The interaction of Cognitive Control Mechanisms and Language Processing: An Investigation with Methylphenidate

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON48291

Source
ToetsingOnline

Brief title
Cognitive Control & Language

Condition

- Other condition

Synonym
executive function, reading

Health condition

Cognitive and attention disorders and disturbances

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Catecholamine, Cognitive Control, Language Processing, Methylphenidate

Outcome measures

Primary outcome

Primary study parameters include participants' task behavioral performance

(e.g. accuracy, reaction times) and electroencephalographic (EEG) measures.

Secondary outcome

Secondary study parameters include participants' baseline characteristics (e.g.

working memory capacity, linguistic experience), and general processing speed.

Study description

Background summary

One of the hottest topics in the psycholinguistics research is the relationship between individuals* general cognitive control ability and language processing efficiency. However, the nature of such a relationship remains unclear, such as when and how cognitive control operations are recruited during language processing, and whether there is a causal interplay between these two cognitive operations. Recent studies have shown that both cognitive control and language processing are affected by the individuals* catecholaminergic (CA) level. We proposed that investigating the role of CA for language and cognitive control operations via a pharmacological manipulation, would provide a causal link to understand the nature of the relationship between these two most essential human abilities.

Catecholamine (CA) neurotransmitters, such as dopamine (DA) and noradrenaline (NA), have long been implicated playing a critical role in cognitive functions, such as working memory (WM), inhibition, learning, decision making, and language processing. However, the question of what kind of influence that CA might exert on language is still open. In a recent study, through the

administration of a CA agonist (i.e., methylphenidate), Tan and Hagoort (in preparation) found that increased CA level enhanced participant*s sensitivity to semantically incongruent information even when language processing per se was actually goal irrelevant. Moreover, the results showed that participants with lower cognitive control capacity benefited more from MPH administration. These results shed light on the relation among language processing, cognitive control, and catecholaminergic level, but also lead to further questions, such as whether the interaction between CA and semantic processing is language-specific or mediated by the relation between CA and the general cognitive control ability, and whether CA also has influence on other aspects of language processing, such as syntactic processing.

In the present study, we aim to further investigate the nature of the interplays between language, cognitive control and CA level through administrating methylphenidate (MPH) to healthy participants. MPH is an indirect CA agonist, which is the most commonly prescribed drug for attention deficit/hyperactivity disorder (ADHD). Previous studies have shown that MPH could efficiently increase the extracellular levels of CA in the brain by blocking their reuptake.

Study objective

Our primary objectives are: 1) to further investigate the effect of CA on semantic and syntactic processing during sentence comprehension; 2) to investigate the effect of CA on the general cognitive control ability, and further evaluate whether there is a causal relationship of cognitive control and language processing.

Our secondary objective is to further examining the relation between the MPH effects and the baseline characteristics (e.g., as eye-blink rate, WM capacity) of individual participants.

Study design

This study will use a within-subject, double-blind, placebo-controlled, randomized, crossover design, similar to CMO-approved protocol 2010/283, 2013/568, and 2015/1532. Participants will either orally receive a 20mg methylphenidate or placebo capsule in each session. Methylphenidate has been approved for clinical use in the Netherlands and the drug can be administered safely without any relevant risk of serious adverse events. Primary study parameters will include sentence comprehension capacity, attention and processing speed. In addition, several other measures will be included to monitor participants* baseline characteristics (e.g. working memory capacity, vocabulary size) and the general modulation effects of MPH (e.g. heart rate, blood pressure, subjective feeling).

Intervention

Not applicable.

Study burden and risks

Participants will have to visit the laboratory site three times. During each visit they will have to complete a series of language and cognitive function tasks after receiving 20mg methylphenidate or placebo. In the information brochure shared with each participant at least 1 week before their first visit, they will be instructed to adhere to some simple restrictions regarding medication (especially recreational drugs), alcohol and drug intake. In the morning of each visit they will have to refrain from smoking and stimulant-containing drinks. The most common side effects of methylphenidate include headache, dizziness, nausea and anxiety1. However, previous studies conducted at the DCCN (CMO2013/568, ABR number NL47166.091.13; CMO2014/289, ABR number NL49516.091.14; CMO2015/1532, ABR number NL51075.091.14) have shown that a single dose of 20mg (or even higher) methylphenidate is well tolerated in healthy adults. Considering the extensive exclusion criteria, screening procedure and constant monitoring of the subjects, we do not expect serious side effects.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Healthy volunteers between 18 and 45 years old;
Native Dutch speakers.
Right-handed

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• (History of) psychiatric treatment;
• (History of) psychosis or mania;
• (History of) neurological diseases (e.g. Parkinson, epilepsie);
• (History of) neurological treatment;
• (History of) endocrine treatment;
• (History of) cardiac or vascular diseases;
• (History of) blood illness (e.g. anemia, porphyria);
• (History of) endocrine / metabolic disease;
• (History of) of stomach or gastrointestinal tract disease;
• (History of) vasovagale reflex syncope;
• Experience of irregular sleep-wake rhythm;
• (History of) obstructive respiratory disease
• (History of) frequent autonomic failure (e.g. vasovagal reflex syncope);
• (History of) clinically significant renal or hepatic disease;
• (History of) epilepsy in adulthood (i.e. no insult after 18 years of age, no current medication for epilepsy, and no insult in the last five years);
• (History of) glaucoma;
• (History of) drug addication (e.g. opiate, (meth)amphetamine, lysergic acid diethylamide, cocaine, solvents or barbiturate) or alcohol dependence;
• One first degree or two or more second degree family members with a history of sudden death or ventricular arrhythmia;
• Problems slicking or problems with the esophagus ();
• Frequent experience of headrush (vertigo);

• Past or current treatment of hyperthyroidism;
• Current experience of an acute infection (e.g. fever);
• First degree family member with schizophrenia or bipolar disorder;
• Abnormal hearing or (uncorrected) vision;
• Use of psychotropic medication or recreational drugs weekly or more over a period of more than three months in the last 6 months;
• Use of drug within 2 weeks prior to the start of the study;
• Use of alcohol within the last 24 hours before each test session;
• Dependence on cannabis or weekly cannabis usage for the last 6 months;
• Strong smoking behaviour starting at more than 1 package of cigarettes per week;
• Hypersensitivity for e.g. beta blockers or methylphenidate;
• Previous use of Methylphenidate (Ritalin);
• Uncontrolled hypertension, defined as diastolic blood pressure at rest >95 mmHg or systolic blood pressure at rest >180 mmHg;
• Irregular sleep/wake rhythm (e.g. regular nightshifts or cross timeline travel);
• Possible pregnancy or breastfeeding;
• Lactose intolerance (because the placebo pill will be a lactose product);
• Language related disabilities (e.g. dyslexia, stuttering);
• Daily intense physical training.

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	26-11-2019
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	24-07-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL69700.091.19