Effects of catecholamines on memory retention; an exploratory study

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The current study aims to investigate the effects of catecholamine modulation by methylphenidate during initial stages of consolidation on memory retention and the underlying neural correlates of memory retrieval.

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

Summary

ID

NL-OMON41056

Source
ToetsingOnline

Brief title
Catecholamines and memory retention

Condition

- Other condition

Synonym
long-term memory, memory consolidation

Health condition

fundamental cognitive neuroscience research of memory consolidation and retention with possible future implications in psychopharmacy and treatment for patients with memory deficits

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universiteit Nijmegen
Source(s) of monetary or material Support: European Union; European Research Council Grant 2010- AdG 268800 - Neuroschema

Intervention

Keyword: catecholamines, functional neuroimaging, memory retention, neural processes

Outcome measures

Primary outcome

1) Memory retention on the associative memory task

At behavioural level, the primary study measure is memory performance, quantified as the number of correctly learned associative memories and measured directly at the end of the learning task (Test 1 on Day 1) and on the second testing day to check long-term memory performance (Test 2 on Day 2). The main study parameter is the comparison of memory retention (i.e., the difference in memory performance between Test 1 and 2) between the MPH and placebo group to test if modulation of catecholamines affects memory retention

2) At neural level, the primary study parameters are activation and functional connectivity during memory retrieval on the second study day, to test if modulation of catecholamines is associated with between-group differences in neural responses to memory retrieval, potentially explaining the behavioral differences. Furthermore, we will investigate functional connectivity during resting-state of the MTL and mPFC with each other and with other (neo)cortical regions.

Secondary outcome

The outcome on three questionnaires will be used as baseline measures of impulsivity and possible ADHD symptoms. In addition, the outcome of the Daneman and Carpenter listening span test will be used as a baseline estimate of working memory capacity, which has been found to be a valid surrogate measure of catecholamine levels at baseline

Study description

Background summary

Adequate memory is essential for normal functioning in daily life. Memory consolidation refers to the processes that stabilize initially fragile memories for long-term use. Memory for most experiences fades quickly while memories of some, usually more significant, events can persist for decades. Release of catecholamines (noradrenaline and dopamine) during initial stages of consolidation is thought to underlie this enhanced memory persistence. In rodents, it has been shown that catecholamine modulation augments memory retention by influencing consolidation processes. In humans, however, the effects of catecholamines on memory retention are not yet well investigated. Also, the mechanistic underpinnings of catecholamine enhanced memory consolidation are unclear. Methylphenidate (MPH) enhances catecholamine levels and is currently widely used both as treatment for Attention Deficit Hyperactivity Disorder (ADHD) as in the healthy student population to improve study performance.

Study objective

The current study aims to investigate the effects of catecholamine modulation by methylphenidate during initial stages of consolidation on memory retention and the underlying neural correlates of memory retrieval.

Study design

A randomized, between-subject, double-blind, placebo-controlled, design will be employed.
All subjects will visit the Donders Centre for Cognitive Neuroimaging (DCCN) for one screening session and two testing sessions. During the first testing session (study Day 1), the subjects will perform a learning task during which they are instructed to learn the associations between objects and locations. During this task, 30 subjects will receive an oral capsule of 20mg MPH and 30

subjects will receive an oral placebo capsule. The drug will be administered halfway during the task to have maximum effect on the consolidation phase after learning but no effect on learning itself (based on prior studies and pharmacokinetics). On the second testing day (study Day 2), all subjects will return and their memory for the learned associations will be tested in a recall task while measuring brain activity using fMRI. Additionally, brain activity will be measured during a resting-state period.
The total duration of the experiment is approximately 8 hours per subject, divided over a screening session (1 hr), study Day 1 (5 hrs) and Day 2 (1,75 hr). The experimental procedures (= study procedures minus the screening procedures) take place on two days that are 45 to 75 hrs apart.

Intervention

Subjects will receive an oral capsule of 20mg MPH or placebo. These can be administered safely without any relevant risk of serious adverse events ((S)AEs) and have been approved for clinical use in the Netherlands.

Study burden and risks

Subjects will perform a learning task prior and immediately after administration of 20mg MPH or placebo. On the second study day, subjects will perform a recall task while lying in an MRI scanner. On the day preceding the drug first study day, subjects will have to adhere to some simple restrictions with respect to alcohol and drug intake. Also, subjects will have to refrain from smoking and stimulant containing drinks on the morning of the first day.
The most common side effect of taking methylphenidate MPH is mild headache (occurring in about 10% of people who take the drug). Less common side effects include feeling dizzy, nauseous or anxious. However, numerous research studies have demonstrated that 20mg (or more) of MPH is well tolerated in healthy volunteers between 18 and 35 years of age. Another possible source of discomfort to participants is the completion of the MRI measurements. Although the noise and the relative confined space of the MRI scanner may cause discomfort to some subjects, MRI measurements themselves do not pose any risk, if appropriate precautions are made.
Considering the extensive exclusion criteria, screening procedure, and constant monitoring of the subjects we do not expect (S)AEs. The consent discussion starts sufficiently in advance of the initiation of study-related procedures to allow potential subjects time to reflect on the potential benefits and risks and possible discomforts. We estimate the risk associated with participation in this study as minimal.

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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 right-handed male volunteers between 18 and 35 of age. Normal or corrected-to-normal vision and willingness and ability to sign informed consent

Exclusion criteria

• (History of) psychiatric treatment
• (History of) neurological treatment
• (History of) endocrine treatment
• (History of) autonomic failure (e.g., vasovagal reflex syncope).
• (History of) clinically significant hepatic, cardiac, obstructive respiratory, renal, cerebrovascular, metabolic or pulmonary disease
• Family history of sudden death or ventricular arrhythmia
• (History of) epilepsy
• (History of) drug dependence (opiate, LSD, (meth)amphetamine, cocaine, solvents, or

barbiturate) or alcohol dependence
• Family history of schizophrenia or bipolar disorder
• Current or past use of psychotropic medication
• Regular use of corticosteroids.
• Suicidality
• Diabetes
• Uncontrolled hypertension, defined as diastolic blood pressure at rest > 95 mmHg or systolic blood pressure at rest > 180 mmHg
• Hypotension, defined as diastolic blood pressure < 50 mm Hg or systolic < 95 mm Hg or resting pulse rate < 45 beats/min
• Abnormal hearing or (uncorrected) vision.
• Lactose intolerance (placebo pill is a lactose product)
• Irregular sleep/wake rhythm (e.g., regular nightshifts or cross timeline travel).
• Current use of oral medication aside from occasional use of paracetamol
• Use of recreational drugs or alcohol over a period of 24 hours prior to the first study day
• Subjects with any personal characteristics that make him/her ineligible for MR scanning

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-11-2014
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	03-09-2014
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	NL49516.091.14