Cannabis modulation of the link between dopamine and creativity

Published: 11-02-2011
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Primary objectiveDoes administration of THC produce an increase in subcortical dopamine level of chronic cannabis users? Does this effect on dopamine modulate the link between spontaneous eye blink rate, performance on divergent and convergent...

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

Summary

ID

NL-OMON38033

Source
ToetsingOnline

Brief title
CDC

Condition

- Other condition

Synonym
none

Health condition

none

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Leiden
Source(s) of monetary or material Support: VENI grant

Intervention

Keyword: cannabis, creativity, delta-9-tetrahydrocannabinol, dopamine

Outcome measures

Primary outcome

The main study parameter is the difference between spontaneous eye blink rates of subjects measured before and after intoxication with THC. Groups with varying dosages of THC and the placebo group will be compared in this regard.

Secondary outcome

A secondary study parameter is the correlation between spontaneous eye blink rates, performance on the Alternate uses task and Remote associates task and mood as indicated on the Affect grid. Additionally, performance on the Global-local and Stop-signal tasks will be measured. The ERN will also be recorded during completion of a flanker task. Groups with varying dosages of THC and the control group will be compared in these aspects. Moreover, in the groups where THC is administered, three visual analogue scales will be used in order to assess the subjective effects of the drug.

Study description

Background summary

An aspect of cannabis intoxication that is frequently mentioned by users is enhanced creative thought. Self-reports indicate openness to contradictory ideas and spontaneous insights during intoxication (Tart, 1971). However, the

impact of delta-9-tetrahydrocannabinol (THC) on creativity has not yet been investigated, apart from one study that identified potential acute effects on divergent and convergent thinking tasks (Weckowicz et al., 1975). Additionally, no data can be found on the chronic impact of THC on performance on creativity tasks. The issue of creativity has lately been linked to dopaminergic functioning (Akbari Chermahini, & Hommel, 2010a). Given this finding, apart from investigating the impact of THC on creativity itself, it is currently possible to gain insight into how THC modulates the reciprocal relationship between dopamine (DA) and creativity, both directly, as well as in the long-term. Measures of creativity can be used to indirectly investigate the effect of THC on dopaminergic functioning, which has been shown in a recent study by Akbari Chermahini and Hommel (2010a).

The above-mentioned study established a direct link between individual DA level and performance on divergent and convergent thinking creativity tasks. Particularly, it has been shown that individual spontaneous eye blink rate (EBR) predicted performance on these tasks. EBR is a clinical marker of striatal DA production (Karson, 1983; Shukla, 1985; Taylor et al., 1999). The relation between EBR and performance followed an inverted-U function for divergent thinking, pointing to best performance with a medium DA level. Convergent thinking followed a more linear relationship indicating best performance with the lowest DA level. In the light of such evidence, it is possible that a potential detrimental long-term effect of THC on striatal DA level could also be observed in regard to performance on the two creativity tasks.

It needs to be mentioned that EBR provides only a basic, subcortical measure of dopaminergic functioning (Akbari Chermahini, & Hommel, 2010a). Although performance on creativity tasks can also be treated as an indirect indicator of DA level, better discrimination between the different dopaminergic pathways is required. Measures of performance on various cognitive tasks can be considered as indirect assessments of DA level in different regions of the brain. For instance, an aspect that has been linked to deregulation of subcortical DA level is inhibitory control. Particularly, too high or too low striatal DA has been shown to impair the ability to inhibit a response in the Stop-signal task (Colzato, van den Wildenberg, van der Does, & Hommel, 2010). Additionally, task-switching performance has been shown to be a reliable indicator of cognitive flexibility, which is also related to DA level in the striatum (Colzato et al., 2010). Therefore, tasks which evaluate inhibitory control and cognitive flexibility need to be applied in combination with EBR measures, in order to give a better understanding of the impact of THC on dopaminergic functioning.

Another cognitive function related to DA transmission is performance monitoring. Performance monitoring describes the process of ensuring that the results of an action are consistent with the goal. A neural indicator associated with this process is the error-related negativity (ERN), a negative event-related potential (ERP) generated in the anterior cingulate cortex. The ERN can be observed when human participants commit errors in a variety of psychological tasks (Holroyd, & Coles, 2002). Holroyd and Coles (2002)

suggested that the ERN signal is transmitted to the anterior cingulate cortex by means of the mesencephalic DA system. It has also been shown that chronic cannabis use impairs the process of performance monitoring (Hester, Nestor, & Garavan, 2009). Therefore, it can be assumed that there is a long-term effect of THC on the mesencephalic DA pathway. However, there is no data about the acute effects of THC on performance monitoring. Due to the fact that cognitive impairments of chronic users seem to diminish after administration of THC (Kelleher, Stough, Sergejew, & Rolfe, 2004), it might be expected that intoxicated users will demonstrate improved performance monitoring, as compared to non-intoxicated ones. In any case, inclusion of performance monitoring to the study might provide data on the direct effect of THC on the mesencephalic DA pathway, as well as on the impact of the drug on this particular cognitive function.

Study objective

Primary objective
Does administration of THC produce an increase in subcortical dopamine level of chronic cannabis users? Does this effect on dopamine modulate the link between spontaneous eye blink rate, performance on divergent and convergent thinking tasks and mood outlined by Chermahini and Hommel (2010a, 2010b)?

Secondary objectives
Does administration of THC to chronic cannabis users affect performance monitoring during a flanker task, as indicated by the ERN component?
Does administration of THC to chronic cannabis users affect performance on the Stop-signal and Global-local processing tasks?

Study design

We will employ a randomized, double-blind, between-subjects design. Each participant will take part in one laboratory session during which they will undergo two eye blink rate and four mood measurements. Each subject will also be required to complete divergent and convergent thinking, Stop-signal and Global-local processing tasks. An ERP recording during a flanker task will additionally be applied. Two-third of participants will be administered THC, one-third will be administered placebo. Three different dosages of THC will be used: 2 and 8 mg. Neither the subjects nor the investigator conducting the experiment will know which dosage is administered. The study will last 120 minutes.

Intervention

Participants will inhale vapor obtained from medical grade Cannabis sativa (Bedrocan) or placebo from a non-transparent polythene bag using a mouthpiece with a valve, which prevents loss of THC between inhalations. Subjects will be

required to completely inhale the contents of the bag. Vapor will be produced using the Volcano® vaporizer. Dosages of 2 and 8 mg of THC will be used.

Study burden and risks

There is a variety of potential effects of cannabis reported. These include changed mood, insomnia, palpitations, relaxation, laughter, hunger, greater sensitivity to sensations of color and music, a disturbed time-space experience and lethargy. Also at higher doses a subjective *high* feeling can occur, which is a state of mild euphoria gradually turning into a satisfied state of calmness. It is difficult to predict exactly which effects may appear after intoxication. All the effects disappear after a few hours.
Recent studies have indicated that chronic users of cannabis show some tolerance to the subjective *high* effects (Ramaekers et al., 2009) and to the cognitive impairing effects (Hart et al., 2010) of cannabis. Therefore, it can be assumed that even a high (8 mg) single dose of THC administered to chronic users will not likely result in adverse effects, such as psychotic symptoms. In the case of the research by Ramaekers et al. (2009), a single high dose of THC (500 µg/kg) did not produce any negative effects both in chronic, as well as occasional users.

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

A weekly consumption of cannabis (at least 4 joints) for a minimum of 2 years.

Exclusion criteria

History or presence of an Axis 1 psychiatric disorder (DSM-IV; assessed with the use of the Mini International Neuropsychiatric Interview; M.I.N.I: Lecrubier et al., 1997), clinically significant medical disease, use of psychotropic medication, current or previous regular use of other drugs except cannabis, abuse of alcohol (more than 14 units a week). Additionally, consumption of caffeine, chocolate or alcohol 12 h before the experimental session, consumption of nicotine 2 h before the experimental session. Participants are also not allowed to use cannabis within 2 days before the experiment.

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):	24-09-2012
Enrollment:	100

Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Bedrocan
Generic name:	Cannabis Flos
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	11-02-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	12-04-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	18-05-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	20-06-2011
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	01-08-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	28-12-2012
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO	

Date:	08-01-2013
Application type:	Amendment
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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
EudraCT	EUCTR2010-024233-23-NL
CCMO	NL34823.058.11