# Effects of coffee on the brain

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## History of coffee
### Description of the properties of coffee

- Coffee was first consumed as a "medical nutrient" because of its stimulatory effects on digestion...
- In the 11th century, the virtues of caffeine were described by Avicenne
- Prosper Alpin, an Italian botanist and medical doctor studied coffee during a trip to Egypt in 1580
- The first citations of coffee are from Antoine de Jussieu in 1713 and Carl von Linné in 1753
- The Encyclopedia by Diderot and d'Alembert (1751-1772) describes the virtues of coffee in "obesity and migraine"

## Caffeine, the main psychoactive component of coffee

- Caffeine
  - isolated from coffee beans in 1820
  - the psychoactive substance most widely consumed throughout the world
  - coffee, tea, mate, sodas; chocolate products; cola nuts; analgesic and sliming medications, and in stimulants
- World consumption of caffeine
  - adults: mean world consumption: 1-2 mg/kg/d (1-2 cups); 2.4-4.0 mg/kg/j in the USA (2-4 cups) and the UK and up to 7.0 mg/kg/j in Scandinavia (7 cups)
  - children: 1.0 mg/kg/j in the USA and 1.8 mg/kg/j in Danemark

## Concentrations of caffeine in coffee

- Content on caffeine in a cup of coffee (150 ml)
- Arabica: 50-120 mg
- Robusta: 100-250 mg
- Filtered coffee: 50-175 mg
- Espresso: 40-110 mg
- Soluble coffee: 35-110 mg
- Decaffeinated coffee: 1-6 mg

- Low to moderate consumption: 1-3 cups/day
- High consumption: over 5 cups/day

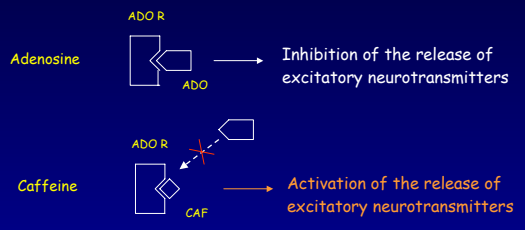
## Effects of coffee and caffeine

- Low to moderate consumption (50-250 mg in one sitting = 1 small cup to two large cups of coffee)
  - positive effects: feeling of well-being, relaxation, positive mood, energy, increased alertness, higher capacity of concentration
- High to very high doses (400-800 mg in one sitting = 5 to 10 large cups of coffee)
  - negative effects: nervousness, anxiety, aggressiveness, insomnia, tachycardia, trembling
- Moderate consumption of coffee and caffeine is not considered to be a health concern

## Mechanism of action of caffeine in the brain

- At the doses reached after the ingestion of one or several cups of coffee
  - main effects by binding to adenosine receptors, mainly A1 and A2a subtypes
- Adenosine acts as a neuromodulator
  - by limiting or inhibiting the release of most excitatory neurotransmitters
- Distribution of adenosine receptors
  - A1: in all cerebral regions
  - A2a: mainly in the striatum

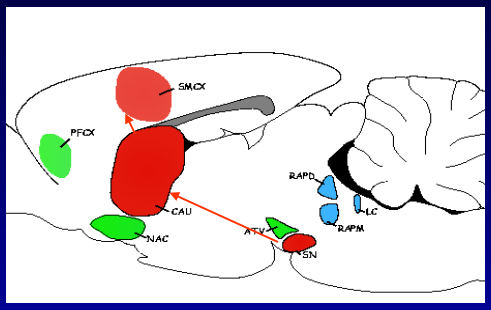
## Mechanism of action of caffeine in the brain



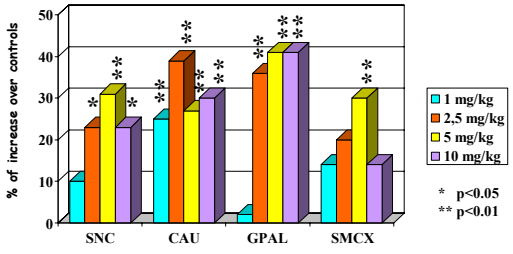

## Effects of caffeine on the brain: Locomotion

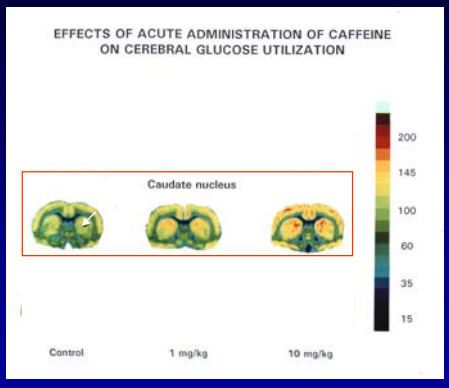
- The effects of caffeine on locomotion have been known for quite a long time
- Biphasic effects
  - Low to moderate doses: stimulation of motor activity
  - High doses: reduction of motor activity
- In the rat, activation at a low dose: 1 mg/kg (1 cup of coffee) increases functional and electrophysiological activity in the striatum, cerebral area mediating locomotion

## Sagittal section of the rat brain




## Caffeine and locomotion

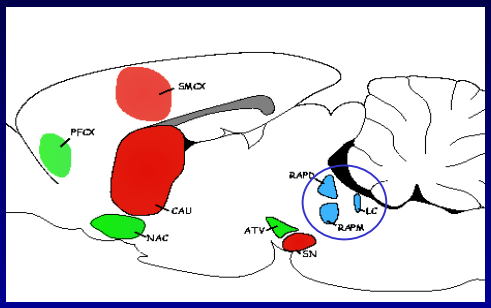


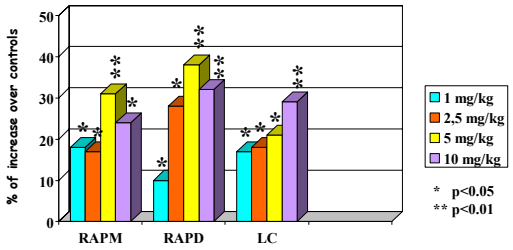

## Effects of caffeine on the brain: Sleep

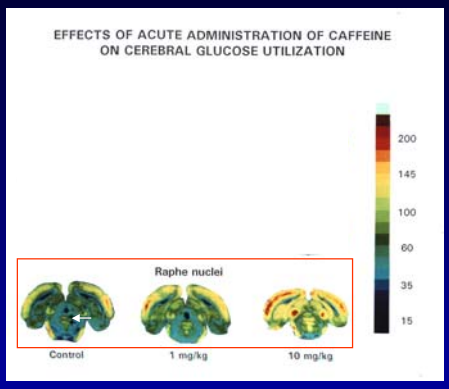
- Sleep is one of the functions most sensitive to the effects of coffee and caffeine. These effects reflect the blockade of the hypnotic properties of adenosine by caffeine
- In humans, 100 mg of caffeine (one cup of coffee) at bedtime:
  - increases the latency to sleep and decreases the quality of sleep, mainly the phases of deep sleep, but has no effect on REM sleep
  - the effect is persisting for about 3-4 h, sometimes longer
- In the rat, a low dose of 1 mg/kg caffeine (one cup of coffee) increases functional activity in brain regions mediating the sleep-wake cycle

## Sagittal section of the rat brain




## Caffeine and sleep




## Effects of caffeine on the brain: Alertness, mood and performance

- Low doses of caffeine (20-200 mg in one sitting) have positive effects on mood, vigilance and energy
  - improvement of self-confidence, concentration abilities and efficacy in intellectual tasks
  - effects mostly marked in situations with reduced vigilance: after lunch, regular cold...
- Effects of caffeine on memory and performance appear to be rather indirect effects:
  - on vigilance, concentration, information processing and reduction of fatigability

## Effects of caffeine on the brain: Headache and migraine

- Pain during headache and migraine is partly resulting from the vasodilation of cerebral blood vessels induced by A2 adenosine receptors located on blood vessels

➢ Caffeine contained in coffee
  - reduces pain during headache and migraine via its vasoconstrictive properties

➢ Caffeine alone
  - is present in analgesic preparations
  - is able to potentiate the analgesic properties of some drugs (aspirin, ibuprofen) by a mechanism not yet clarified

## Effects of coffee and caffeine on brain: Anxiety

- Caffeine may generate anxiety
  - only at doses much larger than the regular doses in the normal population
  - at low doses in a subset of sensitive individuals

🗁 This leads some sensitive individuals to a spontaneous reduction of coffee consumption

## Effects of coffee and caffeine on brain diseases: Parkinson's disease (1)

- Parkinson's disease (PD) is the result of the degeneration of dopaminergic cell bodies in the substantia nigra which connects to the striatum
  - Treatment by an analogue of dopamine, L-dopa which looses its efficacy in the long term, leading to the aggravation of trembling and difficulties to walk
  - Since the molecular target of caffeine at low doses is located in the striatum, caffeine has been suggested as an adjunctive drug to L-dopa therapy; caffeine leads to an improvement of trembling

## Effects of coffee and caffeine on brain diseases: Parkinson's disease (2)

- Mayo Clinic study: Coffee consumers reduce their risk to develop PD by a factor of about 2 compared to non-consumers
- Study performed over 30 years on 8.000 Japanese-American men in Hawaii:
  - the more the subjects consume coffee, the lower the incidence of PD. Those who consume 3-4 cups/day have a 5-fold lower risk than non-consumers to develop PD
- Mechanism is unknown
  - aversion for coffee long the development of the disease?
  - Protective effect of caffeine against dopamine depletion?

## Effects of coffee and caffeine on brain diseases: Parkinson's disease (3)

- In women
  - the risk of PD is similar when using hormones or not
  - use of hormones associated with a 34% lower risk with low coffee consumption (less than half a cup/day)
  - use of hormones associated with a 55% higher risk with high coffee consumption (over 5 cups/day)
  - caffeine-estrogen interaction is postulated
- In the elderly population
  - no association between signs of PD and coffee consumption

## Effects of coffee and caffeine on brain diseases: Stroke and epilepsy

- Stroke
  - Potential "neuroprotective" effects of chronic coffee consumption: postulated in humans, demonstrated in stroke models in rodents
- Epilepsy
  - in rodents: chronic treatment by caffeine in drinking water decreases the susceptibility to seizures and is neuroprotective
  - chronic treatment could reduce cerebral excitability (mechanism not yet clarified)

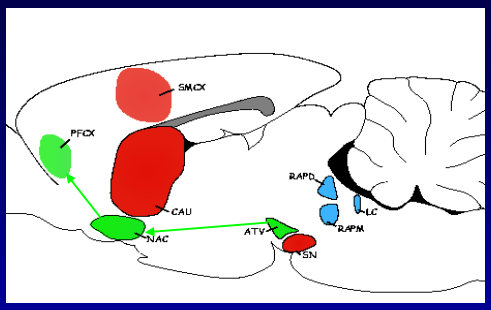
## Are we dependent on coffee and caffeine? (1)

- Caffeine most often in coffee is consumed daily by most individuals: some of them pretend they cannot cut of or stop drinking coffee
- Arguments for a dependence?
  - The abrupt cessation of caffeine consumption can lead to a withdrawal syndrome: headache, feeling of weakness and nervousness
  - These symptoms are only found in some individuals, they are light to moderate and last for only about 24-48 h
  - They are by no means comparable ro those induced by hard drugs (cocaine, amphetamine, morphine or nicotine)
- Arguments against a dependence?
  - There is no tolerance to the central effects of caffeine

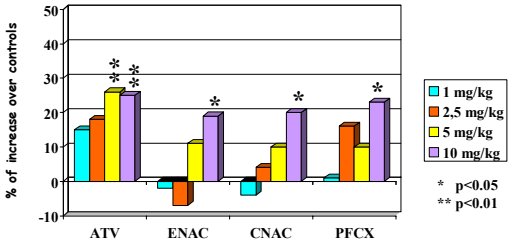
## Are we dependent on coffee and caffeine? (2)

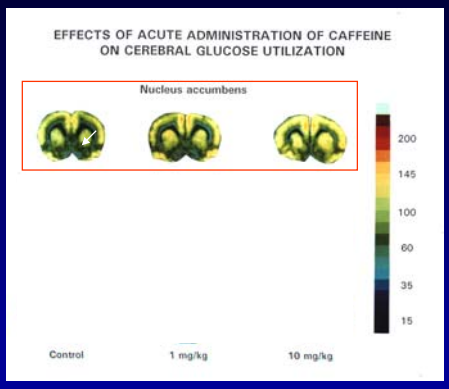
- Characteristics of drugs of dependence (cocaine, amphetamine, morphine, nicotine)
  - specific increase of functional activity in the shell of the nucleus accumbens (NA)
  - induction of the release of dopamine in the shell of the NA
- These two effects are specific and occur at low doses of these drugs: these properties reflect their high addictive potential

## Sagittal section of the rat brain




## Caffeine and dependence




## Are we dependent on coffee and caffeine? (3)

- Conversely to hard drugs, the activation of the shell of the NA by caffeine only occurs at high doses
  - at 10 mg/kg (8-10 cups of coffee in one sitting) and this non specific effect occurs simultaneously to the activation of numerous brain regions
  - these generalized increases in functional activity most likely reflect the negative and aversive effects of the ingestion of high doses of caffeine
- Caffeine does not induce any release of dopamine in the shell of the NA (0.5-5 mg/kg)

## Properties of other constituents of coffee

- Composition of coffee is very complex
  - in addition to caffeine, coffee contains: proteins, minerals, vitamins and a multitude of other compounds
- Phenolic compounds
  - chlorogenic acids: antioxidant properties and cellular detoxification in vitro and in vivo (ongoing research)
- Diterpenes
  - kawheol and cafestol: antioxidant properties and cellular detoxification in vitro and in vivo (ongoing research)

## Conclusions

### Coffee and caffeine

- stimulate locomotion and disturb sleep
- ameliorate mood and performances
- act on headaches and are able to potentiate the effects of analgesic medications
- do not activate the circuits of dependence

### Moderate consumption of coffee and caffeine

- has beneficial effects
- can contribute to a healthy and balanced daily diet