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Cocaine and the Endocannabinoid System

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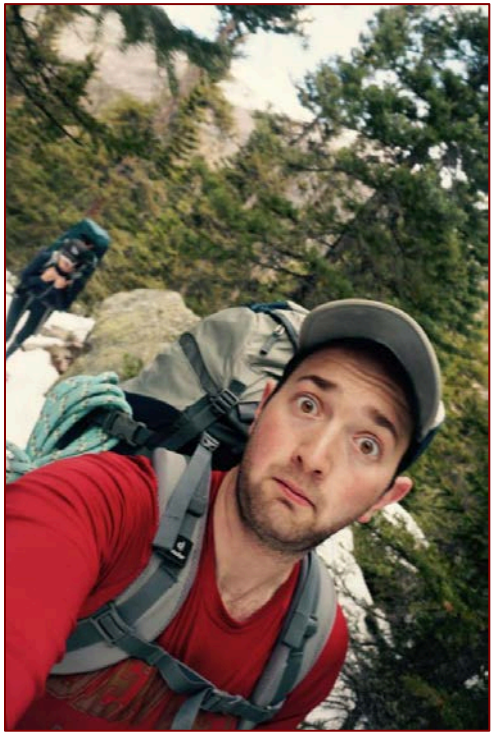
About Me



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- Founded in 1870
- Eugune “Bleuler
  - Introduced the term Schizophrenia in 1908
- Carl Jung
  - Large supporter of Freudian psychiatric theories
- Eduard Einstein

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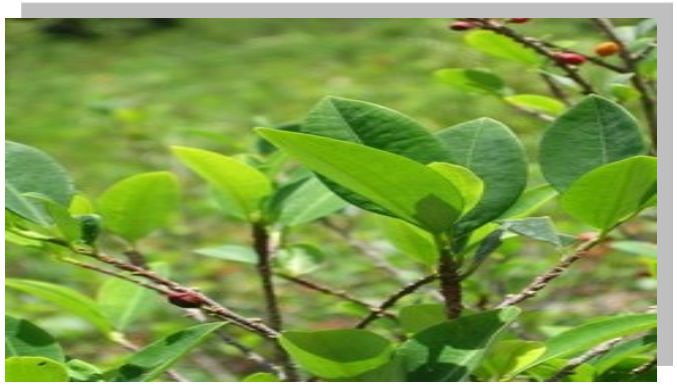
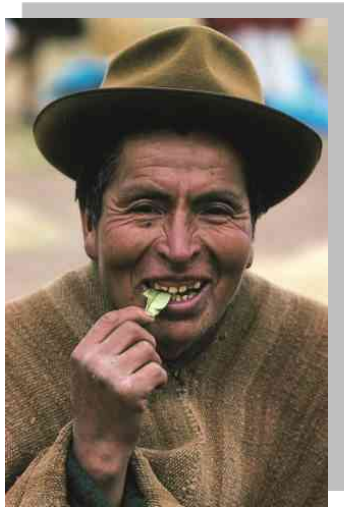
Cocaine

- Since about 5000 years cultivation of coca in the northern Andes
- In the Andes broad use of coca leaves as natural stimulant and tonic to date





- 1750: first coca plants arrive in Europe
- 1860: Albert Niemann firstly isolates and named cocaine in Göttingen
- From 1879 fast distribution as local anaesthetics and treatment for morphine addiction

Addictive potential of cocaine

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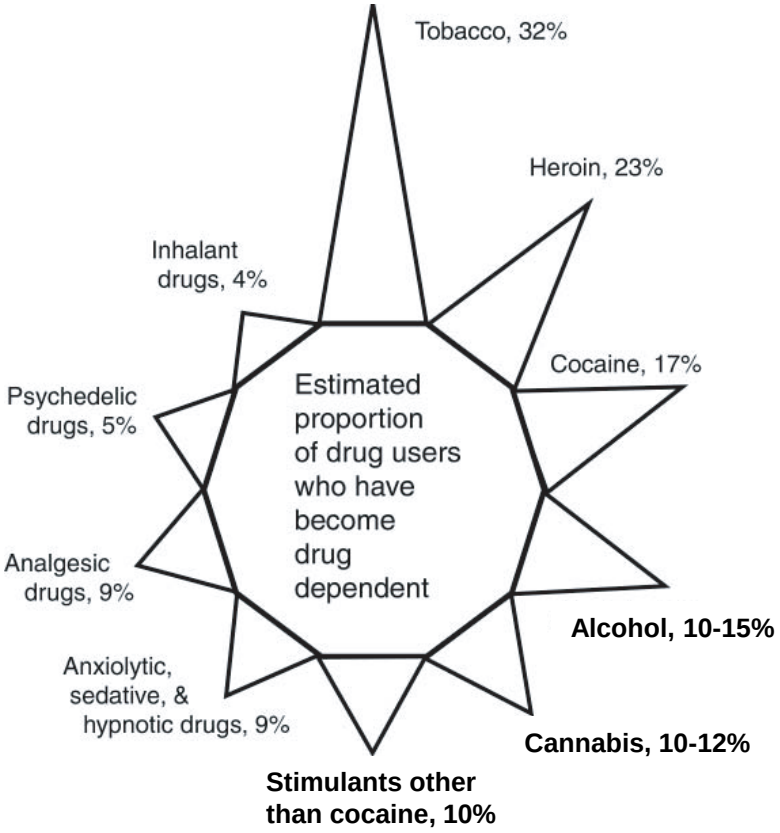
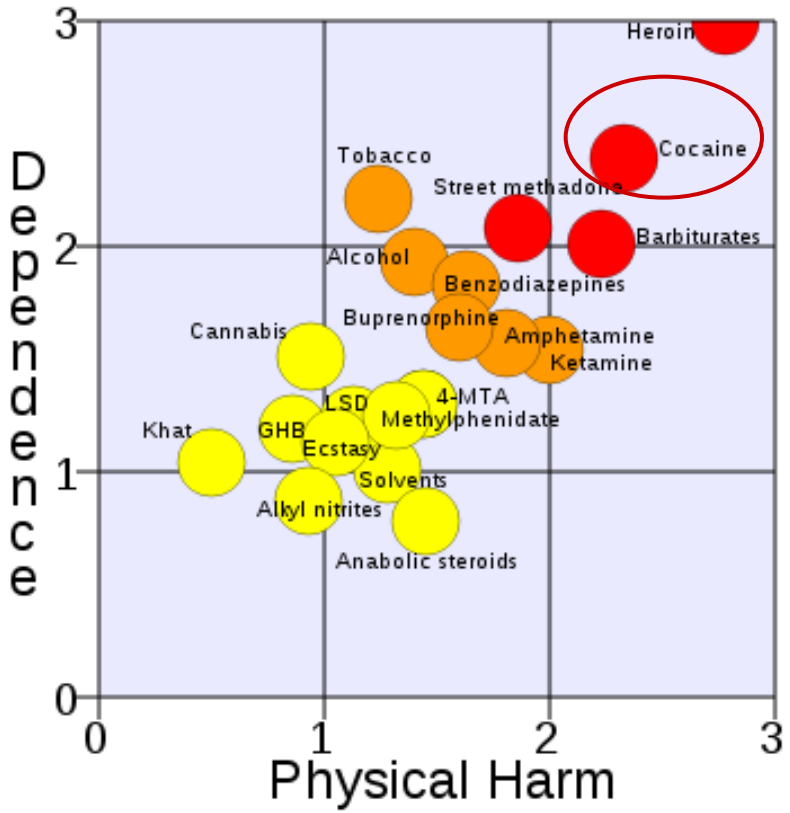


Estimated probability for addiction in specific substance user group

Anthony 2002, updated



Expert estimations (Delphi study) regarding the risk of drug consumption

Nutt et al. 2007

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Epidemiology of cocaine

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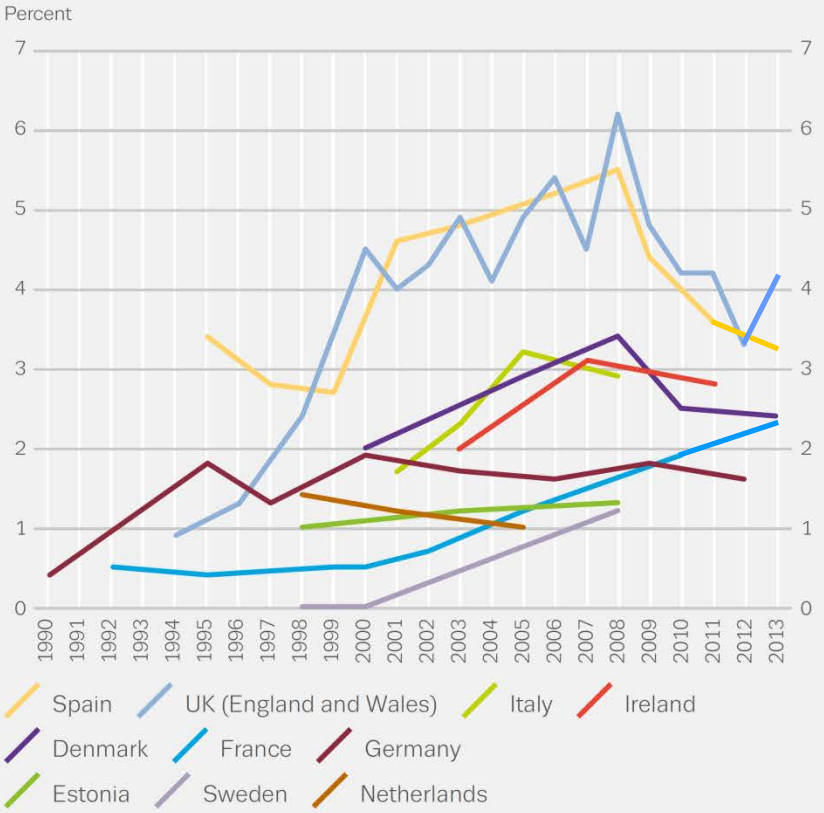
- Cocaine is worldwide as in Europe the second most prevalent illicit drug after cannabis.

Last year prevalence of cocaine use among young adults (15–34): selected trends (left) and most recent data (right)

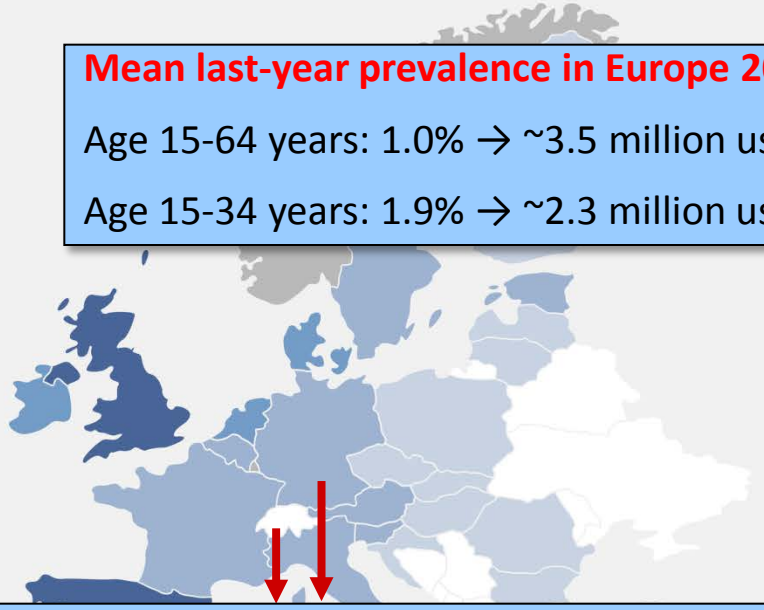
EMCDDA, 2014, 2015



Mean last-year prevalence in Europe 2014

Age 15-64 years: 1.0% → ~3.5 million users

Age 15-34 years: 1.9% → ~2.3 million users



Germany: Age 15-34: 1.6% → ~300k users (EMCDDA, 2015)
Switzerland: Age 15-34: 1.2% → ~24k users (BAG, 2012)

NB: Trends for ten countries with the highest prevalence and three or more surveys. Percent 0.1–1.0 1.1–2.0 2.1–3.0 >3.0 No data

Wastewater epidemiology of cocaine

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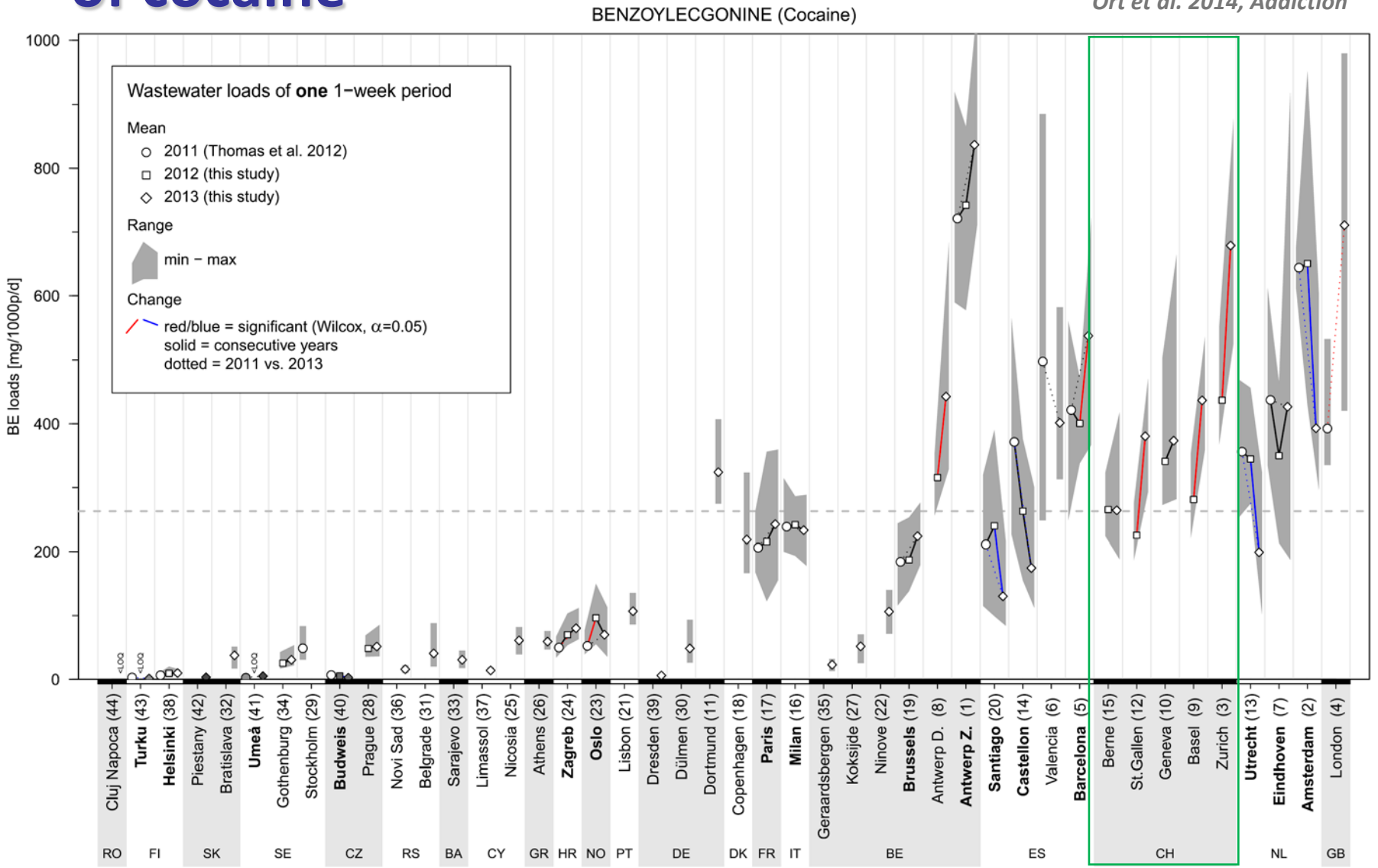
Ort et al. 2014, Addiction



Zürich Cocaine Cognition Study (ZuCo²St)

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Neuropsychology + Psychophysiology + Genetics

1. Baseline (cross-sectional)

73 recreational users
35 dependent users
96 stimulant-naïve controls
204 participants

12 month

Neuropsychology + Psychophysiology

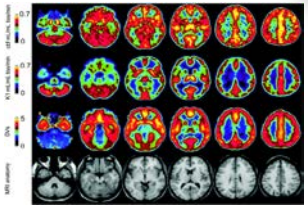
2. Follow-up (longitudinal)

64 recreational users
17 dependent users
51 stimulant-naïve controls
132 participants

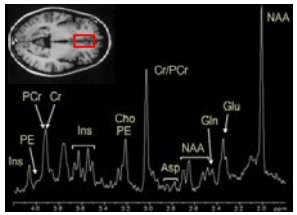
PET + MRS + MRI

PET + MRS (cross-sectional)
18 chronic users
18 stimulant-naïve controls
36 participants

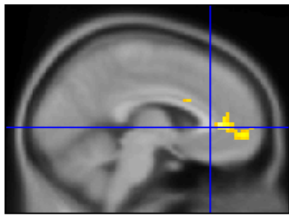
fMRI + VBM + resting-state + ASL
25 chronic users
25 stimulant-naïve controls
50 participants



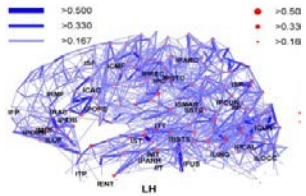
[^{11}C]-ABP688 PET



[^{1}H]NMR spectroscopy



Functional MRI



Resting-state connectivity

- Early information processing
- Classical neuropsychology
- Social Cognition
- Decision-making and impulsivity
- Social decision-making and neuroeconomics
- Genetics and gene expression

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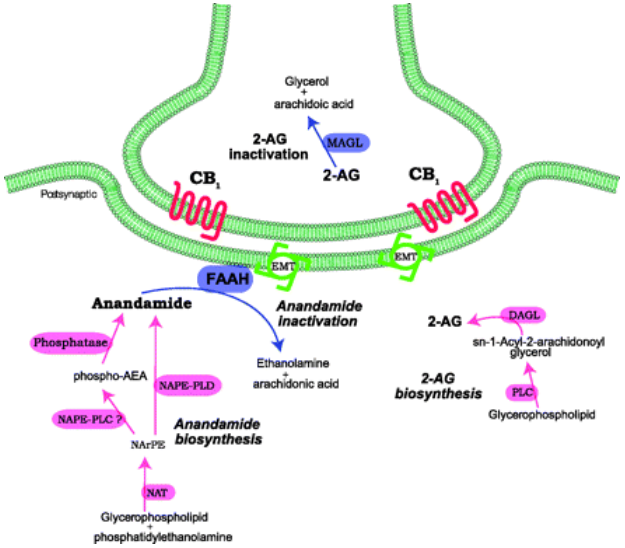
Sample Results

Mean and SD, numbers	Stimulant-naive controls (n=68)	Recreational cocaine users (n=68)	Dependent cocaine users (n=30)	F/Chi²/t	df/df$_{err}$	*P*
Age	30.3 (9.2)	28.7 (6.2)	32.5 (9.0)	2.38	2/163	0.10
Sex (m, f)	21 / 47	48 / 14	23 / 8	0.38	2	0.83
Years of school education	10.7 (1.8)	10.5 (2.0)	9.5 (1.2)	4.82	2/163	**<0.01**
Verbal IQ (MWT-B)	104.4 (9.7)	103.2 (9.6)	99.7 (9.1)	2.46	2/163	0.09
Smoker/non-smoker	53 / 15	53 / 15	24 / 6	0.06	2	0.97
Cocaine Craving (CCQ)	-	19.0 (9.1)	20.3 (11.4)	0.36	96	0.55
Cocaine self report						
g/week	-	1.1 (1.0)	7.9 (15.8)			
Duration (years)	-	6.5 (4.0)	9.4 (6.5)			
Cumulative lifetime dose (g)	-	520 (751)	5501 (9635)			
Last consumption (days)	-	27.5 (37.6)	21.0 (33.6)			
Quantitative hair toxicology						
Cocaine (pg/mg)	-	2739 (4628)	22164 (32609)			
Benzoylecgonine (pg/mg)	-	546 (919)	5048 (7711)			
Cocaethylene (pg/mg)	-	276 (318)	2006 (3656)			
Norcocaine (pg/mg)	-	62.4 (100)	586 (758)			
Alcohol (g/week)	116.8 (122.6)	167.8 (117.5)	188.5 (260.6)			
Amphetamine (g/week)	-	0.1 (0.2)	0.0 (0.2)			
MDMA (tablets/week)	-	0.1 (0.3)	0.4 (1.8)			
Cannabis (g/week)	0.5 (1.0)	0.9 (2.1)	1.2 (3.7)			

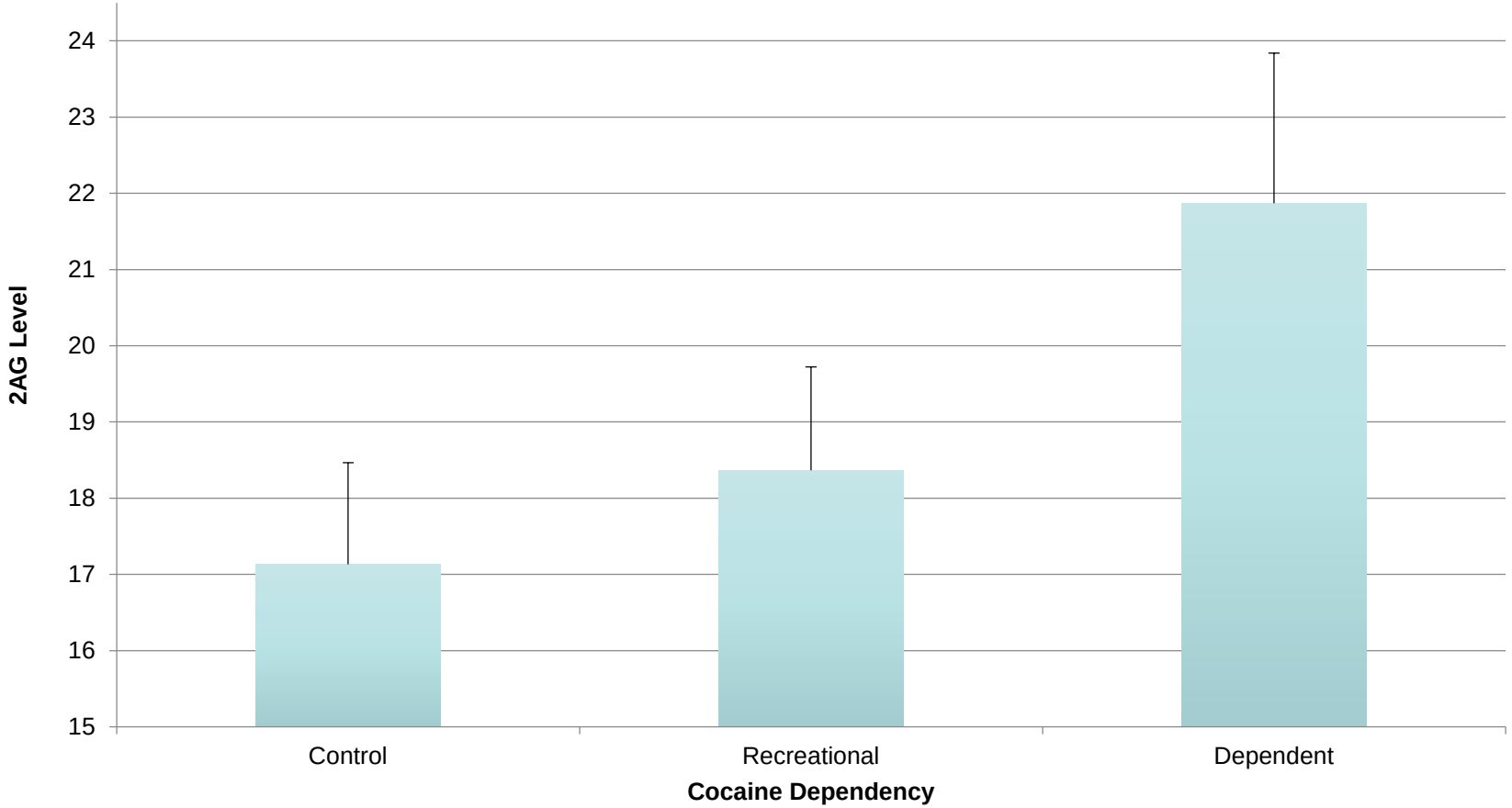
Endocannabinoids

- 1970s: THC (one of around 60 to be found in Cannabis, but the only that is psychoactive) found to connect with the CB_1 receptor in the brain.
  - They are the most abundant receptors in the mammalian brain but are also present in lower concentrations throughout the peripheral nervous system.

- 1992: Discovered endogenous ligands that also connect to the CB_1 receptor, beginning with Anandamide (AEA) and 2-arachidonoylglycerol (2-AG)



2AG vs. Cocaine Dependency



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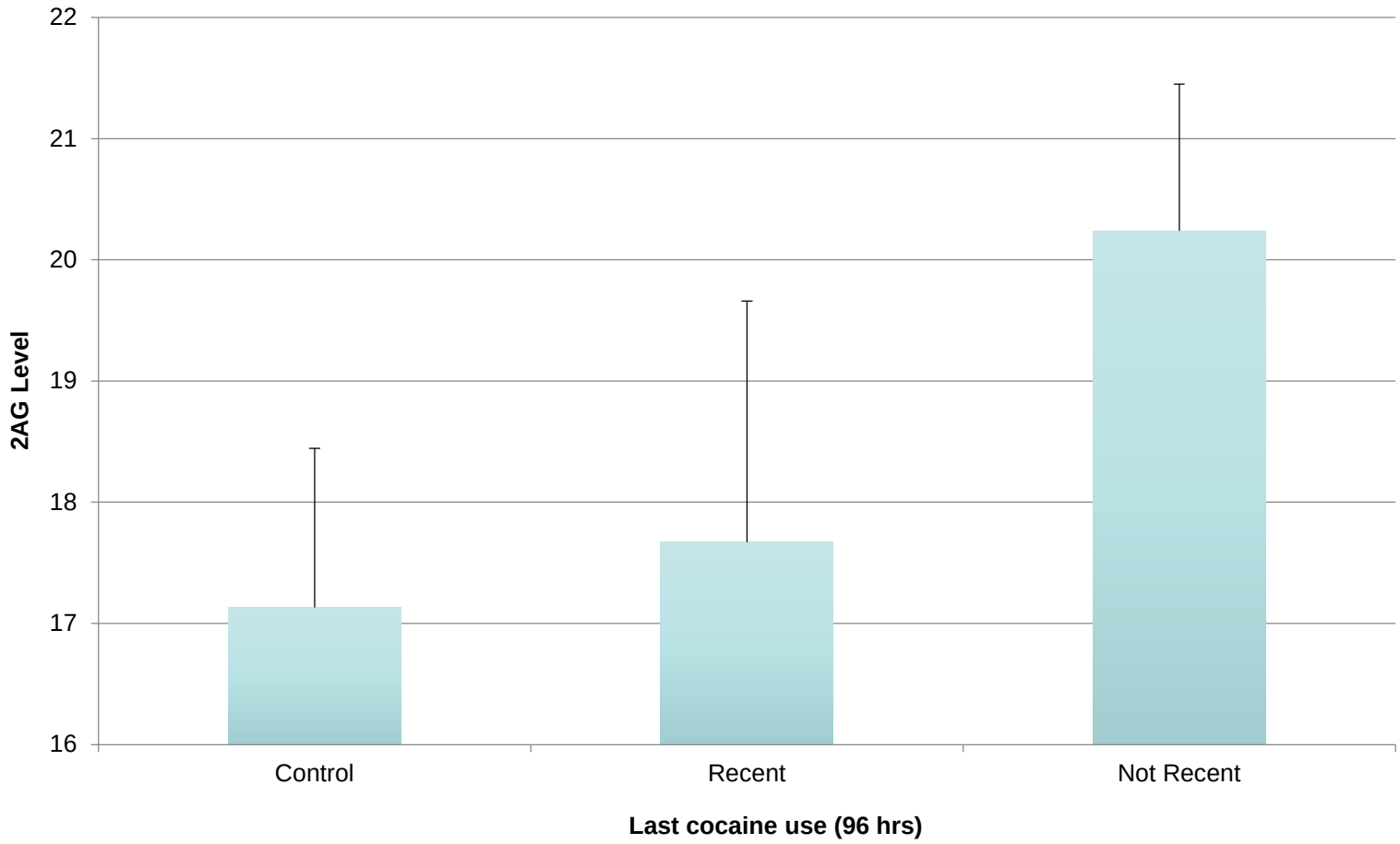
2AG vs. Recent Use



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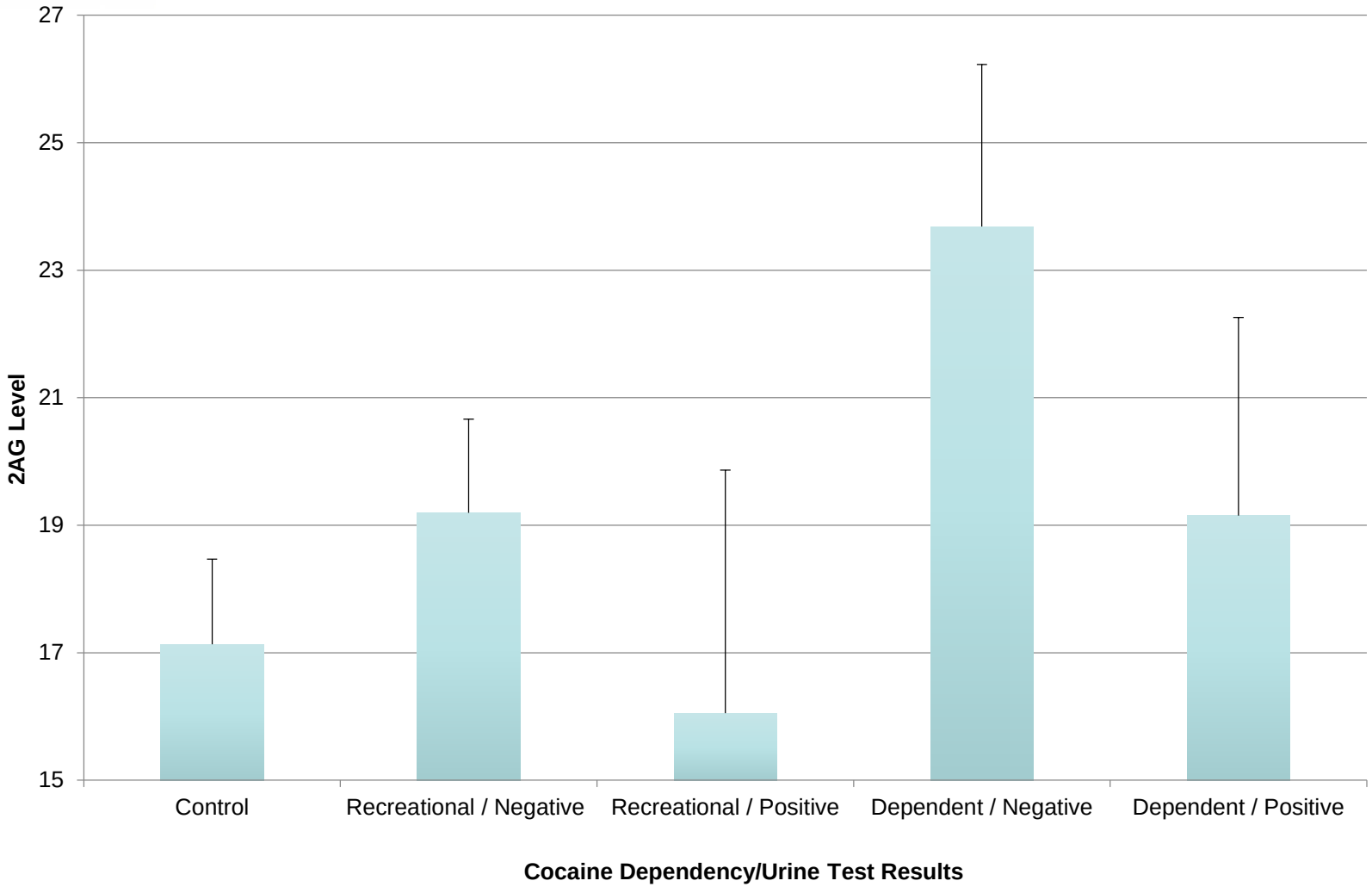
2AG vs. Dependency and Urine Test



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Thank You

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