



Clinical trial results:

NEUPRO DB, efficacy profile of Neurexan in an experimental acute stress setting – an explorative double blind study in healthy probands

Summary

EudraCT number	2012-002358-22
Trial protocol	DE
Global end of trial date	02 April 2013

Results information

Result version number	v1 (current)
This version publication date	28 October 2017
First version publication date	28 October 2017
Summary attachment (see zip file)	C1201 NEUPRO double blind study (Neurexan) (C1201_20131212_C1201_NEUPRO_DB_synopse_CSR_03Dec2013_redacted.pdf)

Trial information

Trial identification

Sponsor protocol code	C1201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01703819
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biologische Heilmittel Heel GmbH
Sponsor organisation address	Dr.-Reckeweg-Str. 2-4, Baden-Baden, Germany, 76532
Public contact	Biologische Heilmittel Heel GmbH, Biologische Heilmittel Heel GmbH, +49 7221-501-0, info@heel.com
Scientific contact	Biologische Heilmittel Heel GmbH, Biologische Heilmittel Heel GmbH, +49 7221-501-0, info@heel.com

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	02 April 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 April 2013
Global end of trial reached?	Yes
Global end of trial date	02 April 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is the efficacy of Neurexan® on tension and nervousness perception using visual analogue scales (VAS) when study participants undergo an emotional stressful condition as compared to Placebo. The test method for this study is the TSST protocol.

Protection of trial subjects:

Routine monitoring was performed to verify that rights and well being of participants were protected.

Background therapy:

6 subjects took contraceptives (2 in the Neurexan Group, 4 in the Placebo Group)

Evidence for comparator: -

Actual start date of recruitment	18 October 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	66
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment was carried out in 2 outpatient clinics in Germany (Marburg and Essen). 35 subjects were enrolled in Marburg and 31 in Essen.

Pre-assignment

Screening details:

Telephone pre-screening was carried out and individuals received gross Information about the study. If they were suited for study participation an appointment for the medical and psychological screening was made.

Interested volunteers were invited to the study site for the 1st visit and received oral and written Information about study and ICF.

Period 1

Period 1 title	overall trial (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:

Participants were randomly allocated to either treatment group in a 1:1 randomisation. Randomisation was stratified by site and by gender.

Arms

Are arms mutually exclusive?	Yes
Arm title	Neurexan group

Arm description:

34 participants were randomized to Neurexan. All randomized participants in this Group formed the full analysis set for analysis of efficacy and safety.

Subjects took 6 Neurexan tablets over a period of 2.5 hours (one tablet every 30 minutes).

Arm type	Experimental
Investigational medicinal product name	Neurexan
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

One Neurexan tablet contains: 0.6 mg Avena sativa (dil. D2), 0.6 mg Coffea arabica (dil. D12), 0.6 mg Passiflora incarnata (dil. D2), 0.6 mg Zincum isovalerianum (dil. D4), lactose monohydrate and magnesium stearate

Route of administration: oral

Total administered: 6 tablets (over a period of 2.5 hours - one tablet every 30 minutes)

Arm title	Placebo group
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Arm description:

32 participants were randomized to placebo. Two premature terminators could not be evaluated for primary efficacy, so only 30 participants in this group formed the full analysis set for analysis of efficacy. All randomised participants (32) were included in the safety analysis.

Subjects took 6 placebo tablets over a period of 2.5 hours (one tablet every 30 minutes)

Arm type	Placebo
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Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Each placebo tablet contains: lactose monohydrate and magnesium stearate

Route of administration: oral

Total administered: 6 tablets (over a period of 2.5 hours - one tablet every 30 minutes)

Number of subjects in period 1	Neurexan group	Placebo group
Started	34	32
Completed	34	30
Not completed	0	2
Consent withdrawn by subject	-	1
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups

Reporting group title	Neurexan group
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Reporting group description:

34 participants were randomized to Neurexan. All randomized participants in this Group formed the full analysis set for analysis of efficacy and safety.

Subjects took 6 Neurexan tablets over a period of 2.5 hours (one tablet every 30 minutes).

Reporting group title	Placebo group
-----------------------	---------------

Reporting group description:

32 participants were randomized to placebo. Two premature terminators could not be evaluated for primary efficacy, so only 30 participants in this group formed the full analysis set for analysis of efficacy. All randomised participants (32) were included in the safety analysis.

Subjects took 6 placebo tablets over a period of 2.5 hours (one tablet every 30 minutes)

Reporting group values	Neurexan group	Placebo group	Total
Number of subjects	34	32	66
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	34	32	66
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	41.1	40.7	
standard deviation	± 7	± 8.2	-
Gender categorical			
Units: Subjects			
Female	16	16	32
Male	18	16	34
Ethnic origin			
Units: Subjects			
white	34	32	66
Body mass index (BMI)			
Units: kg/m2			
arithmetic mean	24.31	24.68	
standard deviation	± 2.94	± 2.85	-
Trier Inventory for Chronic Stress - screening scale of chronic stress (SCSS)			
includes scores from five scales (chronic worrying, work and social overload, excessive demands and lack of acceptance).			
Units: score points			
median	8	10	

full range (min-max)	0 to 17	0 to 26	-
Global Severity Index (GSI) of psychological distress			
Derived from Symptom Checklist 90.			
Units: score points			
median	0.122	0.144	
full range (min-max)	0.01 to 0.46	0 to 0.38	-
Screening height			
Units: cm			
arithmetic mean	173.5	174.1	
standard deviation	± 8.8	± 9.3	-
Screening weight			
Units: kg			
arithmetic mean	73.43	75.11	
standard deviation	± 11.76	± 12.56	-

Subject analysis sets

Subject analysis set title	Neurexan Essen group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The secondary endpoint "Change in natural killer (NK) cells" was analysed in the Essen subgroup only.	
Subject analysis set title	Placebo Essen group
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The secondary endpoint "Change in natural killer (NK) cells" was analysed in the Essen subgroup only.	

Reporting group values	Neurexan Essen group	Placebo Essen group	
Number of subjects	15	16	
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)	15	16	
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
arithmetic mean			
standard deviation	±	±	
Gender categorical			
Units: Subjects			
Female			
Male			

Ethnic origin			
Units: Subjects			
white			
Body mass index (BMI)			
Units: kg/m2			
arithmetic mean			
standard deviation	±	±	
Trier Inventory for Chronic Stress - screening scale of chronic stress (SCSS)			
includes scores from five scales (chronic worrying, work and social overload, excessive demands and lack of acceptance).			
Units: score points			
median			
full range (min-max)			
Global Severity Index (GSI) of psychological distress			
Derived from Symptom Checklist 90.			
Units: score points			
median			
full range (min-max)			
Screening height			
Units: cm			
arithmetic mean			
standard deviation	±	±	
Screening weight			
Units: kg			
arithmetic mean			
standard deviation	±	±	

End points

End points reporting groups

Reporting group title	Neurexan group
Reporting group description: 34 participants were randomized to Neurexan. All randomized participants in this Group formed the full analysis set for analysis of efficacy and safety. Subjects took 6 Neurexan tablets over a period of 2.5 hours (one tablet every 30 minutes).	
Reporting group title	Placebo group
Reporting group description: 32 participants were randomized to placebo. Two premature terminators could not be evaluated for primary efficacy, so only 30 participants in this group formed the full analysis set for analysis of efficacy. All randomised participants (32) were included in the safety analysis. Subjects took 6 placebo tablets over a period of 2.5 hours (one tablet every 30 minutes)	
Subject analysis set title	Neurexan Essen group
Subject analysis set type	Sub-group analysis
Subject analysis set description: The secondary endpoint "Change in natural killer (NK) cells" was analysed in the Essen subgroup only.	
Subject analysis set title	Placebo Essen group
Subject analysis set type	Sub-group analysis
Subject analysis set description: The secondary endpoint "Change in natural killer (NK) cells" was analysed in the Essen subgroup only.	

Primary: Tension

End point title	Tension
End point description: Tension was self-assessed by the participants on a 0 to 100 millimeter (mm) Visual Analogue Scale (VAS), ranging from 0="not at all" to 100="highly", before and after a stress test. The measurements started with first intake of Neurexan or Placebo and were repeated until 100 minutes after the end of the stress test. The total stress was then summarized with the Area under the curve (AUC) method. AUC of VAS Tension value was measured from -210 min to +100 min.	
End point type	Primary
End point timeframe: From first intake of Neurexan or Placebo until 100 minutes after end of the stress test, i.e.: -210 min, -180 min, -150 min, -120 min, -90 min, -60 min, -30 min, -15 min, 0 min, +15 min, +30 min, +45 min, +60 min, +75 min, +100 min	

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: mm* min				
median (full range (min-max))	3335.7 (345 to 16411)	3360.3 (0 to 21115)		

Statistical analyses

Statistical analysis title	Descriptive statistics
Statistical analysis description:	
Standard descriptive statistics were calculated for continuous variables. All analyses were performed using Version 9.1.3 or later of SAS Software.	
Comparison groups	Neurexan group v Placebo group
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence ^[1]
P-value	= 0.7726
Method	ANCOVA
Parameter estimate	LS-Mean difference
Point estimate	186.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1099.1
upper limit	1472.2
Variability estimate	Standard error of the mean
Dispersion value	642.5

Notes:

[1] - Null-hypotheses of no Treatment differences were tested by the two-sided-t-tests from the respective ANCOVAs.

Primary: Nervousness

End point title	Nervousness
End point description:	
Nervousness was self-assessed by the participants on a 0 to 100 millimeter (mm) Visual Analogue Scale (VAS), ranging from 0="not at all" to 100="highly", before and after a stress test. The measurements started with first intake of Neurexan or Placebo and were repeated until 100 minutes after the end of the stress test.	
The total stress was then summarized with the Area under the curve (AUC) method. AUC of VAS Nervousness value was measured from -210 min to +100 min.	
End point type	Primary

End point timeframe:

From first intake of Neurexan or Placebo until 100 minutes after end of the stress test, i.e.: -210 min, -180 min, -150 min, -120 min, -90 min, -60 min, -30 min, -15 min, 0 min, +15 min, +30 min, +45 min, +60 min, +75 min, +100 min

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: mm* min				
median (full range (min-max))	3147.4 (247 to 17050)	3022.5 (0 to 21409)		

Statistical analyses

Statistical analysis title	Descriptive statistics
Statistical analysis description: Standard descriptive statistics were calculated for continuous variables. All analyses were performed using Version 9.1.3 or later of SAS Software.	
Comparison groups	Neurexan group v Placebo group
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	equivalence ^[2]
P-value	= 0.5702
Method	ANCOVA
Parameter estimate	LS-Mean difference
Point estimate	335.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-839.3
upper limit	1509.4
Variability estimate	Standard error of the mean
Dispersion value	586.9

Notes:

[2] - Null-hypotheses of no Treatment differences were tested by the two-sided-t-tests from the respective ANCOVAs.

Secondary: Salivary alpha amylase

End point title	Salivary alpha amylase
End point description: The stress biomarker salivary alpha amylase was measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.	
End point type	Secondary

End point timeframe:

60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: IU/ml				
median (full range (min-max))				
-60 min	112.9 (19.65 to 353.65)	133.3 (23.73 to 421.05)		
+15 min	201.9 (78.41 to 729.7)	216 (49.3 to 670.89)		
+45 min	140.8 (25.55 to 420.4)	142.1 (37.1 to 484.75)		
+100 min	149.9 (29.19 to 465.07)	140.6 (35.11 to 417.27)		

Statistical analyses

No statistical analyses for this end point

Secondary: Saliva cortisol

End point title	Saliva cortisol
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End point description:

The stress biomarker saliva cortisol was measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: nmol/l				
median (full range (min-max))				
-60 min	7.1 (2.96 to 17.44)	7.1 (2.73 to 32.43)		
+15 min	19.4 (7.18 to 120.83)	20 (6.14 to 86.62)		
+45 min	15.3 (6.96 to 80.66)	21.3 (3.93 to 81.35)		
+100 min	6.4 (3.74 to 20.94)	8.9 (3.61 to 21.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Adrenocorticotrophic Hormone (ACTH)

End point title	Adrenocorticotrophic Hormone (ACTH)
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End point description:

The stress biomarker Adrenocorticotrophic Hormone was measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: ng/L				
median (full range (min-max))				
-60 min	22.5 (9.17 to 330.41)	19.1 (5.45 to 493.16)		
+15 min	37.7 (13.87 to 124.21)	37 (13.63 to 209.74)		
+45 min	20.3 (7.49 to 42.29)	20.7 (7.47 to 79.36)		
+100 min	11.3 (3.18 to 24.44)	10.7 (5.44 to 23.96)		

Statistical analyses

No statistical analyses for this end point

Secondary: Epinephrine

End point title	Epinephrine
End point description: The stress biomarker epinephrine (adrenaline) measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.	
End point type	Secondary
End point timeframe: 60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min	

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: ng/l				
median (full range (min-max))				
-60 min	42.6 (10 to 98)	35.6 (8.1 to 146)		
+15 min	32.9 (10 to 116)	47.4 (10 to 126)		
+45 min	41.4 (10 to 152)	26.4 (10 to 101)		
+100 min	31.9 (0 to 91.3)	41.1 (11.3 to 89.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Norepinephrine

End point title	Norepinephrine
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End point description:

The stress biomarker norepinephrine was measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: ng/l				
median (full range (min-max))				
-60 min	463 (99 to 990)	457 (253 to 1329)		
+15 min	584 (150 to 1352)	591.5 (316 to 1856)		
+45 min	481 (231 to 1530)	476 (168 to 1189)		
+100 min	451.5 (215 to 1318)	482.5 (230 to 815)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Cortisol

End point title	Plasma Cortisol
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End point description:

The stress biomarker plasma cortisol was measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: nmol/l				
median (full range (min-max))				
-60 min	331.6 (97.61 to 614.82)	325.5 (54.18 to 1006.68)		
+15 min	441.1 (281.35 to 987.1)	569.8 (174.14 to 1048.65)		
+45 min	403.1 (223.67 to 1259.65)	535.4 (142.47 to 841.16)		
+100 min	228.4 (94.57 to 671.77)	273.3 (108.54 to 658.03)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in natural killer cells

End point title	Change in natural killer cells
End point description: The Natural Killer (NK) Cells as immune cells and stress biomarkers were measured before and after a stress test. The measurements started 60 minutes before stress test and were repeated until 100 minutes after the end of the stress test.	
End point type	Secondary
End point timeframe: 60 minutes before until 100 minutes after stress test, i.e.: -60 min, +15 min, +45 min, +100 min	

End point values	Neurexan Essen group	Placebo Essen group		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	15	16		
Units: % of lymphocytes				
median (full range (min-max))				
-60 min	13.5 (5.5 to 23.2)	11.65 (6.3 to 21)		
+15 min	21 (9.1 to 36.2)	20.4 (8 to 37.3)		
+45 min	10.3 (3.3 to 20.4)	9.1 (5.4 to 18.6)		
+100 min	13.1 (4.3 to 20.9)	8.65 (5.5 to 21.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Systolic blood pressure

End point title	Systolic blood pressure
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End point description:

Systolic blood pressure was measured before and after a stress test by continuous cardiovascular recording.

The measurements started 30 minutes before stress test and were repeated until 45 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

30 minutes before until 45 minutes after stress test, i.e.: -15 min, 0 min, +15 min, +45 min

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: mmHg				
median (full range (min-max))				
-15 min	122 (96 to 153)	123.5 (102 to 147)		
0 min	132 (106 to 201)	142 (110 to 168)		
+15 min	125 (99 to 164)	133.5 (105 to 153)		
+45 min	121.5 (96 to 163)	125 (101 to 182)		

Statistical analyses

No statistical analyses for this end point

Secondary: Diastolic blood pressure

End point title	Diastolic blood pressure
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End point description:

Diastolic blood pressure was measured before and after a stress test by continuous cardiovascular recording.

The measurements started 30 minutes before stress test and were repeated until 45 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

30 minutes before until 45 minutes after stress test, i.e.: -15 min, 0 min, +15 min, +45 min

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: mmHg				
median (full range (min-max))				
-15 min	79.5 (58 to 109)	81.5 (61 to 98)		
0 min	81 (66 to 117)	91 (63 to 107)		
+15 min	83.5 (65 to 115)	89 (63 to 109)		
+45 min	81 (34 to 113)	83 (63 to 113)		

Statistical analyses

No statistical analyses for this end point

Secondary: Heart rate

End point title	Heart rate
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End point description:

Heart rate was measured before and after a stress test by continuous cardiovascular recording. The measurements started 30 minutes before stress test and were repeated until 45 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

30 minutes before until 45 minutes after stress test, i.e.: -15 min, 0 min, +15 min, +45 min

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: bpm				
median (full range (min-max))				
-15 min	70 (55 to 96)	69 (52 to 94)		
0 min	88 (65 to 115)	89.5 (65 to 131)		
+15 min	69.5 (56 to 94)	71 (53 to 119)		
+45 min	71 (59 to 106)	71 (55 to 91)		

Statistical analyses

No statistical analyses for this end point

Secondary: Modified somatic SCL90

End point title	Modified somatic SCL90
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End point description:

The SCL90 has 90 items and covers dimensions like depression, somatization, obsessive-compulsive disorder, social insecurity, anxiety, phobic anxiety, aggression/hostility, paranoid ideation, psychoticism. A new instrument covering potential somatic stress consequences was used in this study, the modified somatic SCL90 that uses the SCL90 somatization items, but instead of a 7 day timeframe asking for "now" (current state). The corresponding items from SCL90 were: 1, 4, 12, 27, 40, 42, 48, 49, 52, 53, 56, 58 and the introductory question had to be: "How much do you currently suffer from..." ("Wie sehr leiden Sie momentan unter:").

End point type	Secondary
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End point timeframe:

210 minutes before and 100 minutes after stress test, i.e: -210 min, +100 min

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	33	30		
Units: score points				
median (full range (min-max))				
-210 min	0 (0 to 10)	0 (0 to 5)		
+100 min	0 (0 to 9)	0 (0 to 4)		

Statistical analyses

No statistical analyses for this end point

Secondary: State anxiety and stress perception measured by State-Trait Anxiety Inventory X1

End point title	State anxiety and stress perception measured by State-Trait Anxiety Inventory X1
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End point description:

State anxiety and stress perception were measured by State-Trait Anxiety Inventory X1 before and after a stress test. The measurements took place 90 minutes before stress test and were repeated 15 and 100 minutes after the end of the stress test.

End point type	Secondary
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End point timeframe:

90 minutes before stress test and 15 and 100 minutes after the end of the stress test, i.e.: -90 min, +15 min, +100 min

End point values	Neurexan group	Placebo group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	30		
Units: score points				
median (full range (min-max))				
-90 min	31 (21 to 45)	29.5 (22 to 50)		
+15 min	54.5 (24 to 74)	51.5 (23 to 68)		

+100 min	33 (20 to 69)	32.5 (20 to 69)		
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Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Randomization until individual study end, i.e.: -180 min, -150 min, -120 min, -90 min, -60 min, -30min, -15 min, 0 min, +15 min, +30 min, +45 min, +60 min, +75 min, +100 min

Adverse event reporting additional description:

All adverse events that occurred after the participant has received at least one dose of the product under investigation were to be collected and reported.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	15.1
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Reporting groups

Reporting group title	Neurexan group
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Reporting group description:

34 participants were randomized to Neurexan. All randomized participants in this group formed the full analysis set for analysis of efficacy and safety.

Reporting group title	Placebo Group
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Reporting group description:

32 participants who were randomized to placebo were included in the safety Analysis.

Serious adverse events	Neurexan group	Placebo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)	0 / 32 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Neurexan group	Placebo Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 34 (11.76%)	3 / 32 (9.38%)	
Investigations			
decreased blood pressure			
subjects affected / exposed	0 / 34 (0.00%)	2 / 32 (6.25%)	
occurrences (all)	0	3	
Nervous system disorders			
dizziness			

subjects affected / exposed	1 / 34 (2.94%)	1 / 32 (3.13%)	
occurrences (all)	2	2	
headache			
subjects affected / exposed	2 / 34 (5.88%)	0 / 32 (0.00%)	
occurrences (all)	2	0	
tremor (legs)			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
fatigue			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	1	
feeling cold			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
nausea			
subjects affected / exposed	1 / 34 (2.94%)	0 / 32 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 34 (0.00%)	1 / 32 (3.13%)	
occurrences (all)	0	2	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/17615391>

<http://www.ncbi.nlm.nih.gov/pubmed/16952284>

<http://www.ncbi.nlm.nih.gov/pubmed/8255414>

<http://www.ncbi.nlm.nih.gov/pubmed/19837490>

<http://www.ncbi.nlm.nih.gov/pubmed/4303377>

<http://www.ncbi.nlm.nih.gov/pubmed/5535207>

<http://www.ncbi.nlm.nih.gov/pubmed/10600217>

<http://www.ncbi.nlm.nih.gov/pubmed/8598500>

<http://www.ncbi.nlm.nih.gov/pubmed/9491439>