Clinical trial results:
The effect of dopamine on reading motivation and achievement.

Summary

EudraCT number	2014-001352-36
Trial protocol	NL
Global end of trial date	17 July 2017

Results information

Result version number	v1 (current)
This version publication date	14 January 2022
First version publication date	14 January 2022
Summary attachment (see zip file)	Swart & Sikkema-de Jong (2021) - Current Psychology (Swart, Sikkema-deJong (2021)_CurrentPsychology.pdf)

Trial information

Trial identification

Sponsor protocol code	DOPAREAD1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Leiden University
Sponsor organisation address	Wassenaarseweg 52, Leiden, Netherlands, 2333AK
Public contact	Dr. E.K. Swart, Leiden University, e.k.swart@fsw.leidenuniv.nl
Scientific contact	Dr. E.K. Swart, Leiden University, e.k.swart@fsw.leidenuniv.nl

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	11 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	17 July 2017
Global end of trial reached?	Yes
Global end of trial date	17 July 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main goal of the study is to investigate if small amounts of dopamine could influence engagement during reading, comprehension of the story and vocabulary learning and to investigate if the effect of dopamine is different for carriers of the long or short variant of the DRD4 gene. Additionally, the effect of dopamine on how participants value reading is investigated.

Protection of trial subjects:

Students with dyslexia, medical illnesses indicating a risk in using haloperidol (e.g. cardiac illness, depression, thyroid disorders, or glaucoma), or known drug allergies were excluded from participation in the study. Also students were excluded if they were using medication (other than contraceptives) or drugs in the two weeks prior to the experiment or if they were pregnant or lactating during the experiment.

During study sessions participants were constantly accompanied by a researcher. Participants were informed beforehand that side-effects of the one-time administration of the drug were unlikely to occur, but that they should tell the researcher immediately if they thought they would possibly suffer from side-effects.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2014
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	Netherlands: 80
Worldwide total number of subjects	80
EEA total number of subjects	80

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	80
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total number of 200 undergraduate students from universities in the Netherlands signed up for participation in our study. After genotyping, 80 students (40 carriers of the DRD4-7r allele, and 40 participants who did not) were selected to participate in the experimental sessions. Recruitment took place between in 2015 and 2016.

Pre-assignment

Screening details:

Inclusion criteria: Women, 18 years or older, right-handed.
Exclusion criteria: Dyslexia, medical illnesses indicating a risk in using haloperidol (e.g. cardiac illness, depression, thyroid disorders, or glaucoma), known drug allergies, using medication or drugs in the two weeks prior, pregnancy or lactating during the experiment

Period 1

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

Blinding implementation details:

To ensure that the study design was double-blind, randomization of the order of treatments (Sinemet125 or placebo) and the order of texts that were read in both experimental sessions (text A and text B) was carried out by the university hospital pharmacy, resulting in four different combinations of the order of treatment condition and text.

Arms

Are arms mutually exclusive?	No
Arm title	Dopamine-condition

Arm description:

The study had a randomized, double-blind placebo-controlled within-subjects experimental design. A total of 80 participants were submitted to both experimental conditions (dopamine and placebo) at two separate lab sessions.

Arm type	Experimental
Investigational medicinal product name	SINEMET 125
Investigational medicinal product code	RVG 08740
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

At the beginning of the lab sessions, participants received capsules containing Sinemet125 and took the capsules orally.

Arm title	Placebo-condition

Arm description:

A total of 80 participants were submitted to both experimental conditions (dopamine and placebo) at two separate lab sessions.

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

Dosage and administration details:
Lactose monohydrate with 1 % magnesium stearate (125mg)

Number of subjects in period 1	Dopamine-condition	Placebo-condition
Started	80	80
Completed	80	80

Baseline characteristics

Reporting groups	
Reporting group title	Experimental sessions
Reporting group description:	
80 students (mean age 21.38 years, SD = 1,84; 40 participants carrying the DRD4-7R allele, and 40 participants who did not) were selected to participate in the experimental sessions (both the dopamine and placebo condition). Students in the two groups (DRD4-7R+ and DRD4-7R-) did not differ in age, reading motivation, language skills, executive functioning in daily life, attentional control in daily life, or baseline reading speed.	

Reporting group values	Experimental sessions	Total	
Number of subjects	80	80	
Age categorical Units: Subjects			
Adults (18+)	80	80	
Age continuous Units: years			
arithmetic mean	21.38		
standard deviation	± 1.84	-	
Gender categorical Units: Subjects			
Female	80	80	
Male	0	0	
Reading motivation			
Participants completed a researcher-constructed reading motivation survey. The survey consisted of three subscales: engagement in reading related activities, attitude towards reading for pleasure, and reading in spare time. Higher scores reflected higher reading motivation.			
Units: 0.1			
arithmetic mean	0.00		
standard deviation	± 1.00	-	
Language skills			
Participants completed a researcher-constructed language test, containing of four subtests: spelling, grammar, vocabulary and syntax.			
Units: 0.1			
arithmetic mean	0.00		
standard deviation	± 1.00	-	
Executive functioning			
Participants completed the Behavior Rating Inventory of Executive Function—Adult version (BRIEFA; Scholte & Noens, 2011), a self-report questionnaire of 75 items designed to examine adult's executive functions in daily life.			
Units: 1.0			
arithmetic mean	102.91		
standard deviation	± 20.33	-	
Attentional Control			
Participants completed a Dutch translation of the Attentional Control Scale (ACS; Derryberry & Reed, 2002).			
Units: 1.0			
arithmetic mean	53.55		
standard deviation	± 8.51	-	

Subject analysis sets	
Subject analysis set title	DRD4 7R+
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The final sample consisted of 40 students with the DRD4 7R+ genotype and 40 students with the DRD4 7R- genotype.

Subject analysis set title	DRD4 7R-
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The final sample consisted of 40 students with the DRD4 7R+ genotype and 40 students with the DRD4 7R- genotype.

Reporting group values	DRD4 7R+	DRD4 7R-	
Number of subjects	40	40	
Age categorical Units: Subjects			
Adults (18+)	40	40	
Age continuous Units: years			
arithmetic mean	21.18	21.58	
standard deviation	± 1.65	± 2.01	
Gender categorical Units: Subjects			
Female	40	40	
Male	0	0	
Reading motivation			
Participants completed a researcher-constructed reading motivation survey. The survey consisted of three subscales: engagement in reading related activities, attitude towards reading for pleasure, and reading in spare time. Higher scores reflected higher reading motivation.			
Units: 0.1			
arithmetic mean	0.11	-0.11	
standard deviation	± 0.95	± 1.05	
Language skills			
Participants completed a researcher-constructed language test, containing of four subtests: spelling, grammar, vocabulary and syntax.			
Units: 0.1			
arithmetic mean	0.03	-0.03	
standard deviation	± 1.08	± 0.92	
Executive functioning			
Participants completed the Behavior Rating Inventory of Executive Function—Adult version (BRIEFA; Scholte & Noens, 2011), a self-report questionnaire of 75 items designed to examine adult's executive functions in daily life.			
Units: 1.0			
arithmetic mean	102.00	103.82	
standard deviation	± 20.82	± 19.83	
Attentional Control			
Participants completed a Dutch translation of the Attentional Control Scale (ACS; Derryberry & Reed, 2002).			
Units: 1.0			
arithmetic mean	53.80	53.30	
standard deviation	± 8.00	± 9.01	

End points

End points reporting groups

Reporting group title	Dopamine-condition
Reporting group description:	
The study had a randomized, double-blind placebo-controlled within-subjects experimental design. A total of 80 participants were submitted to both experimental conditions (dopamine and placebo) at two separate lab sessions.	
Reporting group title	Placebo-condition
Reporting group description:	
A total of 80 participants were submitted to both experimental conditions (dopamine and placebo) at two separate lab sessions.	
Subject analysis set title	DRD4 7R+
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The final sample consisted of 40 students with the DRD4 7R+ genotype and 40 students with the DRD4 7R- genotype.	
Subject analysis set title	DRD4 7R-
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
The final sample consisted of 40 students with the DRD4 7R+ genotype and 40 students with the DRD4 7R- genotype.	

Primary: Attentional control - average frontal TBR

End point title	Attentional control - average frontal TBR[1]
End point description:	
End point type	Primary
End point timeframe:	
during reading	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A repeated measures ANOVA with condition (dopamine vs. placebo) and type of attentional control measure (frontal TBR during reading, SD in frontal TBR during reading and self-reports of attentional control during reading) as within-subjects factors showed no main effect of condition ($F(1,75) = 1.48$, $p = 0.23$). Attentional control during reading did not differ between the levodopa condition and the placebo condition.

End point values	Dopamine-condition	Placebo-condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	80		
Units: 0.01				
arithmetic mean (standard deviation)	.40 (± .20)	.39 (± .17)		

Statistical analyses

No statistical analyses for this end point

Primary: Attentional control - SD in frontal TBR

End point title	Attentional control - SD in frontal TBR[2]

End point description:

End point type	Primary

End point timeframe:

during reading

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A repeated measures ANOVA with condition (dopamine vs. placebo) and type of attentional control measure (frontal TBR during reading, SD in frontal TBR during reading and self-reports of attentional control during reading) as within-subjects factors showed no main effect of condition ($F(1,75) = 1.48$, $p = 0.23$). Attentional control during reading did not differ between the levodopa condition and the placebo condition.

End point values	Dopamine-condition	Placebo-condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	78	79		
Units: 0.01				
arithmetic mean (standard deviation)	.09 (± .06)	.09 (± .05)		

Statistical analyses

No statistical analyses for this end point

Primary: Attentional control - self-reports

End point title	Attentional control - self-reports[3]

End point description:

End point type	Primary

End point timeframe:

during reading

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A repeated measures ANOVA with condition (dopamine vs. placebo) and type of attentional control measure (frontal TBR during reading, SD in frontal TBR during reading and self-reports of attentional control during reading) as within-subjects factors showed no main effect of condition ($F(1,75) = 1.48$, $p = 0.23$). Attentional control during reading did not differ between the levodopa condition and the placebo condition.

End point values	Dopamine-condition	Placebo-condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	79	79		
Units: 1.00				
arithmetic mean (standard deviation)	3.09 (± 2.47)	2.97 (± 2.76)		

Statistical analyses

No statistical analyses for this end point

Primary: Summary task

End point title	Summary task[4]

End point description:

End point type	Primary

End point timeframe:

post-test

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A repeated measures ANOVA was performed with condition (dopamine vs. placebo) and type of reading comprehension measure (summary task, text-level comprehension questions, spelling questions, open word meaning questions, and MC word meaning questions) as within-subjects factors. There was a significant main effect of condition on reading comprehension ($F(1,79) = 11.55$, $p = 0.001$). Participants performed worse on reading comprehension in the levodopa condition than in the placebo condition.

End point values	Dopamine-condition	Placebo-condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	80		
Units: 1.00				
arithmetic mean (standard deviation)	24.70 (± 13.61)	25.47 (± 13.14)		

Statistical analyses

No statistical analyses for this end point

Primary: Text-level comprehension questions

End point title	Text-level comprehension questions[5]

End point description:

End point type	Primary

End point timeframe:

post-test

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A repeated measures ANOVA was performed with condition (dopamine vs. placebo) and type of reading comprehension measure (summary task, text-level comprehension questions, spelling questions, open word meaning questions, and MC word meaning questions) as within-subjects factors. There was a significant main effect of condition on reading comprehension ($F(1,79) = 11.55$, $p = 0.001$). Participants performed worse on reading comprehension in the levodopa condition than in the placebo condition.

End point values	Dopamine-condition	Placebo-condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	80		
Units: 0.1				
arithmetic mean (standard deviation)	31.82 (± 17.63)	36.72 (± 17.61)		

Statistical analyses

No statistical analyses for this end point

Primary: MC word meaning questions

End point title	MC word meaning questions[6]

End point description:

End point type	Primary

End point timeframe:

post-test

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A repeated measures ANOVA was performed with condition (dopamine vs. placebo) and type of reading comprehension measure (summary task, text-level comprehension questions, spelling questions, open word meaning questions, and MC word meaning questions) as within-subjects factors. There was a significant main effect of condition on reading comprehension ($F(1,79) = 11.55$, $p = 0.001$). Participants performed worse on reading comprehension in the levodopa condition than in the placebo condition.

End point values	Dopamine-condition	Placebo-condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	80		
Units: 1.00				
arithmetic mean (standard deviation)	44.00 (± 9.42)	46.88 (± 13.56)		

Statistical analyses

No statistical analyses for this end point

Primary: Open word meaning questions

End point title	Open word meaning questions[7]

End point description:

End point type	Primary

End point timeframe:

post-test

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A repeated measures ANOVA was performed with condition (dopamine vs. placebo) and type of reading comprehension measure (summary task, text-level comprehension questions, spelling questions, open word meaning questions, and MC word meaning questions) as within-subjects factors. There was a significant main effect of condition on reading comprehension ($F(1,79) = 11.55$, $p = 0.001$). Participants performed worse on reading comprehension in the levodopa condition than in the placebo condition.

End point values	Dopamine-condition	Placebo-condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	80		
Units: 1.00				
arithmetic mean (standard deviation)	4.79 (± 5.66)	6.42 (± 7.21)		

Statistical analyses

No statistical analyses for this end point

Primary: Spelling questions

End point title	Spelling questions[8]

End point description:

End point type	Primary

End point timeframe:

post-test

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: A repeated measures ANOVA was performed with condition (dopamine vs. placebo) and type of reading comprehension measure (summary task, text-level comprehension questions, spelling questions, open word meaning questions, and MC word meaning questions) as within-subjects factors. There was a significant main effect of condition on reading comprehension ($F(1,79) = 11.55$, $p = 0.001$). Participants performed worse on reading comprehension in the levodopa condition than in the placebo condition.

End point values	Dopamine-condition	Placebo-condition		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	80		
Units: 1.00				
arithmetic mean (standard deviation)	8.33 (± 5.76)	10.50 (± 7.89)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Experimental sessions

Adverse event reporting additional description:

None of the participants suffered from serious adverse events during or after our study related to the intake of Sinemet125 or the placebo treatment. Except for one participant reporting nausea in the placebo condition, no side effects of the medication were reported by the participants.

Assessment type	Non-systematic

Dictionary used

Dictionary name	N.A.
Dictionary version	N.A.

Reporting groups

Reporting group title	Dopamine condition
Reporting group description: -	
Reporting group title	Placebo condition

Reporting group description: -

Serious adverse events	Dopamine condition	Placebo condition	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 80 (0.00%)	0 / 80 (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: 1 %

Non-serious adverse events	Dopamine condition	Placebo condition	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 80 (0.00%)	1 / 80 (1.25%)	
Injury, poisoning and procedural complications			
Nausea			
subjects affected / exposed	0 / 80 (0.00%)	1 / 80 (1.25%)	
occurrences (all)	0	1	

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

N.A.

Notes: