

Blood concentrations of THC: Relationship with degree of impairment

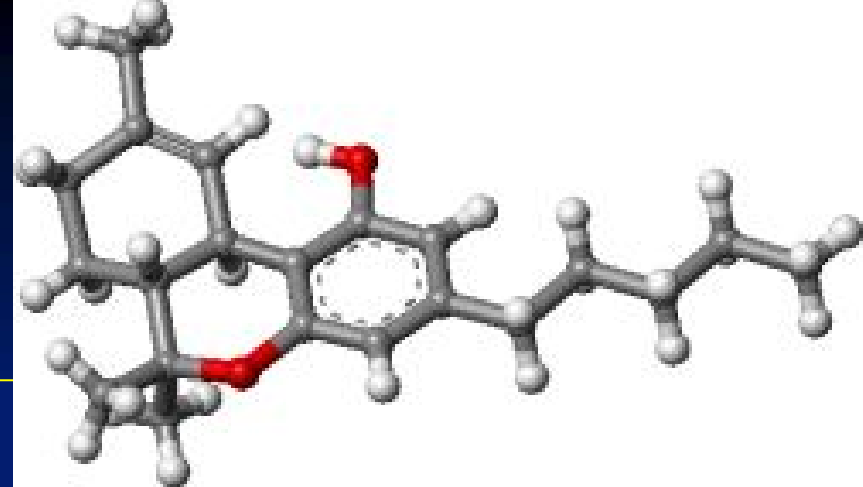


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Chemistry



- Extremely complex
- 1940s; The isolation of cannabinal and canabidiol provided the general structure of the active principle of cannabis.
- 1960s; Mechoulam et al., isolated Δ^9 -tetrahydrocannabinol (THC), which was later found to be primarily responsible for the psychoactive properties of the plant.
- Synthetic THC is available on prescription in the U.S., Canada and several other countries as Marinol.

- Is there a relationship between blood concentration of THC and psychomotor and cognitive impairment?
- Do the impairments eventually increase the risk of becoming involved in traffic accidents?



- The use of cannabis does not increase traffic accident
- The effects of cannabis on driver risk are likely to be small
- Much of the elevated traffic accident risk found among cannabis users is likely to be more due to the characteristics of those who use cannabis than to the effects of cannabis use on driver performance

Robbe 1994, Chesher 1995, Fergusson 2001

The LaGuardia report; Mayor's Committee on Marihuana; 1944

Examined the effect of "moderate" and "high" doses of orally ingested Marihuana:

1. Body sway
2. Hand steadiness
3. "Speed of tapping"
4. Strength of hand grip

The LaGuardia report; Mayor's Committee on Marihuana; 1944

Results:

Both hand unsteadiness and body sway were increased in both groups

Speed of tapping was only slightly affected by the large dose and not by the smaller dose

The peak effect was not reached until the fourth hour after administration

Impairment continued until eighth hour

Experimental studies

Psychomotor tests

Cognitive tests

Coordination

Perception

Memory (Short-term or working memory)

Reaction time

Sustained attention

Tracking

etc

Moskowitz 1985

Chesher 1986

Chait and Pierri 1992

Wilson et al. 1994

Robbe 1994

Berghaus et al. 1995

Berghaus et al. 1998

Heishman et al. 1998

Kurzthaler et al. 1999

Mènètrety et. al. 2005

Numerous Experimental studies

THC in doses between 40-300 $\mu\text{g}/\text{kg}$ causes a dose dependent reduction in performance testing

Memory function

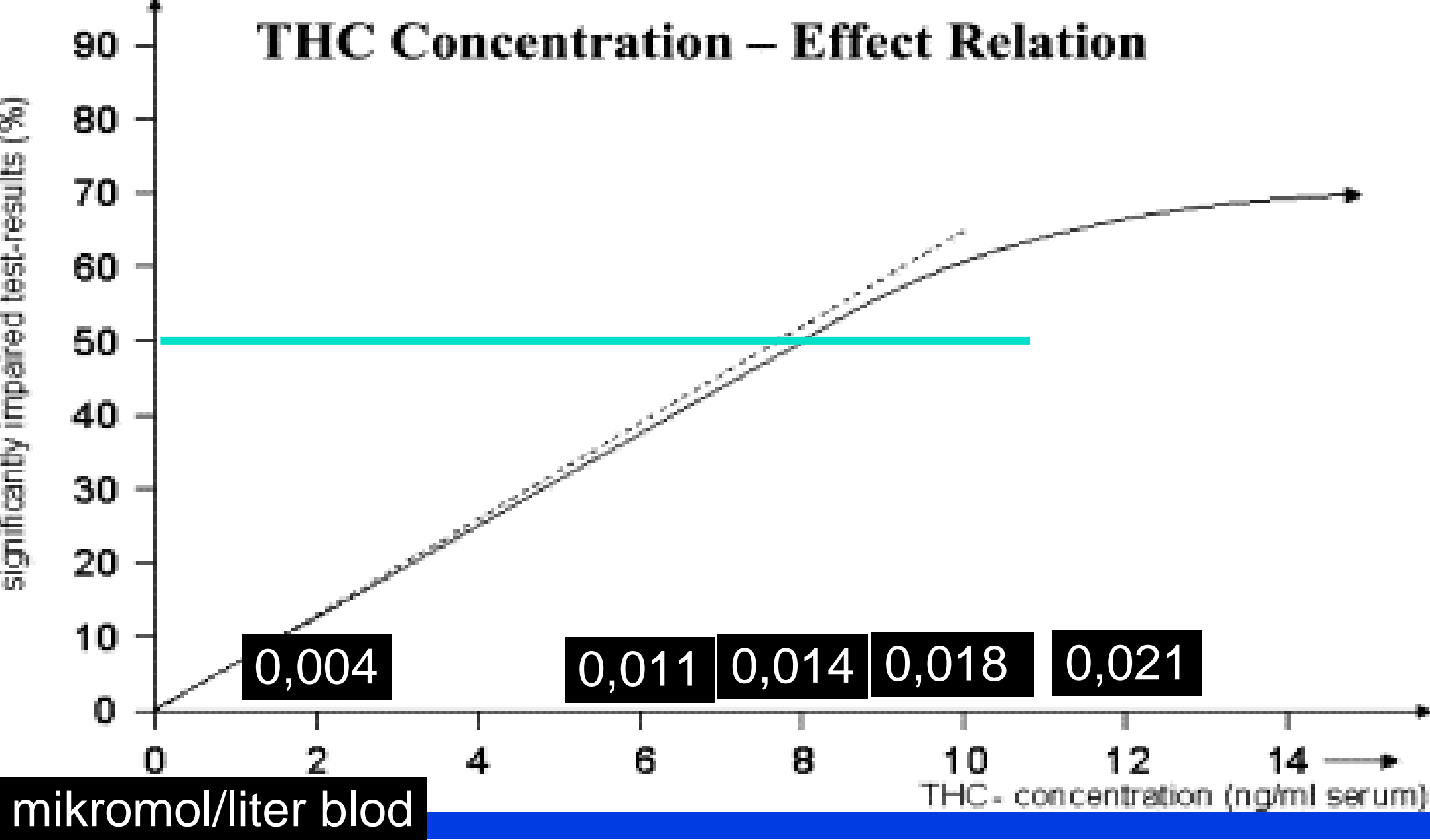
learning and the acquisition of information

Reaction time

Tracking

Motor control

THC Concentration – Effect Relation



Frequency of performance decrements (%) observed in the total number of psychomotor tests applied in 87 experimental studies as a function of THC concentration in plasma after eating (---) and smoking (—) cannabis

(adapted from [[Berghaus et al., 1998a](#)])

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Substance	Authors	Odds ratio	95% CI
Drug free cases		1.0	
Alcohol	Terhune and Fell (1982);	5.4*	2.8–10.5
	Williams et al. (1985);	5.0*	2.1–12.2
	Terhune et al. (1992);	5.7*	5.1–10.7
	Drummer (1994);	5.5*	3.2–9.6
	Hunter et al. (1998);	6.8*	4.3–11.1
	Lowenstein and Koziol-Mclain (2001);	3.2*	1.1–9.4
	Drummer et al. (2003b)	6.0*	4.0–9.1
THC—COOH	Terhune and Fell (1982);	2.1	0.7–6.6
	Williams et al. (1985);	0.2	0.2–1.5
	Terhune et al. (1992);	0.7	0.2–0.8
	Drummer (1994);	0.7	0.4–1.5
	Hunter et al. (1998);	0.9	0.6–1.4
	Lowenstein and Koziol-Mclain (2001)	1.1	0.5–2.4
THC (range: ng/ml)			
<1.0	Hunter et al. (1998)	0.35	0.02–2.1
1.10–2.0		0.51	0.2–1.4
>2		1.74	0.6–5.7
1–100	<u>Drummer et al. (2003a,b)</u>	2.7*	1.02–7.0
5–100		6.6*	1.5–28.0
<u>Alcohol/THC or THC-COOH</u>	Williams et al. (1985);	8.6*	3.1–26.9
	Terhune et al. (1992);	8.4*	2.1–72.1
	Drummer (1994);	5.3*	1.9–20.3
	Hunter et al. (1998);	11.5*	4.6–36.7
	Lowenstein and Koziol-Mclain (2001)	3.5*	1.2–11.4

Summary of OR of becoming involved in fatal or injurious traffic accidents under the influence of cannabis, alcohol or their combination as reported in culpability studies.

- Increased culpability when THC found in blood samples
- (dose related)

Significance of changes in OR is indicated as follows: *<0.05. Ramaekers et al. 2004

Cases:

900 drivers involved in a non-fatal accident

Controls:

900 patients who attended the same emergency units for a non-traumatic reason

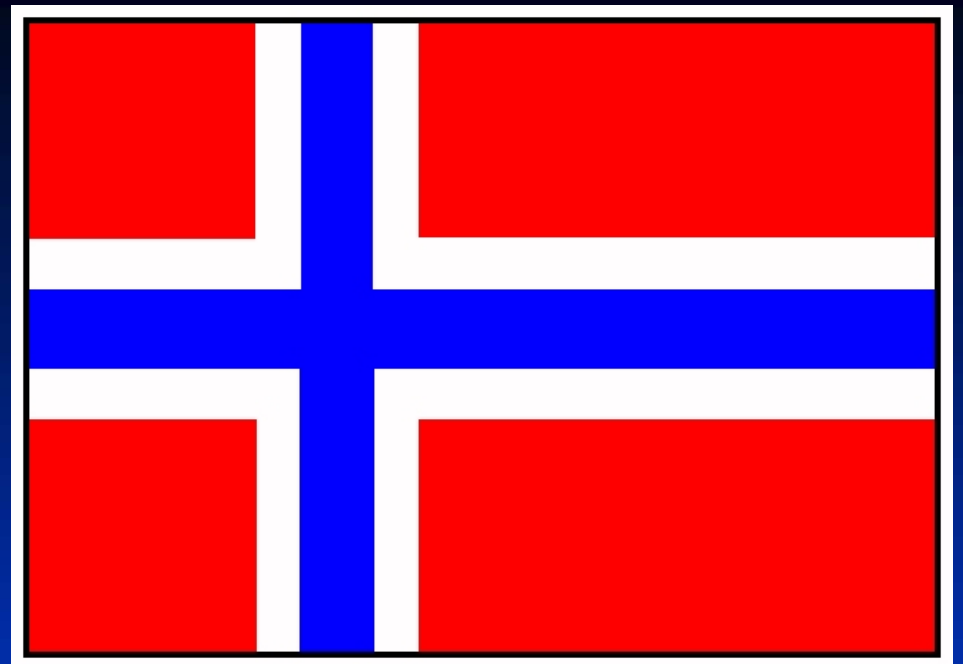
THC > 1 ng/ml

In accordance with French laws, subjects were considered to be positive when THC blood concentration exceeded 1 ng/ml. Accordingly, when only THC-COOH was found, subjects were considered to be negative since the presence of this compound can only attest for a previous consumption of cannabis but not for impairment at the time of blood sampling.

Drugs (positivity thresholds)	Positive (%)		Odds-ratios (95% confidence interval)
	Drivers	Controls	
Alcohol only (>0.5 g/l) ^a	17.0	5.0	3.8 (2.1–6.8)
THC only (>1 ng/ml) ^a	14.1	6.7	2.5 (1.5–4.2)
Alcohol + THC ^a	9.5	2.2	4.6 (2.0–10.7)
Morphine (>20 ng/ml) ^b	2.7	0.3	8.2 (2.5–27.3)
Benzodiazepines only	9.4	5.8	1.7 (1.2–2.4)

^a less than 27 years old
^b all ages included

The difference between the two groups was highly significant in 18–22 ($P < 0.01$) and 23–26 ($P < 0.05$) years age ranges.

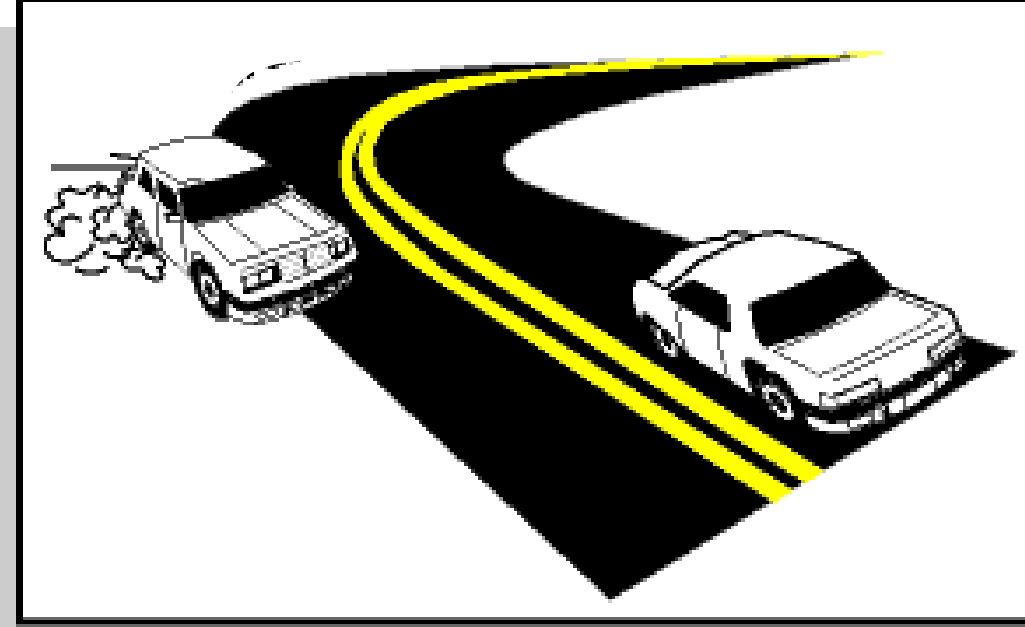


Background

- Non-alcoholic drugged driving is becoming more common
- Δ 9-tetrahydrocannabinol (THC) is one of the most frequently detected drugs in blood samples from suspected drugged drivers



Aim



Is there any relation between
THC-concentration in blood and
impairment in apprehended drivers ?

Material

456 samples from approximately 30 000 cases of suspected drugged driving from the period 1997-1999 contained only cannabis with CTI conclusion available:

- Male 95 %
- 230 (51%) were considered not impaired
- 226 (49 %) were considered impaired

Background characteristics of the studied population according to gender. Only significant differences are depicted.

Characteristic	Male N=437 (95.8%)	Female N=19 (4.2%)
<i>The suspected driver</i>		
Age (years) (mean \pm SD) ^a	25 \pm 7	28 \pm 8
BMI (kg/m ²) (mean \pm SD) ^a	23 \pm 5.7	21 \pm 2.4 ^d
Regular use of cannabis ^b	170 (39%)	7 (37%)
<i>Signs of i.v. abuse</i>		
Needle marks (%) ^b	119 (27 %)	9 (47 %)
Trombosis (%) ^b	48 (11 %)	5 (26 %)
<i>The incident</i>		
Accident (number of accidents) (%) ^b	52 (12 %)	7 (37 %) ^e
Type of vehicle (number of private cars) (%) ^b	414 (95 %)	19 (100 %)
<i>Examination and analytical results</i>		
Number of impaired drivers (%) ^b	213 (49 %)	13 (68 %)
Blood Δ^9 -THC concentration (ng/mL) (median; range) ^c	2,2 (0.3-45.3)	1.3 (0.3-18.9) ^e

^aResult based on Student's *t*-test ($P < 0.01$)

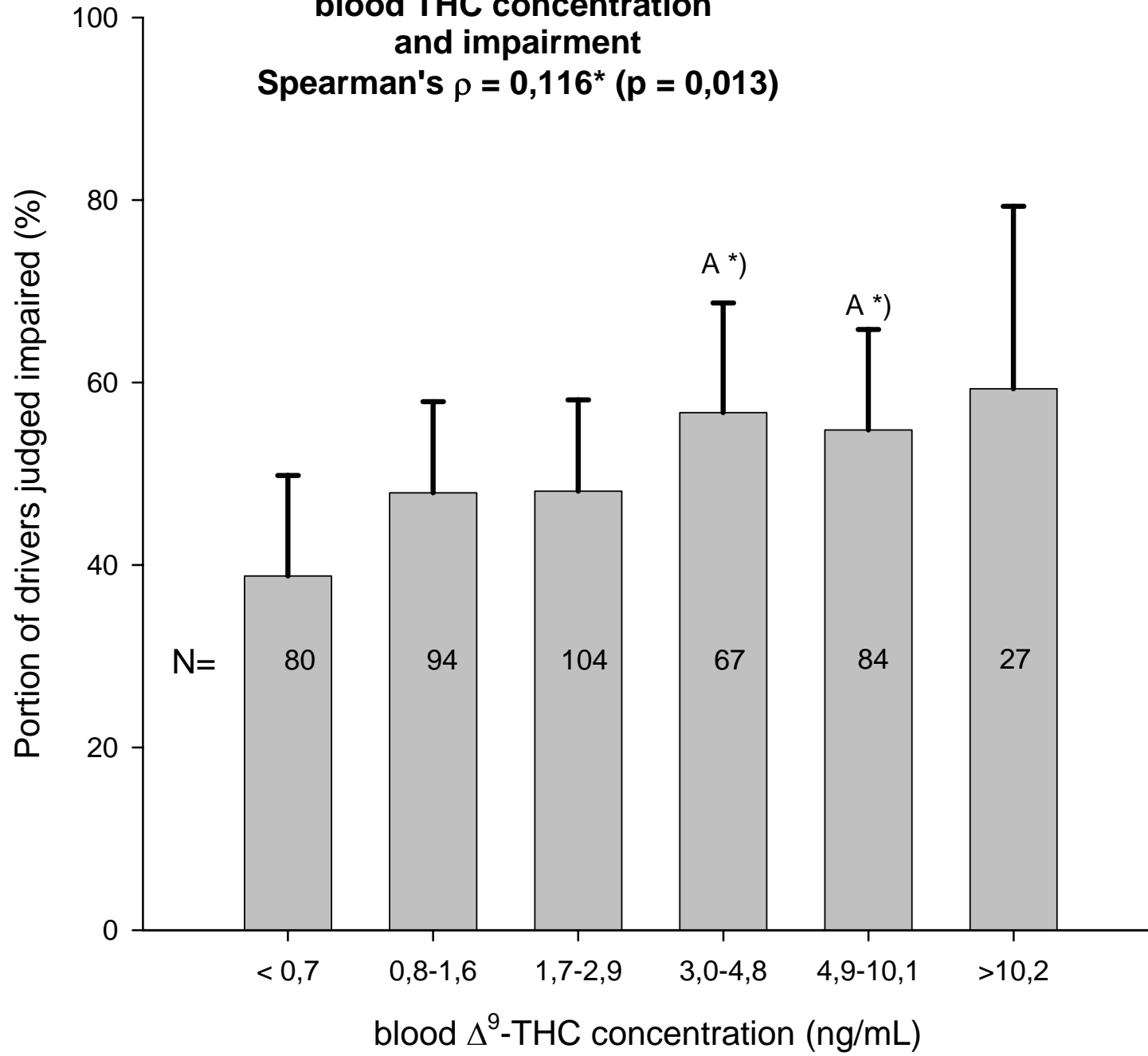
^bResult based on χ^2 -test ($P < 0.05$)

^cResult based on Mann-Whitney-test ($P < 0.05$)

^d $P < 0.01$

^e $P < 0.05$

**Correlation between
blood THC concentration
and impairment
Spearman's $\rho = 0,116^*$ ($p = 0,013$)**



Odds Ratios (OR) and 95% confidence intervals (CI) for being determined “impaired” at 6 different levels of blood Δ^9 -THC concentrations

	Blood Δ^9 -THC concentrations (ng/mL) and OR (95% CI)					
	< 0.7 ^a	0.8 – 1.6	1.7 – 2.9	3.0 – 4.8	4.9 – 10.1	> 10.2
Drug concentration unadjusted	1	1.5 (0.8-2.7)	1.5 (0.8-2.7)	2.1 (1.1-4.0) ^b	1.9 (1.1-3.6) ^b	2.3 (0.9-5.6)
Drug concentration adjusted for regular use	1	1.5 (0.8-2.8)	1.3 (0.7-2.4)	1.8 (0.9-3.7)	1.8 (0.9-3.4)	2.5 (1.0-6.6)
Drug concentration adjusted for the presence of needle marks	1	1.6 (0.8-3.0)	1.6 (0.9-3.0)	2.6 (1.3-5.3) ^c	2.6 (1.3-5.1) ^c	2.9 (1.2-7.3) ^b
Drug concentration adjusted for gender, needle marks and regular use	1	1.7 (0.9-3.2)	1.6 (0.8-3.0)	2.4 (1.1-5.0) ^b	2.5 (1.3-5.0) ^b	3.2 (1.2-8.7) ^b

^areference category

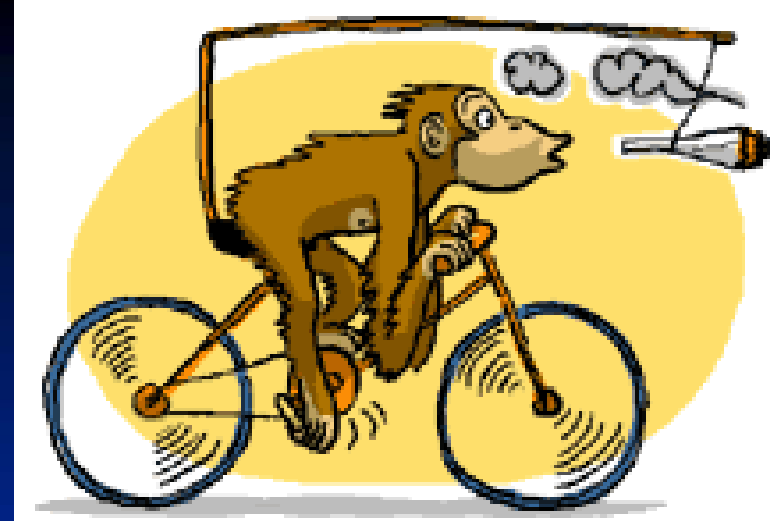
^b $P < 0.05$

^c $P < 0.01$

Limitations

- **All the subjects were already suspected of drugged driving by police (Selection)**
- **No knowledge on time of drug intake**
- **No knowledge on dose ingested**
- **Little knowledge on pattern of use**

Conclusion



The relationship between the concentration of THC in blood and risk of being impaired, supports findings from previous experimental studies of concentration related effects of THC on psychomotor performance and driving skills.

Norway, SRI; 1990-2001

