

Project number: 220139

Project acronym: DA and decisions

Project full name: the role of dopamine and novelty in decision making in humans: behavioural and neuroimaging studies.

Final Report

Period covered: from 01/07/2008 to 30/06/2010

Period number: 1

Start date of project: 01/07/2008

Project beneficiary name: Dr. Marc Guitart Masip

Project beneficiary organization name: University College London

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1. Final publishable summary report

Using fMRI, we showed for the first time that neural responses to rewarding stimuli in the striatum were enhanced in the context of novelty. Using MEG we discovered that neural correlates of reward anticipation emerge as a modulation of oscillatory activity over frontal sensors within 150 ms. Finally, contextual novelty enhanced the effects of reward anticipation on oscillatory activity.

In a series of behavioural experiments we could show that after conditioning abstract stimuli to monetary wins or losses, the incidental presentation of these stimuli as contextual cues in an independent gamble task biased the participants' decisions to choose between a gamble and a sure option. This contextual bias is analogous to the framing effect described in prospect theory of decision making, and suggests that the framing effect could be explained as arising from an influence of conditioned associations on goal directed decision making. Moreover, we conducted an fMRI study using the same task and found that activation of the amygdala was the brain correlate of the observed bias as has been described in previous fMRI experiments of the classical framing effect.

Thereafter, we designed a new behavioural task that allowed us to isolate the brain responses generated by the anticipation of valence (reward and punishment) from the brain responses generated by the preparation of impending motor responses (required to obtain rewards or to avoid punishment). This new approach towards separating the neural signatures of anticipating reward or punishment from preparing for appropriate actions led to new findings that, we believe, will lead to a new concept of the role that dopamine plays in reward processing. Using our new task and fMRI, we found that during anticipation and before any behaviour is generated, the striatum and lateral aspects of the dopaminergic midbrain areas responded to action anticipation in contrast with the generally accepted role of these areas with reward anticipation. Moreover, we found that medial aspects of the dopaminergic midbrain responded to valence in an action dependent way. In a separate learning study we have found that participants are quick to learn to be active in the light of reward and to be passive in the light of punishment whereas it takes much longer for them to learn to be passive in the light of reward and to be active in the light of punishment. We have used computational modelling to establish that this behaviour arises from the interaction of an instrumental system that learns about the value of actions and a Pavlovian system that inhibits or promotes behaviour in the light of punishment or reward respectively. We are currently analyzing the fMRI data for this separate learning study. Finally, we have just completed the pharmacological experiment mentioned earlier. Behaviourally, we see that levodopa increases the accuracy of actions responses while citalopram has no effect. We expect to find that levodopa increases the brain responses to action anticipation irrespective of outcome valence which would change the well-established notion that dopamine is involved in anticipation of reward towards suggesting that dopamine is involved in preparing actions.

The conclusions of these studies are three-fold:

- In the context of novelty the responses to reward predictive stimuli in the striatum are enhanced.
- Biases in economic decision making can be accounted for by the interaction of different valuation systems.

- The striatum and dopaminergic midbrain mainly encode action anticipation instead of valence.
- An account of valence of reward and punishment (and the opponency between reward and punishment) must incorporate action both at a behavioural and at a neurological level.

The results obtained during the development of the project represent a substantial contribution to the understanding of the neurological underpinnings of decision-making. Some of the results enlarge a substantial body of evidence on the effects and neural mechanisms of contextual factors, particularly novelty, to decision making. On the other hand, the last series of experiments performed during the funding period provided new evidence for a reinterpretation of an important body of experimental work relating the striatum and the dopaminergic midbrain with the anticipation of reward. Thus, our findings highlight a need to reformulate the role of these regions in representing reward and punishment. Thus, in our opinion, the results we present will motivate a new line of research towards a better characterization of the role of action and valence processing in these brain systems.

Finally, the results of this research will inform research into aging and neuropsychiatric disorders where aberrant novelty and dopamine processing may reflect a fundamental component such as Parkinson's Disease, ADHD, schizophrenia and depression. This may ultimately result in the development of better diagnostic and therapeutic tools and benefit society.

2. Use and dissemination of foreground

Peer reviewed publications

The results obtained during the fellowship have been published in 2 peer-reviewed journals as research articles:

Guitart-Masip M, Bunzeck N, Stephan KE, Dolan R, Duzel E (2010) Contextual novelty changes reward representations in the striatum. *J Neuroscience*, 30:1721-1726

Guitart-Masip M, Talmi D, Dolan R (2010) Conditioned associations and economic decision biases. *NeuroImage*, in pres [doi:10.1016/j.neuroimage.2010.06.021](https://doi.org/10.1016/j.neuroimage.2010.06.021)

And two reviews have been published:

Düzel E, Bunzeck N, **Guitart-Masip M**, Wittmann B, Schott BH, Tobler PN (2009) Functional imaging of the human dopaminergic midbrain. *Trends Neurosci* 32:321-328.

Düzel E, Bunzeck N, **Guitart-Masip M**, Düzel S (2009) NOvelty-related Motivation of Anticipation and exploration by Dopamine (NOMAD): Implications for healthy aging. *Neurosci Biobehav Rev*, 34:660-669.

Moreover, one other manuscript is currently under consideration

Guitart-Masip M, Fuentemilla LL, Bach D, Huys Q, Dayan P, Dolan R, Duzel E (2010) Disambiguating action and valence representation in the human striatum and dopaminergic midbrain.

One more is under preparation

Bunzeck N, **Guitart-Masip M**, Dolan R, Duzel E (2010) Contextual novelty changes the neural dynamics of reward anticipation, an MEG study.

And at least two more are expected to result from the work developed during the project duration.

Participation in scientific meetings

Guitart-Masip M, Bunzeck N, Dolan R and Düz el E
Contextual novelty changes reward representations in the ventral striatum
4th Alpine Brain Imaging Meeting (2009), Champéry, Switzerland

Guitart-Masip M, Talmi D, Duzel E, Dolan R
Biases in choices emerge from different interacting value systems in the human brain
39th Meeting of the Society for Neuroscience (2010), Chicago, USA

Guitart-Masip M, Fuentemilla LL, Bach D, Huys Q, Dayan P, Dolan R, Duzel E (2010)
Disambiguating action and valence representation in the human striatum and dopaminergic midbrain.
16th Meeting of the Organization for Human Brain Mapping (2010), Barcelona, Spain

Duzel E (2010)
On the Relationship Between Hemodynamic Responses of the Substantia Nigra/Ventral Tegmental Area (SN/VTA) and Dopamine Release
16th Meeting of the Organization for Human Brain Mapping (2010), Barcelona, Spain