM-C Part B - MOD400		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 44 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	AIM-C Part A - Placebo	AIM-C Part B - Placebo	AIM-C Part A - MPH20
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 32 (43.75%)	17 / 44 (38.64%)	12 / 32 (37.50%)
General disorders and administration site conditions			
Sleepy / tired			
subjects affected / exposed	14 / 32 (43.75%)	16 / 44 (36.36%)	5 / 32 (15.63%)
occurrences (all)	14	16	5
dizzy			
subjects affected / exposed	1 / 32 (3.13%)	0 / 44 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
perceived increased heart rate			
subjects affected / exposed	0 / 32 (0.00%)	1 / 44 (2.27%)	5 / 32 (15.63%)
occurrences (all)	0	1	5
feeling unfocused			
subjects affected / exposed	2 / 32 (6.25%)	0 / 44 (0.00%)	1 / 32 (3.13%)
occurrences (all)	2	0	1
feeling restless			
subjects affected / exposed	0 / 32 (0.00%)	0 / 44 (0.00%)	0 / 32 (0.00%)
occurrences (all)	0	0	0
feeling jittery / tingly			
subjects affected / exposed	0 / 32 (0.00%)	0 / 44 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2
feeling nauseous			
subjects affected / exposed	0 / 32 (0.00%)	2 / 44 (4.55%)	1 / 32 (3.13%)
occurrences (all)	0	2	1

Non-serious adverse events	AIM-C Part A - MPH40	AIM-C Part A - ATX40	AIM-C Part A - ATX60
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 30 (36.67%)	19 / 30 (63.33%)	24 / 30 (80.00%)
General disorders and administration site conditions			
Sleepy / tired			
subjects affected / exposed	3 / 30 (10.00%)	14 / 30 (46.67%)	15 / 30 (50.00%)
occurrences (all)	3	14	15
dizzy			
subjects affected / exposed	0 / 30 (0.00%)	1 / 30 (3.33%)	2 / 30 (6.67%)
occurrences (all)	0	1	2

perceived increased heart rate			
subjects affected / exposed	3 / 30 (10.00%)	1 / 30 (3.33%)	3 / 30 (10.00%)
occurrences (all)	3	1	3
feeling unfocused			
subjects affected / exposed	0 / 30 (0.00%)	0 / 30 (0.00%)	5 / 30 (16.67%)
occurrences (all)	0	0	5
feeling restless			
subjects affected / exposed	5 / 30 (16.67%)	0 / 30 (0.00%)	0 / 30 (0.00%)
occurrences (all)	5	0	0
feeling jittery / tingly			
subjects affected / exposed	2 / 30 (6.67%)	1 / 30 (3.33%)	0 / 30 (0.00%)
occurrences (all)	2	1	0
feeling nauseous			
subjects affected / exposed	1 / 30 (3.33%)	5 / 30 (16.67%)	7 / 30 (23.33%)
occurrences (all)	1	5	7

Non-serious adverse events	AIM-C Part B - AMPH10	AIM-C Part B - AMPH20	AIM-C Part B - MOD200
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 41 (53.66%)	15 / 41 (36.59%)	11 / 43 (25.58%)
General disorders and administration site conditions			
Sleepy / tired			
subjects affected / exposed	6 / 41 (14.63%)	0 / 41 (0.00%)	3 / 43 (6.98%)
occurrences (all)	6	0	3
dizzy			
subjects affected / exposed	3 / 41 (7.32%)	7 / 41 (17.07%)	2 / 43 (4.65%)
occurrences (all)	3	7	2
perceived increased heart rate			
subjects affected / exposed	5 / 41 (12.20%)	6 / 41 (14.63%)	1 / 43 (2.33%)
occurrences (all)	5	6	1
feeling unfocused			
subjects affected / exposed	2 / 41 (4.88%)	1 / 41 (2.44%)	0 / 43 (0.00%)
occurrences (all)	2	1	0
feeling restless			
subjects affected / exposed	3 / 41 (7.32%)	1 / 41 (2.44%)	1 / 43 (2.33%)
occurrences (all)	3	1	1
feeling jittery / tingly			

subjects affected / exposed	6 / 41 (14.63%)	0 / 41 (0.00%)	2 / 43 (4.65%)
occurrences (all)	6	0	2
feeling nauseous			
subjects affected / exposed	0 / 41 (0.00%)	0 / 41 (0.00%)	2 / 43 (4.65%)
occurrences (all)	0	0	2

Non-serious adverse events	AIM-C Part B - MOD400		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 44 (36.36%)		
General disorders and administration site conditions			
Sleepy / tired			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences (all)	2		
dizzy			
subjects affected / exposed	3 / 44 (6.82%)		
occurrences (all)	3		
perceived increased heart rate			
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	4		
feeling unfocused			
subjects affected / exposed	1 / 44 (2.27%)		
occurrences (all)	1		
feeling restless			
subjects affected / exposed	4 / 44 (9.09%)		
occurrences (all)	4		
feeling jittery / tingly			
subjects affected / exposed	2 / 44 (4.55%)		
occurrences (all)	2		
feeling nauseous			
subjects affected / exposed	0 / 44 (0.00%)		
occurrences (all)	0		

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