Human neuroscience in Portugal:
Here we go!

Diana Prata

Marie Curie Fellow

Group Leader, **iMM Lisboa**

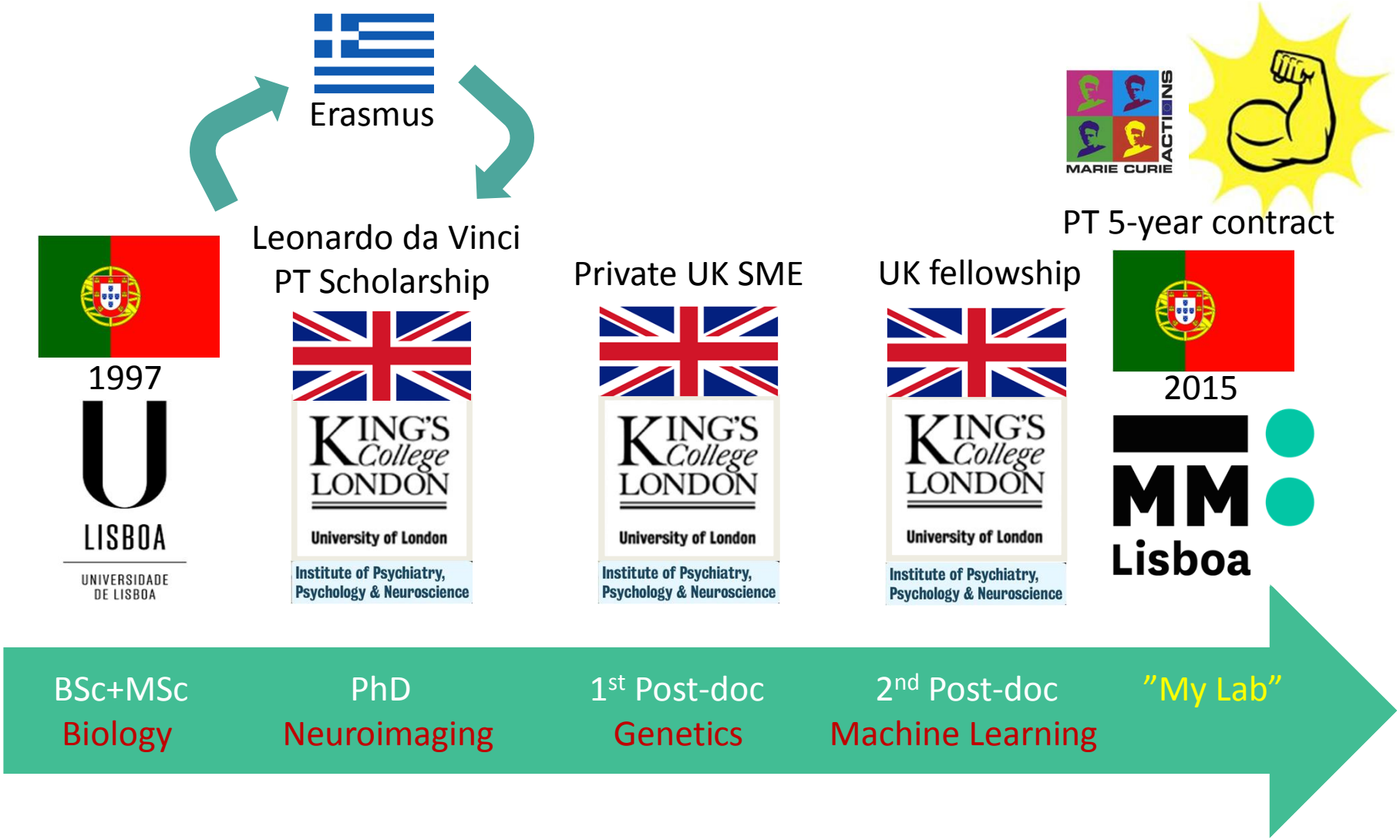
Visiting Lecturer, IoPPN, King's College London

Visiting Lecturer, FMUL

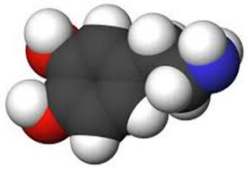
Lecturer, IUL-ISCTE

Co-founder and CSO, NeuroPsyCAD

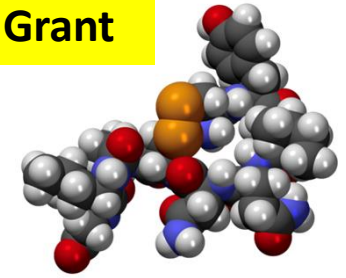

CIHEAM
MAICHANIA
KING'S College LONDON
U LISBOA
UNIVERSIDADE DE LISBOA


Erasmus
MARIE CURIE ACTIONS
PT 5-year contract
1997
Leonardo da Vinci
PT Scholarship
Private UK SME
UK fellowship
2015
LISBOA
UNIVERSIDADE DE LISBOA
KING'S College LONDON
University of London
Institute of Psychiatry, Psychology & Neuroscience
MM Lisboa
BSc+MSc
Biology
PhD
Neuroimaging
1st Post-doc
Genetics
2nd Post-doc
Machine Learning
"My Lab"

FP7 Marie Curie Career Integration Grant



MARIE CURIE ACTIONS

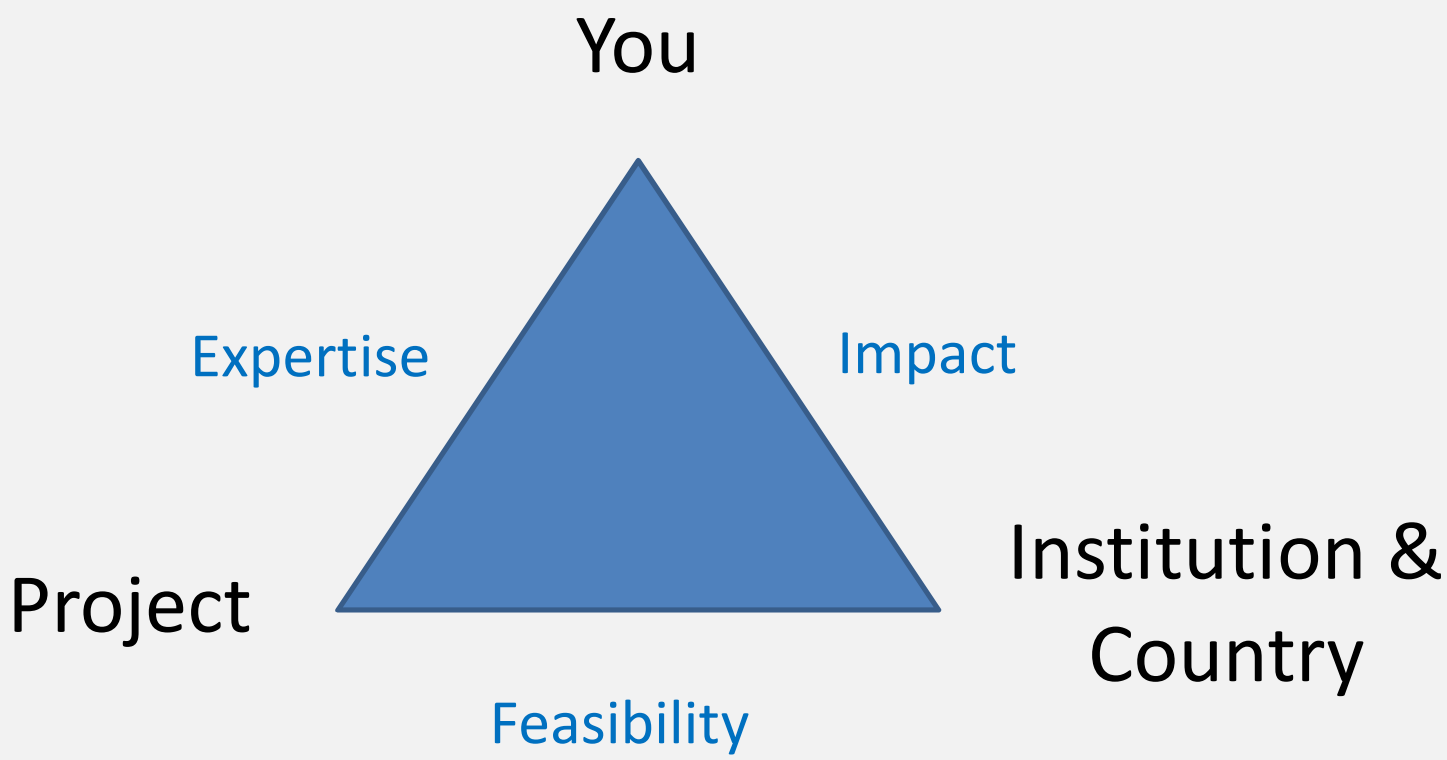


Dopamine

– exploration, learning, new challenges

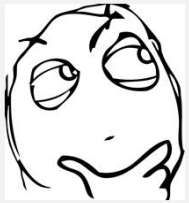
Oxytocin

– familiarity, bonding, building


You
Expertise
Impact
Project
Institution &
Country
Feasibility

WHY?

	Black-box	Mechanisms
ETIOLOGY		
	Descriptive	✓ Quantitative
	Subjective	✓ Objective
	Stigmatizing	✓ Ecological
TREATMENT		
	Trial-and-error	✓ Rational design
	One-size-fits-all	✓ Stratified & personalized
PROGNOSIS		
	Unpredictable	✓ Predictable



How can we get insights into the basic **mechanisms**?
How can we empower psychiatry with **quantitative** biomarkers?

MY TEAM

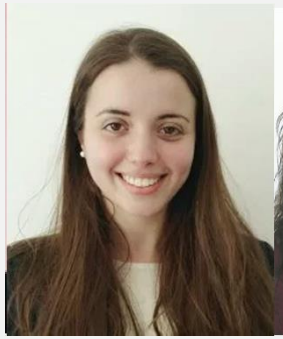
Medics + biomedical engineers + psychologists

Bernardo Neves
(Psychiatrist)

Bernardo Moura
(PhD Student)

André Sousa
(Psychiatrist)

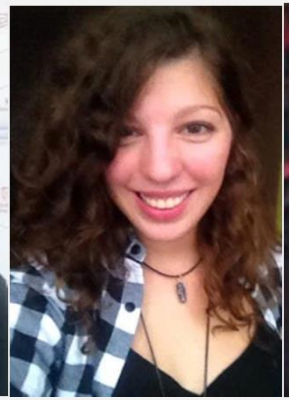
Vânia Tavares
(PhD student)



Marina Balseiro
(MSc student)

Carina Mendes
(Technician)

Katja Brodmann
(Post-doc)



Mónica Costa
(MSc student)

Alessia Ávila
(PhD Student)

Gonçalo Oliveira
(Post-Doc)

+ Many eager volunteers!

MY LAB

MM Lisboa

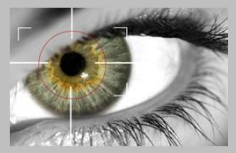
BASIC

APPLIED

What is the role of oxytocin in human social cognition?

Can we develop neuropsychiatric biomarkers/treatments?

Eye-tracking & pupilometry



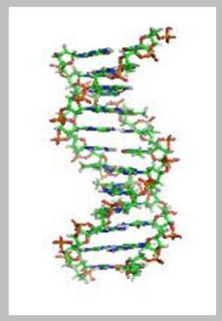
Neuroimaging

Pharmacology

EEG & TMS

Psychology

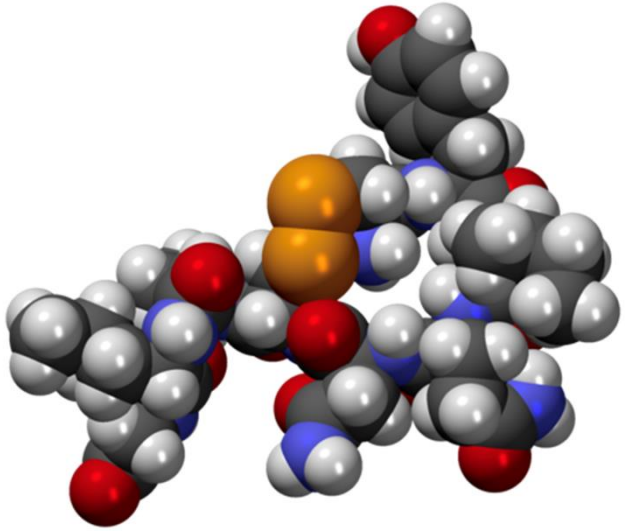
Genetics




BASIC

“Oxytocin” AND “Social” Publications

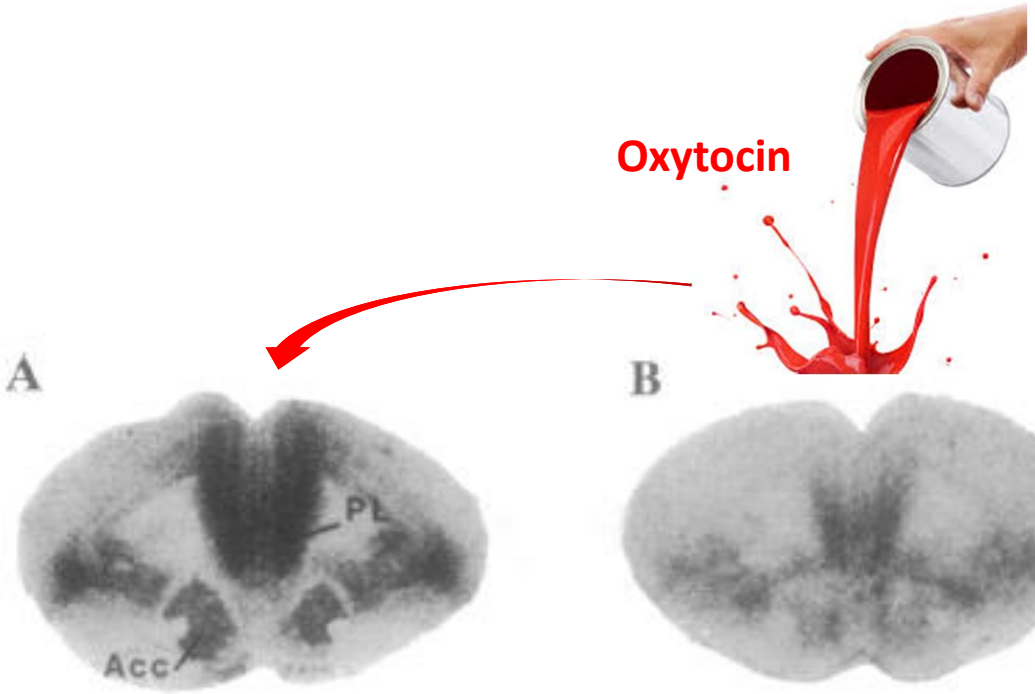
2015



They are **better mothers** if they have ***more*** **oxytocin** receptors in their brain's reward centre.

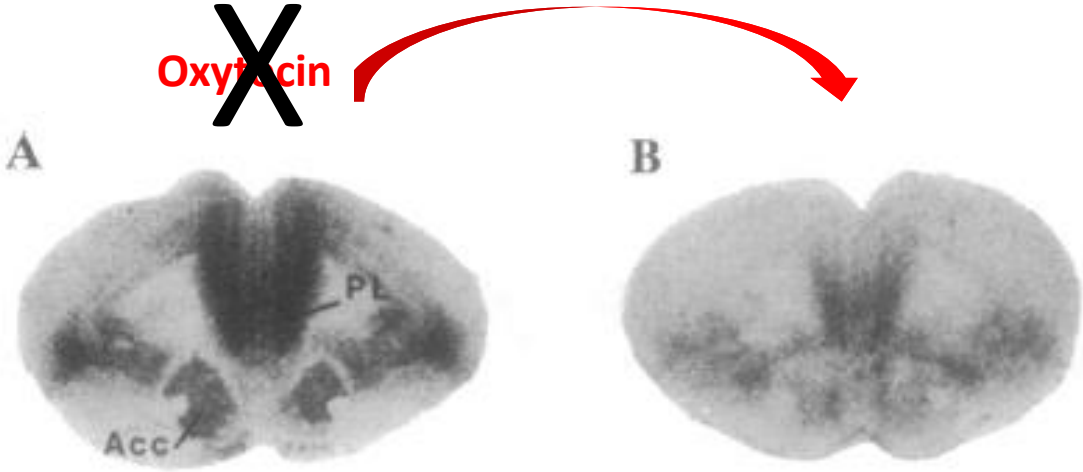
Oxytocin
Further increases this.

Reverted with an antagonist.



Monogamic vole

Polygamic vole



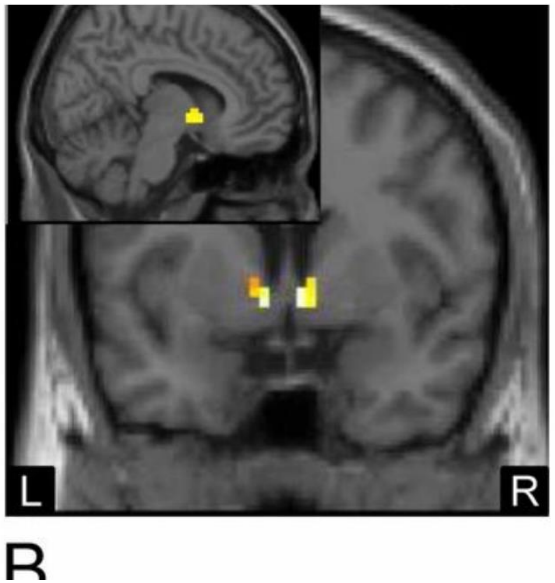
Monogamic vole

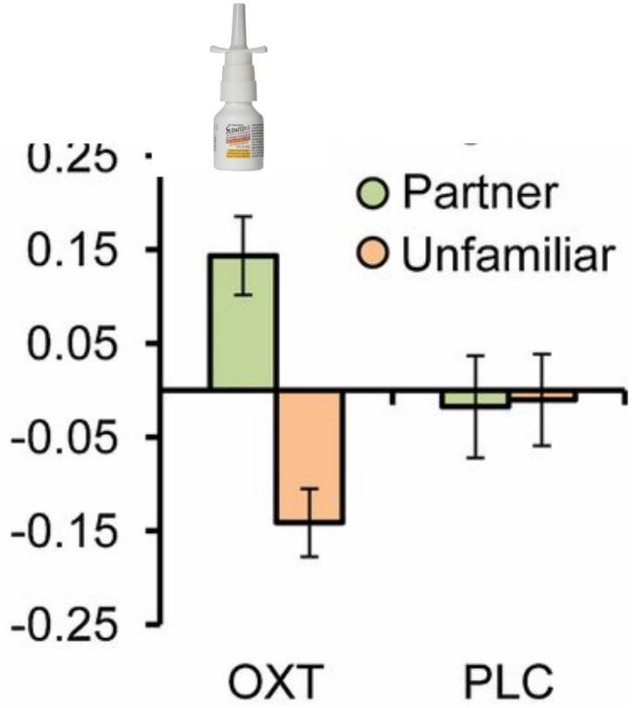
Polygamic vole

Oxytocin=  ?

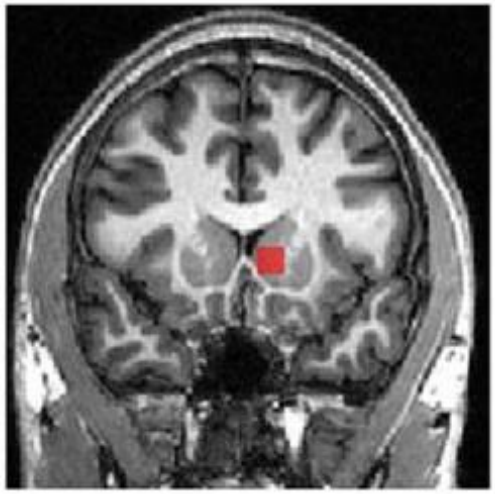
How can we take some of it?!

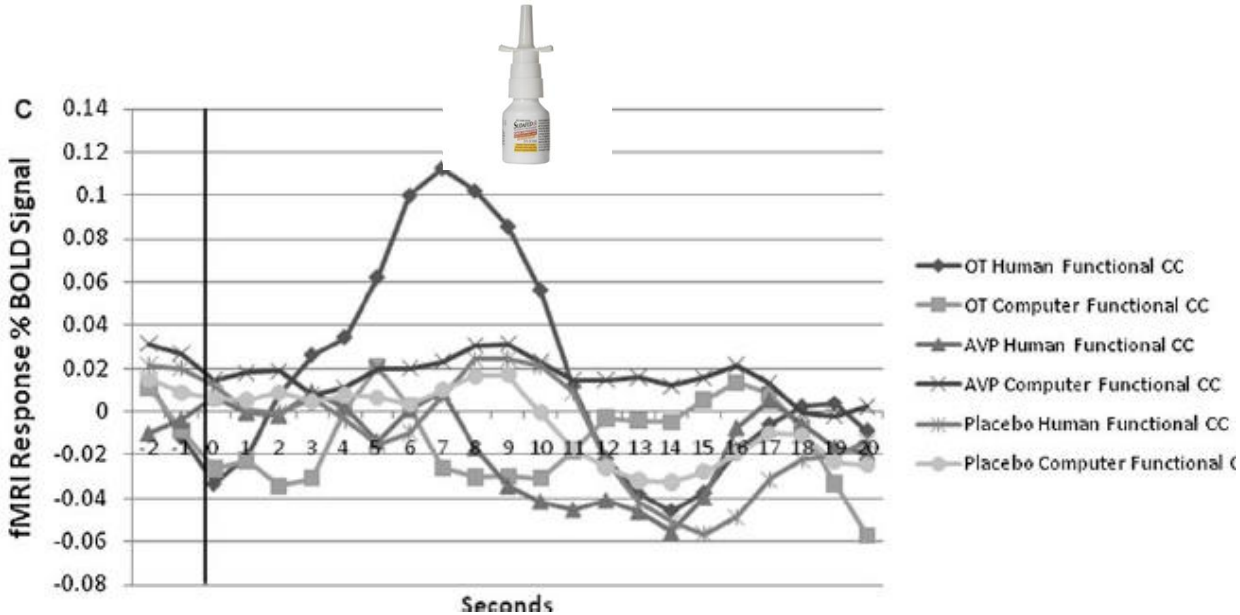
Oxytocin activates our **reward** center when we look at our partner's photo (vs unfamiliar).





… and when others **reciprocate our cooperation** in an economic game.

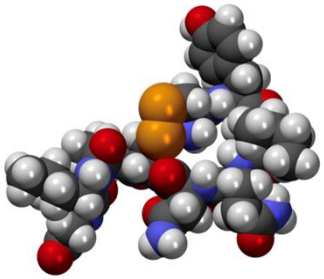


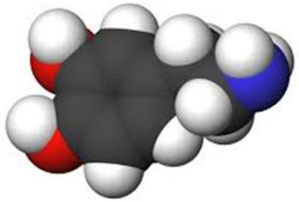


Hypothesis

FP7 Marie Curie Career Integration Grant

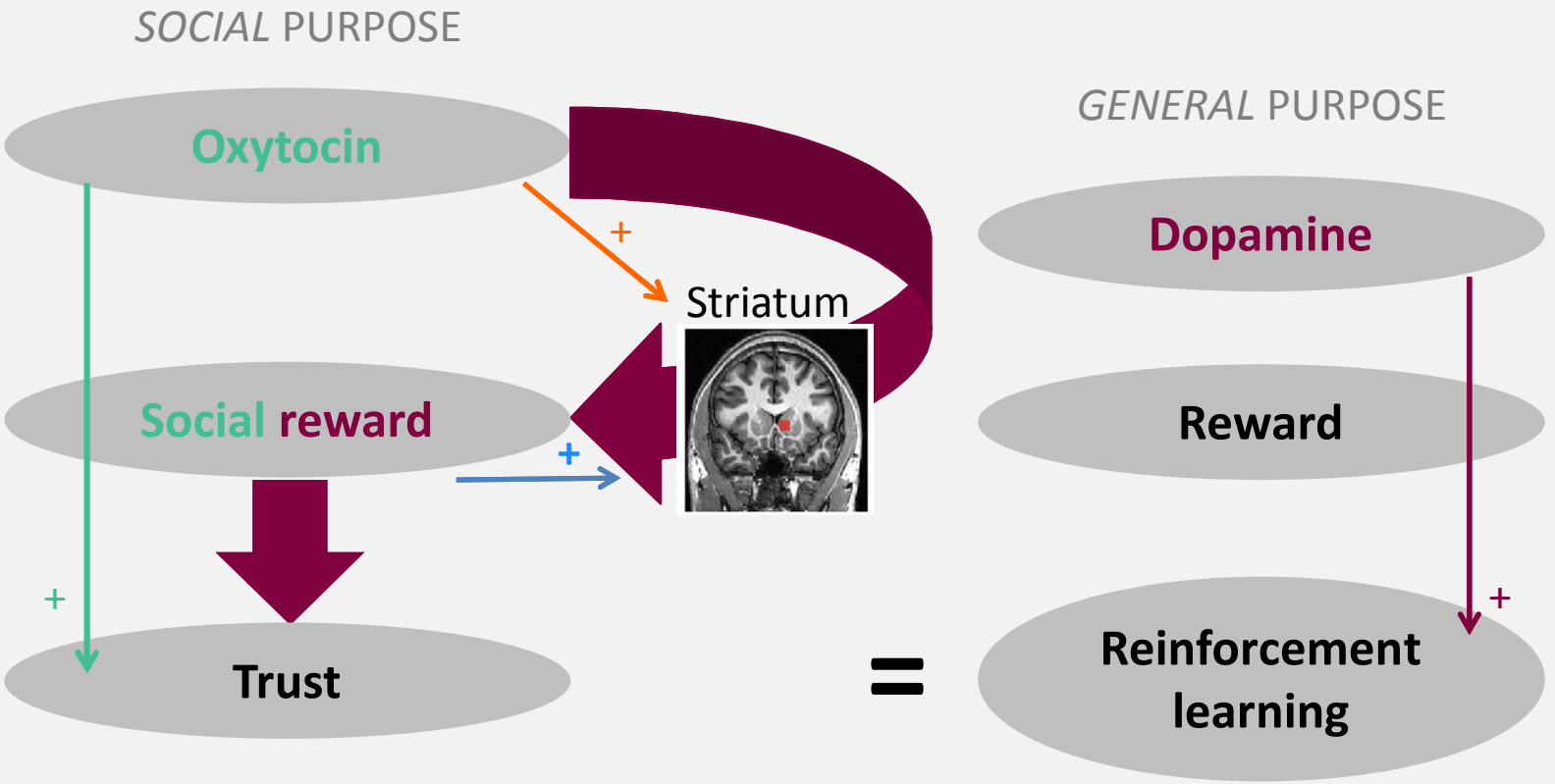
Oxytocin *boosts* the ***reward*** value of good **social** interactions...

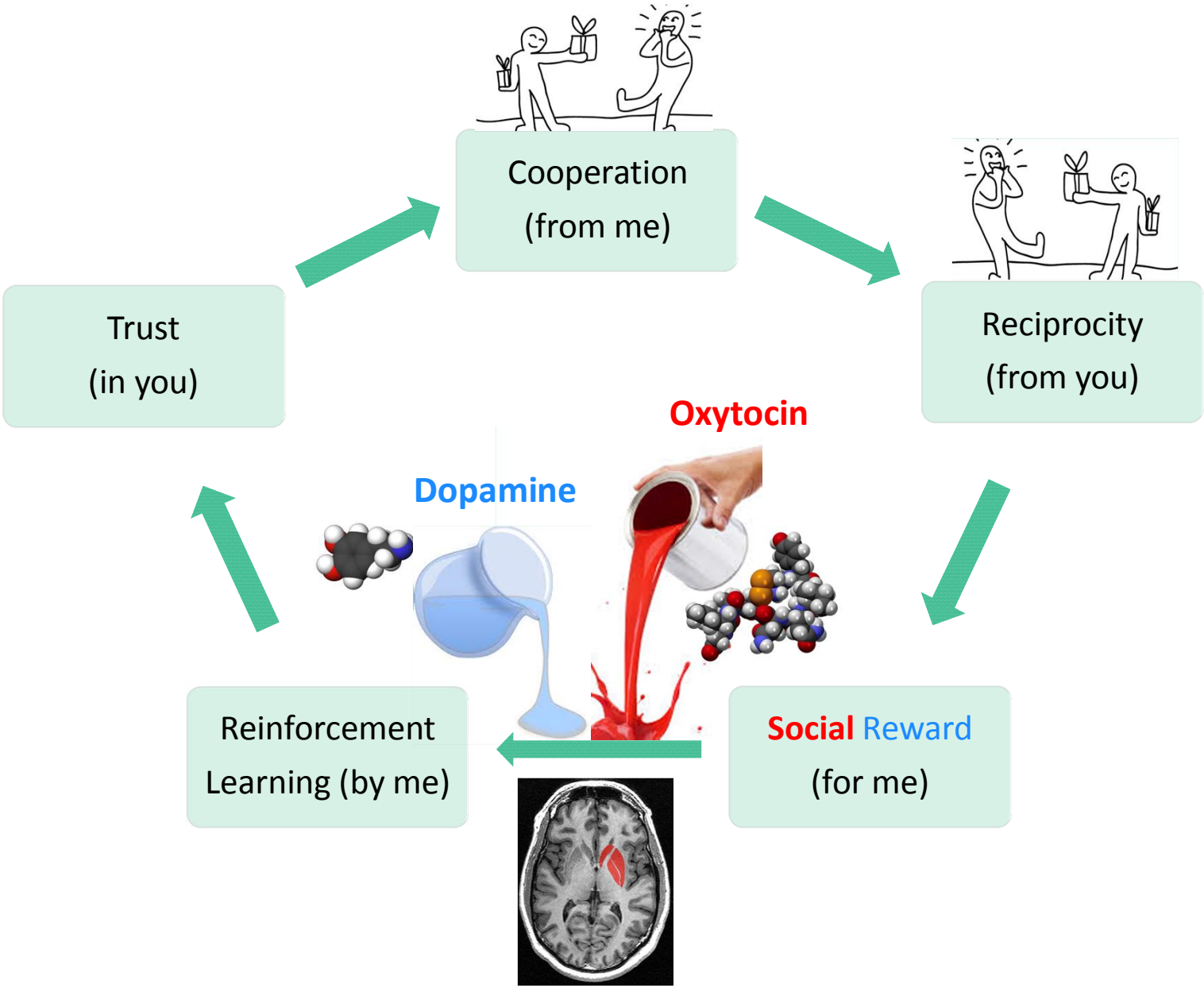




… by “collaborating” with the **dopamine** system.

RATIONALE


SOCIAL PURPOSE
Oxytocin
Social reward
Trust
+
+
+
Striatum
=
GENERAL PURPOSE
Dopamine
Reward
Reinforcement learning
+


Cooperation
(from me)
Reciprocity
(from you)
Social Reward
(for me)
Reinforcement
Learning (by me)
Trust
(in you)
Oxytocin
Dopamine

DM [15]5

Dopamine & Oxytocin **receptor *dimers*** found in mice's "pleasure centre".

Molecular Psychiatry (2013) 18, 849–855

www.nature.com/mp

LETTERS TO THE EDITOR

Evidence for the existence of dopamine d2-oxytocin receptor heteromers in the ventral and dorsal striatum with facilitatory receptor–receptor interactions

Molecular Psychiatry (2013) **18,** 849–850; doi:10.1038/mp.2012.103; published online 24 July 2012

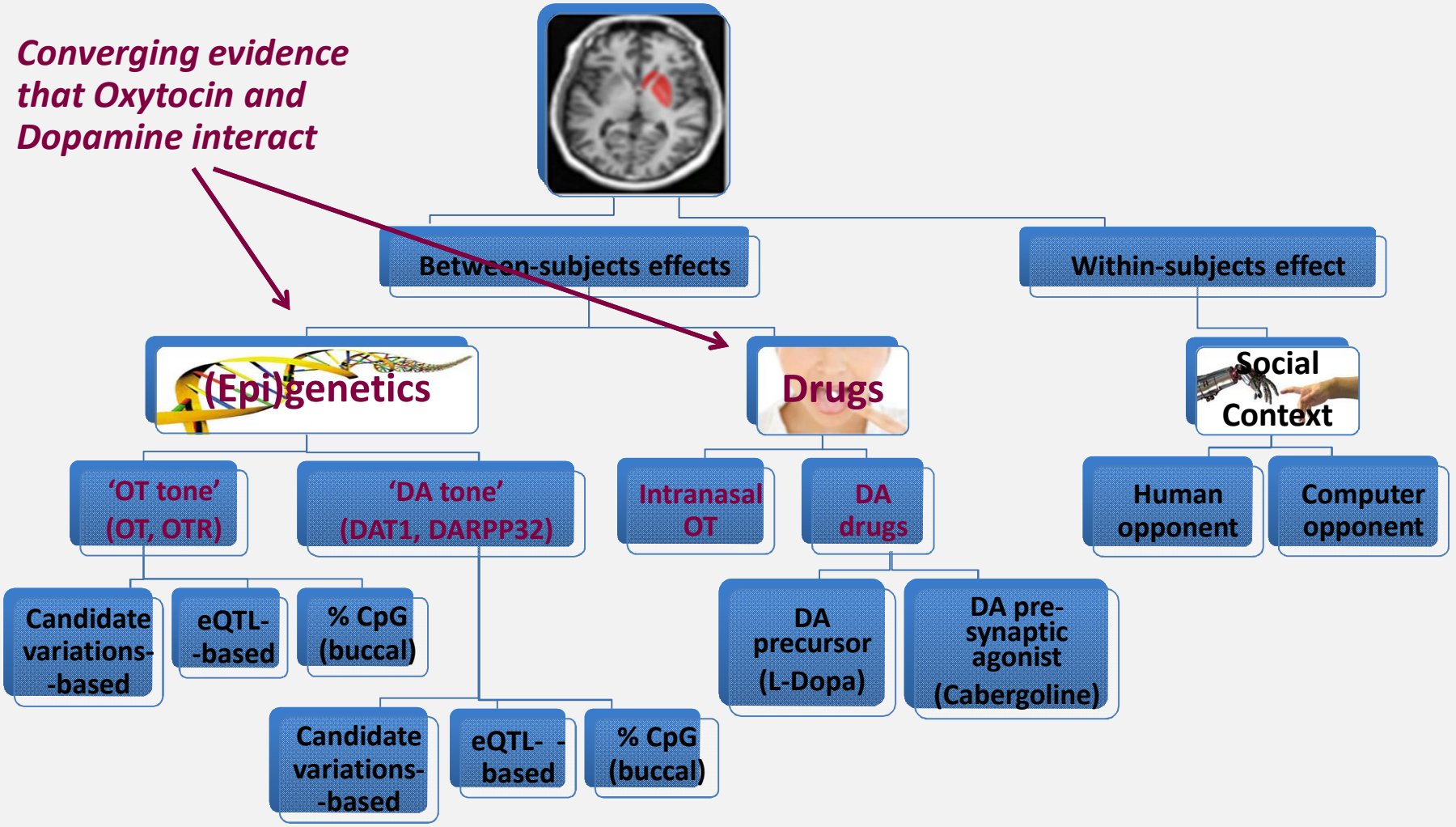
The pioneering work of the Insel group has demonstrated a key role of oxytocin neurons and their striatal oxytocin receptors (OTR) in producing pair bonding in the monogamous prairie vole female,[1,2] with the oxytocin neurons likely communicating mainly

Acb oxytocin at 3 nM, but not at 1 and 100 nM, highly significantly increased the affinity of the high- (Ki_H) but not the low-affinity (Ki_L) agonist state of the D_2R, as seen from a marked reduction of the Ki_H value from 16.58 ± 0.74 to 1.89 ± 0.70 nM (Table 1, Supplementary Figure 6). The major elevation of the OTR-induced increase in D_2R recognition may therefore result from an increase in the affinity of the high-affinity state of the D_2R. The oxytocin actions at 3 nM on D_2R-like recognition are all blocked by the OTR antagonist L-368,899 (30 nM, Supplementary

Diapositivo 21

DM [15]5 faz sentido aparecer antes
Daniel Martins; 04-04-2016

We hypothesize **striatal** activation after **reciprocity** (=social reward) in a social game will be *affected* by:




Av. Prof. Egas Moniz
Av. Prof. Gama Pinto
Av. Prof. Gama Pinto
bon School
& Economics
Hospital de Santa Maria
Av. dos Combatentes
iott
FP7 Marie Curie Career Integration Grant
Barra Lisboa/
iu Jitsu Team
EGOC
Av. das Forças Armadas
Secil
SANA Metropolitan
Google
MARIE CURIE ACTIONS

SET UP = UNPRECEDENTED IMPACT

- **1st Psychophysiological Facility at iMM**
  - Functional MRI access
  - EEG
  - Eye-tracking and pupilometry
  - Galvanic skin response
  - ECG
  - Body temperature and respiration

- 1st collaboration protocol for use of **MRI scanner** on weekends.

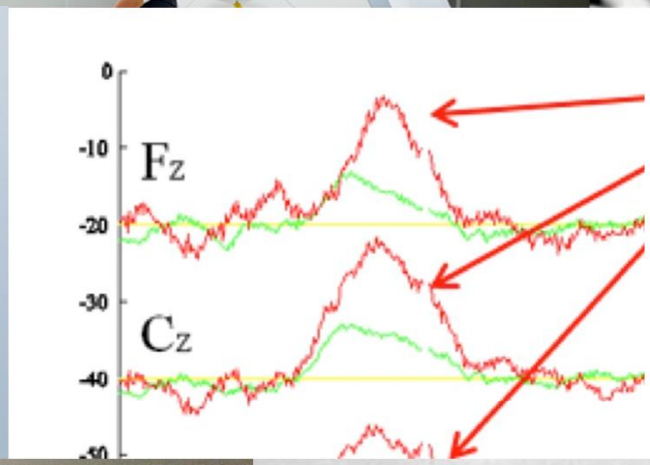
- 1st ethical **approval for a clinical study** with pharmacological administration (different from a clinical trial!)

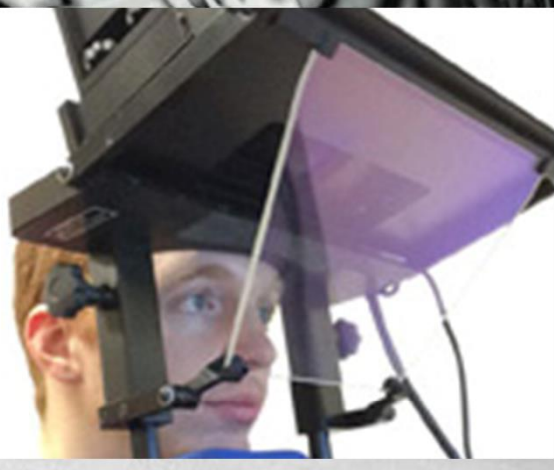
- 1st approval for **drug import** for such type of study

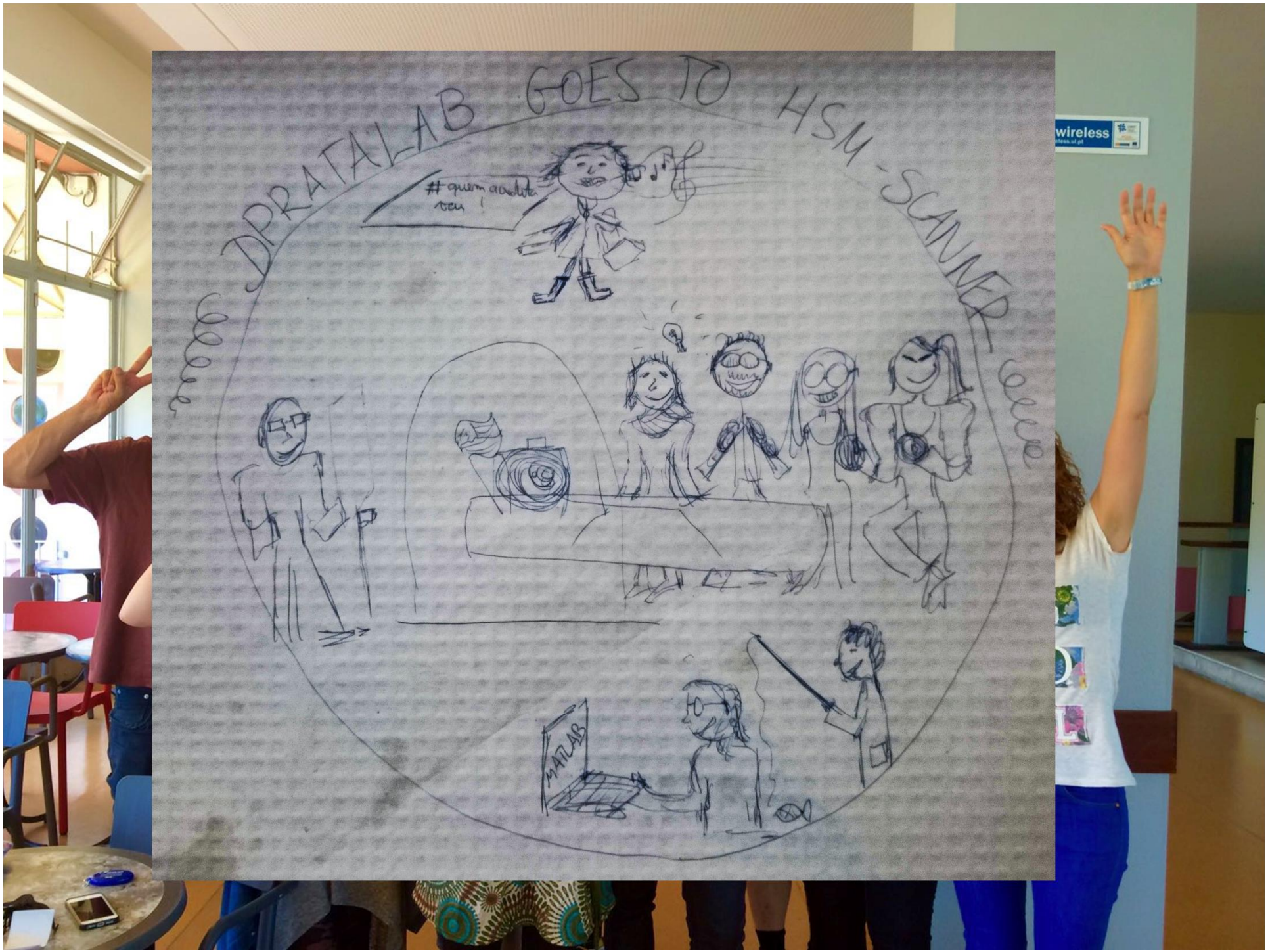
- 1st approval for **drug manipulation** for such type of study.

- 1st general iMM-hospital collaboration protocol for clinical studies initiated by the investigator

SET UP = UPRECEDENTED IMPACT

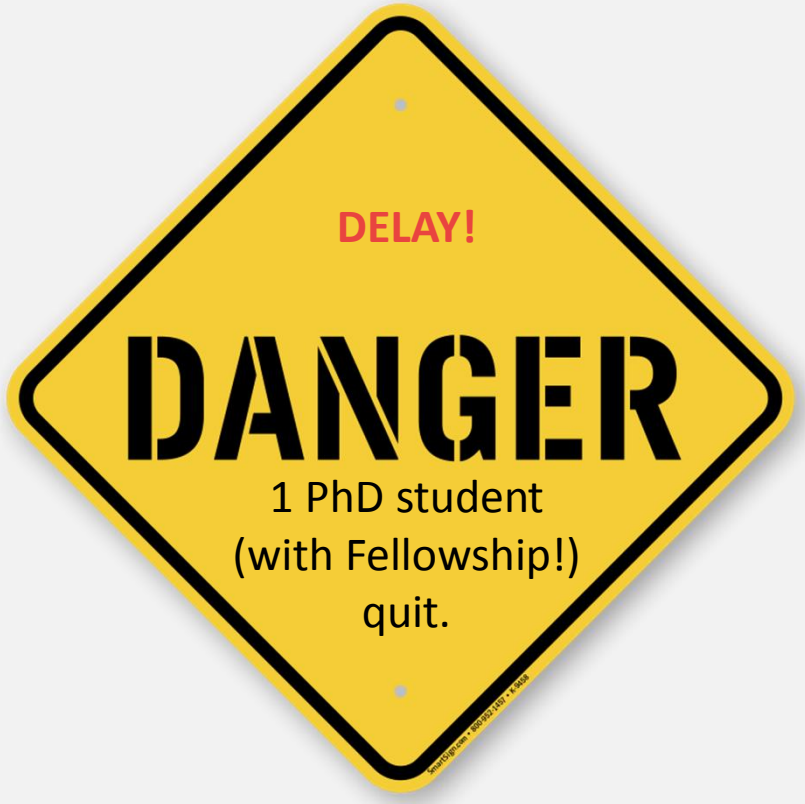





DPRATALAB GOES TO HSM - SCANNER
#quem acredita vou!
MATLAB
wireless

HURDLES FROM LACK OF FAMILIARITY

- **Local ethics committee:**
  - Unprepared, bad coordination between local and national.
- **Nacional ethics committee:**
  - General contact, unprepared.
- **Scientific committee**
  - Lack of Psychiatry research expertise
  - Uncoordinated with Ethics
- **Infarmed**
  - General contact, unprepared.
- **Hospital**
  - Delayed communication with Heads
  - Authority arguments
- **Purchases**
  - 4-6- months delay, public acquisitions




YES
NO
MAYBE

Let’s make Portugal nicer for human neuroscientists.

Law makers need to speak to recently returned scientists.

INNOVATION - INTERDISCIPLINARY

- **1st Lab in Portugal combining** genetics, pharmacology, neuroimaging, electrophysiology and pupilometry to study the physiology of human behaviour.
- **1st Lab at the iMM** to do interdisciplinary human Psychiatric research
- **1st Lab collaborating with the Psychiatry** department of the university hospital
- Unprecedented **hospital-iMM synergiesl**:
  - Pathology Lab
  - Pharmacy
  - Imaging
  - Department for Clinical Research
- Large interest from **students** and **psychiatrists, psychologists, biologists statisticians and engineers** in Portugal
- **Ambassador for PARSUK** (the Portuguese Association for Researchers and Students in the UK).

MSCA 2017 MALTA

MALTA EU2017

MINISTRY FOR EDUCATION AND EMPLOYMENT

Xjenza The Malta Council for Science & Technology

European Commission

MSCA 2017 Prize Awards
Marie Skłodowska-Curie Actions

This is to certify that

Diana Prata

has been awarded

third prize as the most promising scientist

in the category 'Innovation and Entrepreneurship'

Presented by Martine Reicherts on 11 May 2017 in Kalkara, Malta

Martine Reicherts
Director General - DG Education, Youth,
Sport and Culture
European Commission

Martine Reicherts

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 742185

GRANTS AND FELLOWSHIPS AFTER CIG

Caixa Capital Award (€100.000)

Bial Psychophysiology grant, Bial Foundation (€50.000)

1 FCT Post-Doc Fellowship

6 FCT PhD Fellowships

Idea prize to 10 best startup ideas, BornFromKnowledge

AstraZeneca/FMUL grant

'InovPortugal New Ideas B2B' award, Acredita Portugal

Twinning Grant (€1.000.000)

Breakthrough Idea Grant (€100.000), iMM

FCT Investigator Starting Contract

FCT Exploratory Grant (€50.000)

DISSEMINATION

International scientific meetings below:

Invited Oral

- 2016 Summerschool, University of Eastern Finland, Finland
- 8th Workshop on Biomedical Engineering at FCUL, Portugal
- 2017 World Congress of Psychiatry, Germany
- 2017 Summerschool, University of Lancaster, UK

Posters

- Human Brain Mapping conference, USA.

National scientific meetings:

Invited Oral

- I3S, University of Porto.
- Lisbon Social Neuroscience Club, Instituto Superior de Investigação em Psicologia (ISPA)
- Biological Sciences Annual Meeting (BIOSAM) meeting in FCUL.
- NeuroLx conference in Lisbon (Portugal).

PUBLICATIONS - **PI's internationally peer-reviewed N(published)=37, H-index =19**

Not directly related to CIG: 9

Related to CIG (5):

Martins D, Silva M, PRATA D. **"Cracking" the code of human sociability and affiliation: Evidence from neuroimaging (epi)genetics of the oxytocin system.** *In writing.*

Oliveira G, Nobre G, Lima C, Sá R, Rosa P, PRATA D**. Recognizing vocalized emotions in other cultures: a electrophysiological study in Guiné Bissau and Portugal.** *In writing*

Ferreira D, Lopes M, Rilling J, Antunes M, PRATA D. **Computational modelling of oxytocin's and vasopressin's effect in the human brain during a Prisoner's Dilemma: a model-based neuroimaging study.** *In writing.*

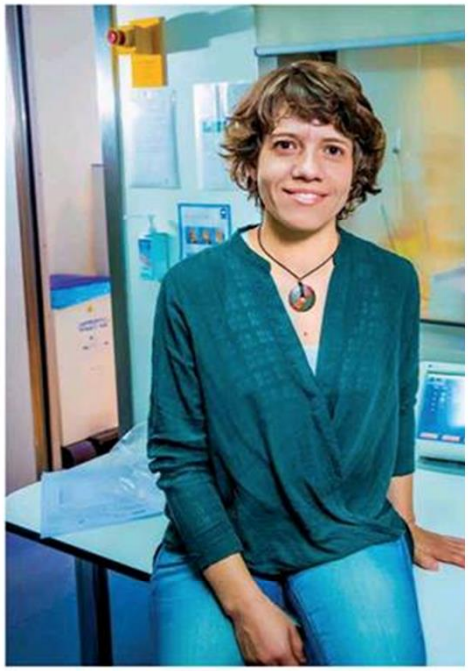
Martins D, Mehta M, PRATA D. "The "highs and lows" of the human brain on dopaminergics: Evidence from neuropharmacology". **Neuroscience and Biobehavioral Reviews**. *2017*

Martins D, Paloyelis Y, PRATA D. **"Shedding light on a dark question": Peripheral oxytocin signalling and neurobehavioral responses to intranasal oxytocin in humans**. **Psychoneuroendocrinology**. 2016

UNIVERSIDADE LUSÓFONA GUINÉ

OUTREACH

- **Interview in Documentary** “Portugal Desconhecido” in History Channel – Portugal
- **TV debate** on the theme “Hug” at “Sociedade Civil” in RTP2
- **Interview** on NeuroPsyCAD startup for “Jornal de Negócios” newspaper
- **Interview** for magazine of “Diário de notícias”
- **TV debate** on the theme “Emotions” at “Sociedade Civil” in RTP2
- **Public Talk** at ComCeptCon, COMCEPT, conference “Esmiuçar o cérebro“
- **Public Talk** at Culturgest “Empatia: Biologia ou Educação?
- **Interview** at Design the Future magazine
- **TV Interview** in News Night piece ‘Reportagem no Jornal da Noite SIC Notícias ‘
- **Magazine article** ‘Investigating Oxytocin’ in Super Interessante magazine
- **Public talk** and **Debate** on ‘The senses’ by news media Observador at CCB
- **Public talk** on ‘The biology of social behaviour’ at Pav. Conhecimento by Ciência Viva
- **Table** at The European Investigators’ Night
- **Public Pub talk** in ‘evening of Science’ at Oxford Science Festival



a função de ajudar as mulheres no parto, promovendo, por exemplo, as contrações. E vai testar o seu efeito em algumas zonas do cérebro: numa pequena estrutura cerebral (amígdala) que sinaliza o medo, num núcleo (estriado) que é responsável pela sensação de recompensa e em partes do córtex frontal e temporal, a área cerebral com a qual conseguimos perceber as emoções nos outros.

Há estudos que indicam, adianta a investigadora, que a oxitocina diminuiu a atividade da amígdala e, portanto, reduz o medo e torna as pessoas mais calmas. Além disso, aumenta a ação do núcleo do prazer e fortalece a sensação de recompensa associada à interação social, o que faz crescer a vontade de confiar nos outros e melhora a capacidade dos neurónios do córtex que nos fazem entender o que uma pessoa está a sentir quando olhamos para ela.

«O que vamos fazer é tentar perceber onde estão e como trabalham os recetores desta substância no cérebro», detalha Diana Prata, que espera ainda descobrir se os genes influenciaram todo este processo do compo genéticos menos ox

Seja co esta subs ra ajudar portame seu traba (Bial, Ins ropeia), q Depois d – já tem s dora que esquizofr

Desde próprio l lecular d estudar a

E agora tância é outros.

SAÚDE

TESTAR A HORMONA DA CONFIANÇA

No Instituto de Medicina Molecular de Lisboa, 200 a 300 doentes vão consumir uma substância enquanto os seus cérebros serão analisados em tempo real. O estudo clínico nunca foi realizado em Portugal.

Diana Prata está a realizar um estudo clínico inédito no país e prepara-se para começar em breve a analisar, em tempo real, o cérebro de 200 a 300 homens, enquanto estes realizam vários jogos – como o dilema do prisioneiro, em que os participantes podem decidir cooperar ou trair os concorrentes.

Aos 38 anos, a investigadora do Instituto de Medicina Molecular de Lisboa procura descobrir de que forma a oxitocina, uma hormona produzida no cérebro, leva as pessoas a colaborarem e confiarem umas nas outras, a serem menos egoístas, a terem mais ou menos receio dos outros. Para isso, os voluntários – uns irão inalar aquela substância e outros consumirão um placebo – serão sujeitos a uma ressonância magnética durante uma hora e durante outra usarão uma touca de elétrodos para lhes registar e gravar a atividade cerebral enquanto observam imagens de pessoas assustadas e contentes, a ouvir sons diferentes e a enfrentar dilemas. «Vou verificar o que, perante certas situações, as pessoas decidem e o que, nesse momento, acontece no cérebro», explica Diana Prata, que em 2002, quando se licenciou em Biologia pela Faculdade de Ciências da Universidade de Lisboa, partiu para Londres. Ao longo de 12 anos na capital britânica realizou, no King's College London, vários estudos sobre os genes e as doenças mentais, como distúrbios alimentares, doença bipolar e esquizofrenia.

Foi durante estes trabalhos que percebeu que há variada medicação para as alucinações e delírios dos esquizofrénicos mas não há fármacos para os ajudar a melhorar em relação aos problemas de comportamento social que os afetam e os levam ao isolamento. A investigadora tem esperança de que, no futuro, este estudo possa contribuir para o desenvolvimento de medicamentos que melhorem estes sintomas comportamentais na esquizofrenia, mas também noutras doenças, como autismo, depressão, ansiedade, anorexia ou até toxicodependência.

Para isso, Diana Prata vai usar a oxitocina – uma hormona que até recentemente se julgava ter apenas

Controlamos o comportamento?

Inve
OXI

**É bom pensar qu
decidimos ou fazer
de olhares ou u
produzir alteraçõ
de nos levar a co
A neurobiólog**

O projeto ganhou forma
meses e, ao longo do
cinco anos, vai estud
portamentos de coope
fiança e competição em cerca de 3
O objetivo é compreender os meca
efeitos da oxitocina, uma substânci
no hipotálamo que tem a capacidad
ciar a nossa disposição para cola
as outras pessoas. Pelo meio, su
perguntas incómodas. Até que po
portamento humano é biologicam
minado? É possível manipulá-lo atr
macos? À frente do estudo, e de u
formada por um médico, um enger
sico, duas psicólogas, uma bióloga e
mática, está a neurobióloga Diana
cedora de uma bolsa Marie Curie de
Carreira, da União Europeia, no va
mil euros.

O quartel-general onde as inv
terão lugar é o Instituto de Medici
lar, da Universidade de Lisboa. Aí,
de dois dias, os candidatos serão s
a uma bateria de testes, com des
as imagens por ressonância magn
ver o que acontece no cérebro em tempo
real. "Estou interessada em jogos que envol-
vam dilemas sociais, para ver o que as pessoas
decidem e o que acontece no cérebro quando
estão a fazê-lo", explica a cientista. Basica-
mente, quer-se saber que zonas se ativam
quando nos decidimos por um comporta-

quem recebia oxitocina dava a outra pessoa
uma maior parte de um prémio entregue
pelo experimentador. Há, igualmente, outros
estudos relacionados com a confiança, em

que demonstram que as pessoas "manipuladas
pela oxitocina, ou seja, quando a inalam pelo
nariz, não só têm comportamentos mais pró-
-sociais, conseguindo adivinhar melhor as emo-
ções de outras pessoas ao olhar para as suas
fotografias, como se revelam mais generosas.
Por exemplo, em alguns testes, e em média,

NEURO COLAB

COLABORA CONNOSCO...

...EM ESTUDOS DE **NEUROCIÊNCIA!**

+

O LADO NEGRO DA OBEDIÊNCIA

Março 20, 2017
Deixe um comentário
Editar

Após as justificações para os actos de genocídio do Holocausto fornecidas nos julgamentos de Nuremberg, o psicólogo Stanley Milgram levantou a hipótese:

"Será que Eichmann e os seu milhões de cúmplices no Holocausto estavam apenas a seguir ordens?"

Construiu uma experiência simples, no *Yale Interaction Laboratory*, para **testar quanta dor um cidadão normal infligiria noutra pessoa simplesmente porque recebeu ordens** de um investigador[1].

Foi pedido aos voluntários, sob a autoridade do experimentador, para **administrarem choques eléctricos** a uma pessoa na sala adjacente **por cada resposta errada**.

Os voluntários foram informados que o objectivo do estudo seria testar aprendizagem e memória,


APPLIED

ENTREPRENEURSHIP

Med-Tech Startup

NEUROPSYCAD

A clinical report for early and accurate diagnosis in neuropsychiatry

www.neuropsycad.com | info@neuropsycad.com

ENTREPRENEURSHIP


Hugo Ferreira
MSc Physics, Medicine, PhD
Diana Prata
MSc Neuroscience, PhD
Ricardo Maximiano
MSc Biomedical Eng
COHiTEC
NEUROPSYCAD
2016: **Idea** Prize to 10 best startup ideas, Born From Knowledge
2016: **'InovPortugal New Ideas B2B'** Award, Acredita Portugal

ENTREPRENEURSHIP

Subjective & delayed diagnosis in neuropsychiatry

With NeuroPsyCAD, clinicians send us the brain scan...

é we use *artificial intelligence* to compare it to a patientsô databaseé

... and provide a report (in hours) for *early and accurate* diagnosis.

REPORT on Patient X:

Alzheimerôs disease: 93%
Mild cognitive impairment: 7%

Model: 94% accuracy
(94% sensitivity; 95% specificity)

- ***Early* disease management**
- **Slowed disease progression**
- **Lower healthcare costs**

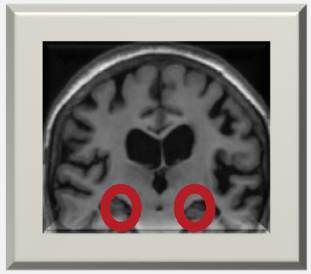
ENTREPRENEURSHIP

NEUROPSYCAD

✓AI platform for Image Recognition of Neuropsychiatric Disorders

'Big Data'

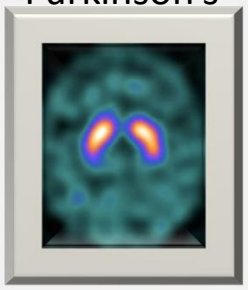
Alzheimer's



61% ➡ 94%

54% more accurate

Parkinson's

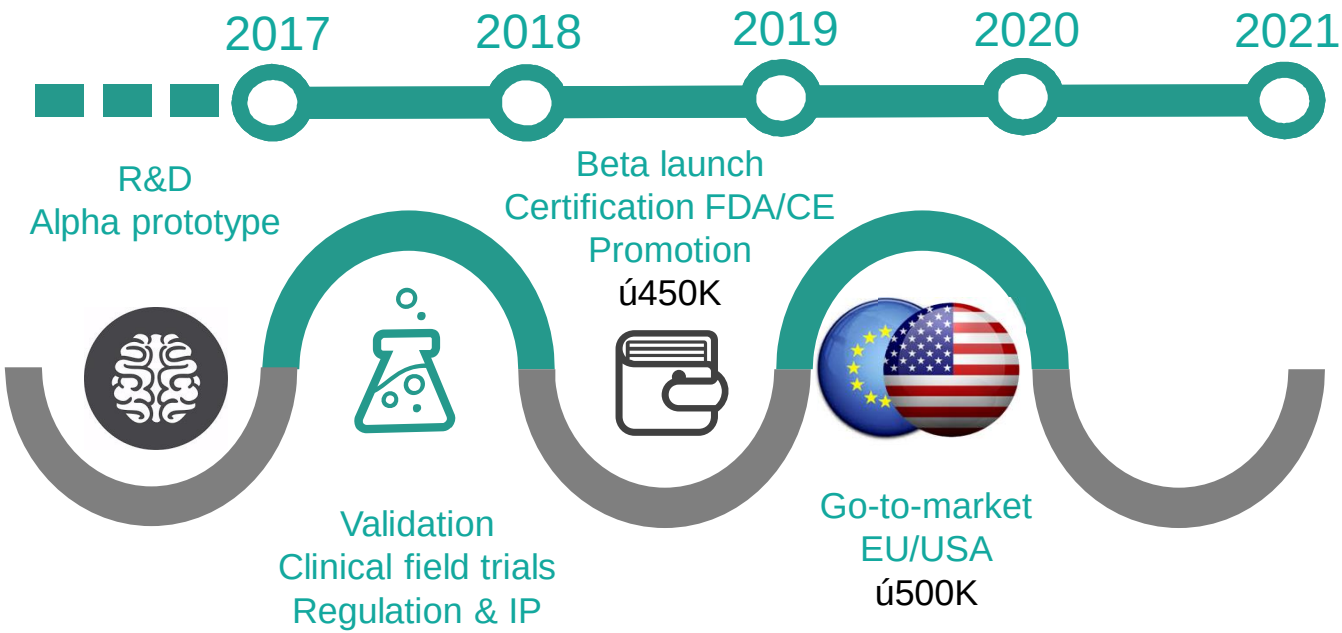


€1500 ➡ €300

5x cheaper

Capitalization on scan's information

No other exams



Clinical Partners

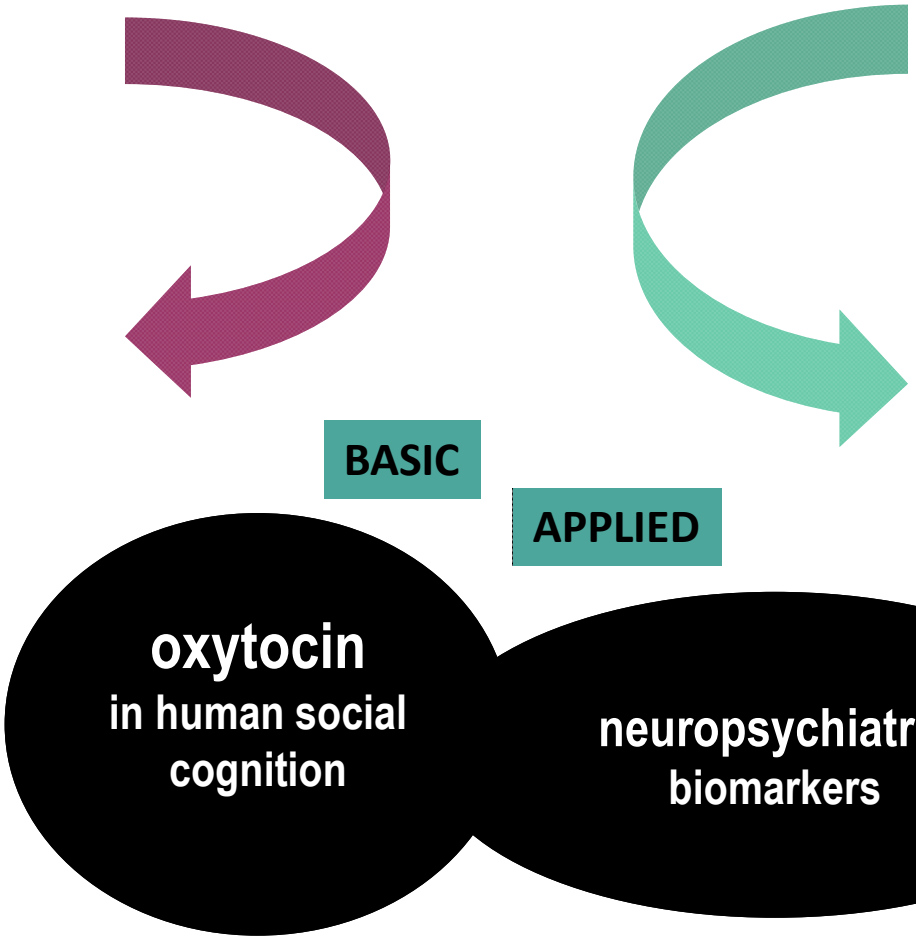
LUZ SAÚDE

UNIVERSITY OF EASTERN FINLAND

KING'S College LONDON

Maccabi Healthcare Services

Using biology and statistics to advance neuropsychiatry



MARIE CURIE ACTIONS

FP7 Marie Curie Career Integration Grant

Thank you!

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www.dpratalab.wordpress.com