

Biomarqueurs en addictologie : place de l'électrorétinogramme (ERG)

Pr Thomas Schwitzer

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Centre Psychothérapique de Nancy

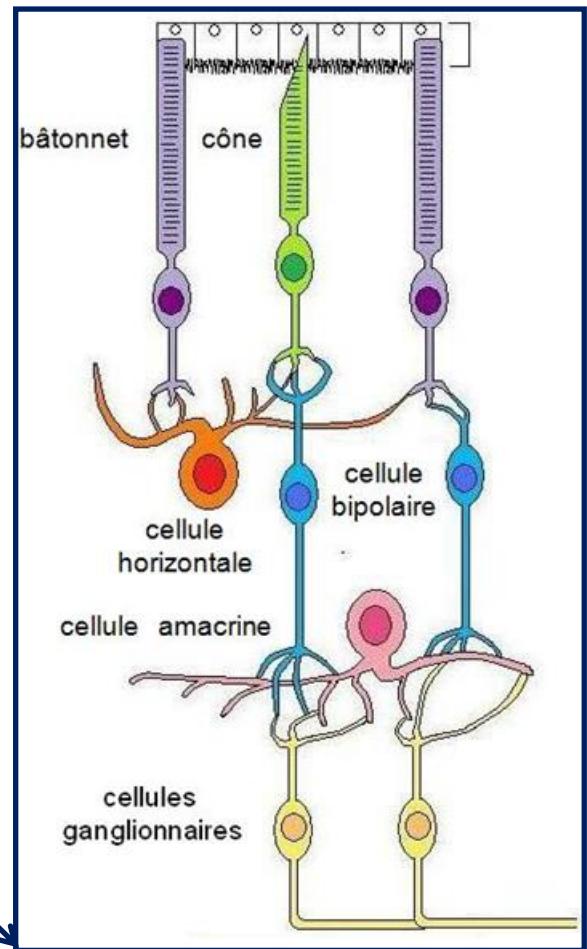
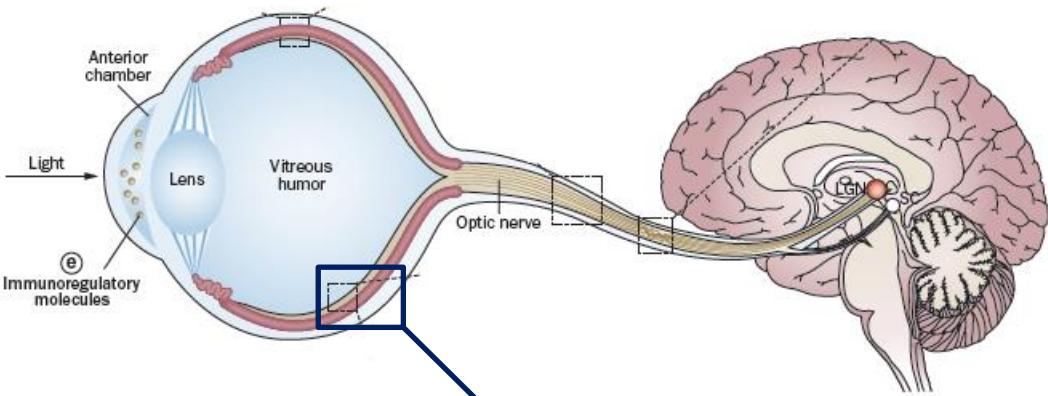
INSERM U1254, Université de Lorraine

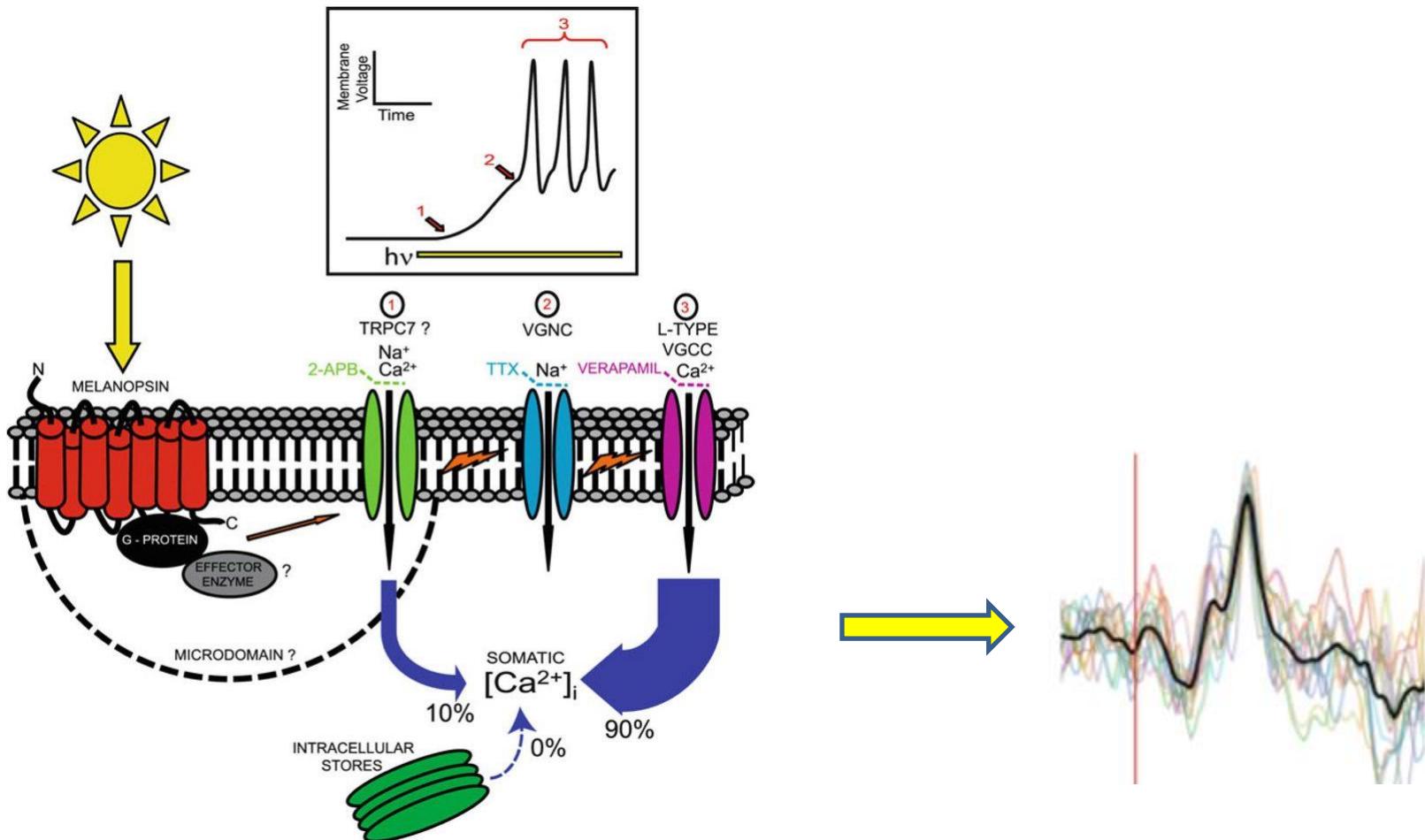


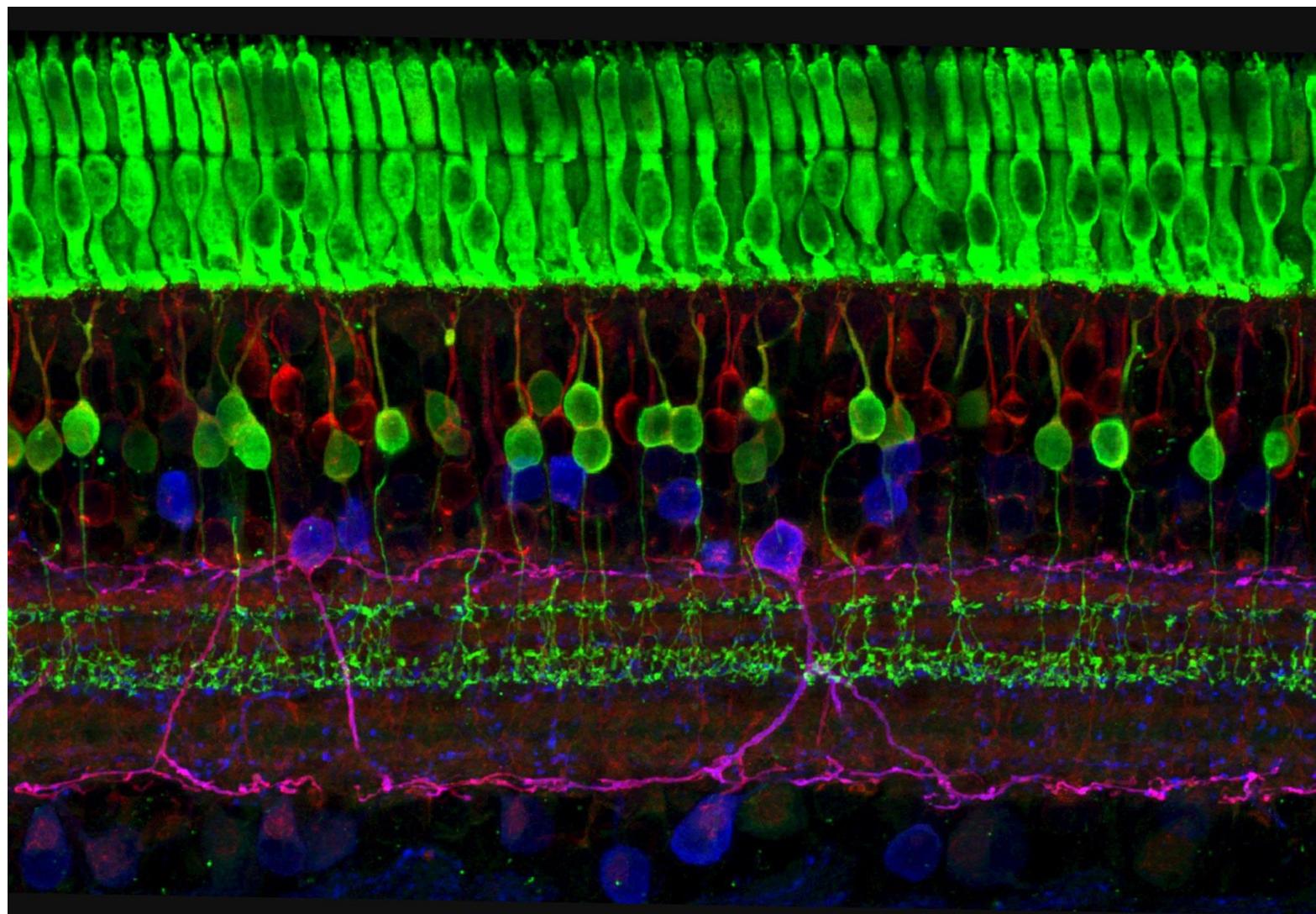
www.chu-nancy.fr



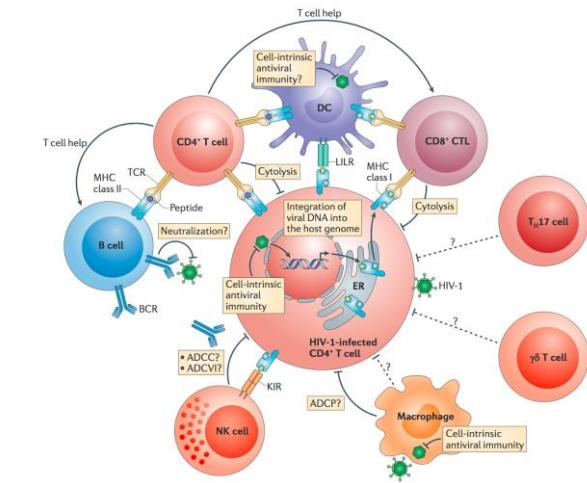
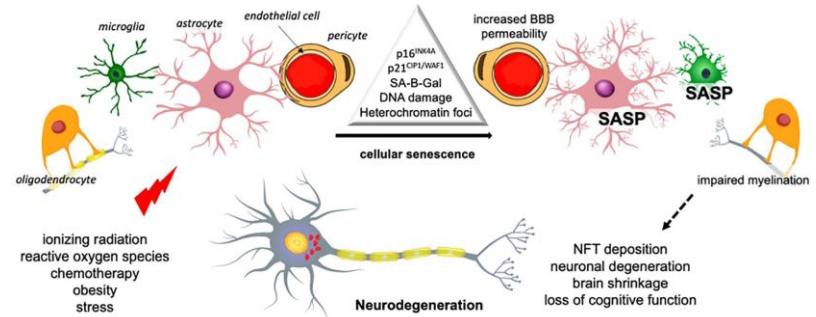
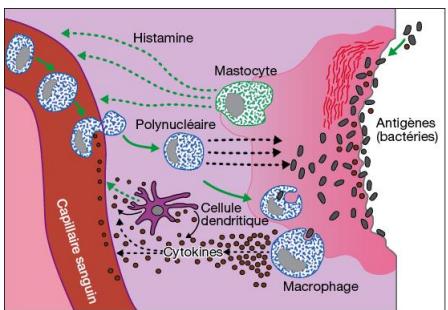
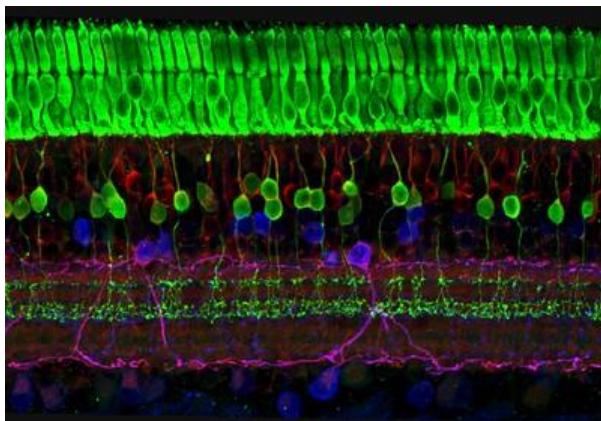
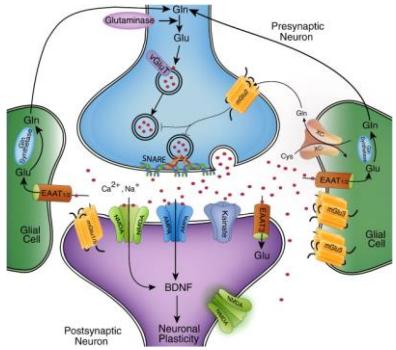
Rétine et ERG

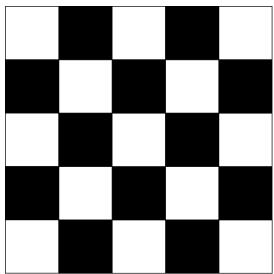






Mécanismes fonctionnels





**STIMULATION
VISUELLE**

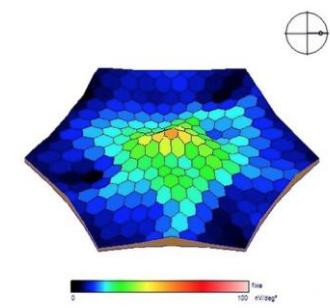
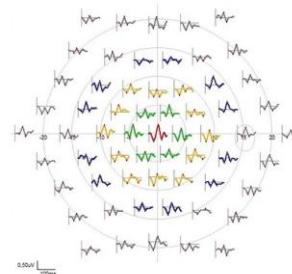
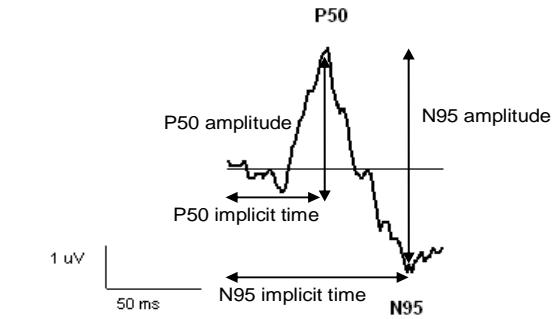


Electrodes

Enregistrement

***Amplification
Filtrage***

***Instrument de
mesure***



***RECUEIL DU SIGNAL BIO-
ELECTRIQUE***

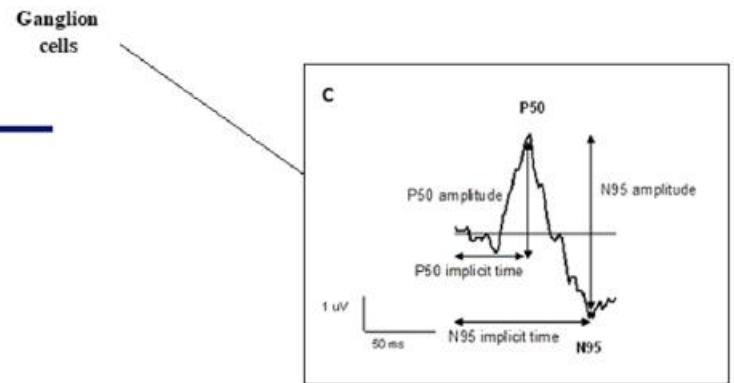
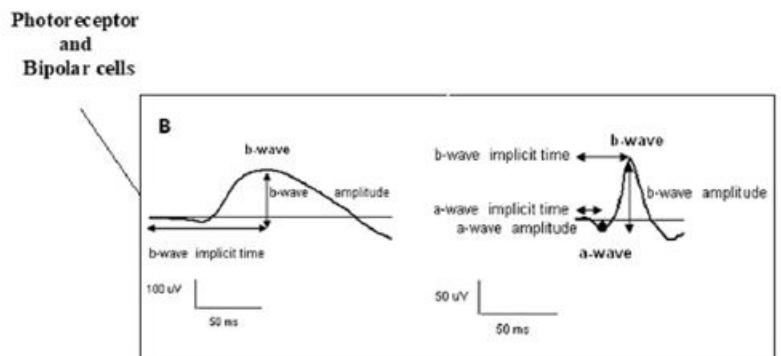
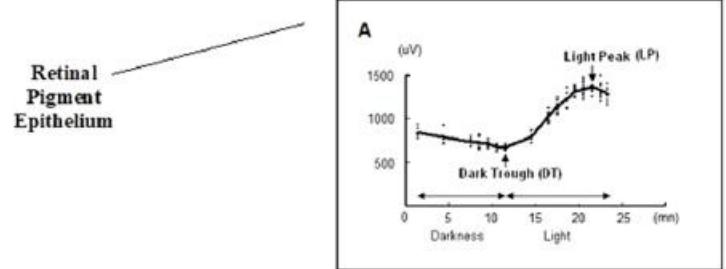
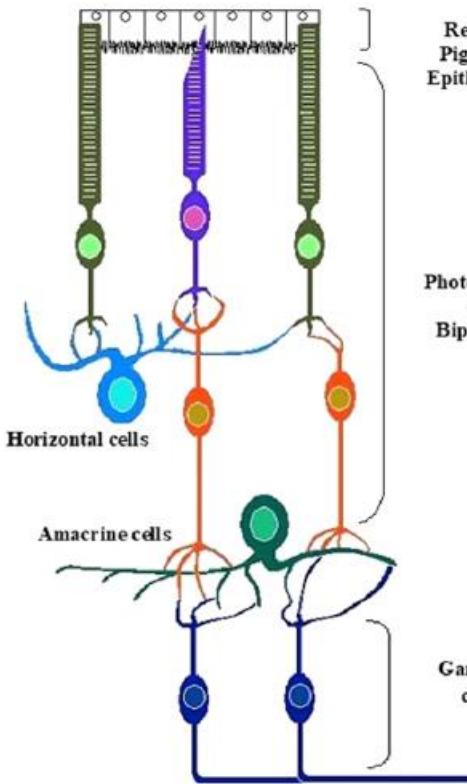
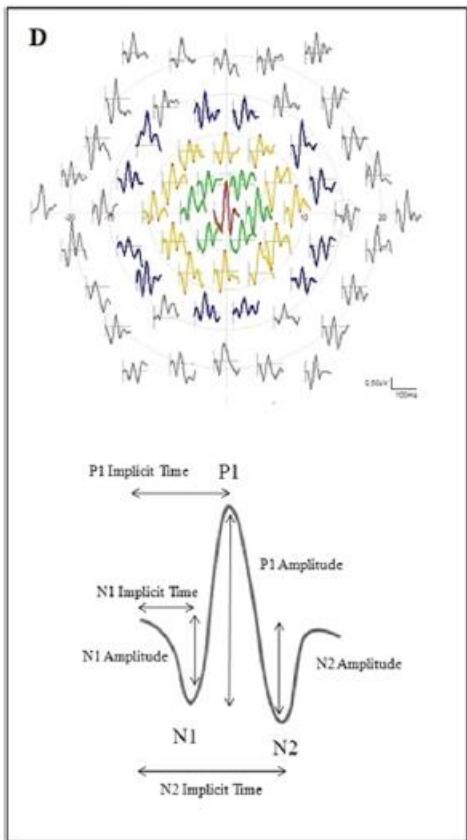


***REPRESENTATION DU
SIGNAL***

Procédure



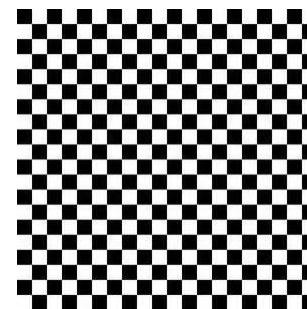
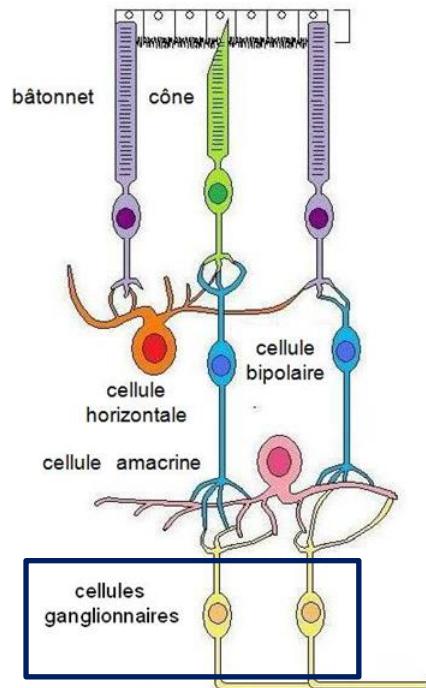
La fonction rétinienne



Schwitzer et al., 2019

USAGE RÉGULIER DE CANNABIS ET FONCTIONNEMENT RÉTINIEN

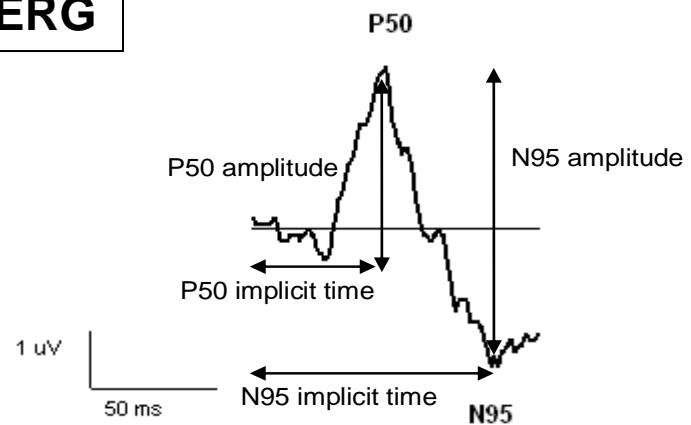
Pattern électrorétinogramme (PERG)



MetroVision, Pérenchies, France

ISCEV Standard pour PERG

0.8° taille
93.3% niveau de contraste
100 cd/m² luminance
4 renversements/s
220 réponses



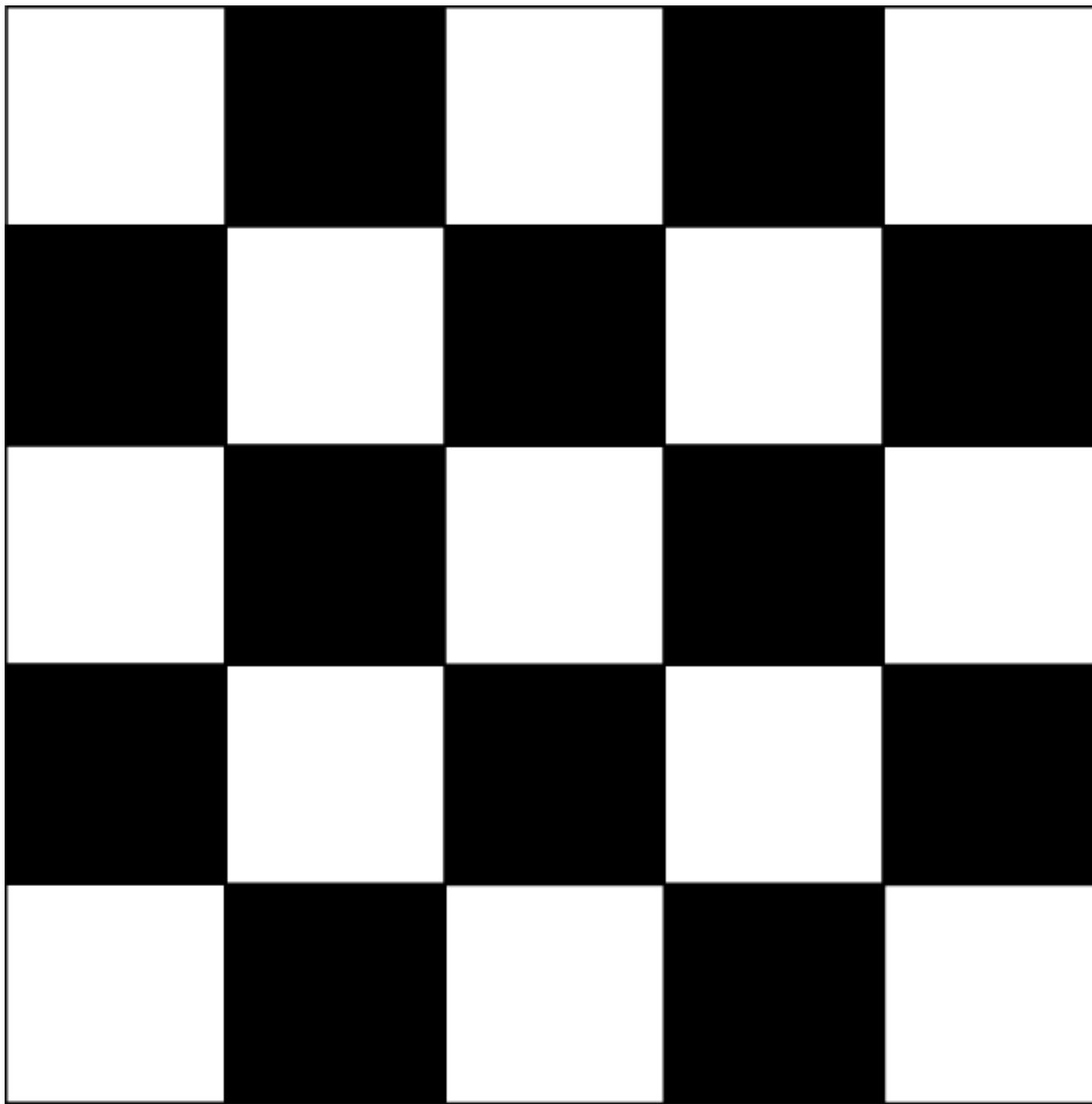


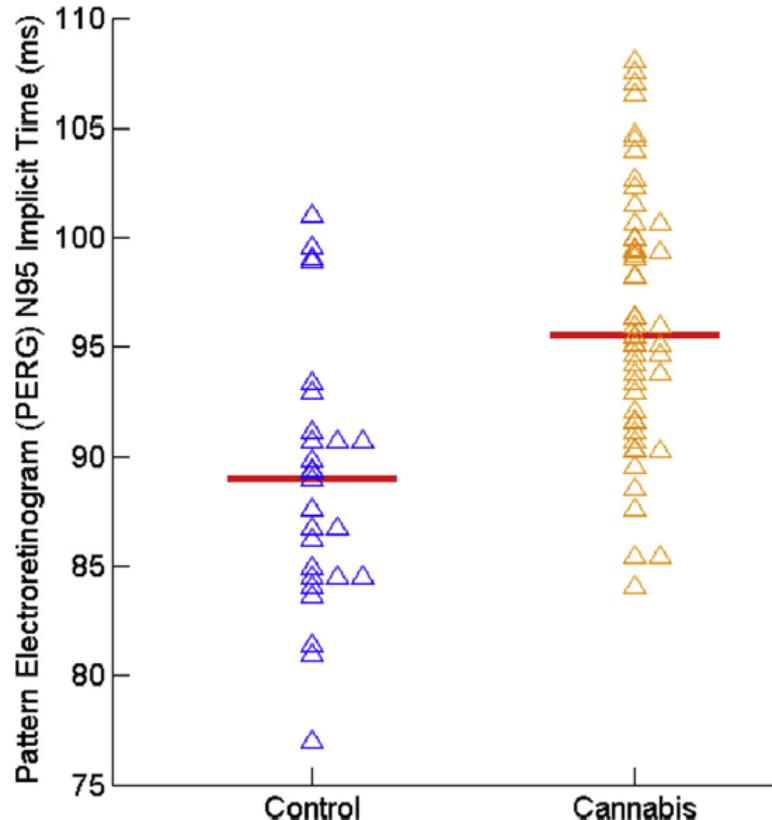
Table 1

Demographic and substance use characteristics of the participants.

	Cannabis users (n = 53)	Controls (n = 29)	P-value
Gender (male/female) ^{a,d}	41/12	21/8	p = 0.618
Age (years) ^{b,c}	23 (21–30)	24 (23–27)	p = 0.517
Education (years) ^{b,c}	13 (12–14)	15 (14–16)	p = 0.0001
Average number of alcohol uses/ week ^{b,c}	4 (1,5–9)	1 (0–3,5)	p = 0.0003
Alcohol Use Disorders Identification Test (AUDIT) scores ^{b,c}	7 (3,5–9)	3 (1–4,5)	p = 0.0001
Fagerström Test scores ^b (n = 44)	1 (0–3)	–	–
Average number of cigarettes/ day ^b	4 (2–10)	–	–
Age of first cannabis use ^b	16 (15–17)	–	–
Total years of cannabis use ^b	7 (5–14)	–	–
Average number of joints/week ^b	20 (14–30)	–	–
Cannabis Abuse Screening Test (CAST) scores ^b	4 (3–5)	–	–
Average number of grams of cannabis/week ^b	4,2 (3–10)	–	–

^a Categorical variable represented as frequencies.^b Quantitative variable represented as median and interquartile range.^c Mann-Whitney U test.^d Chi-Square test.

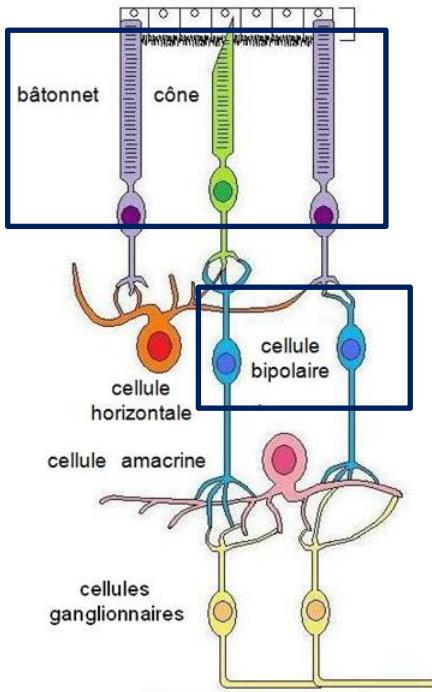
PERG



$p=0.0001$; Mann-Whitney U test

Schwitzer et al., 2017, 2018

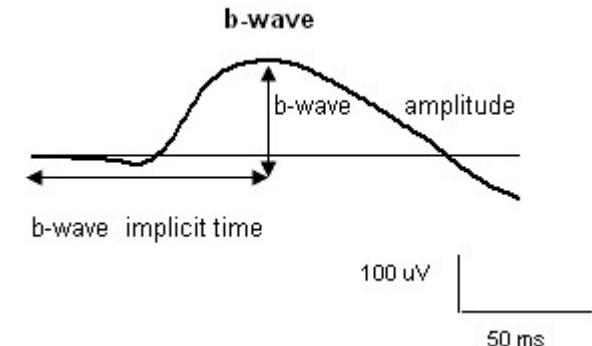
Flash électrorétinogramme (fERG)



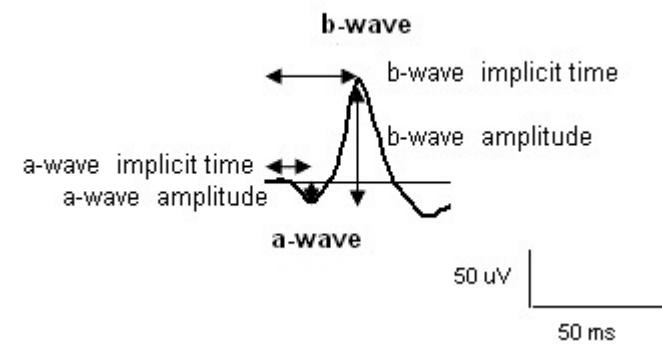
MetroVision, Pérenchies, France

**Scotopique et Photopique
Adaptation à l'obscurité et à la lumière
Dark-adapted 0.01 ERG
Light-adapted 3.0 ERG
8 et 16 réponses**

ISCEV Standard pour fERG



Dark-adapted 0.01 ERG



Light-adapted 3.0 ERG

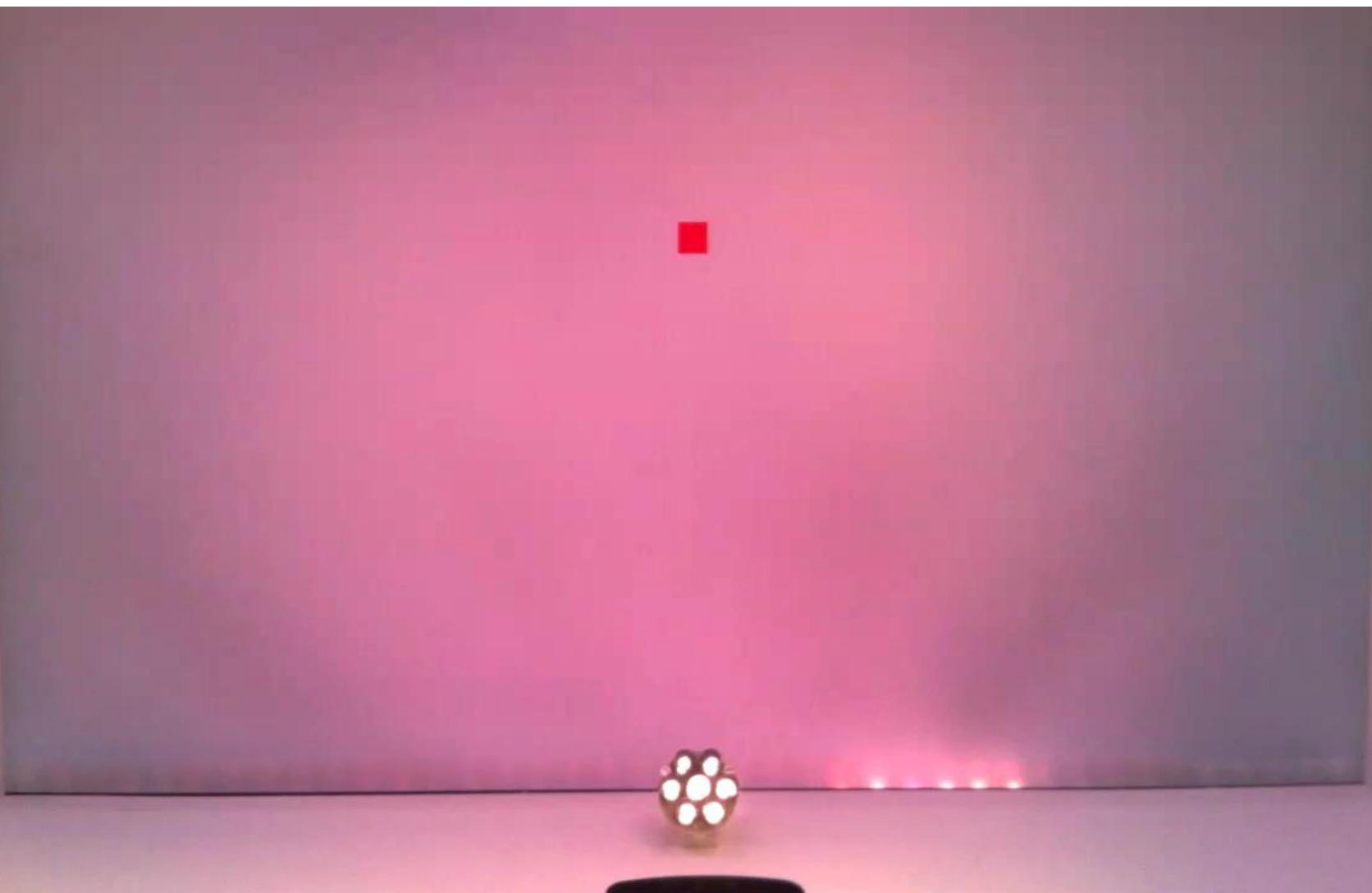
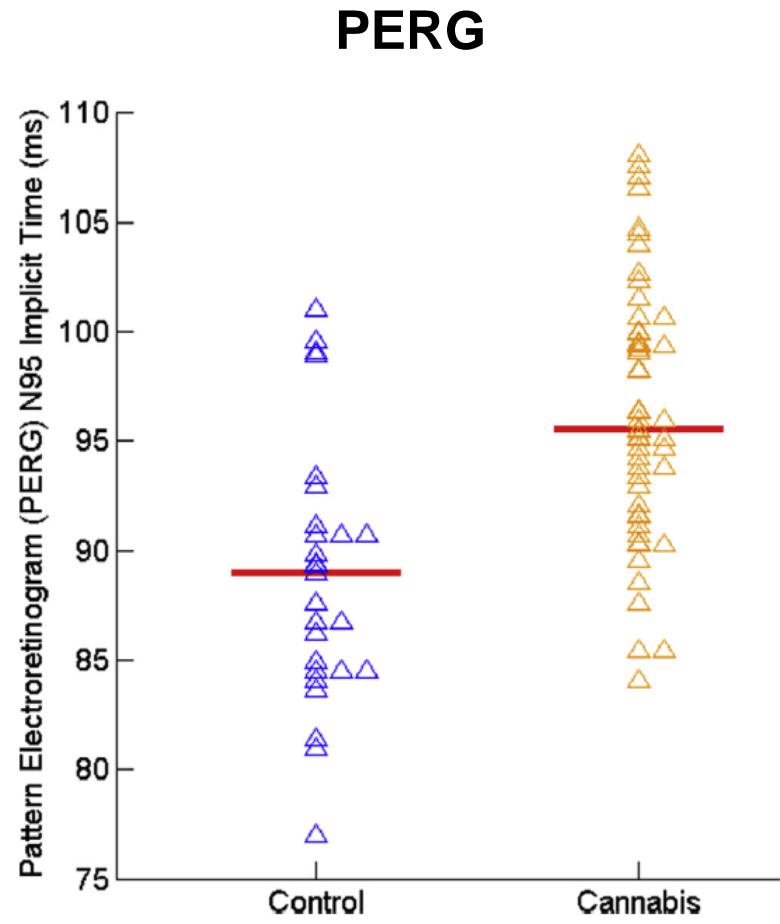


Table 1

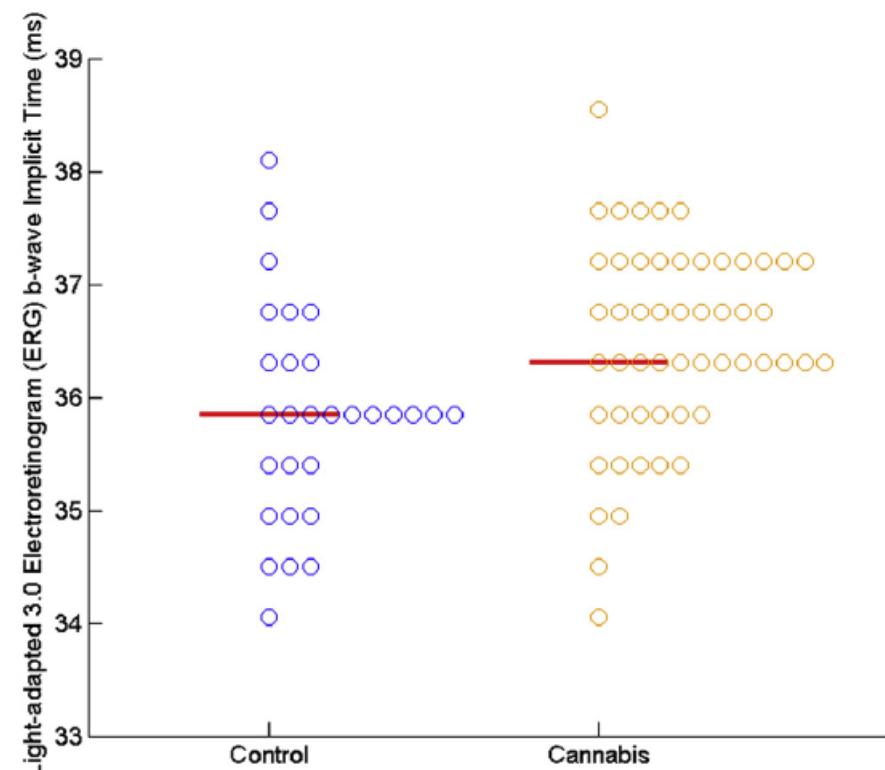
Demographic and substance use characteristics of the participants.

	Cannabis users (n = 53)	Controls (n = 29)	P-value
Gender (male/female) ^{a,d}	41/12	21/8	p = 0.618
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Fagerström Test scores ^b (n = 44)	1 (0–3)	–	–
Average number of cigarettes/ day ^b	4 (2–10)	–	–
Age of first cannabis use ^b	16 (15–17)	–	–
Total years of cannabis use ^b	7 (5–14)	–	–
Average number of joints/week ^b	20 (14–30)	–	–
Cannabis Abuse Screening Test (CAST) scores ^b	4 (3–5)	–	–
Average number of grams of cannabis/week ^b	4,2 (3–10)	–	–

^a Categorical variable represented as frequencies.^b Quantitative variable represented as median and interquartile range.^c Mann-Whitney U test.^d Chi-Square test.

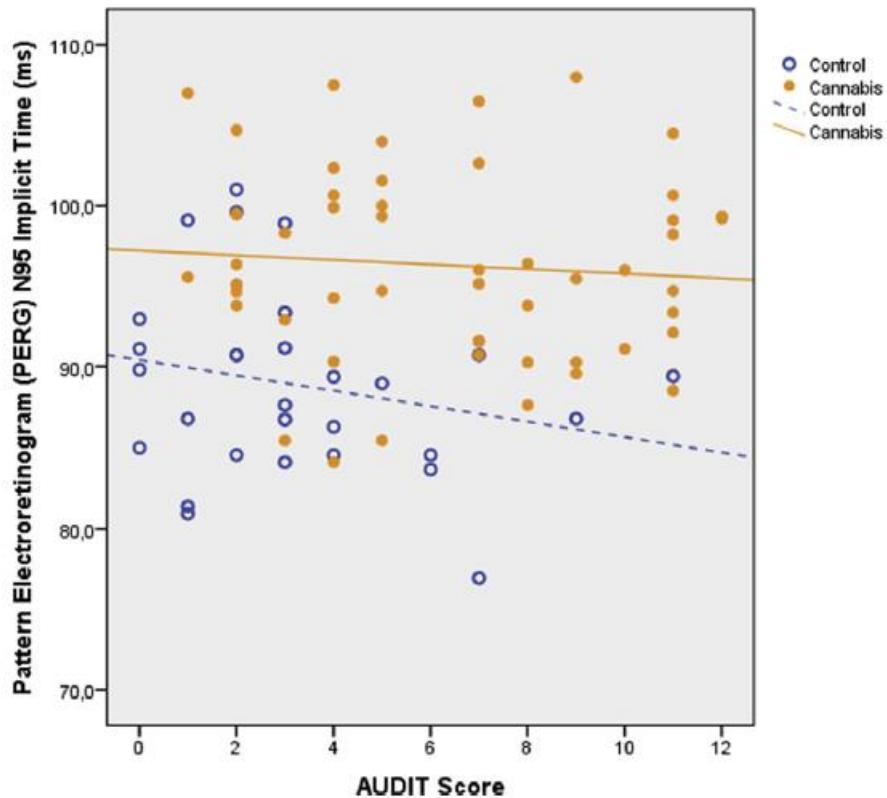


$p=0.0001$; Mann-Whitney U test

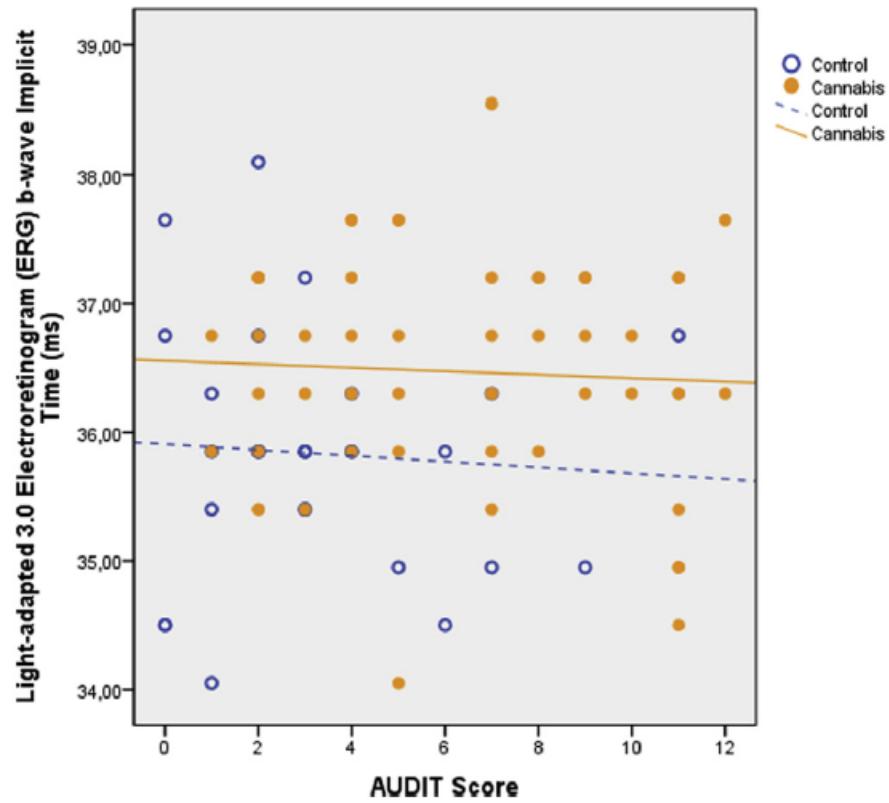


$p=0.002$; Mann-Whitney U test

PERG



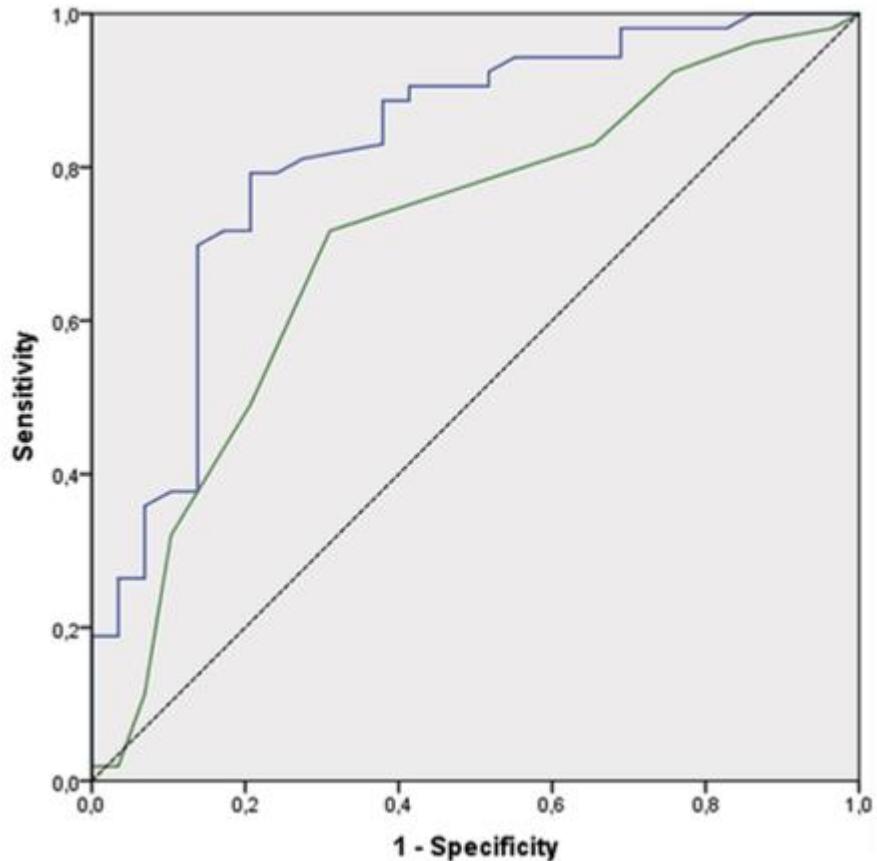
fERG



Investigation graphique de l'interaction entre le temps de culmination de l'onde N95 du PERG et de l'onde b de l'ERG flash série photopique 3.0 et le score d'AUDIT

N95 IT:

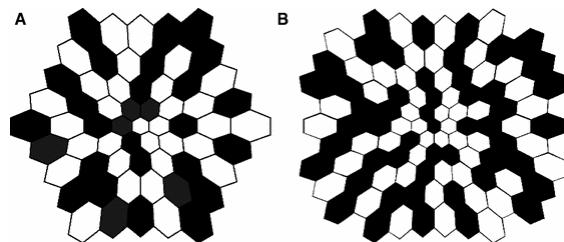
Valeur seuil = 91.3 ms
Sensibilité = 79.2%
Spécificité = 79.3%



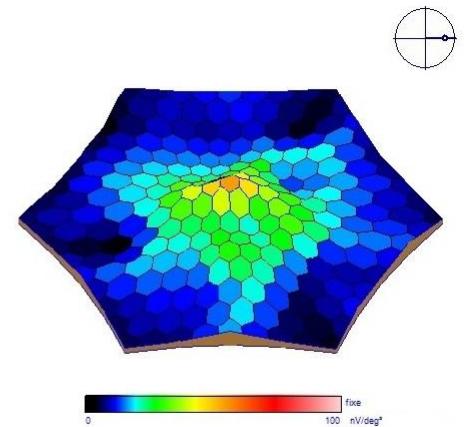
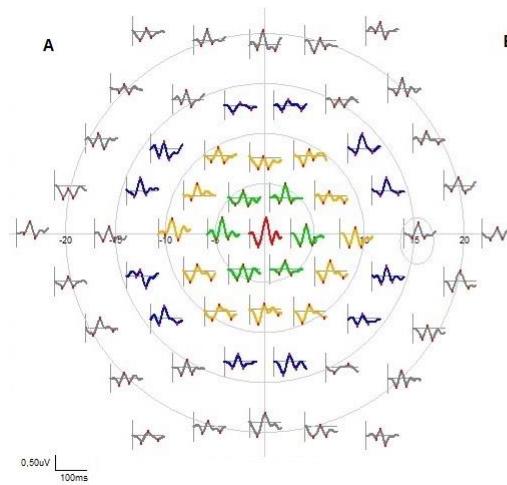
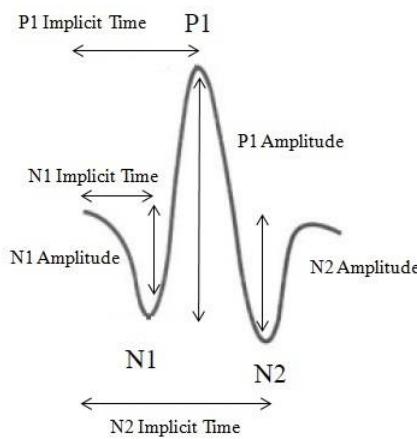
Onde b IT:

Valeur seuil = 36.1 ms
Sensibilité = 71.7%
Spécificité = 69%

Multifocal électrorétinogramme (mfERG)



ISCEV Standard pour mfERG



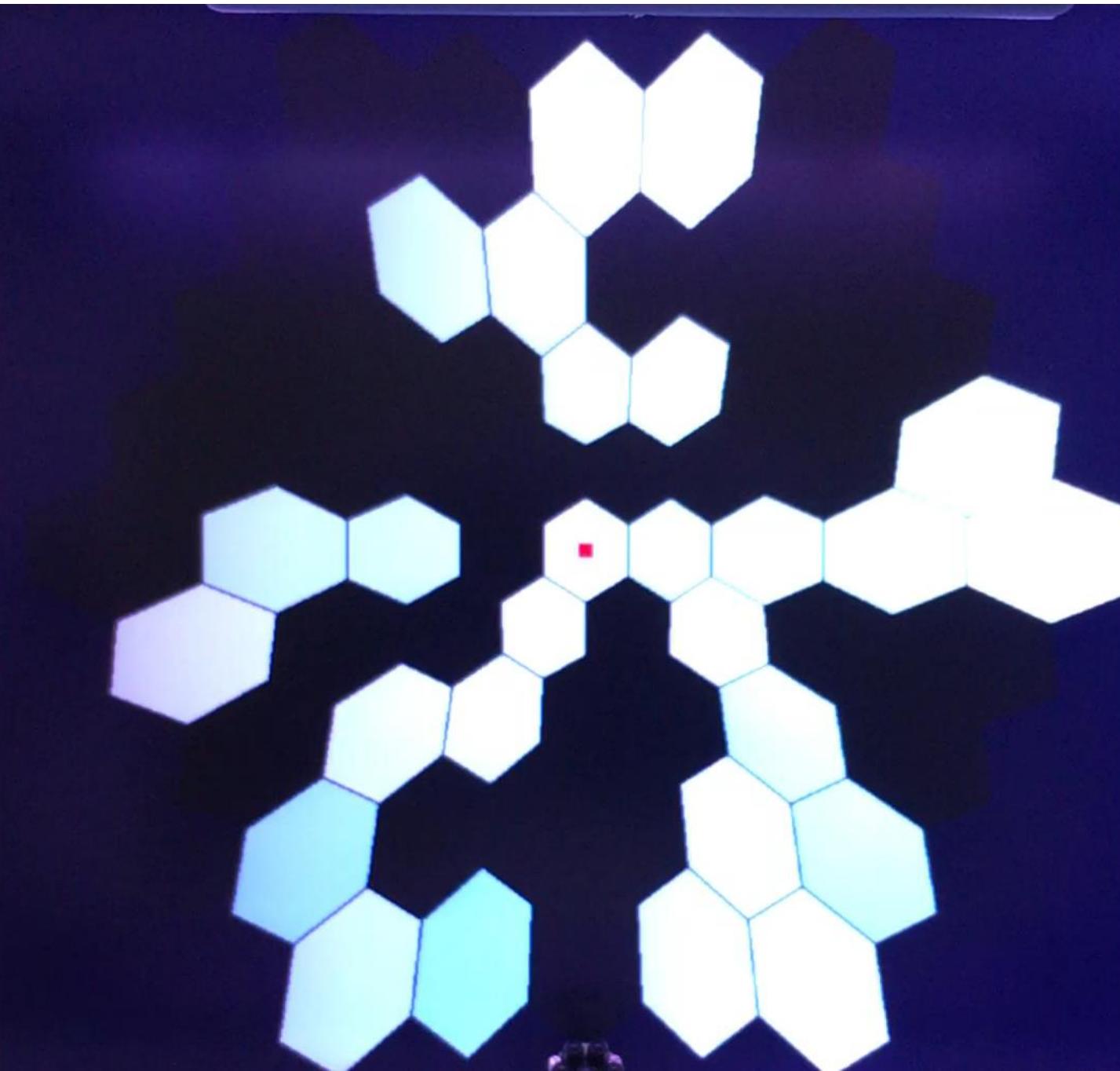


Table 1
Demographic and substance use characteristics of the participants.

	Cannabis users (n = 49)	Controls (n = 21)	p-Value
Gender (male/female) ^{a,d}	37/12	16/5	p = 0,951
Age (years) ^{b,c}	23 [21–30]	24 [22–26]	p = 0,612
Education (years) ^{b,c}	13 [11–14]	15 [14–16]	p = 0,006
Average number of alcohol uses/week (in French standard unit) ^{b,c}	3 [1–7]	1 [0–3,5]	p = 0,055
Alcohol Use Disorders Identification Test (AUDIT) scores ^{b,c}	6 [3–9]	2 [1–5]	p = 0,004
Fagerström Test scores (n = 43) ^b	1 [0–4]	–	–
Average number of cigarettes/day ^b	5 [2–10]	–	–
Average number of pack-year ^b	2 [1–5]	–	–
Age of first cannabis use ^b	16 [15–17]	–	–
Total years of cannabis use ^b	7 [5–14]	–	–
Average number of joints/week ^b	20 [14–30]	–	–
Cannabis Abuse Screening Test (CAST) scores ^b	4 [3–5]	–	–
Average number of grams of cannabis/week ^b	4,2 [3–10]	–	–

Educational level (years) is evaluated by the number of years of study after the first class of primary school.

AUDIT score was performed to assess use, abuse and dependence with respect to alcohol. Fagerström test was performed to assess use, abuse and dependence with respect to tobacco.

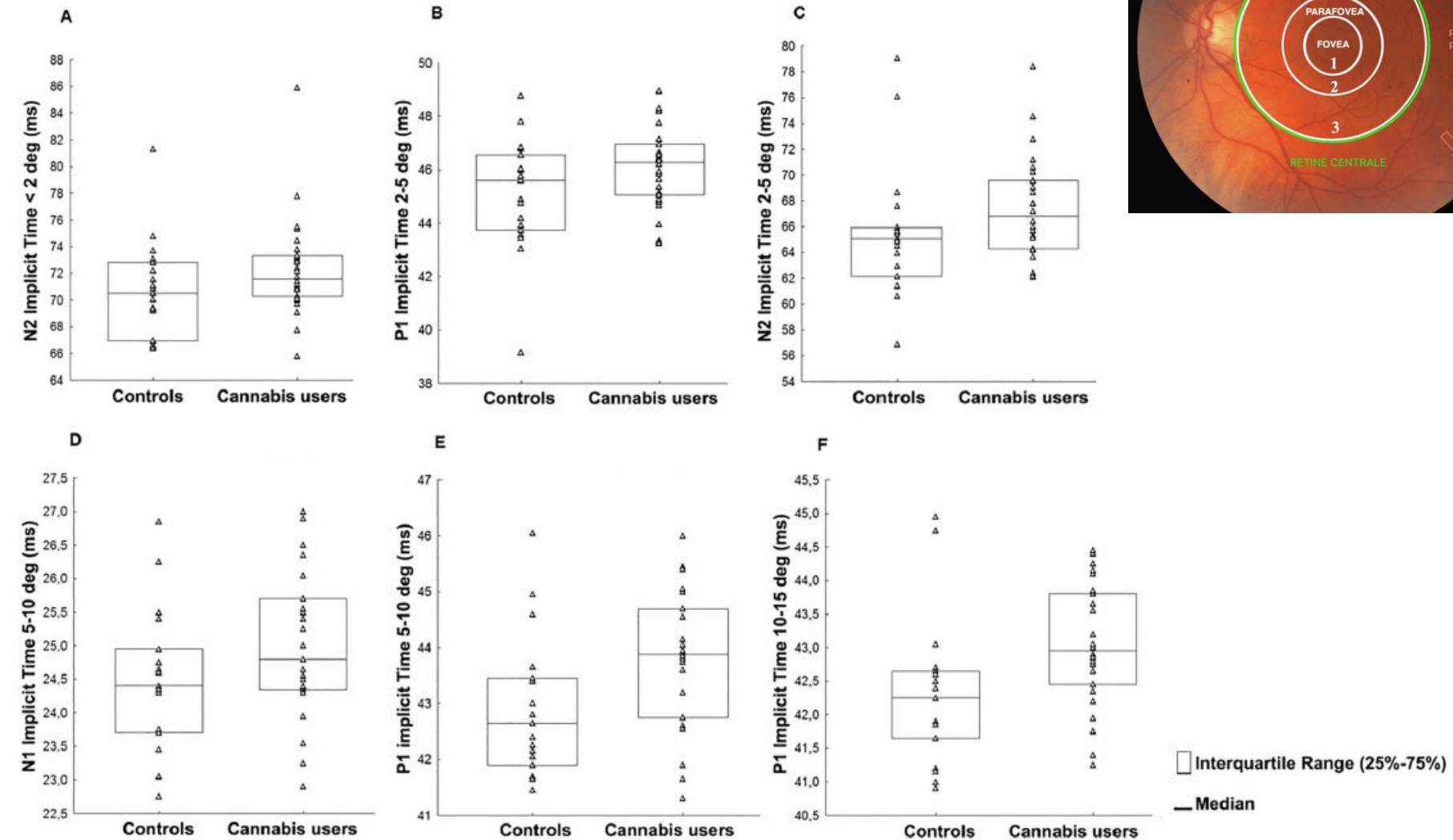
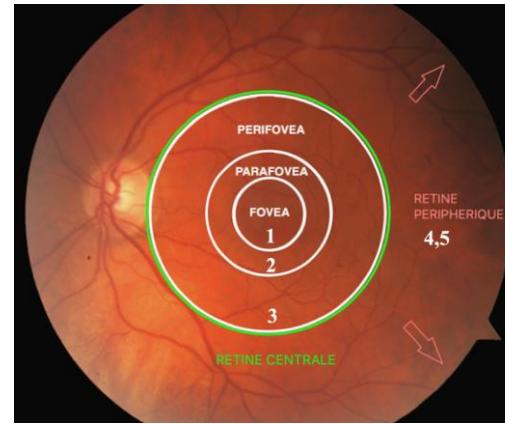
Cannabis Abuse Screening Test (CAST) was performed to assess use, abuse and dependence with respect to cannabis.

^a Categorical variable represented as number.

^b Quantitative variable represented as median and interquartile range.

^c Mann-Whitney U test.

^d Chi-Square test.



Système Cannabinoïde et Rétine: qu'en est-il ?

Chez l'homme:

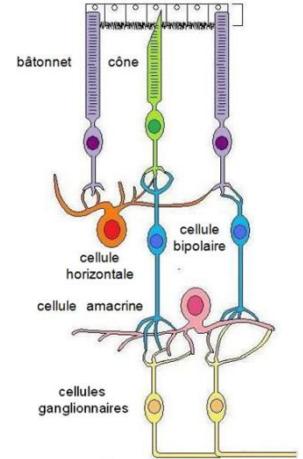
Présence de CB1, CB2, 2-AG et Anandamide

Chez l'animal:

Présence de CB1, CB2, 2-AG et Anandamide

Régulation des canaux ioniques et de la libération synaptique de neurotransmetteurs dans les photorécepteurs, cellules bipolaires et ganglionnaires

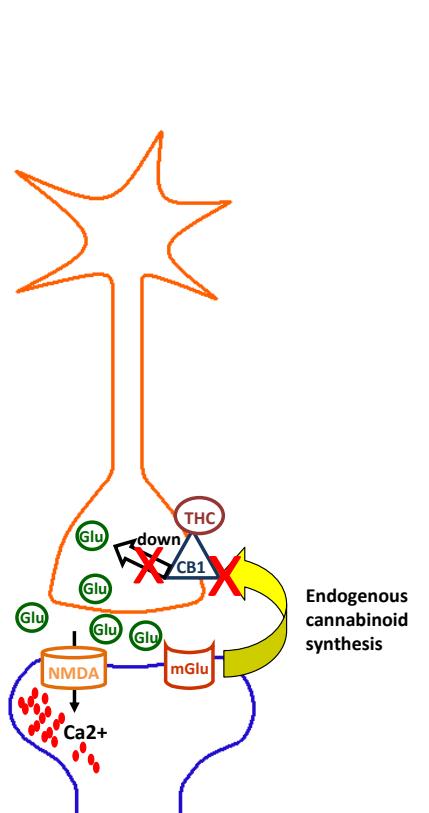
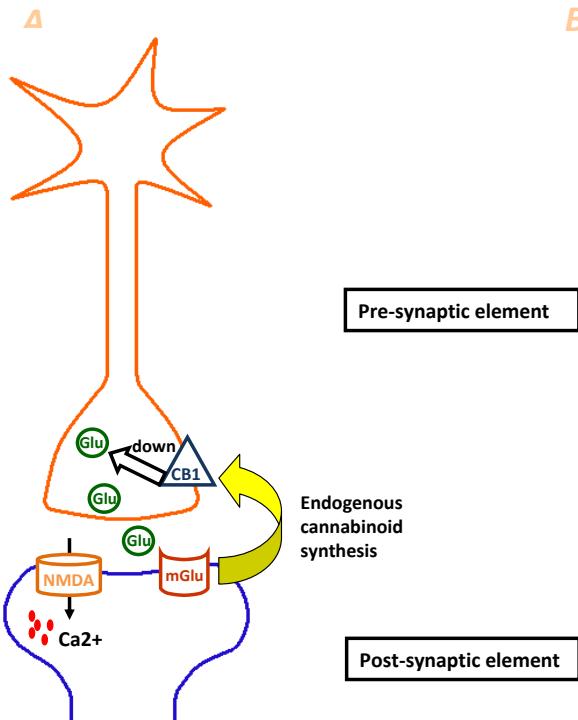
Modifications des ondes a- et b- de l'ERG flash chez des souris avec des CB1 et CB2 inactivés



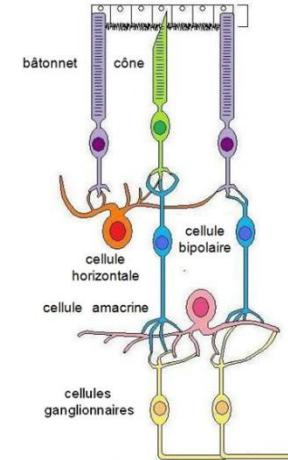
(Yazulla 2008, Schwitzer et al., 2015, 2016)

Un effet du THC sur la NT glutamatergique rétinienne ?

Dans le CNS

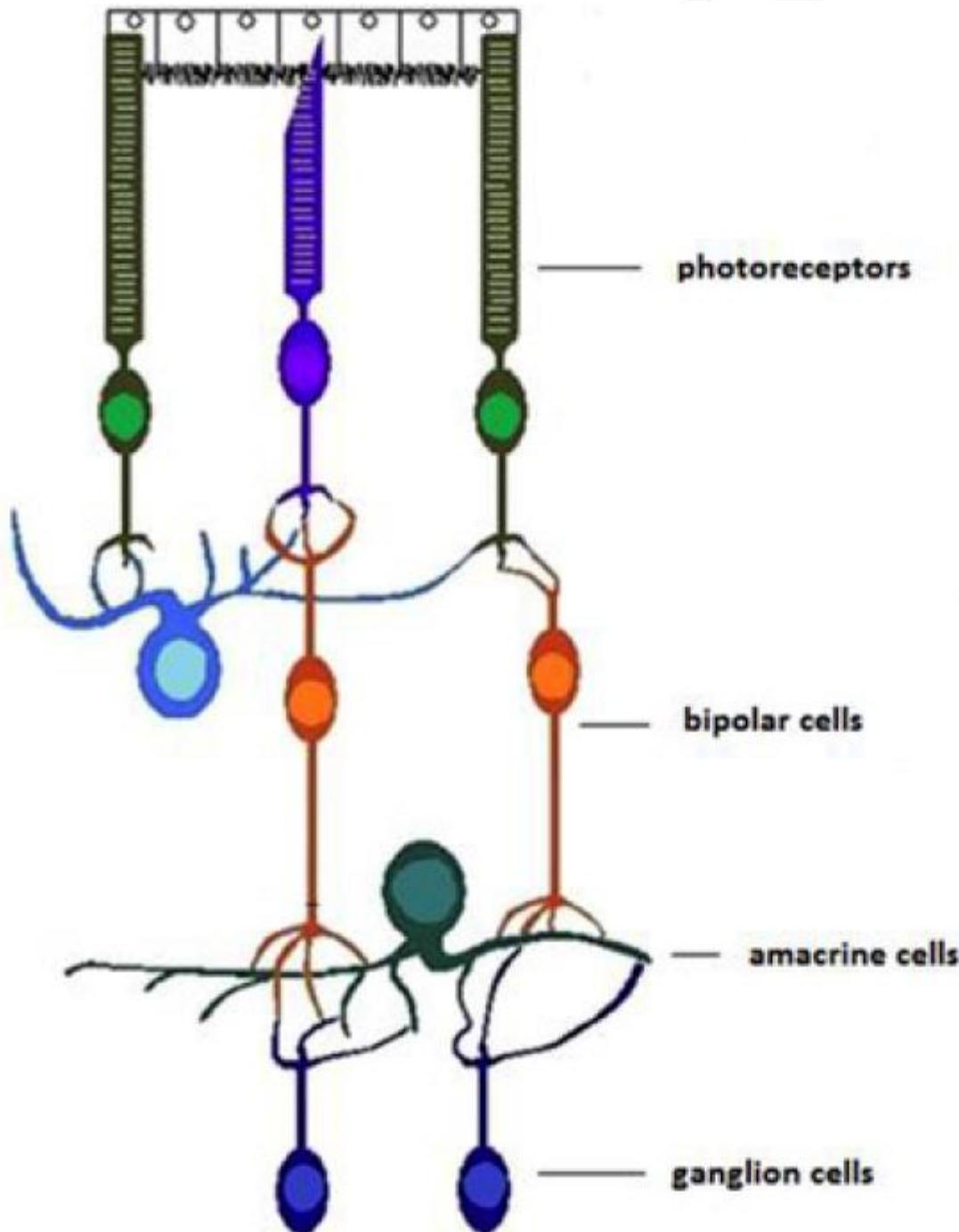


Dans la rétine



Glutamate:

- un NT essentiel
- Transmission verticale du signal
- Libéré par les C. bipolaires et ganglionnaires



no difference

increased of 1ms
b-wave implicit time

no published results

increased of 6ms
N95 implicit time

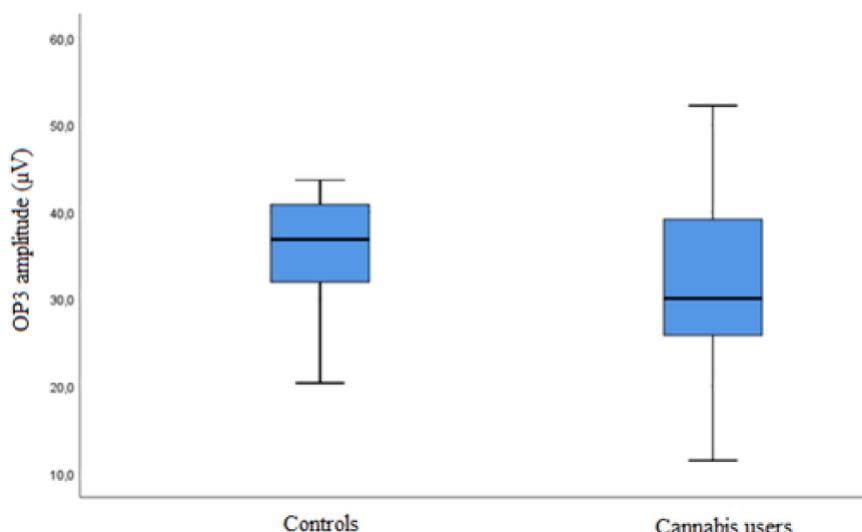
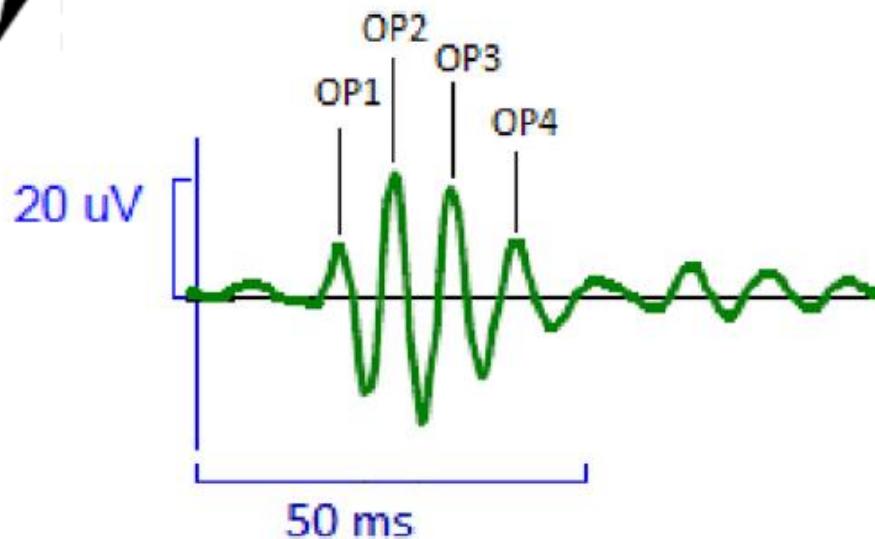


Table 1
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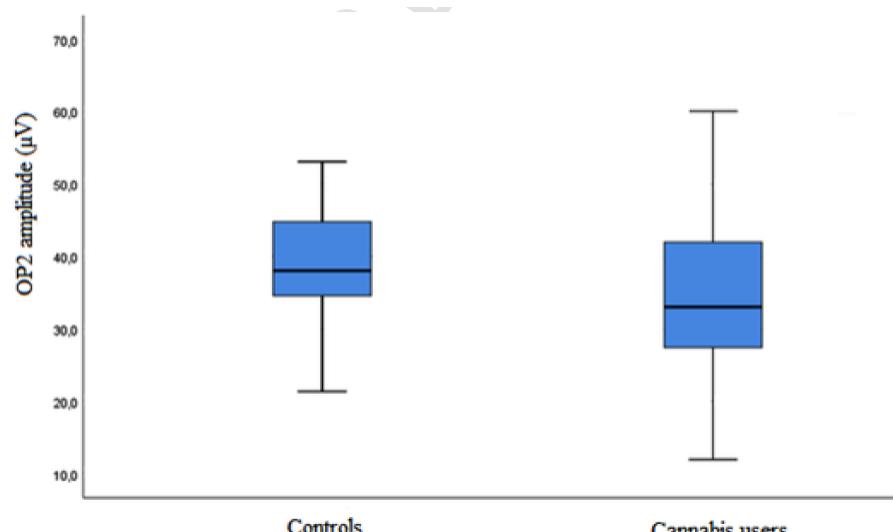
	Cannabis users (n = 56)	Controls (n = 29)	p-value
Gender (male/female) ^{a, d}	44/12	21/8	0.526
Age (years) ^{b, c}	23 (20.5–30)	24 (23–27)	0.466
Education (years) ^{b, c}	13 (12–14)	15 (14–16)	0.0001
Average number of AU/week ^{b, c}	4 (1.5–10)	1 (0–3)	0.0003
AUDIT scores ^{b, c}	7 (3.5–9.5)	3 (1–4)	0.0001
Fagerström test scores (n = 44) ^b	1 (0–3)	–	–
Average number of cigarettes/day ^b	4 (2–10)	–	–
Age of first cannabis use ^b	16 (15–17)	–	–
Total years of cannabis use ^b	7 (5–14)	–	–
Average number of joints/week ^b	20 (14–30)	–	–
CAST scores ^b	4 (3–5)	–	–
Average number of grams of cannabis/week ^b	4.1 (3–10)	–	–

^a Categorical variable represented as frequencies.

^b Quantitative variable represented as median and interquartile range.

^c Mann-Whitney U test.

^d Chi-Square test.

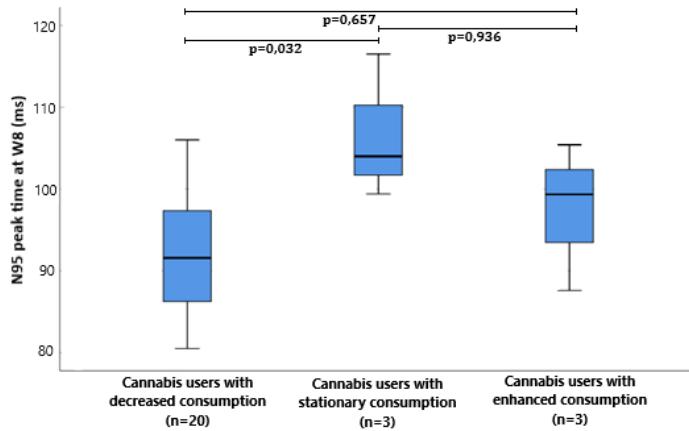
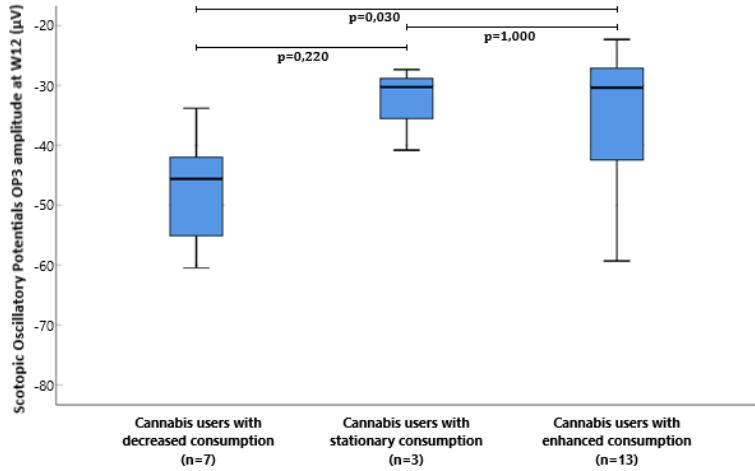
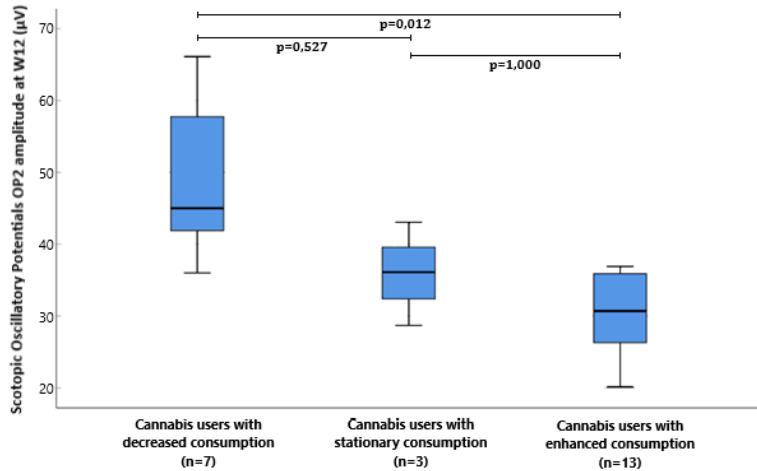


Variation des marqueurs ERG avec le niveau de consommation de cannabis

Test	W0 *	W1 *	W2 *	W3 *	W4 *	W5 *	W6 *	W7 *	W8 *	W10 *	W12 *
Mini International Neuropsychiatric Interview (MINI)	X										
Alcohol Use Disorder Identification Test	X										
Cannabis Abuse Screening Test	X										
Fagerström Test	X										
Fundoscopic examination and visual acuity	X										
Cannabis Withdrawal Scale		X		X		X		X	X	X	X
Urine toxicology for THC	X		X		X		X		X	X	X
TimeLine Follow Back	X	X	X	X	X	X	X	X	X	X	X
Pattern and Flash electroretinogram	X							X			X

	Cannabis users (n = 40)
Gender (male/female) ^a	24/16
Age (years) ^b	37 (27-40)
Education (years) ^b	13 (11-14)
Average number of alcohol uses/week ^b	4 (0-6)
Alcohol Use Disorders Identification Test (AUDIT) scores ^b	6 (3-8)
Fagerström Test scores ^b	2 (0-4)
Average number of cigarettes/day ^b	4 (1-10)
Average number of pack-year of cigarettes ^b	4 (1-10)
Age of first cannabis use ^b	17 (15-19)
Total years of cannabis use ^b	18,5 (9-22)
Average number of joints/week ^b	25 (14-35)
Cannabis Abuse Screening Test (CAST) scores ^b	5 (4-5)
Average number of grams of cannabis/week ^b	5 (2-9)

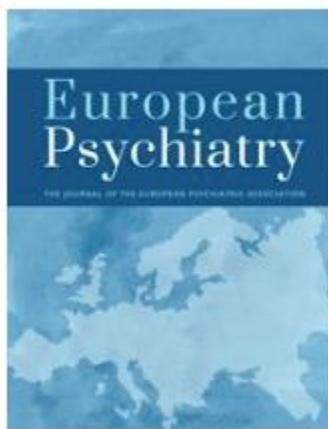
	Inclusion to W8	W8 to W12	Inclusion to W12
Cannabis users with decreased consumption	20	7	19
Cannabis users with stationary consumption	3	3	0
Cannabis users with enhanced consumption	3	13	6
Cannabis users with missing data	14	17	15
Total	40	40	40



Schwitzer et al, 2022

PERSPECTIVES

L'électrophysiologie rétinienne pour la psychiatrie de précision



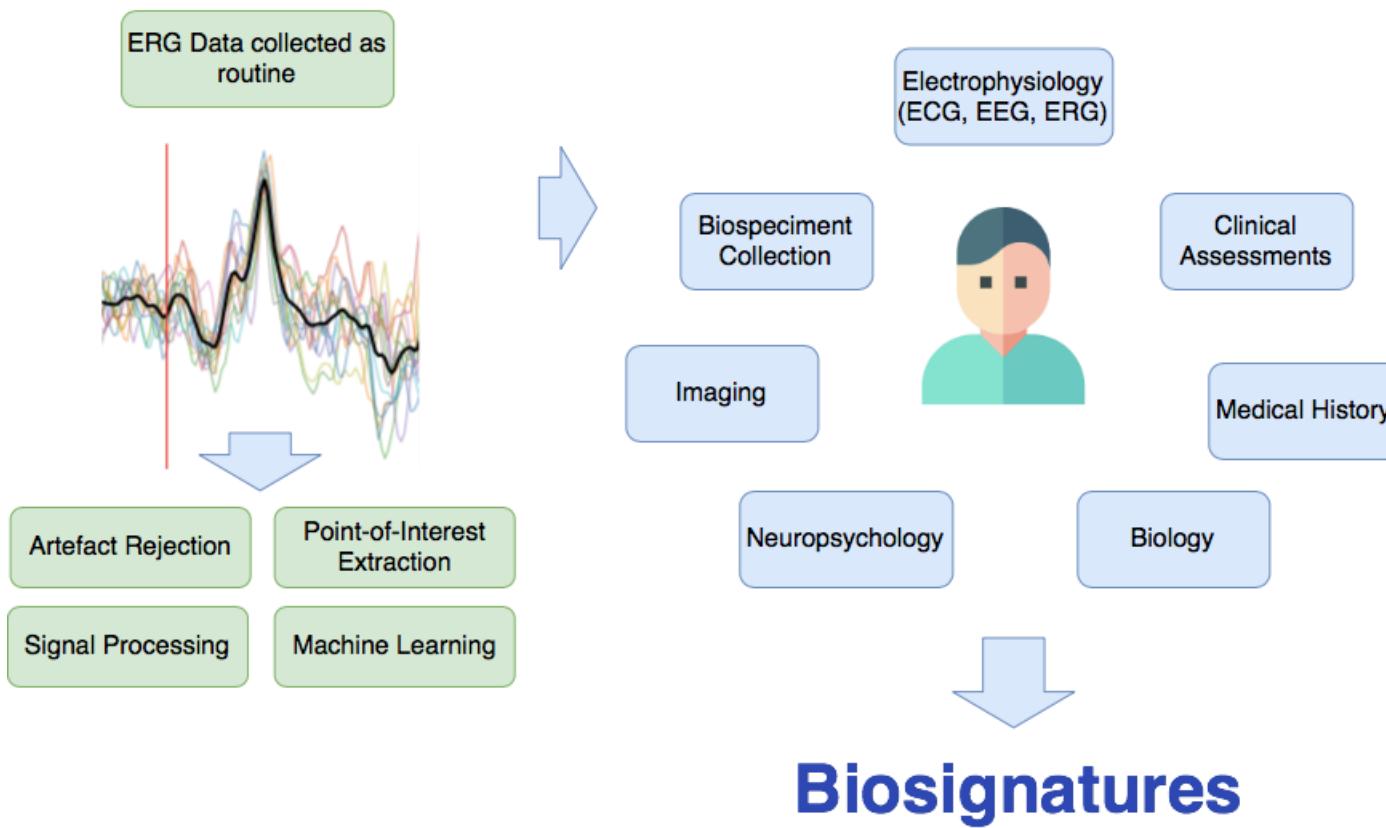
Using retinal electrophysiology towards precision psychiatry

Published online by Cambridge University Press: 14 January 2022

Thomas Schwitzer, Marion Leboyer, Vincent Laprévote, Valérie Louis Dorr and
Raymund Schwan 

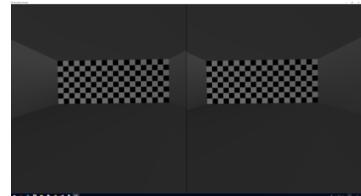
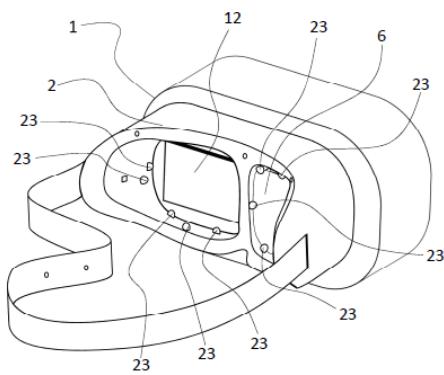
Show author details ▾

Sets of Biomarkers





RETINAUTE

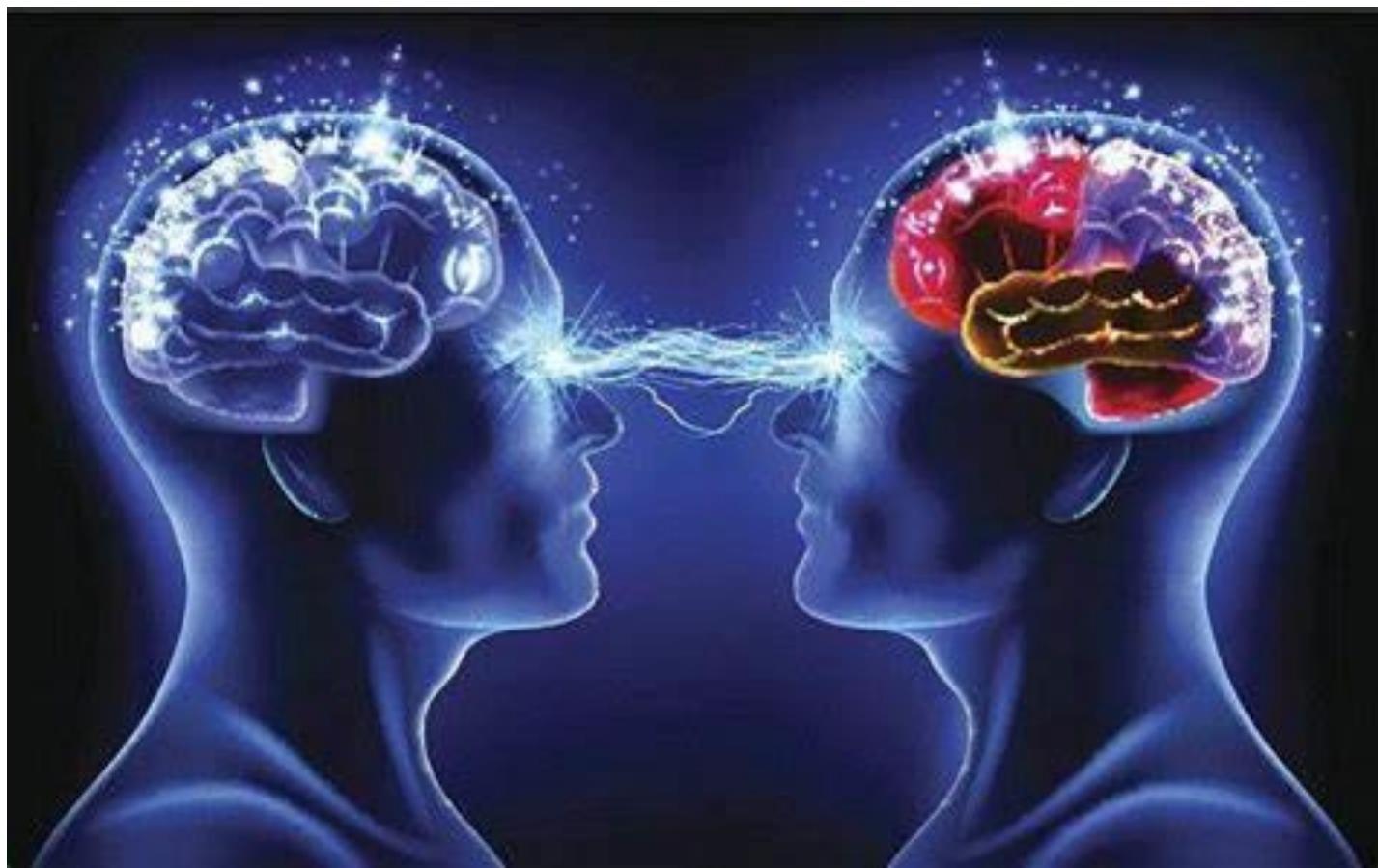


UNIVERSITÉ
DE LORRAINE



BIOSERENITY

1 brevet (FR 18/00175 ; WO2019166704 A1) : dispositif d'exploration du système visuel; Thomas Schwitzer, Raymund Schwan, Valérie Louis-Dorr // X-Novation, E. Polytechnique Paris



TABAC

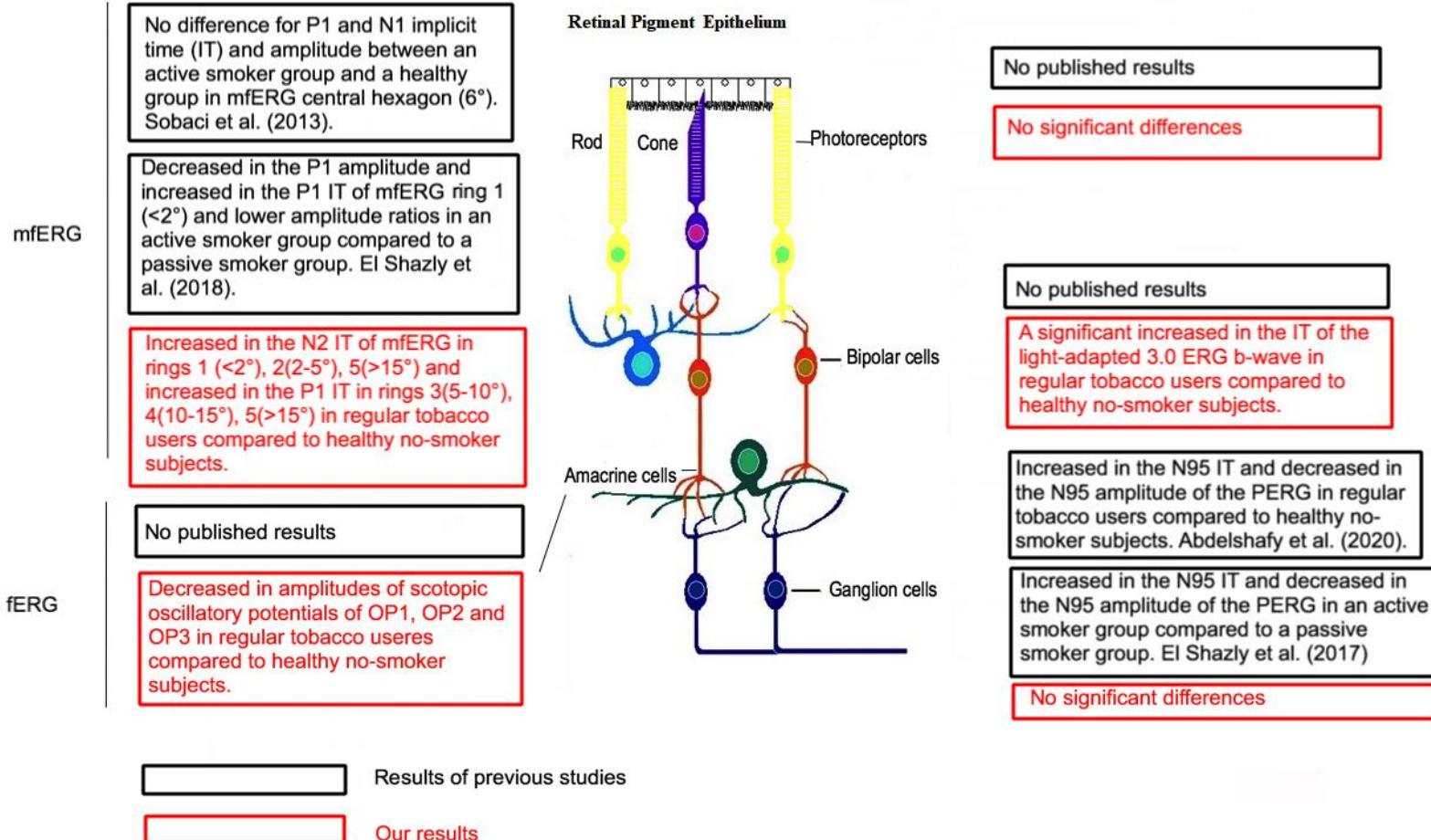


Table 1: Demographic and substance use characteristics of the participants.

	Alcohol users (n = 40)	Controls (n = 20)	p-value
Gender (male/female) ^{a, d}	24/16	7/13	0,07
Age (years) ^{b, c}	25 (3,81)	26 (4,28)	0,398
Education (years) ^{b, c}	17 (3,1)	16 (1,73)	0,305
Total years of alcohol use ^b	8,4 (3,46)	-	-
Number of standard alcohol drink during last month ^b	26,7 (19,32)	-	-
Number of binge drinking episode during the last month ^b	1,5 (1,92)	-	-
Average number of cigarettes / day ^b	0,15 (0,36)	-	-
Severity of Alcohol use disorder (DSM5) ^b	2,15 (2,42)	-	-
Alcohol Use Disorders Identification Test (AUDIT) scores ^b	8,8 (4,84)	-	-
Cognitive assessment (BEARNI) ^{b, c}	24,7 (2,42)	23,4 (5,98)	0,213

Categorical variable represented as frequencies ^aQuantitative variable represented as mean and standard deviation ^bStudent t-test ^cChi-Square test ^d

