Sex differences in impulsivity

Behavioural Brain Research 200 (2009) 134–143

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

Gender differences in delay-discounting under mild food restriction

Susanne Koot[a,b], Ruud van den Bos[a,*], Walter Adriani[b], Giovanni Laviola[b]

Environmental Health Perspectives • VOLUME 111 | NUMBER 4 | April 2003

Research | Articles

Altered Profiles of Spontaneous Novelty Seeking, Impulsive Behavior, and Response to D-Amphetamine in Rats Perinatally Exposed to Bisphenol A

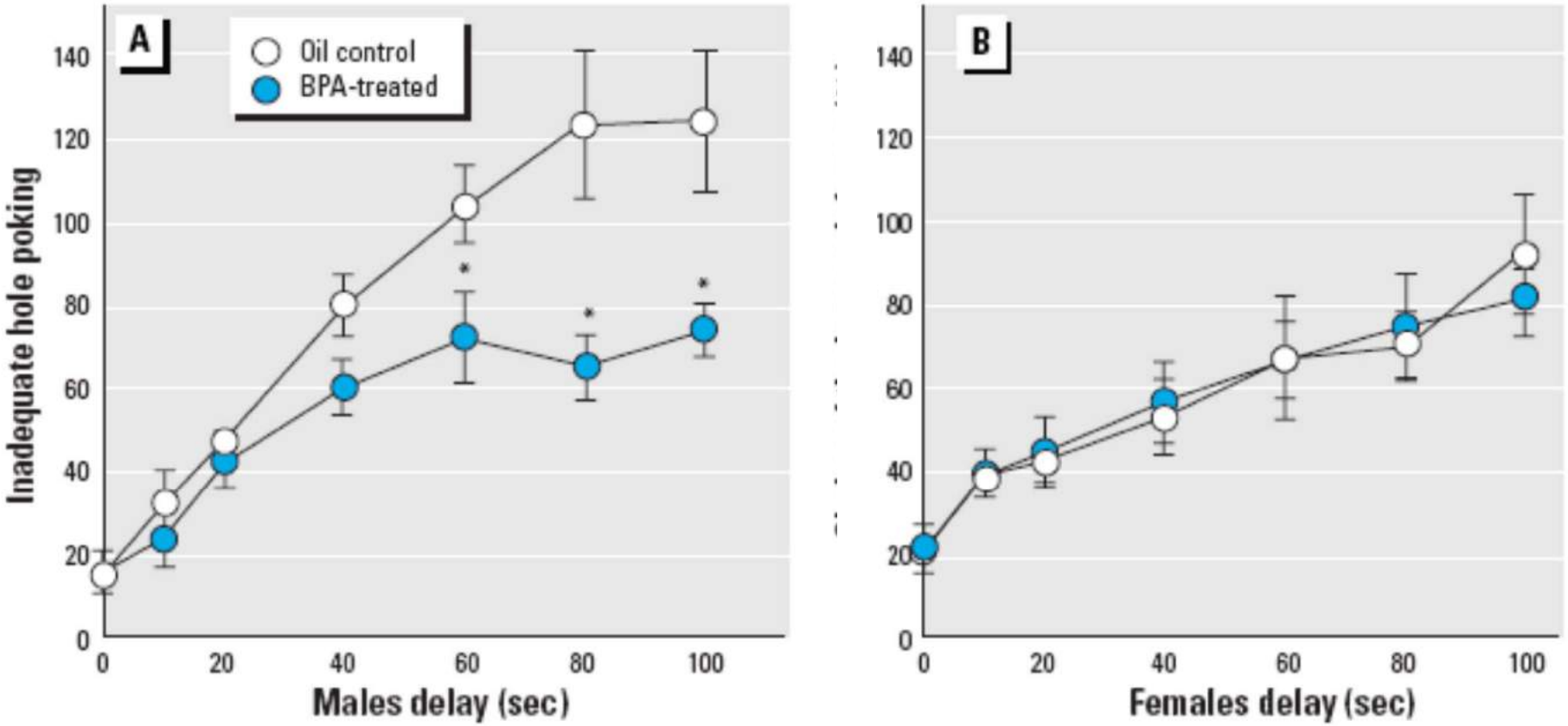
Walter Adriani,[1] Daniele Della Seta,[2] Francesco Dessì-Fulgheri,[3] Francesca Farabollini,[2] and Giovanni Laviola[1]

Environmental Health Perspectives • VOLUME 111 | NUMBER 4 | April 2003

Altered Profiles of Spontaneous Novelty Seeking, Impulsive Behavior, and Response to D-Amphetamine in Rats Perinatally Exposed to Bisphenol A

Walter Adriani,[1] Daniele Della Seta,[2] Francesco Dessì-Fulgheri,[3] Francesca Farabollini,[2] and Giovanni Laviola[1]

Levels of motor impulsivity



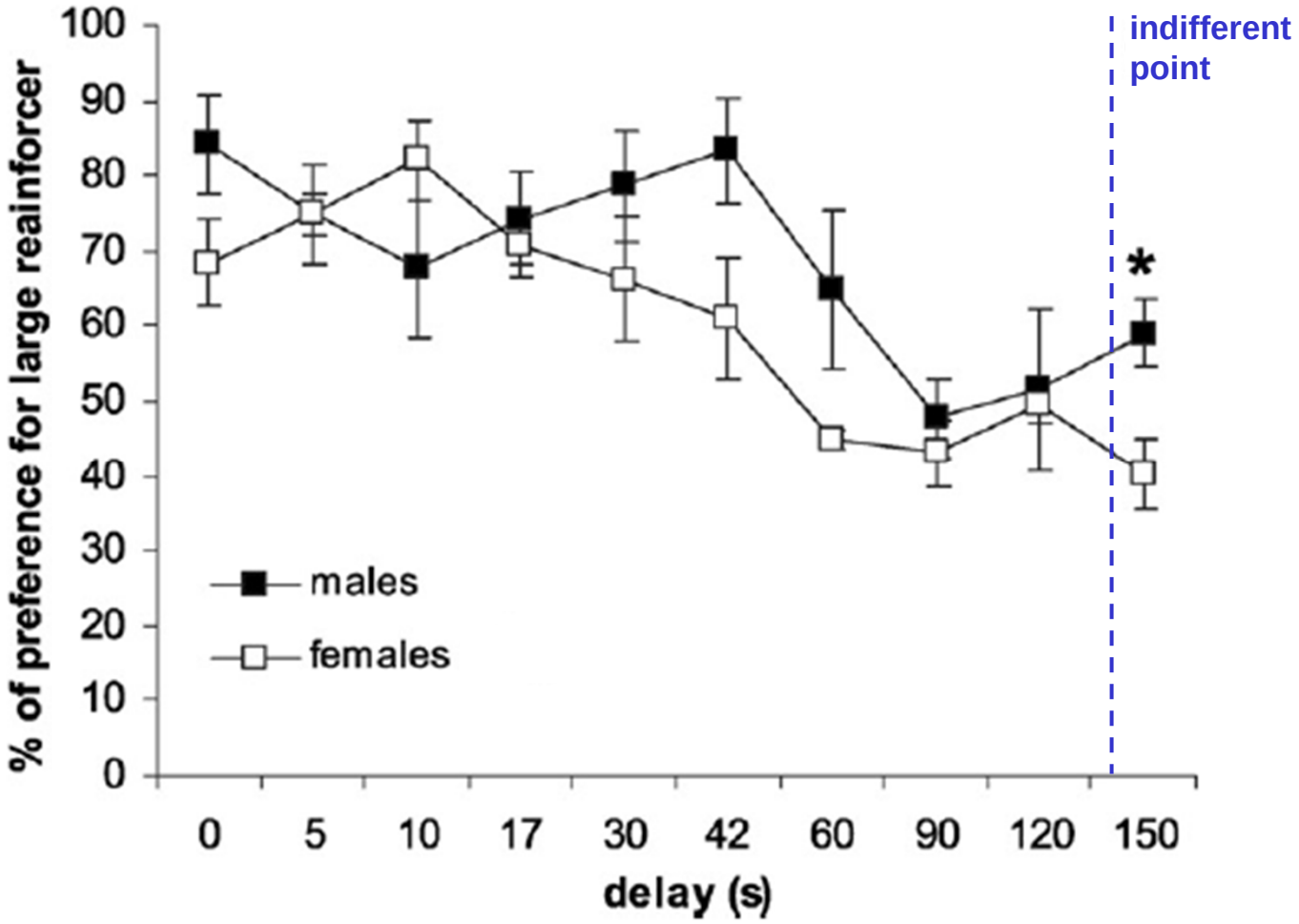
Oil control males are less able than females to inhibit nose poking behaviour during the delay. Interestingly, the profile shown by BPA-treated males is comparable with that expressed by females, suggesting a demasculinization for this measure *(Adriani et al., 2003)*.

Behavioural Brain Research 200 (2009) 134–143

Gender differences in delay-discounting under mild food restriction

Susanne Koot[a,b], Ruud van den Bos[a,*], Walter Adriani[b], Giovanni Laviola[b]

Levels of cognitive impulsivity



Female mice shift towards the economically advantageous option when delays increase earlier than male mice do *(Koot et al., 2009)*.

Sex differences in gambling proneness

Behavioural Brain Research 234 (2012) 375–379

Contents lists available at SciVerse ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Short communication

Male and female Wistar rats differ in decision-making performance in a rodent version of the Iowa Gambling Task

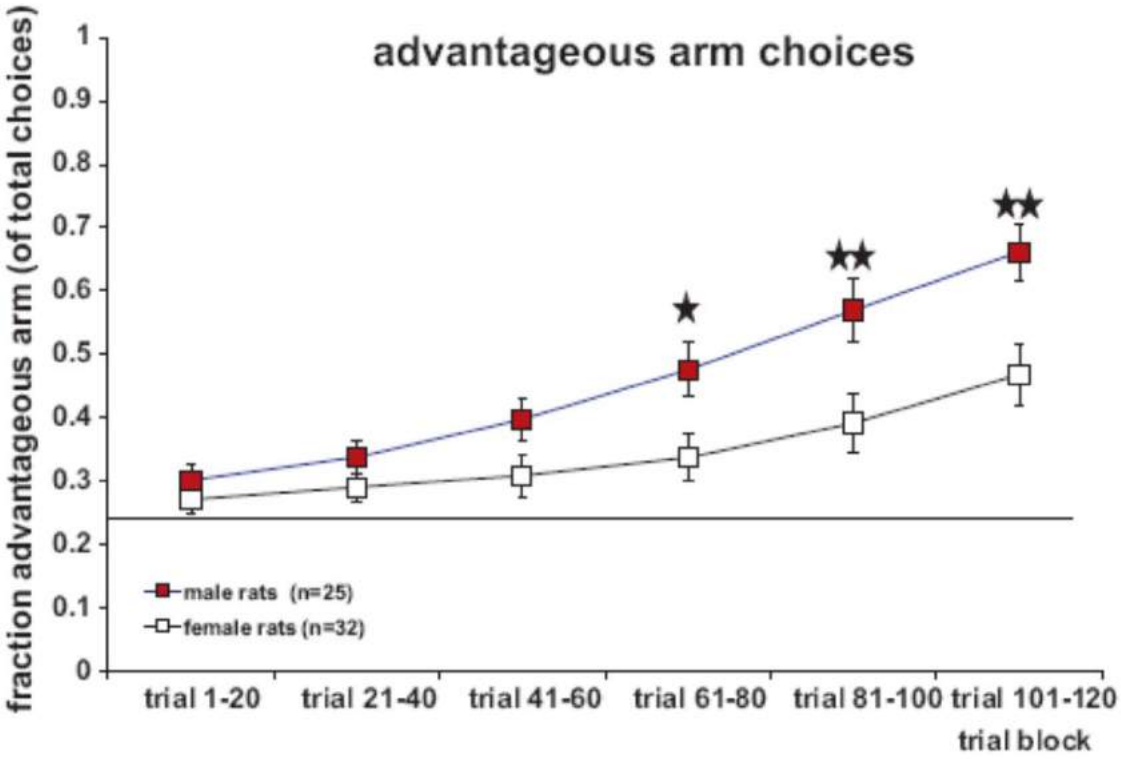
Ruud van den Bos[a,b,*], Jolle Jolles[a,c], Lisette van der Knaap[a], Annemarie Baars[a,d], Leonie de Visser[a,b]

Behavioural Brain Research 234 (2012) 375–379

Male and female Wistar rats differ in decision-making performance in a rodent version of the Iowa Gambling Task

Ruud van den Bos[a,b,*], Jolle Jolles[a,c], Lisette van der Knaap[a], Annemarie Baars[a,d], Leonie de Visser[a,b]

Decision-making performance



As the task progresses male subjects more rapidly chose the best long-term option than female subjects *(van den Bos et al., 2012)*.

Medications used for ADHD treatment: methylphenidate (Ritalin®)

BMC Neuroscience

BioMed Central

Research article

Open Access

Delay aversion but preference for large and rare rewards in two choice tasks: implications for the measurement of self-control parameters

Walter Adriani* and Giovanni Laviola

Neuropsychopharmacology (2006) 31, 1946–1956

www.neuropsychopharmacology.org

Methylphenidate Administration to Adolescent Rats Determines Plastic Changes on Reward-Related Behavior and Striatal Gene Expression

Walter Adriani[1,5], Damiana Leo[2,5], Dario Greco[3], Monica Rea[1], Umberto di Porzio[2], Giovanni Laviola[1] and Carla Perrone-Capano*[,2,4]

[5]Both authors have equally contributed to this work.

ENDURING EFFECT OF ADOLESCENT MPH ADMINISTRATION

Administration of **methylphenidate** (MPH, Ritalin®) may produce its beneficial modulation of impulsive behavior through:

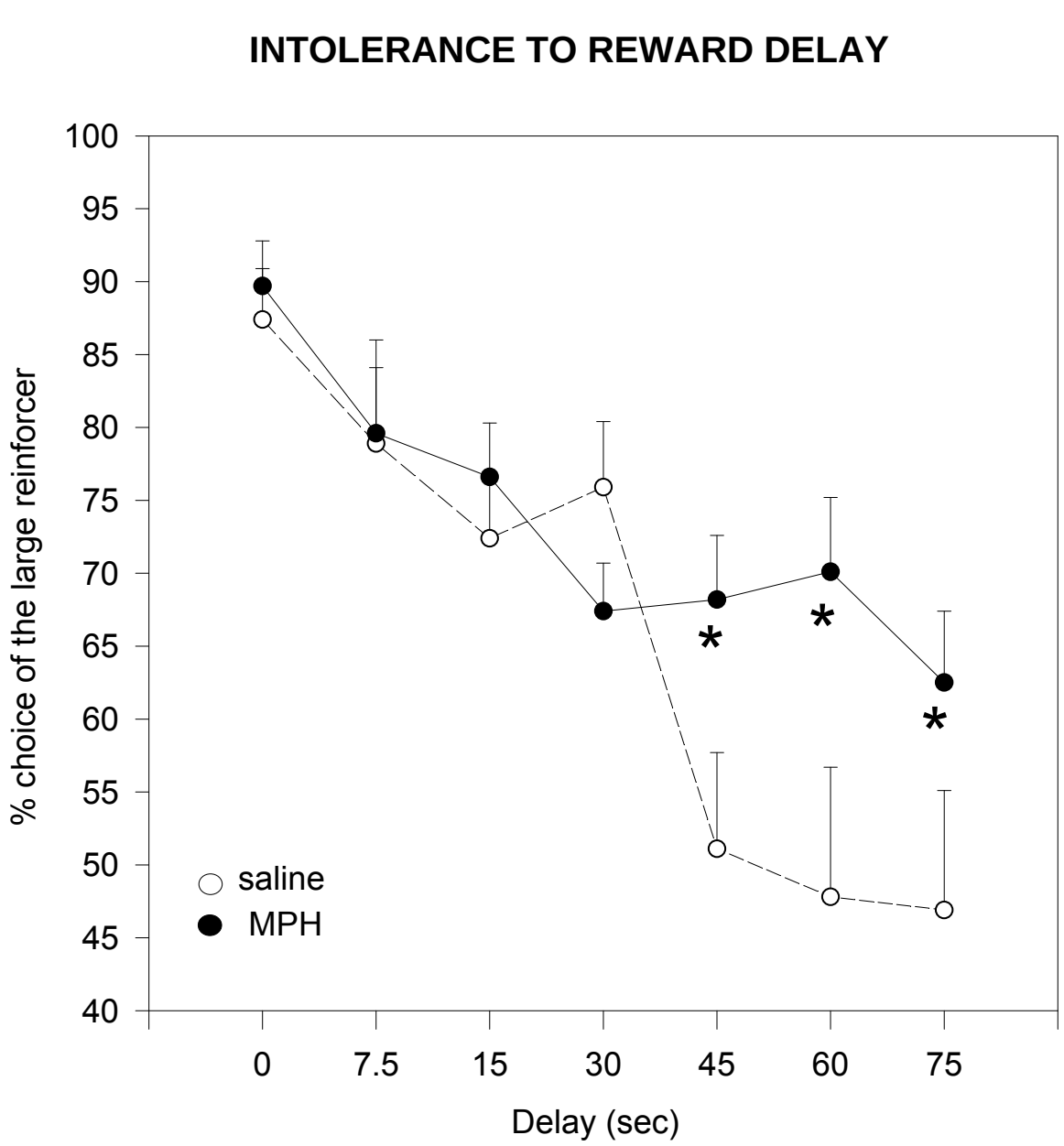
- an enduring **increase** of 5-HT(7) neurotransmission.

- enduring functional changes within **fronto-striatal circuits**.

EXPERIMENTAL DESIGN

Adolescent rats (30- to 44-day-old) were administered MPH (2 mg/kg i.p.) or saline for 14 days, and were tested when adult for :

1) MPH-induced changes in impulsivity (intolerance to delay)
2) blockade of MPH effects with a 5-HT(7) antagonist
3) reproduction of MPH-like effects with a 5-HT(7) agonist (ongoing)
4) magnetic resonance: spectrometry, DTI, fMRI connectivity (ongoing)



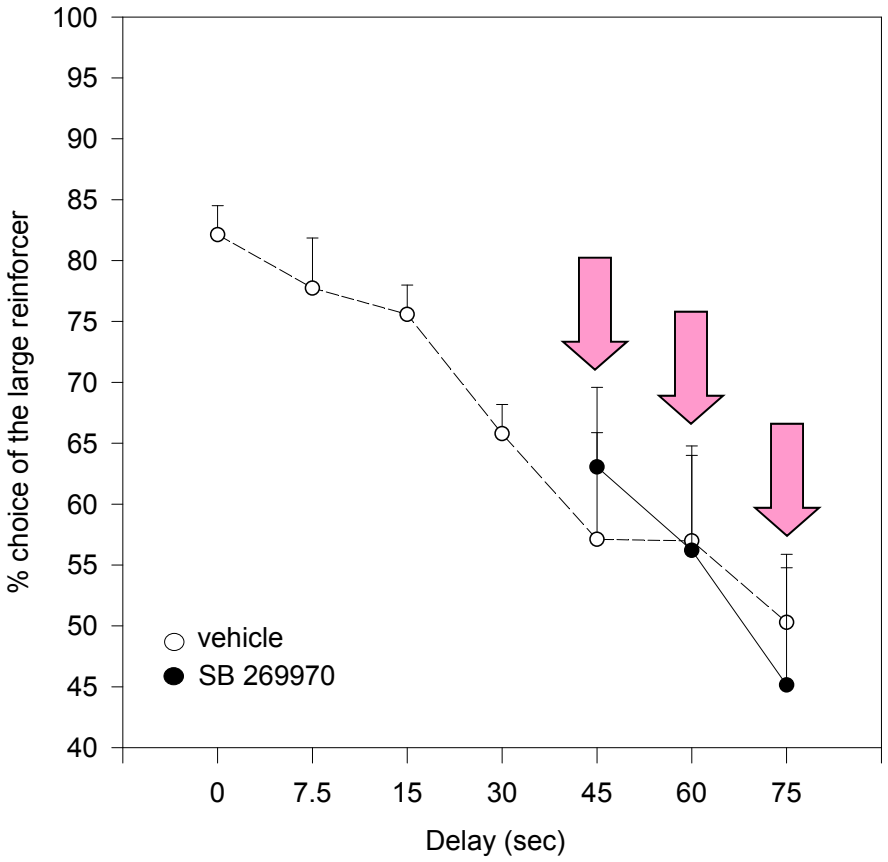
LONG-TERM EFFECT of MPH

RATS TESTED DURING ADULTHOOD, ONE MONTH AFTER MPH PRETREATMENT

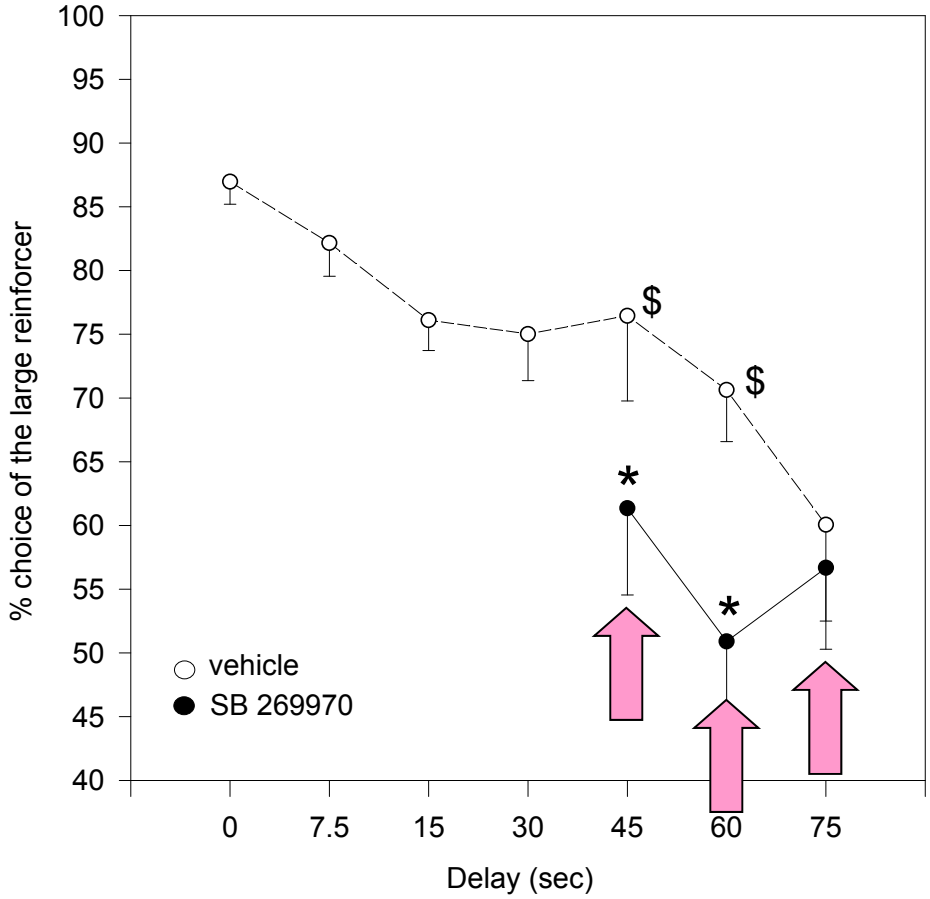
tolerance to delay
= lower impulsivity

the BLOCKADE of MPH-INDUCED LONG-TERM EFFECT with acute administration of the 5-HT(7) selective antagonist

PRE-EXPOSED TO SALINE DURING ADOLESCENCE



PRE-EXPOSED TO MPH DURING ADOLESCENCE



Lentiviral manipulation of DAT expression

Neuroscience 159 (2009) 47–58

INCREASED IMPULSIVE BEHAVIOR AND RISK PRONENESS FOLLOWING LENTIVIRUS-MEDIATED DOPAMINE TRANSPORTER OVER-EXPRESSION IN RATS' NUCLEUS ACCUMBENS

W. ADRIANI,[a1] F. BOYER,[b1] L. GIOIOSA,[a] S. MACRÌ,[a]
J.-L. DREYER[b] AND G. LAVIOLA[a]*

[1] Both authors contributed equally to this work.

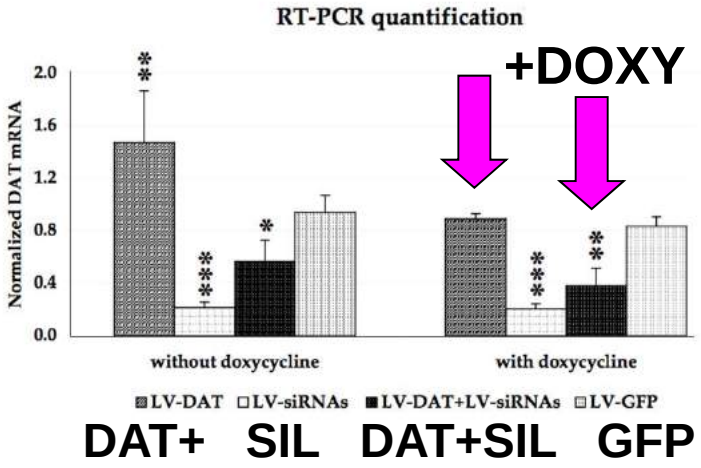
International Journal of Neuropsychopharmacology (2010), **13**, 1329–1342. Copyright © CINP 2010
doi:10.1017/S1461145709991210

Social withdrawal and gambling-like profile after lentiviral manipulation of DAT expression in the rat accumbens

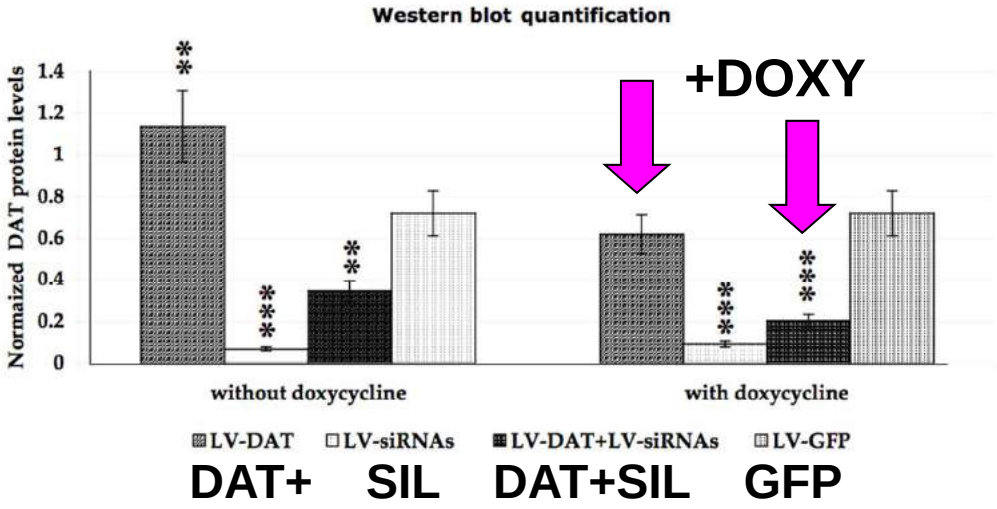
Walter Adriani[1]*, Frederic Boyer[2]*, Damiana Leo[3], Rossella Canese[1], Franca Podo[1], Carla Perrone-Capano[3,4], Jean-Luc Dreyer[2] and Giovanni Laviola[1]

* These authors contributed equally to this work.

MODEL of IMPULSIVITY / GAMBLING



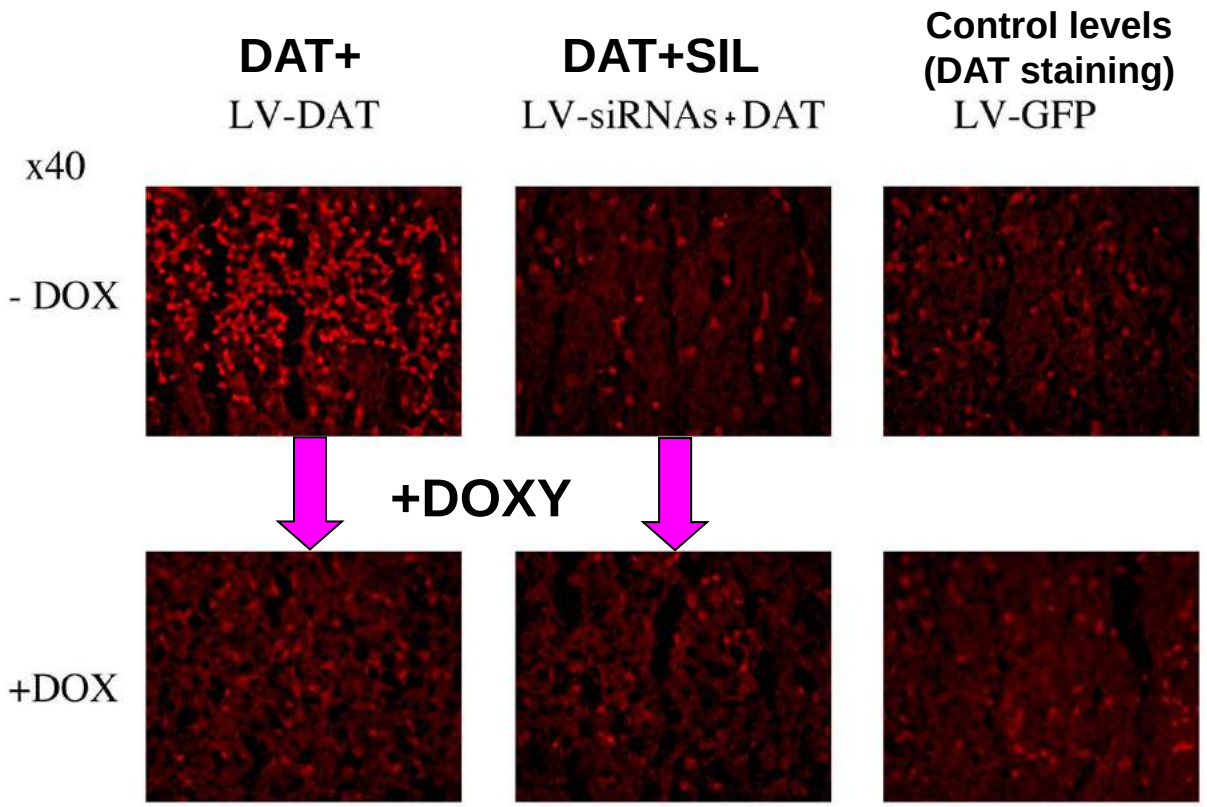
DAT mRNA and protein levels, extracted from the NAcc of rats inoculated with lentivirus vectors.



Doxy switches-off DAT enhancer :

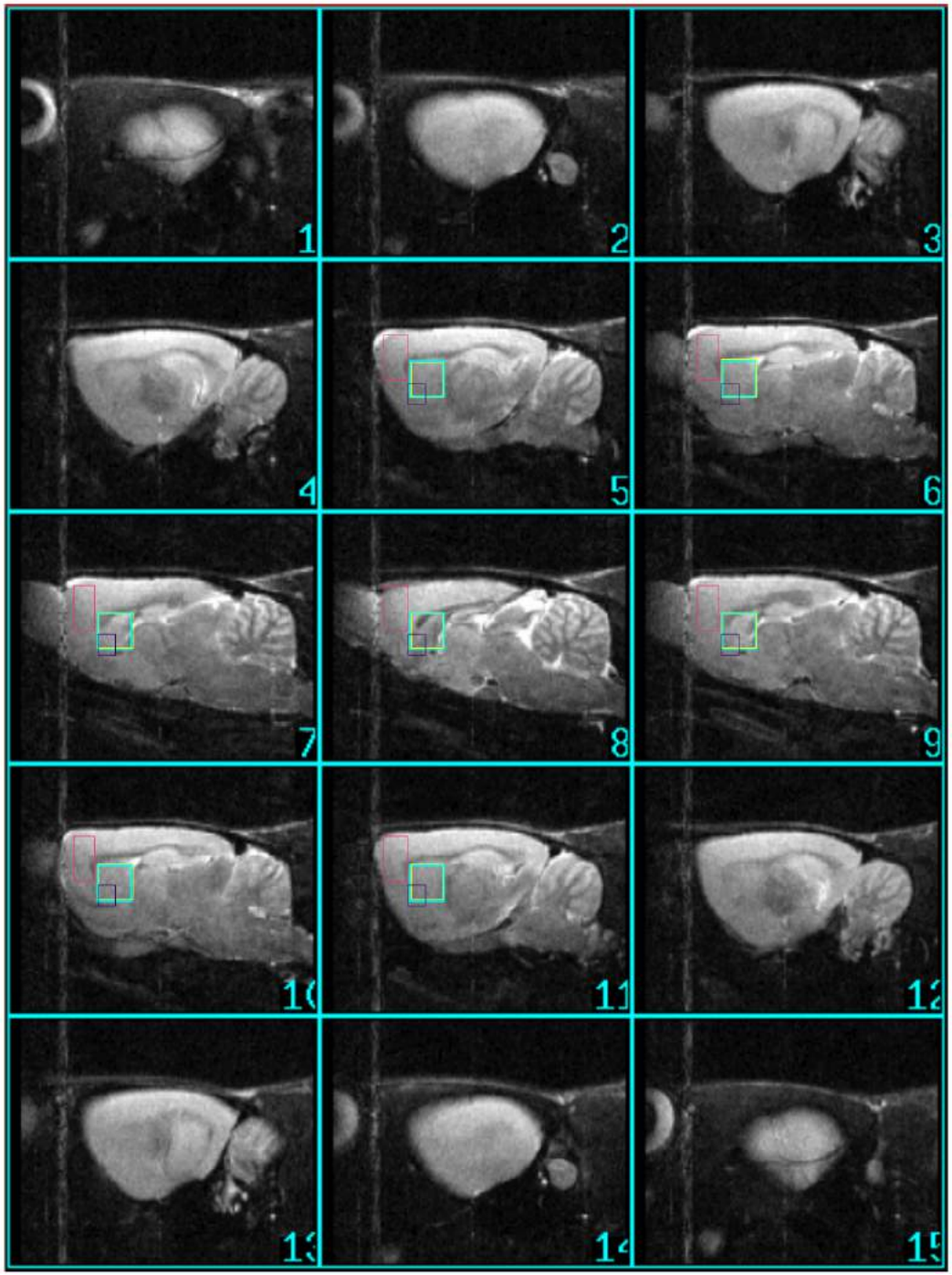
DAT+SIL rats face **strong** silencing.

MODEL of IMPULSIVITY / GAMBLING



Efficacy of lentiviruses inoculated in the NAcc of rats: Lenti-DAT with or without Lenti-DAT-siRNAs.

Adriani W, Boyer F, Gioiosa L, Macrì S, Dreyer J-L, Laviola G (2009) Neuroscience, 159: 47-58.



MAGNETIC RESONANCE SPECTROSCOPY

Data obtained at:
Molecular and Cellular Imaging division at ISS
(dr R. Canese)

Dorsal Striatum
Nucleus Accumbens
Prefrontal Cortex

MAGNETIC RESONANCE SPECTROSCOPY

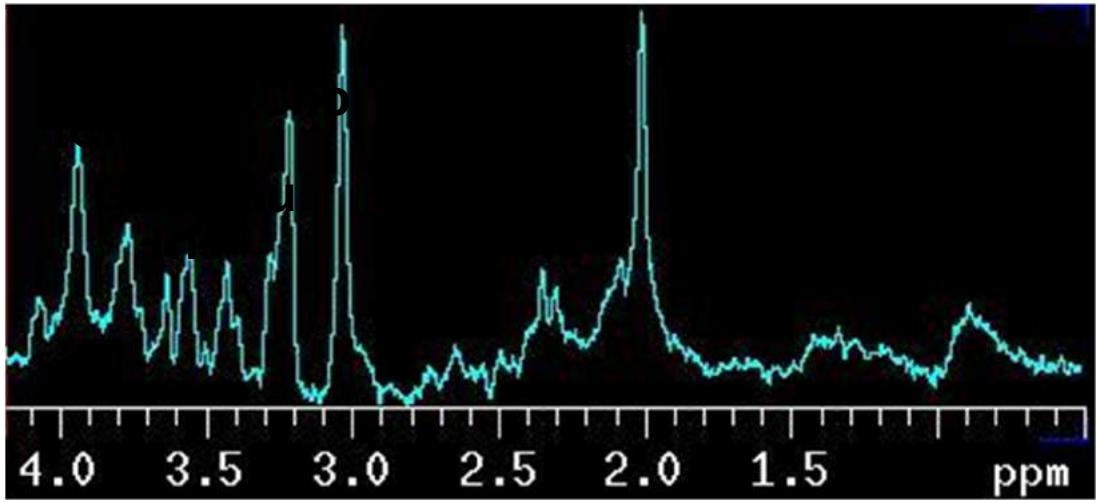
in: striatum, n. accumbens, prefrontal cortex

The major metabolites can be reliably detected in selected voxels.

tCr/PCr= total / phospho- creatine ***tCho = total choline***

NAA = N-acetyl-aspartate ***Glx = glutamine + glutamate***

Tau = taurine ***Ins = inositols phosphates***



MAGNETIC RESONANCE SPECTROSCOPY

in: striatum, n. accumbens, prefrontal cortex

Metabolic parameters in the dStr and the NAcc of adult male rats (n=6) with previous inoculation of lentiviral vectors (DAT+ and/or SIL) into the NAcc.

Dorsal Striatum	**PCr/tot (%)**	**Phospho-creatine**	**Total creatine**
GFP control	**65.4±3.4 %**	**6.29±0.54**	**9.86±0.41**
DAT+	**63.0±2.7 %**	**6.60±0.30 ***	**10.46±0.10 ***
SIL	**64.8±2.6 %**	**6.24±0.52**	**9.57±0.46**
DAT+SIL	**65.5±2.1 %**	**6.97±0.35 ***	**10.62±0.29 ***
N. Accumbens	**PCr/tot (%)**	**Phospho-creatine**	**Total creatine**
GFP control	**64.3±1.5 %**	**6.49±0.17**	**10.10±0.26**
DAT+	**67.5±2.3 %**	**6.72±0.27**	**9.96±0.22**
SIL	**59.7±3.4 % ***	**5.63±0.44 ***	**9.56±0.26**
DAT+SIL	**59.1±3.6 % ***	**5.84±0.32 ***	**9.80±0.26**

Levels of metabolites given in arbitrary units, referred to the unsuppressed water signal. (*) $p < .05$ compared to GFP control rats. Only DAT+SIL rats display changes in both areas.

OPERANT BEHAVIOUR and MR SPECTROSCOPY

Role of dorsal striatum *vs* n. accumbens in self-control

Interestingly, **total creatine** and/or **phospho-creatine** (*bioenergetic metabolites*) were **up-regulated** in the **dStr** and conversely **down-regulated** in the **NAcc** of DAT+SIL rats. The unbalanced influence by these two areas on behavioural output does generate **impulsivity and/or risk-proneness**.

Consistent with the functional role of these two forebrain areas, DAT+SIL animals may display *an enhancement in their coping* ability via **novel behavioural strategies** (**dStr**), and to be *less driven by attractiveness of* reward, or by salient contingencies like *immediacy or binging* - i.e. by **instinct** (**NAcc**).

Lentiviral manipulation of SERT expression

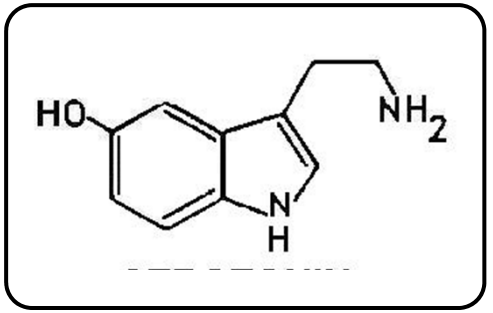
Impulsivity and home-cage activity are decreased by lentivirus-mediated silencing of serotonin transporter in the rat hippocampus

---

Zoratto F., Laviola G., Adriani W.

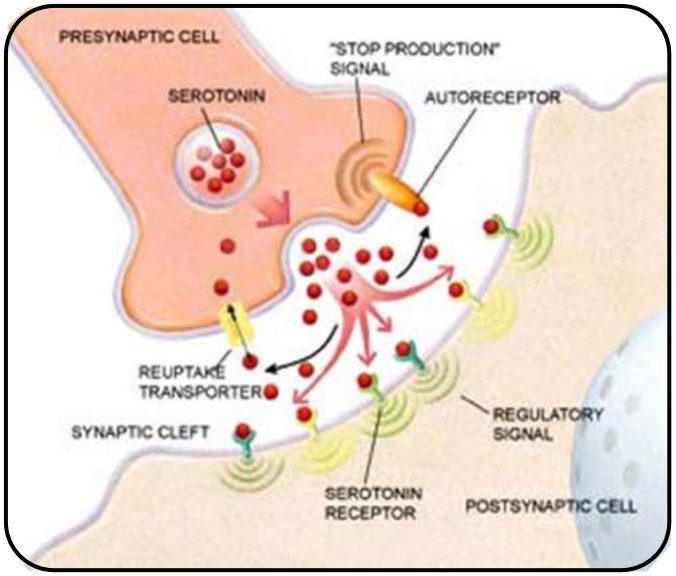
Neuroscience Letters (submitted)

Serotonin (5-HT)



- The serotonergic system is well known for modulation of emotional, cognitive and motivational processes
- Serotonin (5-HT) has a key role in the top-down inhibitory control over behavioural initiation, which is important for withholding of instinctive reactions and for an appropriate feedback regulation of behaviour
- Deficits in the homeostasis of this system play a crucial role in many psychiatric disorders, including affective and impulse-control disorders

Serotonin transporter (SERT)



- SERT, which selectively removes 5-HT out of the synaptic cleft, is a major determinant of serotonergic signalling efficiency
- mutations in the SERT gene promoter do influence the rate of 5-HT reuptake and have been associated with susceptibility towards the development of several psychiatric disorders
- the s-variant of the 5-HTTLPR is associated with reduced SERT gene transcription efficiency, resulting in reduced SERT levels and reduced 5-HT uptake; consequently, the extracellular levels of 5-HT are higher compared to the l-variant

Experimental subjects

❖ **spontaneous locomotor activity:**

- adult male rats
- inside the home-cage, 50 days after inoculation
- continuous automatic registration (15 days) using infrared sensors (20 Hz)
- mean day calculated on 5-days intervals

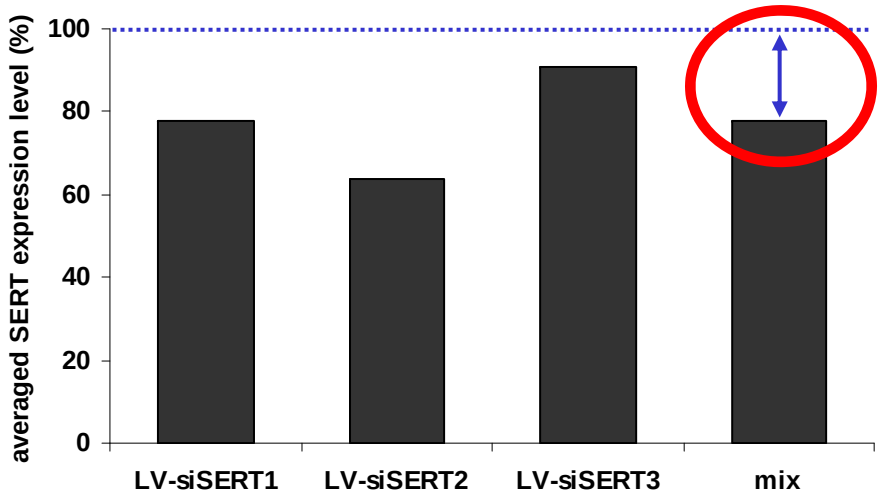
❖ **Intolerance to Delay (ID) task:**

- tested in classical operant chambers during the dark phase of the cycle
- mild food restriction
- testing: 8 days, 1 session per day (40 min), timeout 30 s

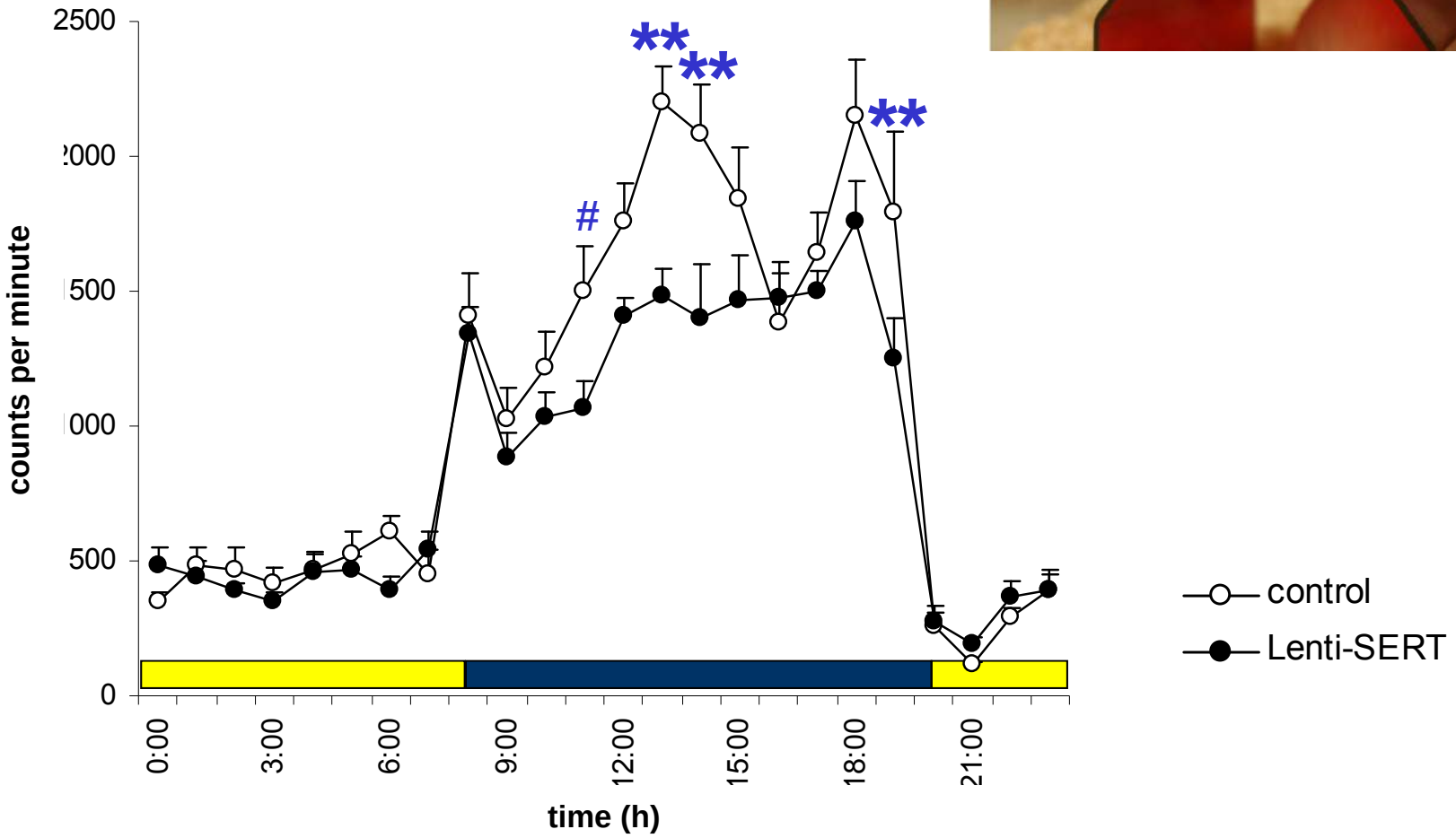
Experimental groups

- **Lenti-SERT** (n=11): inoculation of active lentiviruses
- **control** (n=6): inoculation of heat-inactivated lentiviruses
- bilateral inoculation (volume 1 µl) in the hippocampus; coordinates AP −3.3, ML ±2.0, DV −4.0

In-vitro quantification of SERT silencing

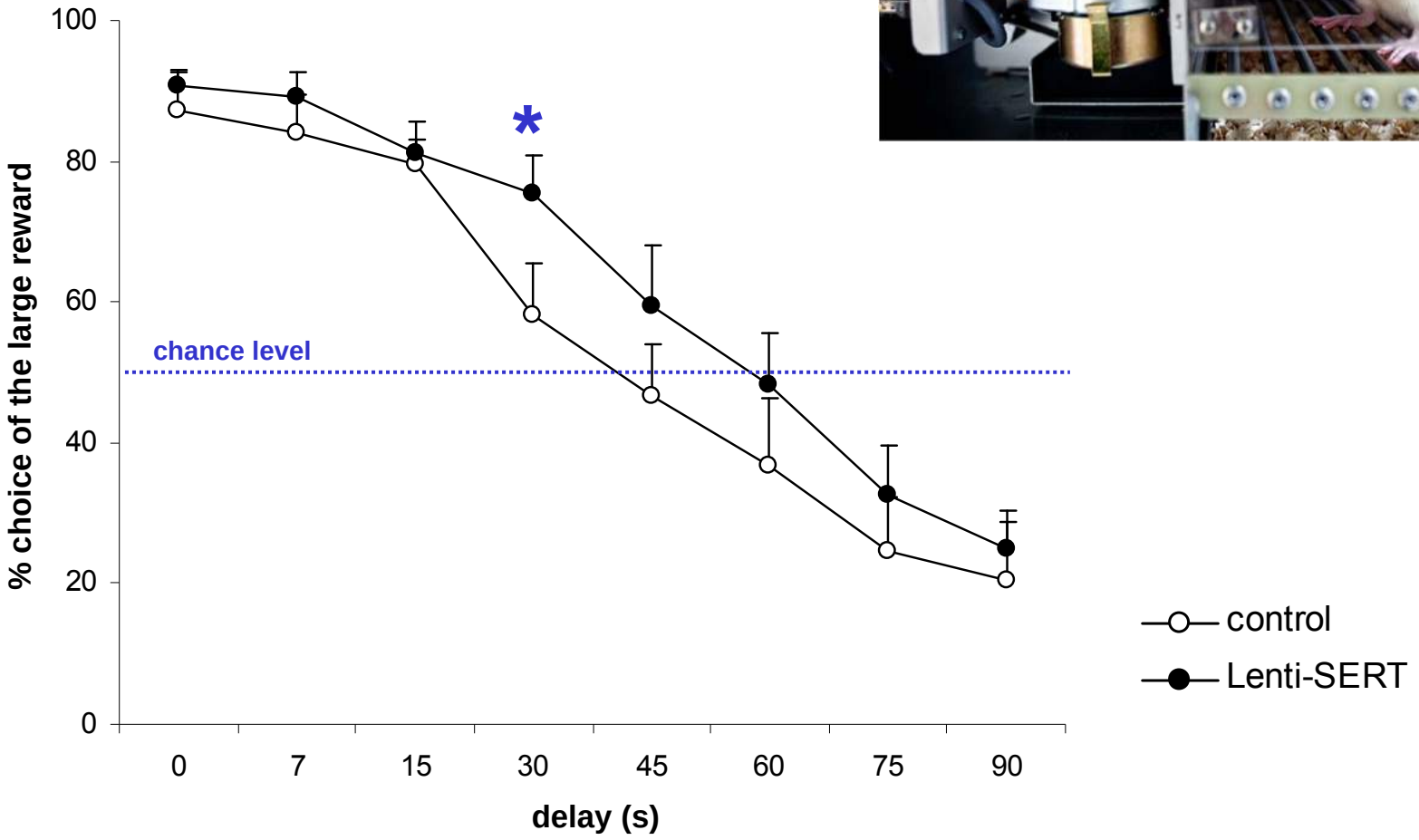


Spontaneous locomotor activity inside the home-cage



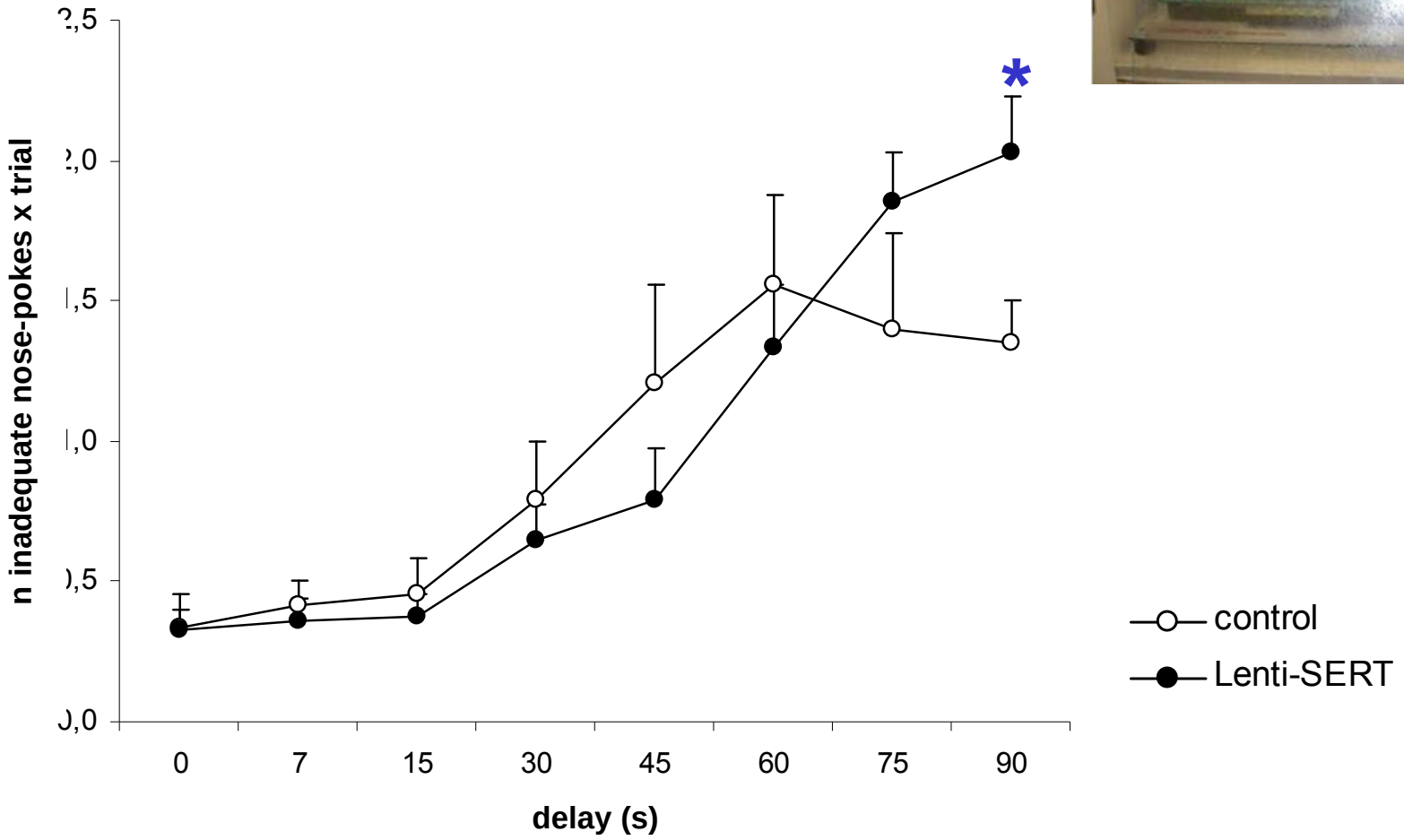
** P < 0.01; # 0.05 < P < 0.1 when comparing Lenti-SERT vs control rats in post-hoc test

Levels of cognitive impulsivity



*** P < 0.05 when comparing Lenti-SERT vs control rats in post-hoc test**

Levels of motor impulsivity



*** P < 0.05 when comparing Lenti-SERT vs control rats in post-hoc test**

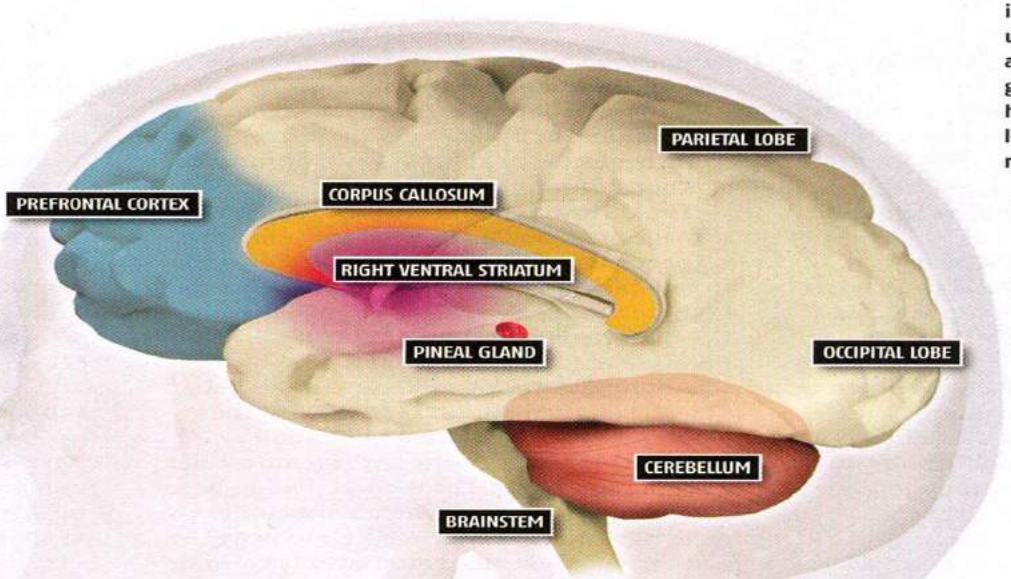
Age differences in humans

Prefrontal cortex

The prefrontal cortex is the home of "executive" functioning, high-level cognitive processes that, among other things, allow us to develop detailed plans, execute them, and block irrelevant actions.

This area undergoes a bulking up between the ages of 10 and 12, followed by a dramatic decline in size that continues into the early 20s. This is probably due to a burst of neuronal growth followed by a "pruning" stage in which pathways that are not needed are lost.

If the adolescent's brain is still bedding down its executive functions, this might help explain why teenagers can sometimes seem so disorganised and irrational.



Corpus callosum

These are nerve fibres linking the left and right sides of the brain.

The parts thought to be involved in language learning undergo high growth rates before and during puberty, but this growth then slows. This might help explain why the ability to learn new languages declines rapidly after the age of 12.

Right ventral striatum

This area of the brain is thought to be involved in motivating reward-seeking behaviour.

A study last year showed that teenagers had less activity than adults in this part of the brain during a reward-based gambling game. The researchers speculate that teens may be driven to risky but potentially high-reward behaviours such as shoplifting and drug-taking because this area is underactive.

Pineal gland

The pineal gland produces the hormone melatonin, levels of which rise in the evening, signalling to the body that it is time to sleep.

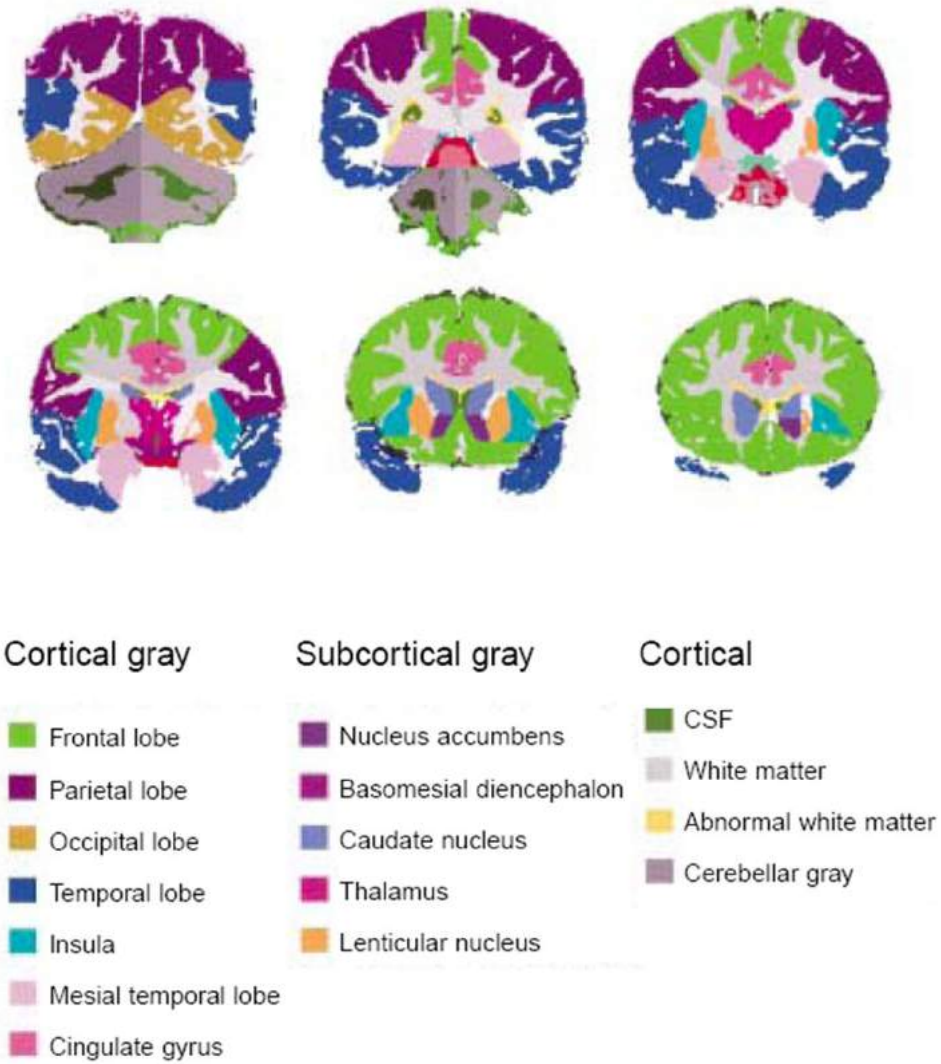
During adolescence melatonin peaks later in the day than in children or adults. This could be why teenagers tend to be so fond of late nights and morning lie-ins.

Cerebellum

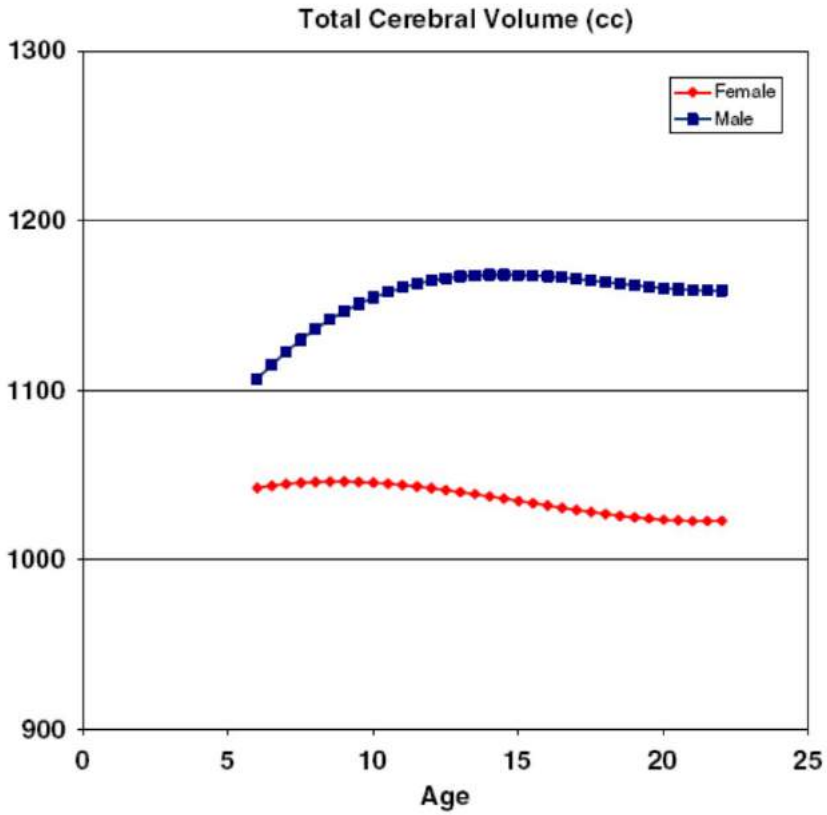
This part of the brain continues to grow until late adolescence. It governs posture and movement, helping to maintain balance and ensure that movements are smooth and directed. It influences other regions of the brain responsible for motor activity and may also be involved in language and other cognitive functions.

New Scientist (5 March 2005)

Sex differences in humans: anatomical MRI



Fully processed images from one 8-year-old female participant *(Sowell et al., 2002)*.

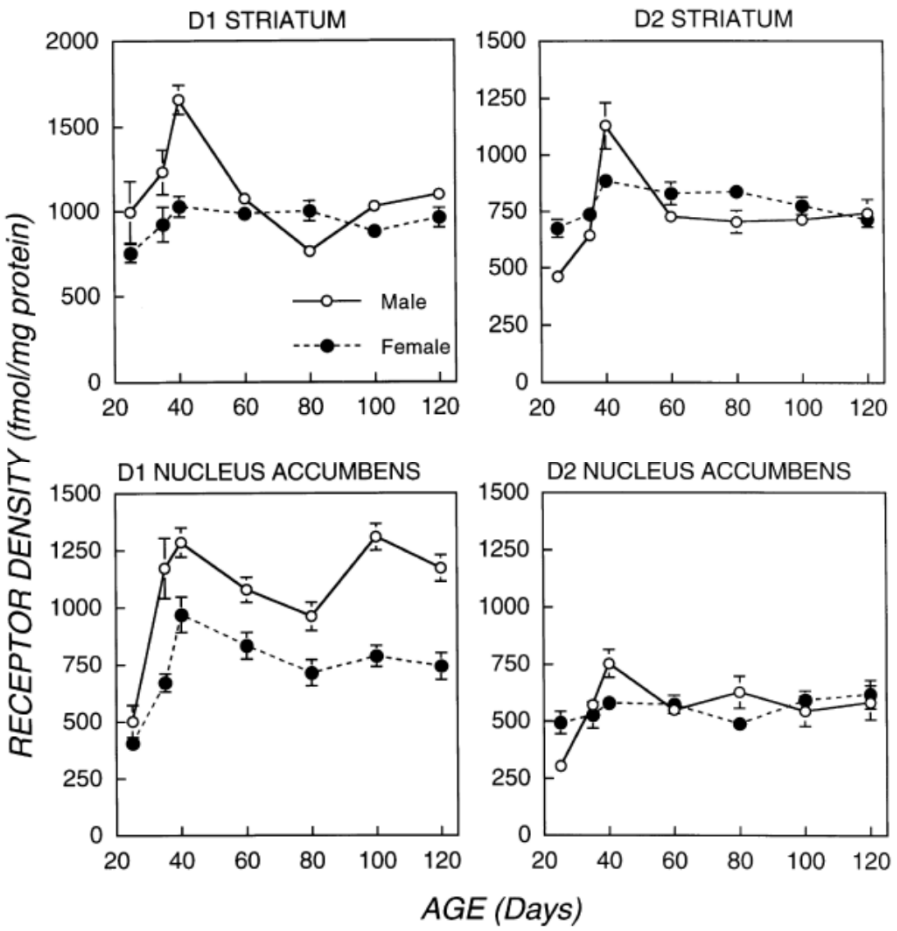


Total cerebral volume peaks at 14.5 years in males and 11.5 years in females.

Male brains are approx. 9% larger than those of females. This difference is statistically significant, even when controlling for height and weight *(Lenroot & Giedd, 2006)*.

Sex differences in dopamine receptors: density

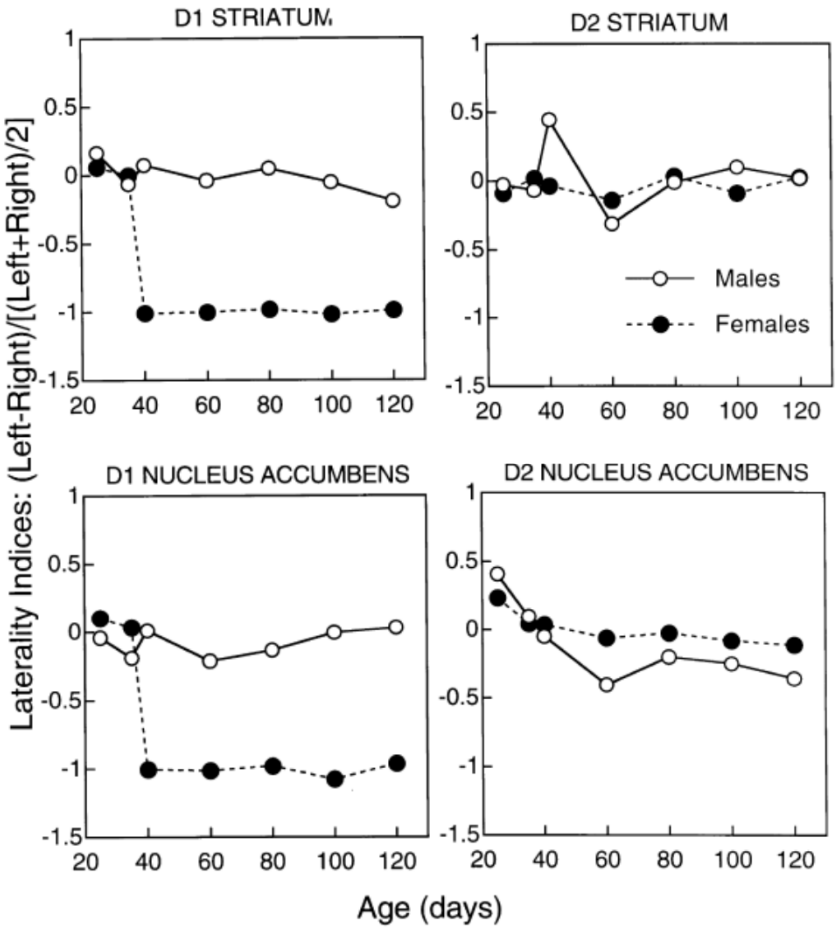
Density of D1 and D2 receptors in male and female rats between 25 and 120 days of age in the striatum and nucleus accumbens.



Males and females differed markedly in their pattern of dopamine receptor development in striatum and nucleus accumbens *(Andersen & Teicher, 2000)*.

Sex differences in dopamine receptors: laterality

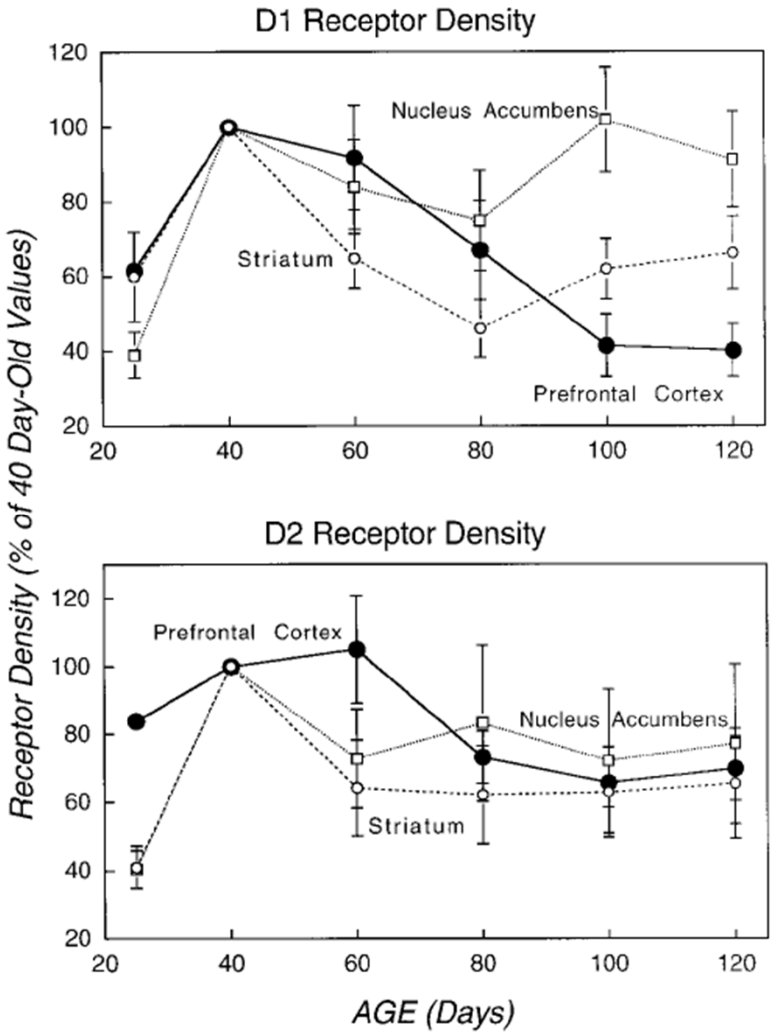
Laterality indices for D1 and D2 receptors in male and female rats between 25 and 120 days of age in the striatum and nucleus accumbens.



These data show the pronounced lateralization of D1 dopamine receptors for females, and the transient expression of D2 receptor lateralization in male striatum at 40 days of age *(Andersen & Teicher, 2000)*.

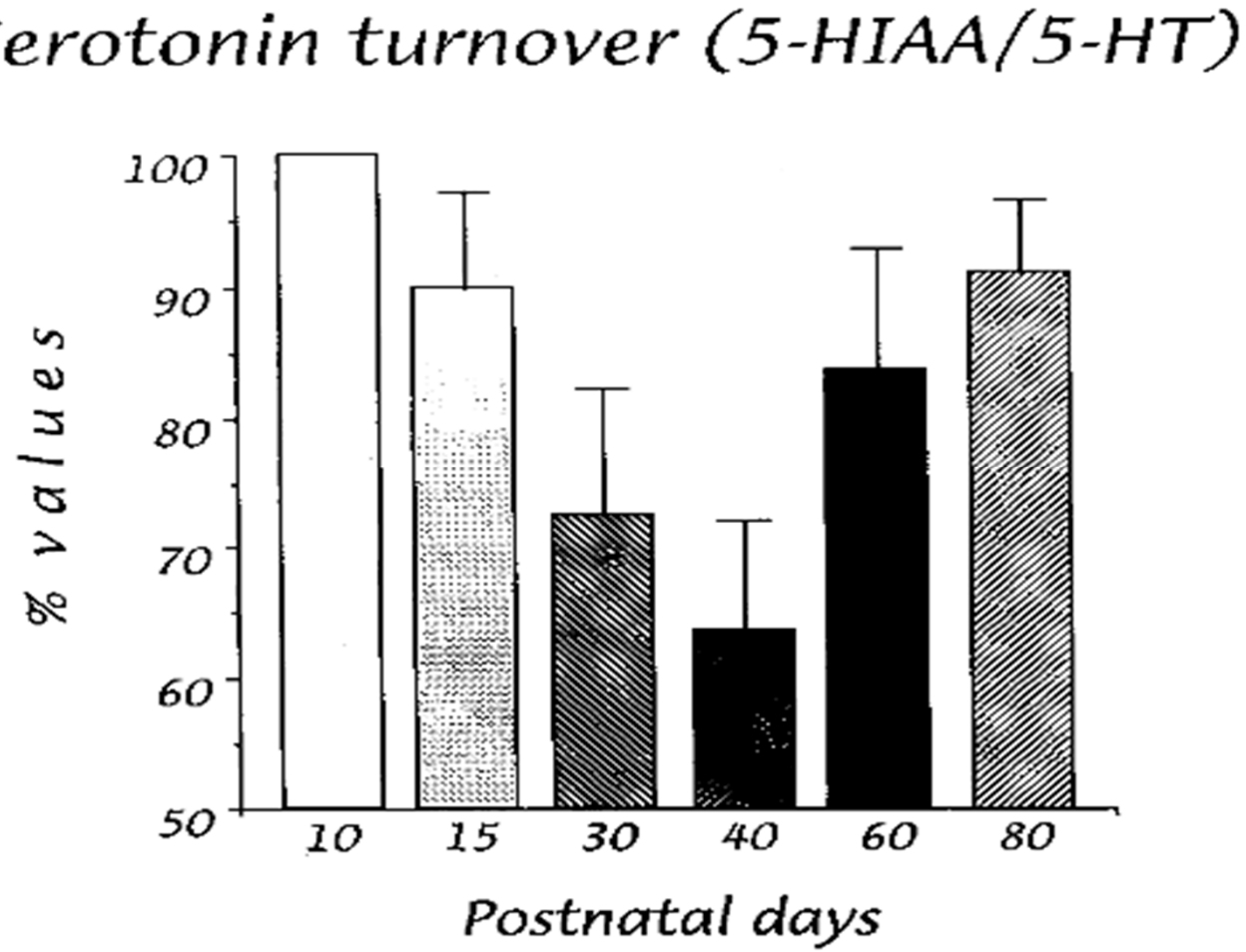
Age differences in dopamine receptors: density

Developmental changes in the density of D1 and D2 receptors from weanling (25 days of age) to the onset of puberty (40 days of age) to full adulthood (120 days) in male rats.

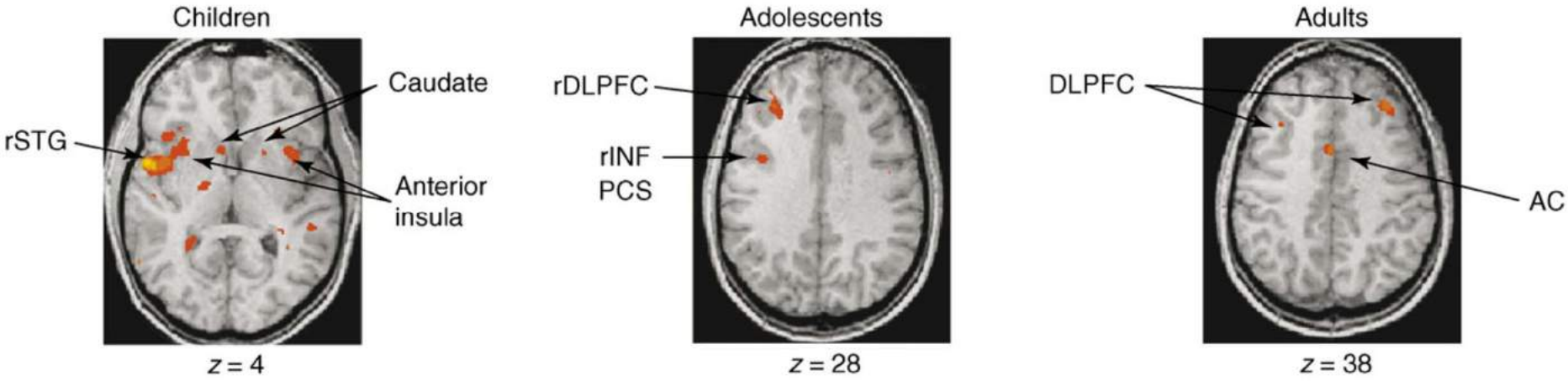


- Marked reduction in the density of D1 and D2 receptors in the prefrontal cortex and striatum between 40 and 120 days of age.
- The pattern of receptor elimination is similar, although more extensive and protracted in prefrontal cortex.
- The nucleus accumbens shows minimal evidence of receptor elimination.

(Andersen & Teicher, 2000)


Serotonin turnover (5-HIAA/5-HT)
% values
100
90
80
70
60
50
10
15
30
40
60
80
Postnatal days

Developmental shifts in the location of active voxels during performance of a visuospatial working memory



The three group-averaged functional maps of percentage signal change illustrate differences in both the magnitude and extent of activation.

Children showed strongest activation bilaterally in the caudate nucleus, the thalamus and the anterior insula. Adolescents showed strongest activation in the right dorsolateral prefrontal cortex (DLPFC), and adults showed concentrated activation in the left prefrontal and posterior parietal regions *(Bunge & Wright, 2007)*.

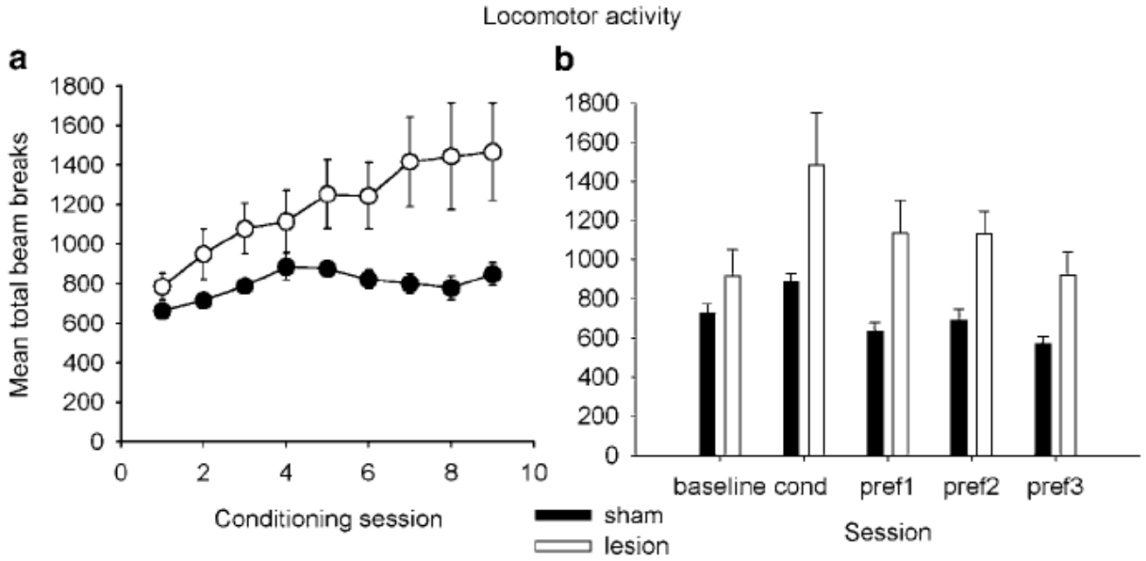
Depletion of forebrain 5-HT levels by means of ICV infusions of the serotonergic neurotoxin 5,7-dihydroxytryptamine

Neuropsychopharmacology (2004) 29, 1331–1343

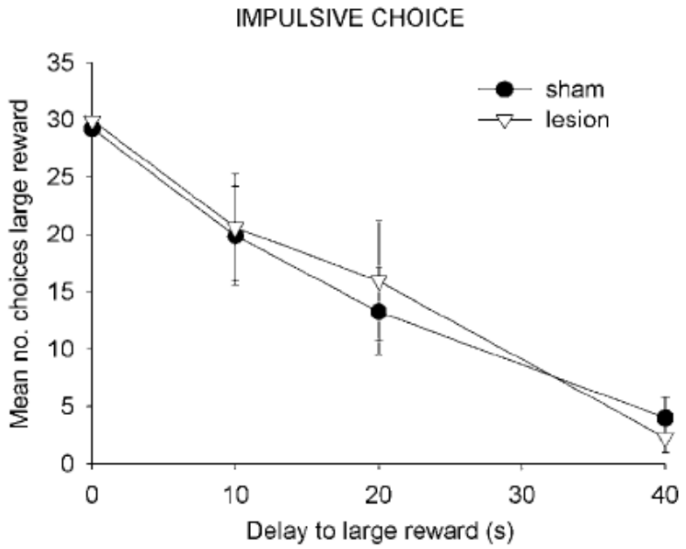
www.neuropsychopharmacology.org

Fractionating Impulsivity: Contrasting Effects of Central 5-HT Depletion on Different Measures of Impulsive Behavior

Catharine A Winstanley*[,1], Jeffrey W Dalley[1], David EH Theobald[1] and Trevor W Robbins[1]



(a) Effects of reducing 5-HT levels in the central nervous system on the acquisition of **conditioned locomotor activity** and **(b)** effects of prefeeding prior to conditioning sessions *(Winstanley et al., 2004)*.



Lack of effect of the same manipulation on **delay-discounting** *(Winstanley et al., 2004)*.

Neonatal serotonin depletion

Psychoneuroendocrinology (2013) 38, 24–39

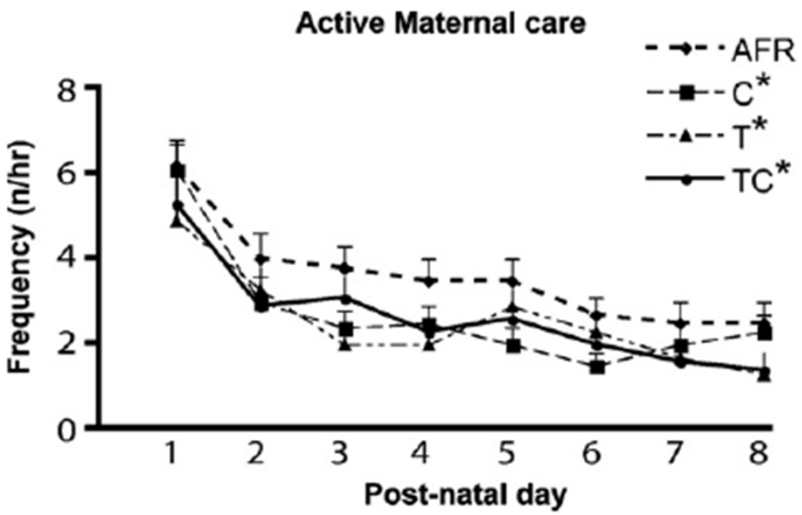
Available online at www.sciencedirect.com

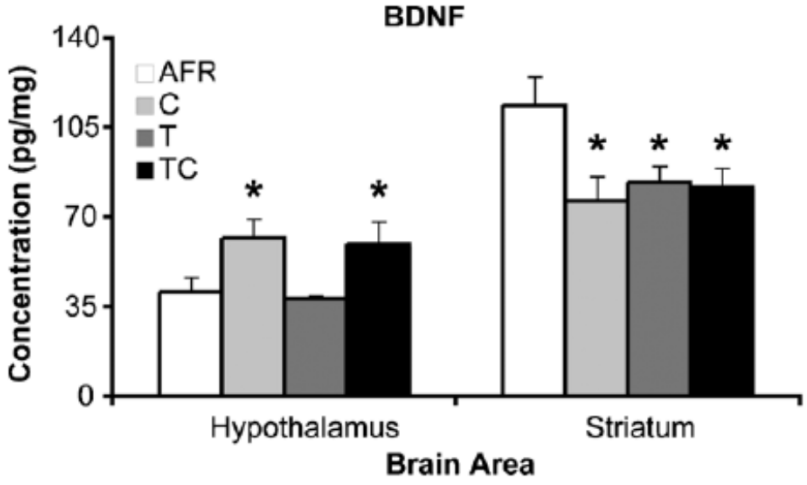
SciVerse ScienceDirect

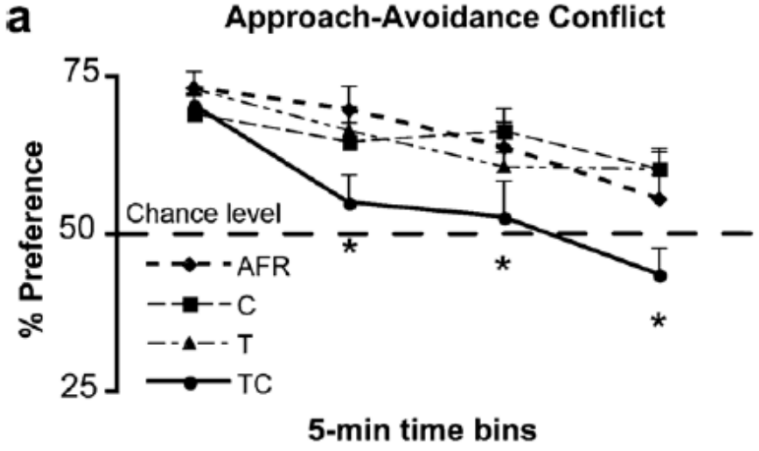
journal homepage: www.elsevier.com/locate/psyneuen

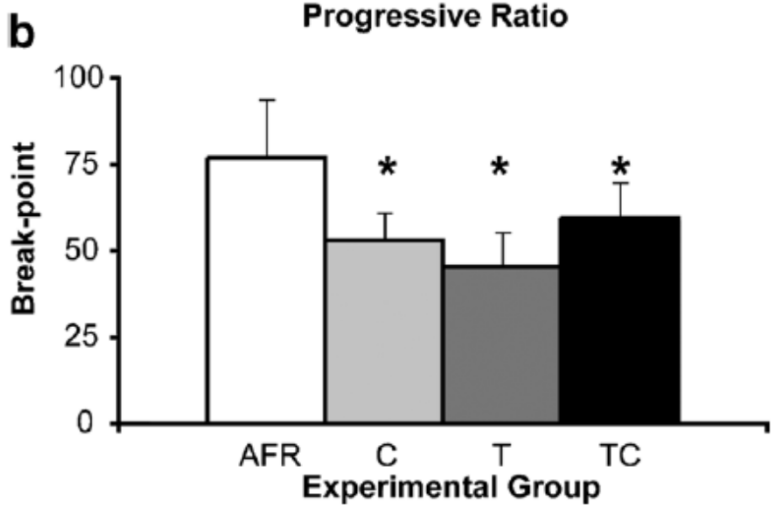
Neonatal tryptophan depletion and corticosterone supplementation modify emotional responses in adult male mice

Francesca Zoratto [a], Marco Fiore [b,c], Syed F. Ali [d], Giovanni Laviola [a], Simone Macrì [a,*]


Active Maternal care
AFR
C*
T*
TC*
Frequency (n/hr)
0
2
4
6
8
1
2
3
4
5
6
7
8
Post-natal day


BDNF
AFR
C
T
TC
Concentration (pg/mg)
0
35
70
105
140
Hypothalamus
Striatum
Brain Area


a
Approach-Avoidance Conflict
% Preference
75
50
25
Chance level
AFR
C
T
TC
5-min time bins


b
Progressive Ratio
Break-point
0
25
50
75
100
AFR
C
T
TC
Experimental Group

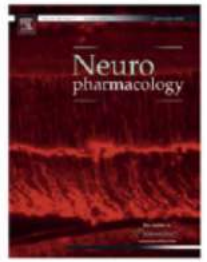
Dietary serotonin depletion

Neuropharmacology 62 (2012) 1640–1650

Contents lists available at SciVerse ScienceDirect

Neuropharmacology

journal homepage: www.elsevier.com/locate/neuropharm



Compromised decision-making and increased gambling proneness following dietary serotonin depletion in rats☆

S. Koot [a,b,c,1], F. Zoratto [a,1], T. Cassano [d], R. Colangeli [e], G. Laviola [a], R. van den Bos [b,c], W. Adriani [a,*]

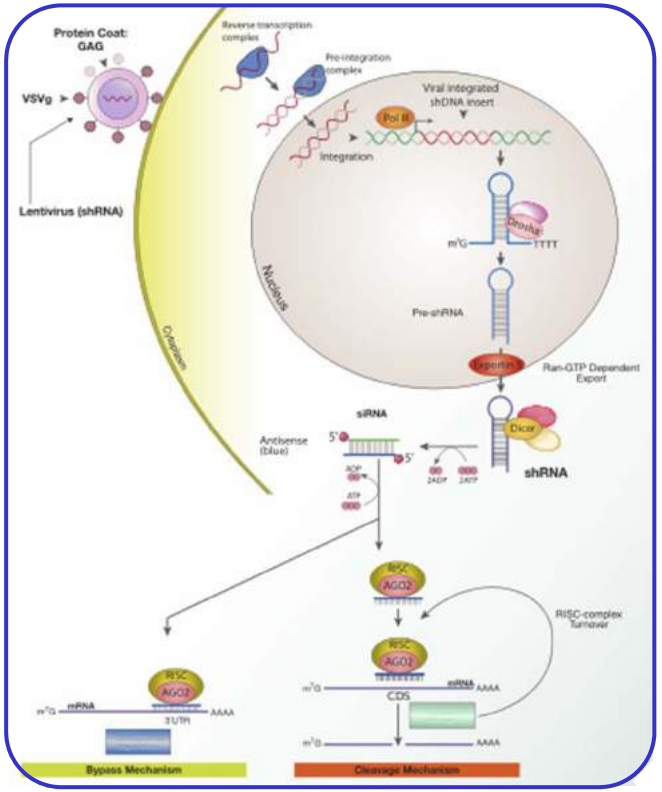
[1] Equally contributed to this work.

The relationship between 5-HT and impulsivity

- Experimental studies with different serotonergic manipulations have demonstrated an inverse relationship between 5-HT levels and impulsivity, with a reduction in the neurotransmitter causing an increase in impulsivity and vice versa.

- However, in humans, an increase in impulsivity appears to be associated with the short (s) allelic variant of 5-HTTLPR, leading to reduced SERT gene transcription.

→ We aimed to determine whether a partial silencing of the SERT-encoding gene within the hippocampus could induce alterations relevant to the modelling of ADHD, in particular symptoms of hyperactivity and impulsivity.



Lentiviral delivery of shRNAs and the mechanism of RNAi interference in mammalian cells (Cojocari D., 2010)

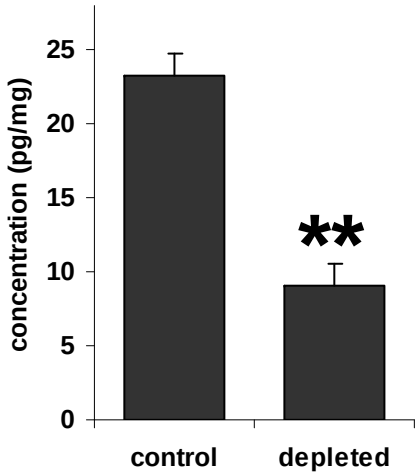
Experimental subjects

- adult male rats tested in classical operant chambers during the dark phase of the cycle
- mild food restriction
- *testing*: 11 days, 1 session per day (25 min), *timeout* 15 s

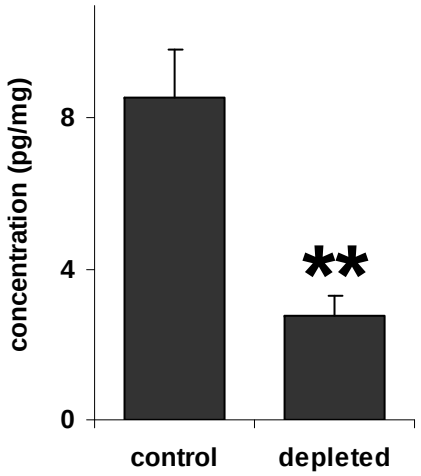
Experimental groups

- **depleted** (n=12): food without TRP (0.0 g/kg)
- **control** (n=12): food with a standard content of TRP (2.8 g/kg)
- from 2 weeks before and throughout the duration of the experiment (until sacrifices)

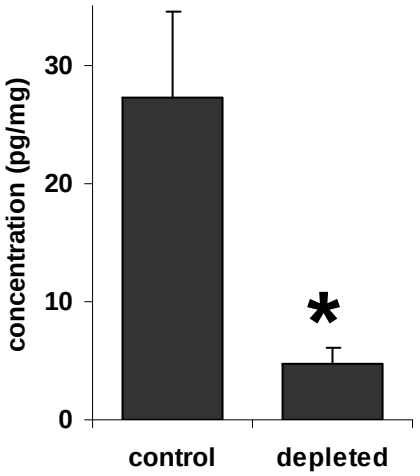
5-HT in prefrontal cortex



5-HT in striatum

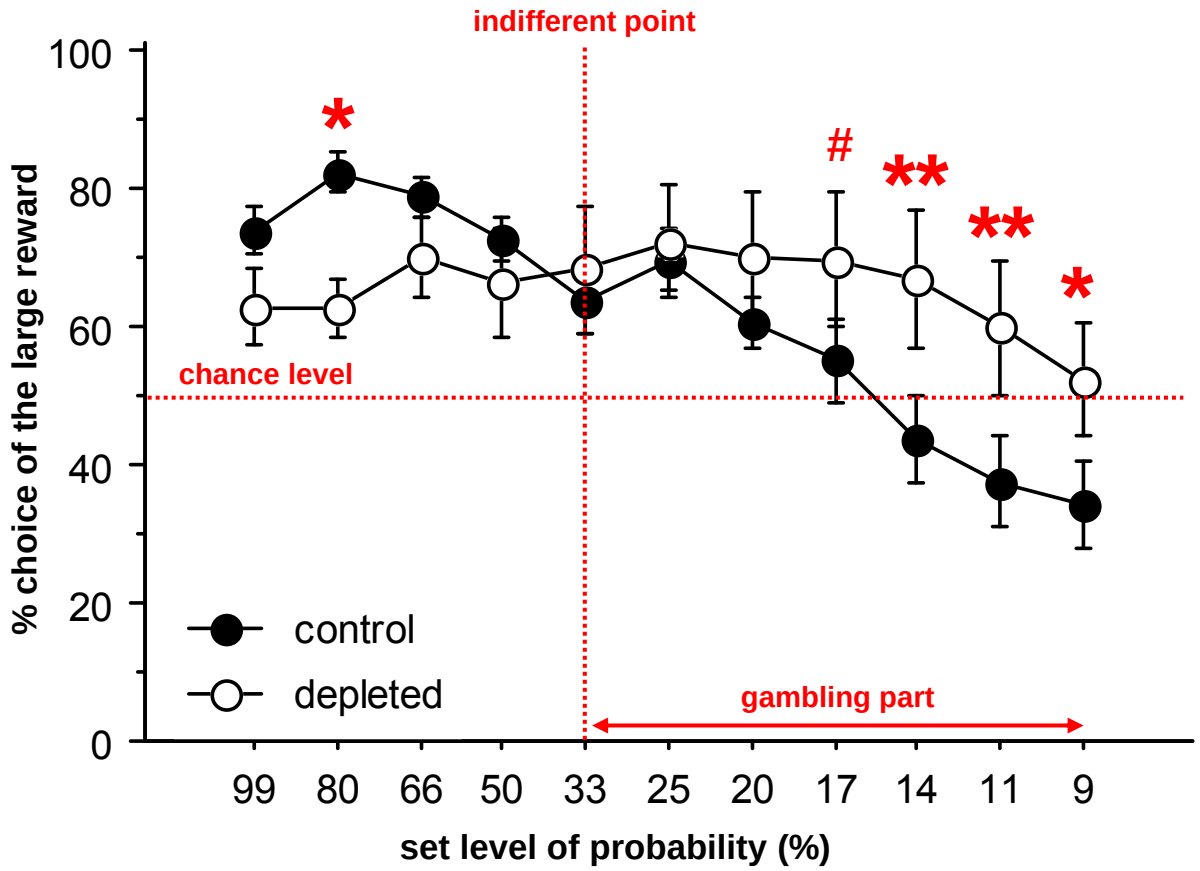


5-HT in hippocampus



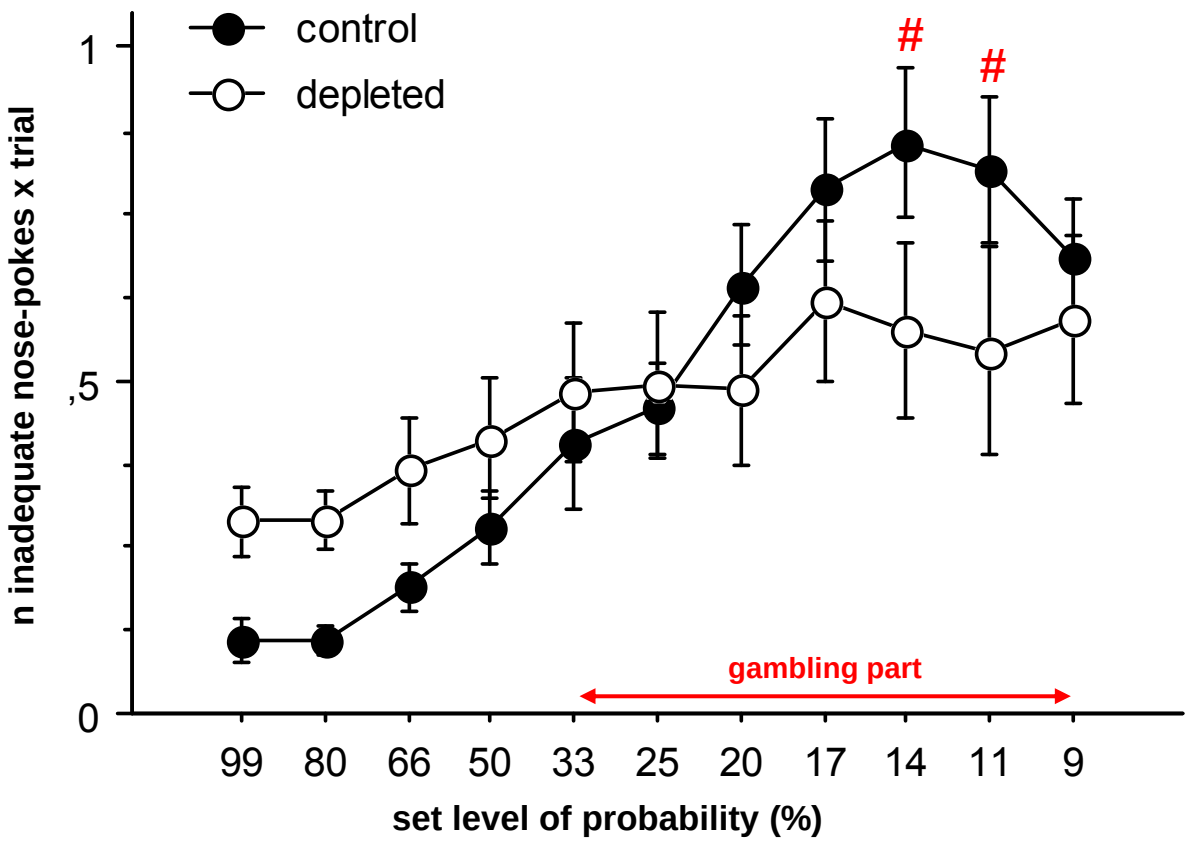
**** P < 0.01; * P < 0.05 when comparing depleted vs control rats in post-hoc test**

Levels of gambling proneness



** P < 0.01; * P < 0.05; # 0.05 < P < 0.1 when comparing depleted vs control rats in post-hoc test

Frequency of inadequate responding, an index of frustration



0.05 < P < 0.1 when comparing depleted vs control rats in post-hoc test

Punishment insensitivity and/or enhanced secondary reinforcement

- In the clinical literature, it has been reported that:

  → gamblers may be insensitive to losses *(Rachlin, 1990)*;

  → despite repeated losses, feelings of “near win” and the occasional large payoff seem to provide sufficient reinforcement *(Walker, 1992)*.

- In our preclinical model, the nose-poking for large reward was constantly turning on the reward-associated lights while occasionally triggering binge reward delivery: this may perhaps reproduce the addictive features of slot machines.

PHARMACOLOGICAL TOOLS

Methylphenidate (MPH, Ritalin) is currently prescribed to ADHD children, since it decreases impulsivity and increases sustained attention (*Ward et al., 1997*).

However, MPH interacts with the same brain pathways activated by drugs of abuse, producing striatal dopamine (DA) overflow similarly to cocaine (Marsteller et al., 2002). Its use raises concerns for public health (*Rapport & Moffitt, 2002; Klein-Schwartz, 2002; Carlezon & Konradi, 2004*).

Great effort is devoted to the identification of novel non-psychostimulant agents.

MAGNETIC RESONANCE SPECTROSCOPY

in: striatum, nucleus accumbens, and prefrontal cortex

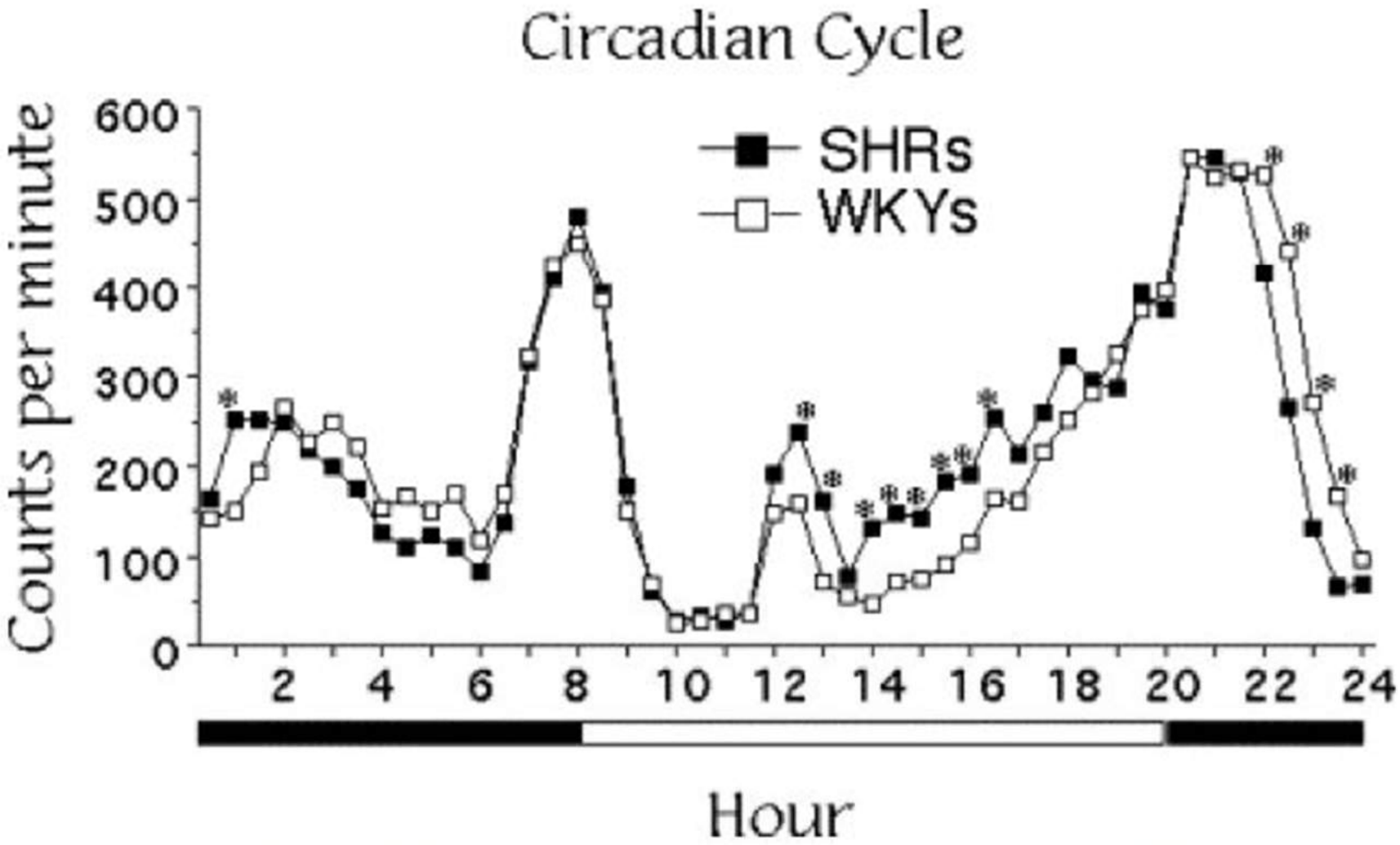
Interestingly, **total creatine** and **taurine**, reputed to be involved in neural activation, were **up-regulated** in the **STRIATUM** and conversely **down-regulated** in the **NUCLEUS ACCUMBENS** of MPH-exposed rats. We suggest that the influence of these two areas on behavioral output was modulated accordingly.

Based on the functional role played by these two brain areas, MPH-exposed animals may be suggested to be more prone to elaborate **novel behavioral habits**, in order to cope with actual reinforcement delay (**STRIATUM**), and to be **less instinctive,** i.e. less affected by the immediacy of reward (**ACCUMBENS**).

IMPULSIVITY IN THE SHR ADOLESCENT

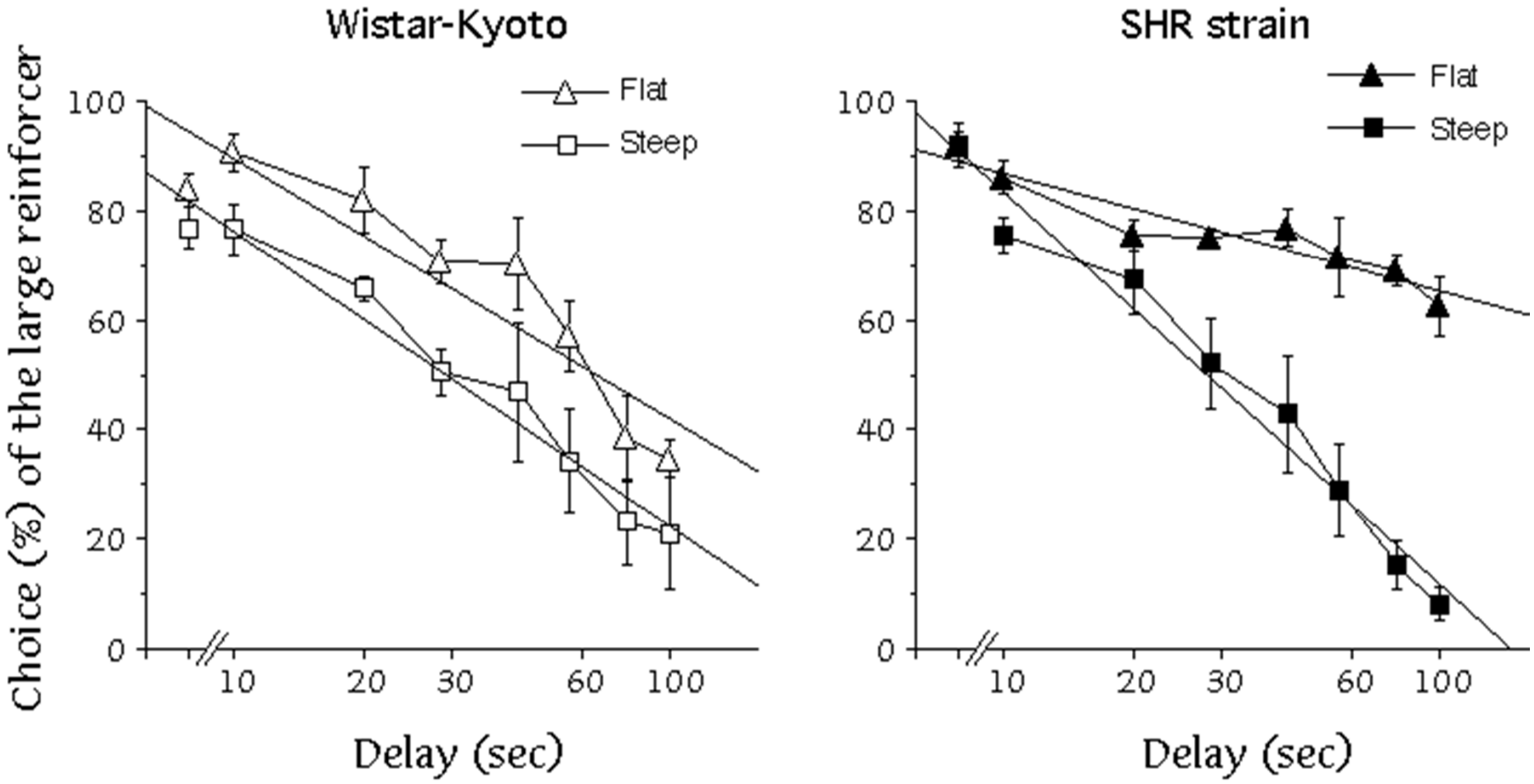
A validated animal model for ADHD is the SHR (Spontaneously Hypertensive Rat) strain.

Aim of the work was to compare SHRs to their Wistar-Kyoto controls in a test for intolerance-to-delay during adolescence (PND 30 to 45), in order to further validate the adolescent SHR as a suitable animal model for ADHD.



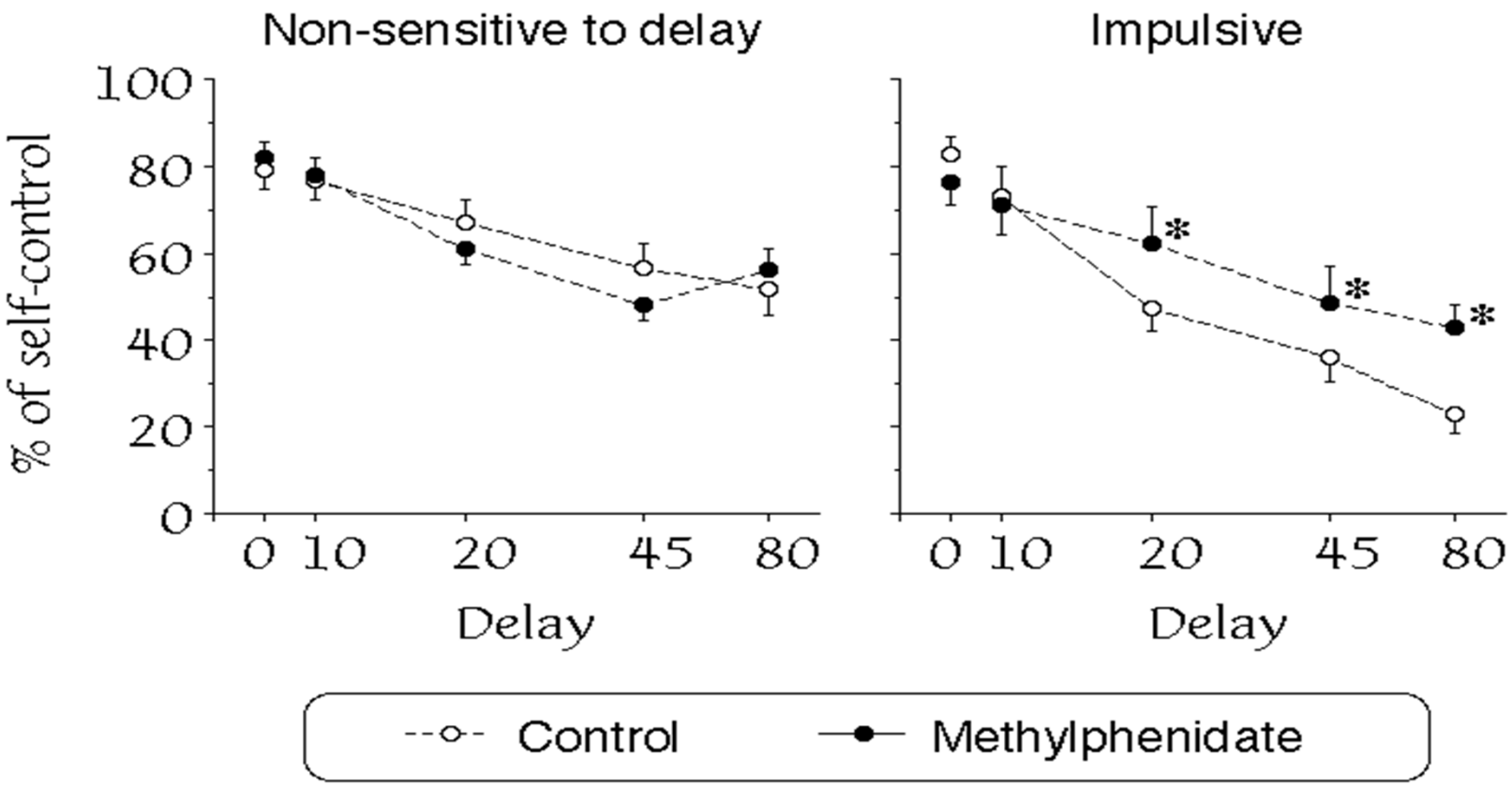
Circadian rhythm in WKYs and SHRs left undisturbed in pairs inside their home-cages. The infrared sensors (20 Hz) detected any movement of rats with a frequency of 20 events per second. Scores were obtained as counts per minute (cpm) expressed during half-hour-periods, and the 24-h profile of daily activity was obtained by averaging seven days of continuous registration.

Adriani W, Caprioli A, Granstrem O, Carli M, Laviola G. (2003). The spontaneously hypertensive-rat as an animal model of ADHD: Evidence for impulsive and non-impulsive subpopulations. Neuroscience & Biobehavioral Reviews 27:639-651.

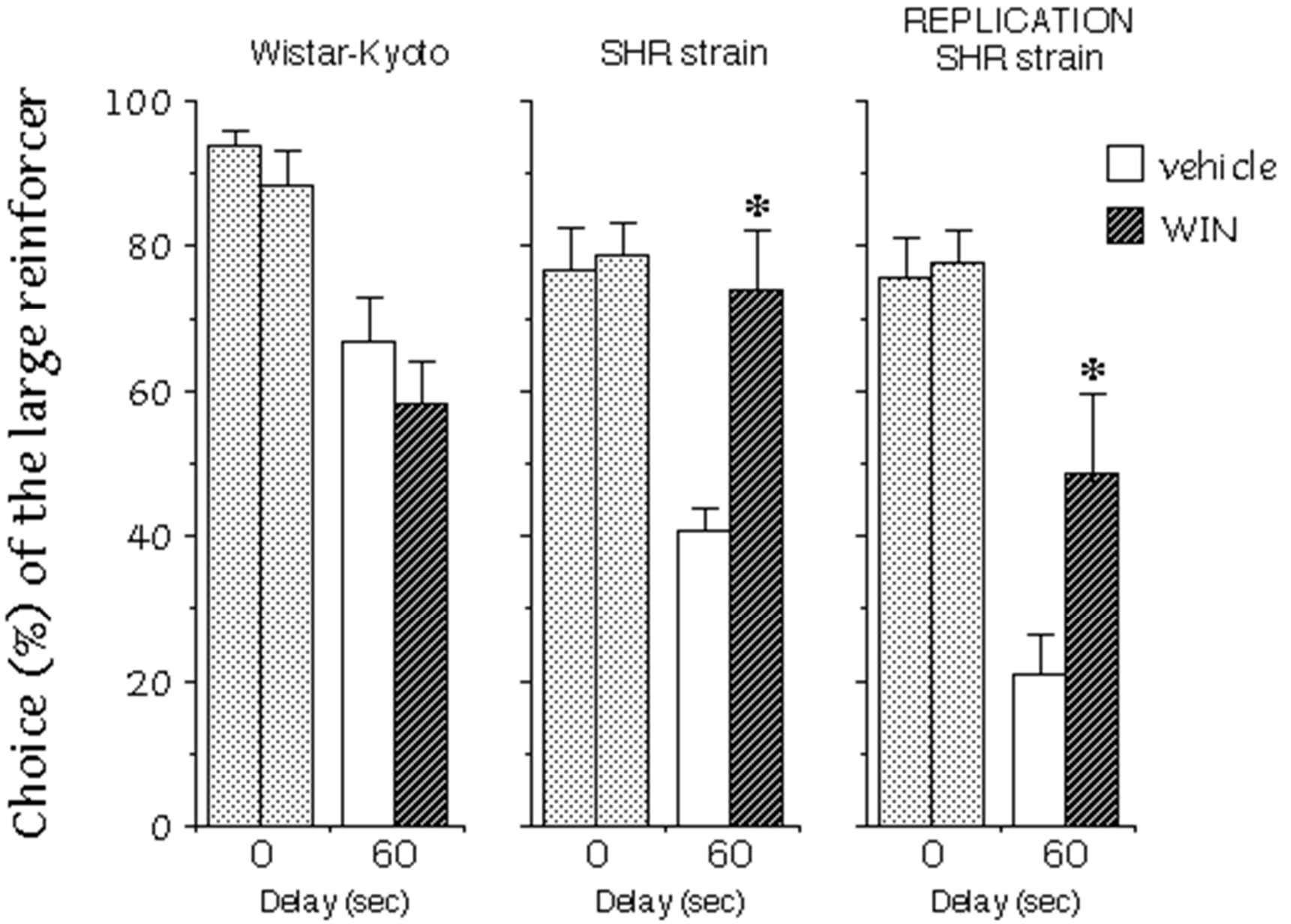


Clear-cut individual differences were evidenced within the SHR model during adolescence.

ONGOING EFFECTS of SUBCHRONIC MPH DURING ADOLESCENCE



The **ongoing** treatment with MPH *(3 mg/kg i.p.)* reduced impulsivity levels


Wistar-Kyoto
SHR strain
REPLICATION
SHR strain
Choice (%) of the large reinforcer
100
80
60
40
20
0
0
60
Delay (sec)
vehicle
WIN
*
*

CONCLUSION - THE ADOLESCENT “SHR”

Clear-cut individual differences were evidenced within the SHR model during adolescence.

« STEEP » subpopulation showed elevated impulsivity. The **ongoing** treatment with MPH (3 mg/kg i.p.) reduced impulsivity levels. **Acute** administration of WIN 55,212 (2 mg/kg s.c.) also reduced impulsivity in **young-adult** SHRs, without effect in WKYs.

FLAT subpopulation kept on choosing H5 even at higher delays

a) animals do not pay attention to the experimental contingency (see Sagvolden et al., 1998; Sagvolden & Sergeant, 1998; Sagvolden, 2000), as expected in an animal model of ADHD;

b) animals are unable to modulate response patterns according to changes in the experimental contingency (perseverative behavior).

CONCLUSIONS

This study combined **behavioural analysis** and **genome-wide approach**, to investigate the molecular and neurobehavioural changes resulting from subchronic **MPH exposure during adolescence**.

In summary, such early treatment was able to modulate striatal gene expression of **Post Synaptic Density** family in the adolescent brain. These changes underlie **enduring plastic rearrangements** in reward-related brain circuits, from **both structural and functional (dendritic spines, neurotransmitter receptors)** viewpoint.

The latter may in turn account for a complex picture of **increased self-control abilities** at adulthood, associated with an **altered processing of incentive values**.

CONCLUSIONS

*** Abnormal Htr7 and/or DAT in adolescents or in ADHD patients is perhaps associated with patterns of impulsive decision-making and with risk-prone behaviours;**

• The impact of stimulant drugs during such important developmental rearrangements received a fast-growing attention in preclinical experimental investigation (i.e. to model cases of illicit use for increased performance);

• It is thus emphasized the importance of characterizing novelty-seeking and risk-prone behaviour in the rodent, during adolescence and/or using new specific models.

Paradigms for the measure of impulsivity and gambling proneness

Intolerance to Delay (ID) task

→ impulsivity

nose-poking in "Small & Soon" hole **(SS)**

⇩

immediate delivery of 1-2 pellets

nose-poking in "Large & Late" hole **(LL)**

⇩

delivery of 5-6 pellets after a delay, which is increased progressively each day

8 testing sessions, from delay 0 s to 90 s
(preceded by 3 training sessions at delay 0 s)

Probabilistic Delivery (PD) task

→ gambling proneness

nose-poking in "Small & Sure" hole **(SS)**

⇩

certain delivery of 1-2 pellets

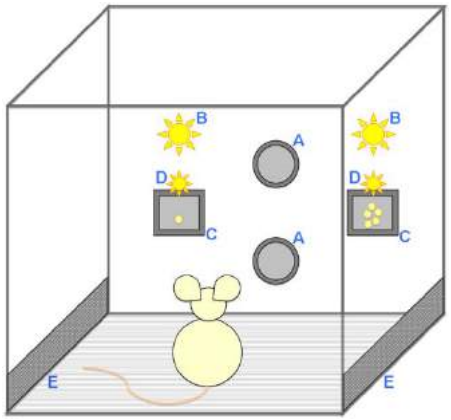
nose-poking in "Large & Luck-Linked" hole **(LLL)**

⇩

delivery (or not) of 5-6 pellets, according to the level of probability "p", which is decreased progressively each day

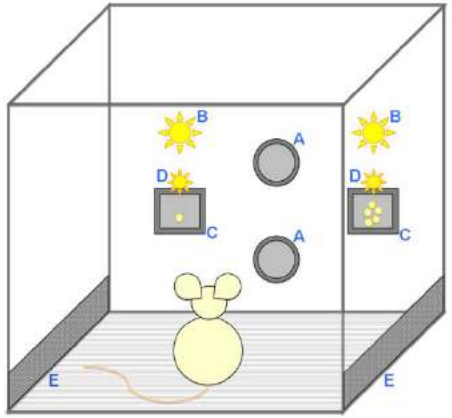
11 testing sessions, from probability 99% to 9%
(preceded by 2 training sessions at probability 99%)

under conditions of mild food restriction
(to increased motivation to work for food delivery)



"Small & Sure" hole ***(SS)*** → *certain* delivery of *2 pellets*

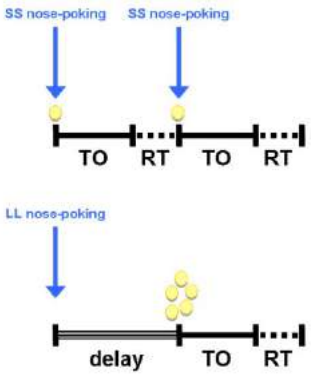
"Large & Luck-Linked" hole ***(LLL)*** → *delivery (or not) of 6 pellets, according to the level of probability "p"*



"Small & Soon" hole ***(SS)*** → *immediate* delivery of *1 pellets*

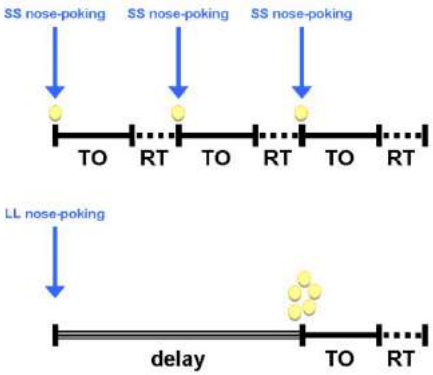
"Large & Late" hole ***(LL)*** → *delivery of 5 pellets, after a delay*

Delay-equivalent odds = delay / mITI = delay / (TO + RT)



odds = 1

il delay è uguale al mITI



odds = 2

il delay è il doppio del mITI

EXPERIMENT OUTLINE