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On-the-Road Driving Tests and Neurocognitive Tests for Measuring the Effects of Cannabis on Driving

by
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On-the-road driving tests and neurocognitive tests for measuring the effects of cannabis on driving

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Introduction

Cannabis – acute effects

- Does cannabis impair psychomotor, cognitive and actual driving performance and increase the risk of becoming involved in traffic accidents?
- Is there a relation between performance impairment and cannabis dose or its concentration in plasma?
- Do combined effects of cannabis and alcohol on driving performance differ from those of either drug alone?
- Limits of impairment

Introduction

Data sources

- Epidemiological surveys
  - Determine the involvement of THC users in traffic crashes
  - Prevalence data
  - Culpability data
  - Case Control data
- Experimental studies
  - Laboratory tests of isolated psychological functions related to driving
  - Driving simulators
  - Actual driving tests

Epidemiology

Prevalence data

Presence of THC is detected in 4-12% of drivers involved in traffic accidents

Caution !!!

Alcohol is also present in 50-80% of these THC positive drivers

Prevalence of THC in general driving population unknown (no control group)

Epidemiology

Culpability data

Classification of culpability

Distinguish between drivers who were responsible for their crash (Cases) and those who were not (Controls).

Compare culpability rates between THC users and drug free drivers that were involved in traffic accidents

(Odds Ratio or Culpability Ratio)

Epidemiology

Culpability data

Substance	Authors	Odds Ratio	95% CI
Drug free cases		1.0	
Alcohol	Terhune & Fell (1982);Williams et al (1985); Terhune et al (1992); Drummer (1994); Hunter et al (1998); Lowenstein & Koziol-McLain(2001); Drummer (2001)	3.2 * – 7.4 *	1.1 – 10.7
THC-COOH	Williams et al (1985); Drummer (1994); Hunter et al (1998); Lowenstein & Koziol-McLain(2001)	0.2 – 1.62	0.2 – 4.8
THC	Terhune & Fell (1982); Terhune et al (1992); Hunter et al (1998); Drummer et al (2004); Laumon et al (2006)	0.7 – 2.7 *	0.2 – 7.6
THC / Alcohol	Williams et al (1985); Terhune et al (1992); Drummer (1994); Hunter et al (1998); Lowenstein & Koziol-McLain(2001); Drummer (2004);	5.3 * - 19 *	1.9 – 136

Epidemiology

Culpability data

Substance	Authors	Odds Ratio	95% CI
Drug free cases		1.0	
THC concentration (ng/ml) in whole blood			
< 1.0	Hunter et al (1998)	0.35	0.02 – 2.1
1.1 – 2.0		0.51	0.2 - 1.4
>2		1.74	0.6 – 5.7
<5	Drummer et al (2004)	0.7	
5 - 100		6.6 *	1.3 - 116
< 1.0	Laumon et al (2006)	1.57	0.8 - 2.9
1 – 2		1.54	1.1 – 2.2
3 – 4		2.13	2.2 – 3.7
>5		2.12	1.3 – 3.4

Epidemiology

Case control

Substance	Authors	Number of cases and controls	THC /THC-COOH Odds rati0 (95% CI)
Mura et al (2003)	Prospective case control Injured drivers vs visitors of same hospitals	900- 900	2.5 (1.5-4.2)
Gerberich-Goodwin et al (2003)	Restrospective cohort in health care program Incidence of traffic injuries in cannabis users vs non users	64,657	2.3 (1.4-2.7)
Fergusson & Horwood (2001)	Retrospective cohort Self reported accident rate and cannabis use Adjusted for lifestyle	907 youngsters	1.6 (1.2 -2.0) 0.97 (0.9-1.1)
Dussault et al (2002)	Prospective case-control Injured drivers vs general driving population	354 – 11,574	2.2 (1.5-3.4)
Movig et al (2004)	Prospective case-control Injured drivers vs general driving population	110 – 816	1.2 (0.5-2.7)

Experimental studies

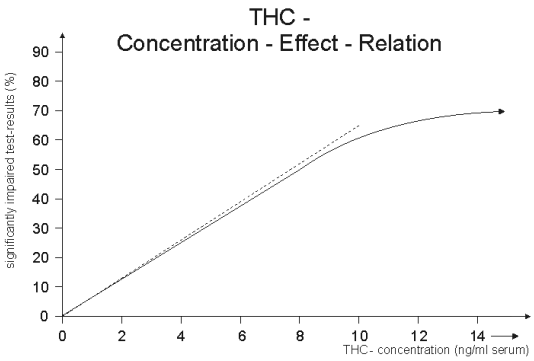
Psychomotor function and cognition

Numerous experimental studies have employed laboratory tests designed to measure cognitive and psychomotor skills related to driving.

- Memory
- Divided and Sustained attention
- Reaction time
- Tracking performance
- Motor control

Experimental studies

Psychomotor function and cognition



Frequency of performance decrements (%) observed in the total number of tests applied in 87 experimental studies as a function of THC concentration after eating (---) and smoking (-) cannabis (Berghaus et al, 1998)

Experimental

Construct validity laboratory tests

- Can results from experimental laboratory studies be generalized to on the road driving ?
- Are these tests relevant to driving ?

Experimental

On-the-road driving studies at Maastricht University (1990-2000)

- Funded by US NHTSA
- Rationale : to assess the effects of cannabis, alone and in combination with alcohol, on actual driving

Experimental studies

Actual driving tests

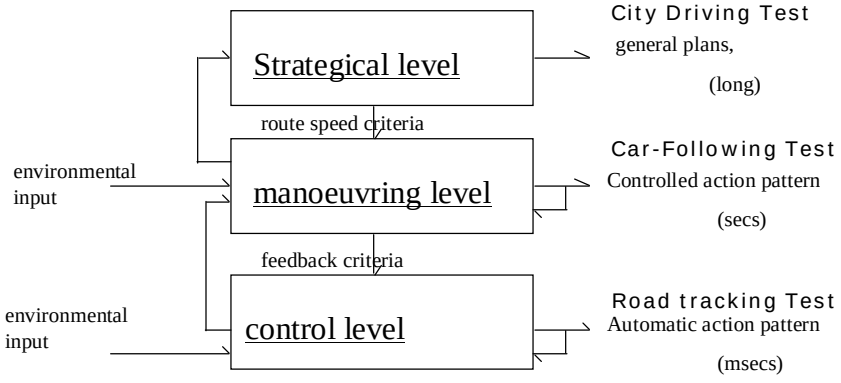
Driving models

- Road tracking performance
  e.g.. weaving, SDLP
- Car-Following performance
  e.g. brake reaction time, time to speed adaptation
- City Driving performance
  e.g. visual search, anticipation traffic, decision making

The effects of cannabis on actual driving were most prominent in tests measuring road tracking precision as compared to tests measuring more complex driving tasks

Robbe (1994); Ramaekers et al. (2000); Lamers & Ramaekers (2001)

Actual driving tests



Experimental studies

Design interaction studies

Study 1

- Balanced 6-way, double-blind, placebo controlled, crossover design (N=18)
- dosages : 0, 100 and 200 µg/kg THC with and without 0.7 g/kg ethanol (mean BAC 0.04 g/dl)
- 19:00 hrs alcohol dose
  20:30 hrs THC smoking

  21.00-23.00 hrs Road Tracking/ Car-Following

Study 2

- Balanced 4-way, double-blind, placebo controlled, crossover design (N=18)
- dosages : 0, 100 THC w µg/kg with and without 0.7 g/kg ethanol (mean BAC 0.04 g/dl)
- 19:15 hrs alcohol dose
  20:00 hrs THC smoking

  20.30-21.30 hrs City Driving Test

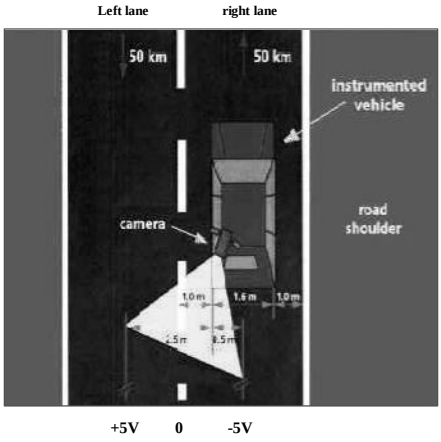
Experimental studies

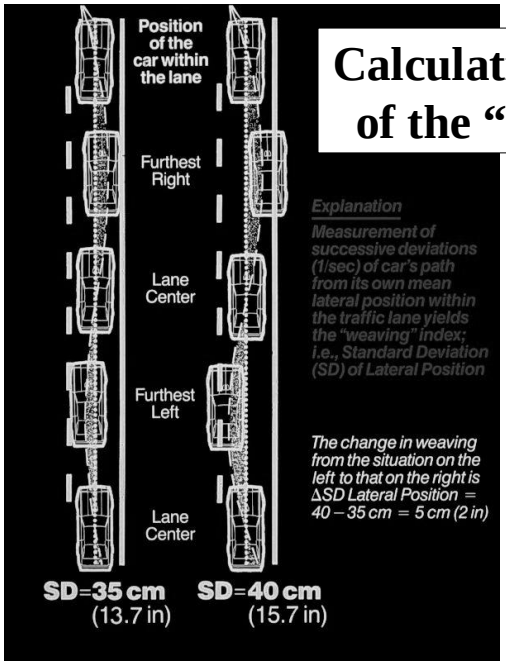
Subject characteristics

- Recreational users of cannabis and alcohol
- Physically and psychologically fit
- Age 21-40 years
- In possession of drivers 'licence
- Driven under the influence of cannabis and alcohol
- Dutch nationality

Experimental studies

Driving at the control level : Road Tracking Test





Calculation and meaning of the "weaving index"

Explanation

Measurement of successive deviations (1/sec) of car's path from its own mean lateral position within the traffic lane yields the "weaving" index; i.e., Standard Deviation (SD) of Lateral Position

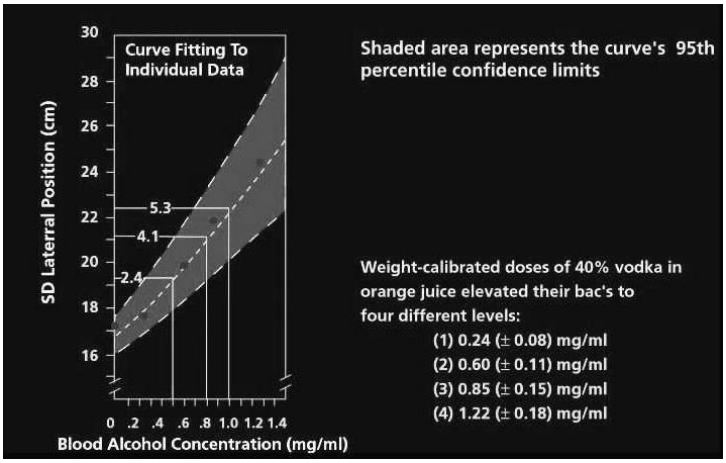
The change in weaving from the situation on the left to that on the right is ΔSD Lateral Position = 40 – 35 cm = 5 cm (2 in)

Experimental studies

Experimental studies

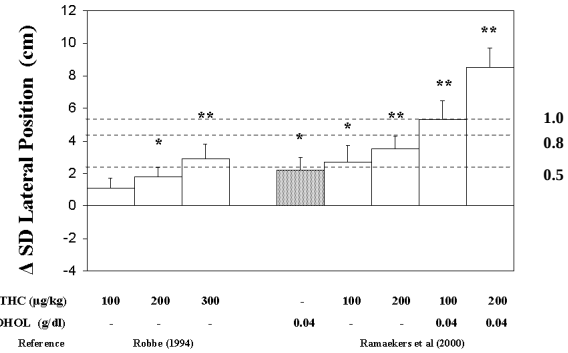
Mean SDLP as a function of BAC

SDLP change scores at legal BAC limits for driving under the influence in EC and US



Experimental studies

Road Tracking test



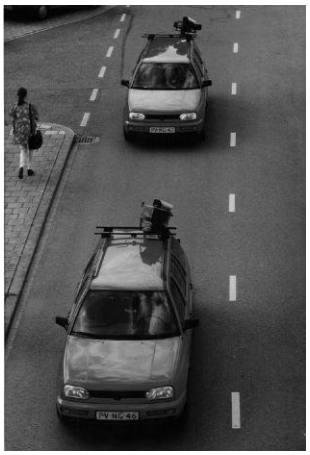
Equivalent effect of BAC (mg/ml)

Mean change in SDLP (weaving) in the Road Tracking Test after incremental doses of THC alone and after THC combined with alcohol.

Mean (range) plasma concentrations after 100, 200 and 300 microg/kg were: 7.9 (0.8-17.2), 12.0 (1.5-27.1) and 16.1 ng/ml (4.7-30.9) ng/ml

Experimental studies

Driving at the Manoeuvring Level



Car-Following Test

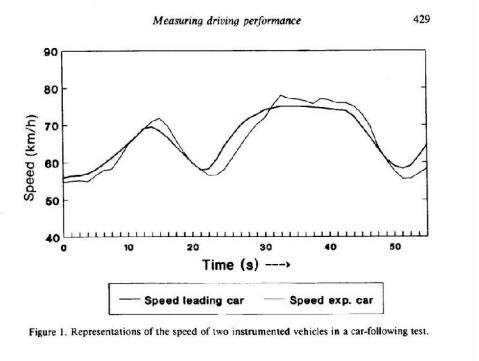
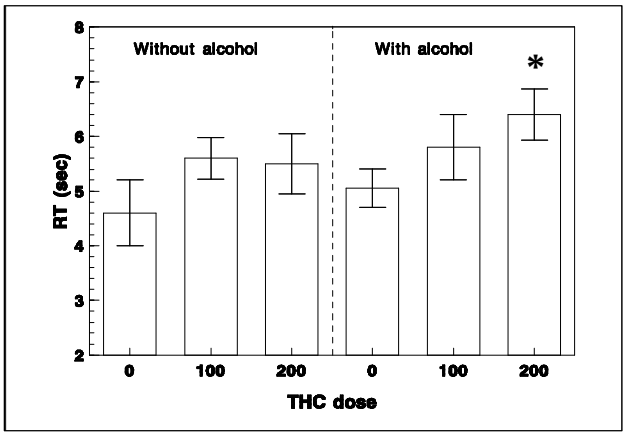


Figure 1. Representations of the speed of two instrumented vehicles in a car-following test.

Experimental studies

Car-Following Test



Mean (±SE) reaction time to speed decelerations in each treatment condition

Experimental studies

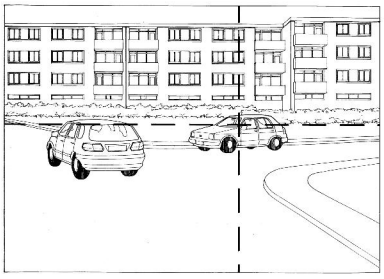
Driving at the Manoeuvring and Strategical level

City Driving Test

Central driving task: driving instructor ratings of vehicle checks, vehicle handling, traffic manoeuvres, observing and understanding traffic, turning

Experimental studies

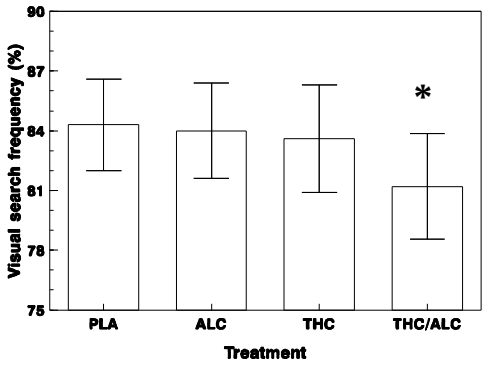
City Driving Test



***Peripheral driving task*: Eye movement recordings of visual search at intersections**

Experimental studies

City Driving Test



Mean (±SE) frequency of visual search for traffic at intersections in the City Driving Test by each treatment condition

Experimental studies

Overall

	Control **Road Tracking**	**Manoeuvring** **Car Following**	**Strategic** **City Driving**
THC 100	*	-	-
THC 200	*	-	
ALC	*	-	-
THC 100 /ALC	*	-	*
THC 200 / ALC	*	*	

summary

Conclusions from experimental studies

- THC has been shown to impair cognition, psychomotor function and actual driving performance in a dose related manner
- The degrees of impairment observed in laboratory or actual driving tests after doses of up to 300 μg/kg THC were comparable to the impairing effects of a dose of alcohol producing a BAC ≥0.05 g/dl, the legal limit for driving under the influence in most European countries.
- Combined use of THC and alcohol severely impairs driving performance, even at low doses.

Summary

… and epidemiological studies

- There is no indication that *past use* of THC alone affects crash risks, but there is growing evidence that *recent use* of THC increases the risk of culpability for motor vehicle accidents compared to drug free drivers, particularly at higher concentrations.
- Combined use of THC and alcohol sharply increases the risk of drivers 'culpability for accidents as compared to drug free drivers, even at low doses.

Motor and cognitive control during cannabis intoxication as a function of THC in plasma: limits of Impairment

Ramaekers JG [1], Kauert G [2], van Ruitenbeek P [1], Theunissen EL[1], Schneider E [3], Moeller MR [4]

1 Dept Neuropscyhology & Psychopharmacology, Faculty of Psychology, Maastricht University, The Netherlands
2 Department of Forensic Toxicology, Institute of Legal Medicine, Goethe University of Frankfurt, Germany
3 Landeskriminalamt, Kriminaltechnisches Institut, Baden-Württemberg, Germany
4 Unikliniken des Saarlandes, Homburg,

Rationale

1) To study the effects of cannabis on skills related to driving as a function of delta-9-THC in plasma

2) To determine plasma THC threshold levels above which (driving) impairment emerges.

Study design

- 20 recreational users of marijuana (14 males, 6 females)
- Placebo controlled, double blind
- 2 doses of THC (250 μg/kg and 500 μg/kg)



Study design

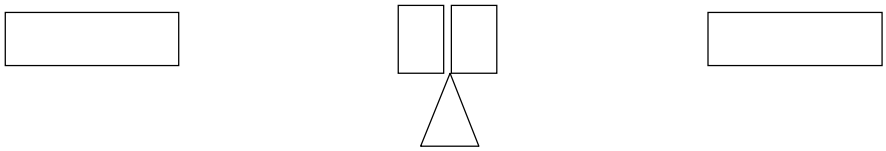
Time post smoking (min)	-30	0	15	30	45	60	120	180	240	300	360
Smoking (-5 minutes)		X									
Blood sample		X	X	X	X	X	X	X	X	X	X
Saliva sample	X		X	X	X	X	X	X	X	X	X
Motor control (Critical Tracking)			X			X		X		X	
Impulsivity (Stop Signal Task)			X			X		X		X	
Cognition (Tower of London)					X		X				X

Intercept (N=10)

Drager Drug Tester (N=10)

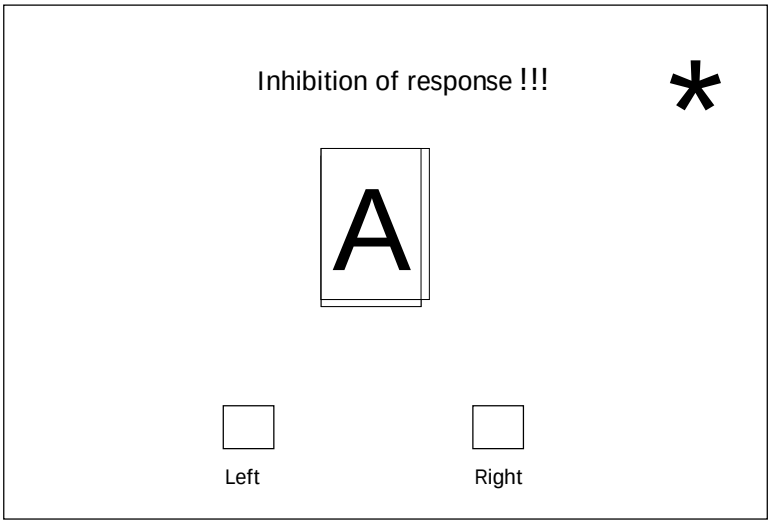
Critical Tracking Task

FAIL



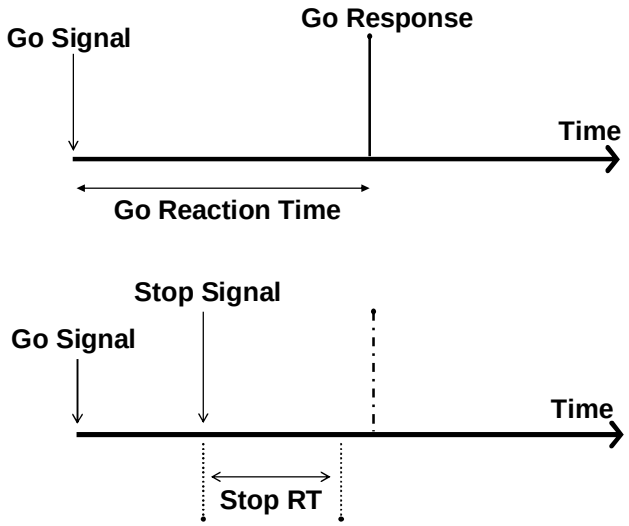
A measure of perceptual motor control. Tracking performance in this task is significantly correlated with Road tracking in on-the-road driving (Ramaekers, 2003)
Dependent measure : Lambda-c (rad/sec)

Stop Signal Task (Logan ,1984)



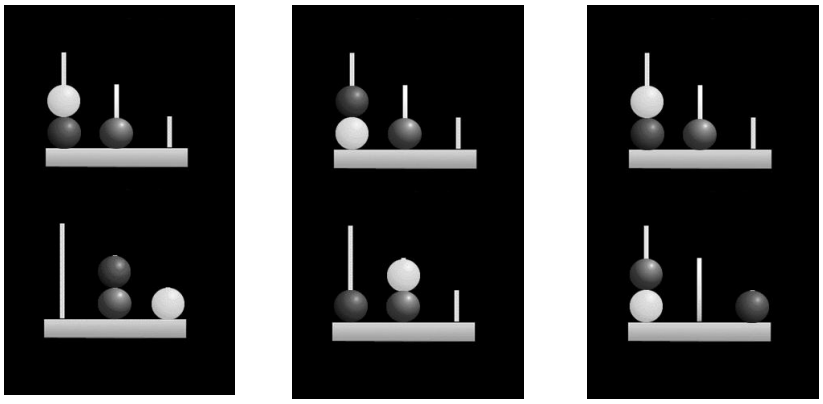
A measure of motor impulsivity or the ability to inhibit an ongoing response.
Dependent measure: Stop reaction time and commission errors (failed inhibitions)

Stop Signal Task (Logan ,1984)



Race model: 2 parallel processes Go RT and Stop RT
Commission error if (stop RT + delay) > Go RT

Tower of London (Shallice , 1982)

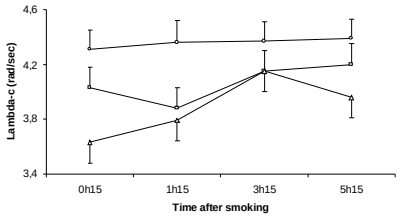


2 Steps 3 Steps 4 Steps

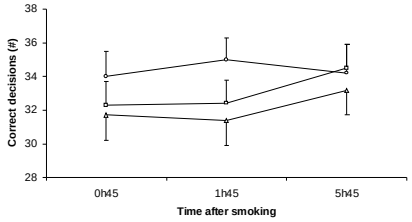
Tower of London provides a measure of planning and cognitive function.
Dependent measure: # correct decisions and RT

Results: skills related to driving

Critical Tracking Task



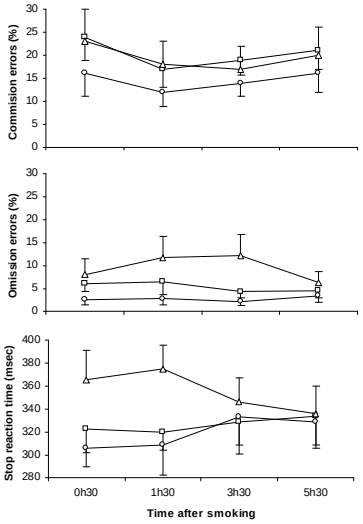
Tower of London



THC 500 = Δ; THC 250 = ~; PLA = O

THC significantly impairs critical tracking performance and decision making ($p<.05$)

Results: skills related to driving



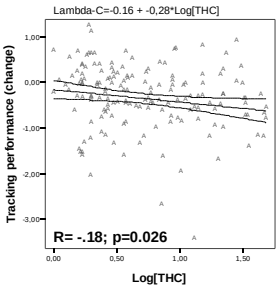
Stop Signal Task

THC significantly ($p<.05$) impairs Stop reaction time and increases the number of commission (misses) and omission errors (false alarms)

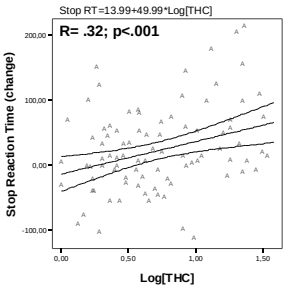
THC 500 = Δ; THC 250 = ~; PLA = O

Results: performance vs THC concentration

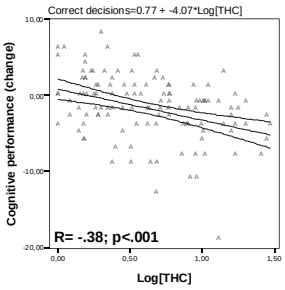
Critical Tracking Task



Stop Signal Task



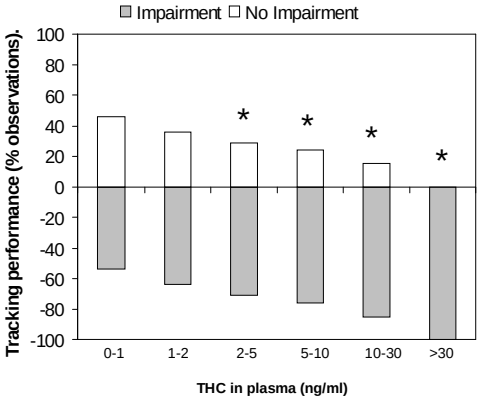
Tower of London



Linear relation between plasma/oral fluid THC and performance.
However correlations are very low

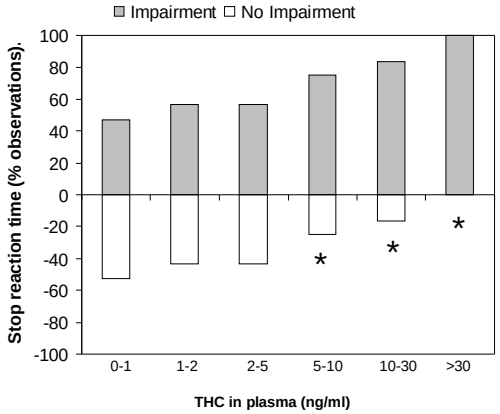
Results: limits of impairment

Critical Tracking Task



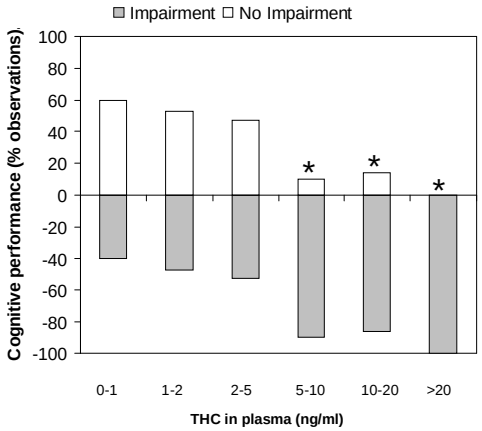
Distributions of observations showing 'impairment' and 'no impairment' as a function of plasma THC in the critical tracking task (* p<.05).

Results: limits of impairment
Stop Signal task



Distributions of observations showing 'impairment' and 'no impairment' as a function of plasma THC in the stop signal task (* p<.05).

Results: limits of impairment
Tower of London



Distributions of observations showing 'impairment' and 'no impairment' as a function of plasma THC in the Tower of London task (* p<.05).

Conclusion: limits of impairment

- 2-5 ng/ml, first sign of impairment (tracking)
- 5-10 ng/ml, impairment in every performance domain
- >30 ng/ml, impairment in each individual

A legal limit for THC in blood plasma of 2–5 ng/ml will reliably separate unimpaired drivers with residual THC concentration from impaired drivers under the influence of cannabis.

Policy ?

per se limits (serum)

Epidemiological data

THC (ng/ml) (serum)	Odds Ratio
<2	ns
2-4	1.54
4-10	2.13
>10	2.12 – 6.16

Experimental data

THC (ng/ml) (serum)	Performance Impairment
<2	ns
2-5	*
5-10	***
>10	***

Cannabis effects on cognition and psychomotor function in occasional and heavy cannabis users

JG Ramaekers, EL Theunissen[1],
G. Kauert[2], S. Toennes[2], M. Moeller[3]

[1] Dept Neuropsychology & Psychopharmacology, Maastricht University
[2] Institute of Legal Medicine, Goethe University of Frankfurt
[3] Unikliniken des Saarlandes, Homburg

Present study

Aim:

acute effects of a high dose of THC on cognitive performance in occasional and heavy cannabis users, up to 8 hours after smoking

Subjects:

	Occasional	Heavy
N	12	12
Males-females	8-4	9-3
Mean age	22.6	23.2
Consumption / month	3.9 (±2.6)	26.8 (±4.9)
Years experience	7.2 (±2.7)	6.1 (±3.4)

Design & dose

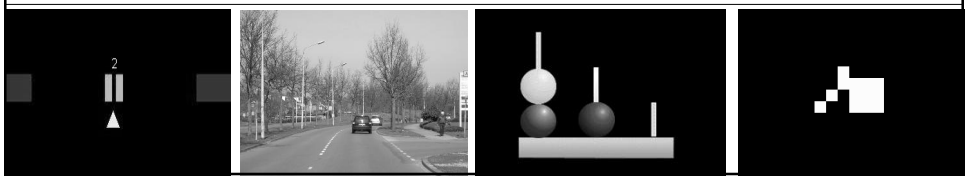
- Double-blind, placebo-controlled, 2-way cross-over
- Treatment:
  - Ø 0 and 500 µg/kg THC
  - Ø total weight cigarette 0,8g
- Wash-out 7 days

Procedure

- Drug screen
  - Ø Heavy users were positive for THC
  - Ø Occasional users were negative
  - Ø Negative for other drugs
- Standard breakfast, lunch and snack
- Smoking routine (10-15min)
- 4 test batteries:
  15min-1,5h, 3-4h, 5-6h and 7-8h

Cognitive tests

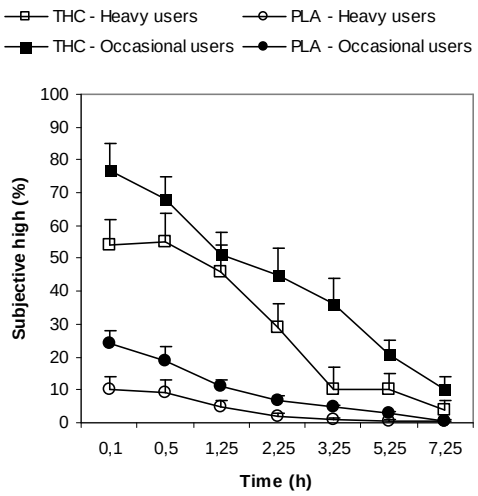
- Critical tracking task (CTT) - psychomotor performance
- Divided attention task (DAT) - divided attention & psychomotor performance
- Stop signal task (SST) - motor impulsivity
- Tower of London (TOL) - executive functioning & planning



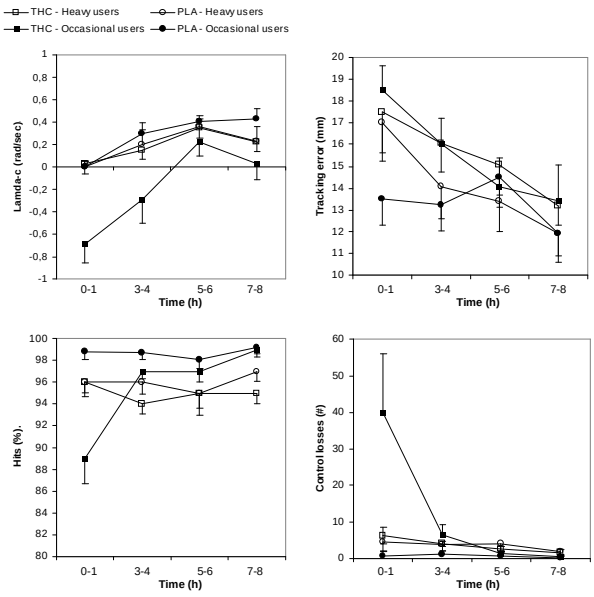
Test schedule

	Baseline	15m-1,5h	3-4h	5-6h	7-8h
CTT	X	X	X	X	X
DAT		X	X	X	X
SST		X	X	X	X
TOL		X	X	X	X
Subjective high (VAS) regular intervals up to 8 hours					

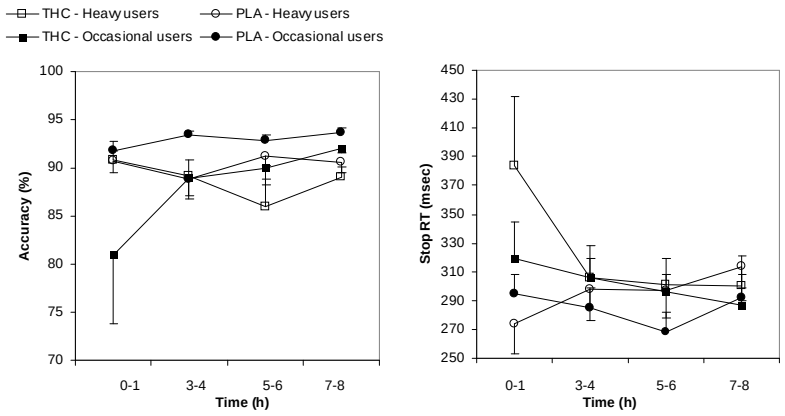
Subjective high



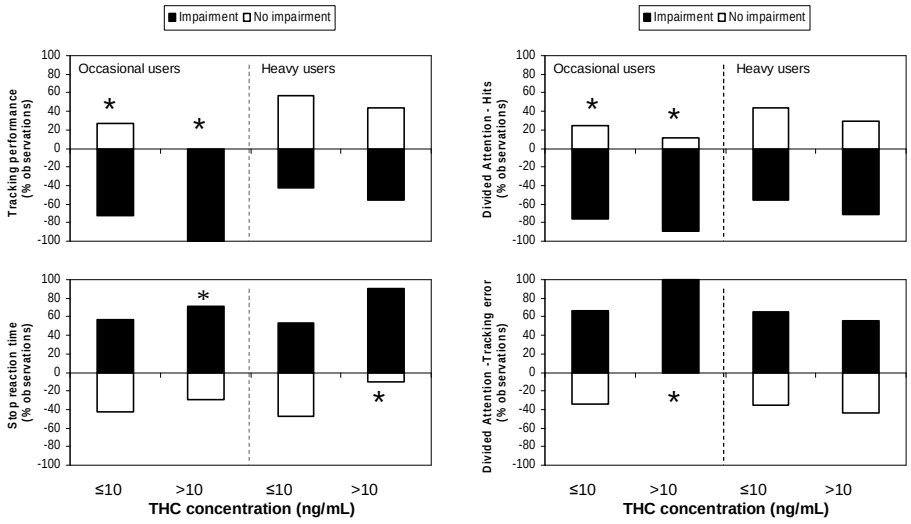
Tracking and divided attention



Stop signal task



Proportion impairment – THC concentration

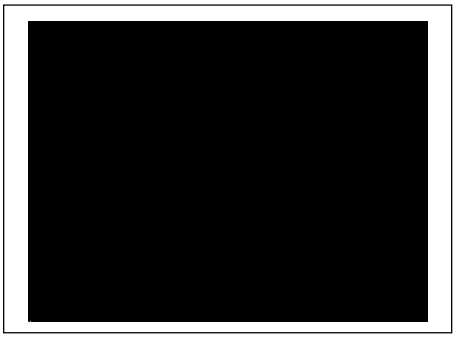


Conclusion

- Motor performance and divided attention and were impaired by THC
- Occasional users are more affected by THC
- THC impairment decreased over time
- Heavy cannabis users developed tolerance for the acute impairing effects of THC

Ø except for motor impulsivity ?

Driving test movie I
Road Tracking / Car Following



Driving test movie II
City Driving