converging evidence that biases implemented through adjustments of the starting point are related to activity in the basal ganglia and fronto-parietal cortical networks [14,15]. Interestingly, the activation of exactly these areas seems to be most severely affected in Parkinson's disease [16]. Conversely, bias implemented through drift rate adjustments has been related to activity in the temporal cortex in a previous functional neuroimaging study [17]. Thus, the failure to use prior knowledge in order to adjust the starting point and the increased use of drift rate adjustments in Parkinson's disease might reflect a shift from activation of more severely to less affected neural networks in Parkinson's disease.

Is the observed behavioural deficit related to dopamine deficiency? Parkinson's disease is a heterogeneous disorder comprising alterations in multiple neurotransmitters and neural networks [2]. Furthermore, dopamine replacement therapy, rather than dopamine deficiency, can affect decision-making by impairing patients' abilities to learn, to express learned information or both [3,18,19]. Since in the work of Basso *et al.* [4] all patients were taking their normal dopaminergic medication, it remains to be elucidated whether dopamine itself affects how people bias their decisions using prior knowledge.

Together, the results by Basso *et al.* [4] showing that Parkinson's disease patients are impaired in using prior information during choice uncertainty are an important new lead in understanding decision-making deficits in Parkinson's disease. It remains an open question for future studies to what extent this contributes to the clinical symptoms of Parkinson's disease, particularly the increased reliance on external stimuli during movement [20].

## REFERENCES

1. Dorsey, E.R., Constantinescu, R., Thompson, J.P., Biglan, K.M., Holloway, R.G., Kieburtz, K., Marshall, F.J., Ravina, B.M., Schifitto, G., Siderowf, A., *et al*. (2007). Projected number of people with Parkinson disease in the most populous nations, 2005 through 2030. Neurology *68*, 384–386.
2. Kalia, L.V., and Lang, A.E. (2015). Parkinson's disease. Lancet *386*, 896–912.
3. Robbins, T.W., and Cools, R. (2014). Cognitive deficits in Parkinson's disease: a cognitive neuroscience perspective. Mov. Disord. *29*, 597–607.
4. Perugini, A., Ditterich, J., and Basso, M.A. (2016). Patients with Parkinson's disease show impaired use of priors in conditions of sensory uncertainty. Curr. Biol. *26*, 1902–1910.
5. Bogacz, R., Brown, E., Moehlis, J., Holmes, P., and Cohen, J.D. (2006). The physics of optimal decision making: a formal analysis of models of performance in two-alternative forced-choice tasks. Psychol. Rev. *113*, 700–765.
6. Ratcliff, R., and McKoon, G. (2008). The diffusion decision model: theory and data for two-choice decision tasks. Neural Comput. *20*, 873–922.
7. Edwards, W. (1965). Optimal strategies for seeking information: Models for statistics, choice reaction times, and human information processing. J. Math. Psychol. *2*, 312–329.
8. Hanks, T.D., Mazurek, M.E., Kiani, R., Hopp, E., and Shadlen, M.N. (2011). Elapsed decision time affects the weighting of prior probability in a perceptual decision task. J. Neurosci. *31*, 6339–6352.
9. Drugowitsch, J., Moreno-Bote, R., Churchland, A.K., Shadlen, M.N., and Pouget, A. (2012). The cost of accumulating evidence in perceptual decision making. J. Neurosci. *32*, 3612–3628.
10. Hamid, A.A., Pettibone, J.R., Mabrouk, O.S., Hetrick, V.L., Schmidt, R., Vander Weele, C.M., Kennedy, R.T., Aragona, B.J., and Berke, J.D. (2016). Mesolimbic dopamine signals the value of work. Nat. Neurosci. *19*, 117–126.
11. Redgrave, P., Gurney, K., and Reynolds, J. (2008). What is reinforced by phasic dopamine signals? Brain Res. Rev. *58*, 322–339.
12. Bogacz, R., and Gurney, K. (2007). The basal ganglia and cortex implement optimal decision making between alternative actions. Neural Comput. *19*, 442–477.
13. Herz, D.M., Zavala, B.A., Bogacz, R., and Brown, P. (2016). Neural correlates of decision thresholds in the human subthalamic nucleus. Curr. Biol. *26*, 916–920.
14. Lauwereyns, J., Watanabe, K., Coe, B., and Hikosaka, O. (2002). A neural correlate of response bias in monkey caudate nucleus. Nature *418*, 413–417.
15. Mulder, M.J., van Maanen, L., and Forstmann, B.U. (2014). Perceptual decision neurosciences - a model-based review. Neuroscience *277*, 872–884.
16. Herz, D.M., Eickhoff, S.B., Lokkegaard, A., and Siebner, H.R. (2014). Functional neuroimaging of motor control in Parkinson's disease: a meta-analysis. Hum. Brain Mapp. *35*, 3227–3237.
17. White, C.N., Mumford, J.A., and Poldrack, R.A. (2012). Perceptual criteria in the human brain. J. Neurosci. *32*, 16716–16724.
18. Frank, M.J., Seeberger, L.C., and O'Reilly, R.C. (2004). By carrot or by stick: cognitive reinforcement learning in parkinsonism. Science *306*, 1940–1943.
19. Smittenaar, P., Chase, H.W., Aarts, E., Nusselein, B., Bloem, B.R., and Cools, R. (2012). Decomposing effects of dopaminergic medication in Parkinson's disease on probabilistic action selection–learning or performance? Eur. J. Neurosci. *35*, 1144–1151.
20. Jankovic, J. (2008). Parkinson's disease: clinical features and diagnosis. J. Neurol. Neurosurg. Psych. *79*, 368–376.

# Neuroscience: Incepting Associations

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http://dx.doi.org/10.1016/j.cub.2016.05.041

**A recent study has used real-time fMRI neurofeedback to induce color-specific activity patterns in early visual cortex as participants viewed achromatic gratings. This procedure resulted in an association between the color and the displayed grating orientation, suggesting that early visual cortex can support associative learning of this type.**

Isolating the role of particular brain regions in learning is complicated by the dense interconnectivity of the brain. When stimuli are displayed, this sets off a cascade of neural activity throughout the visual processing stream. Any of

these areas, from early visual cortex to hippocampus, could be sites where associations are formed between stimuli, and it is difficult to tease apart the role of each site. A recently developed technique, known as real-time functional magnetic resonance imaging (fMRI) neurofeedback, may provide a non-invasive means of establishing where learning is taking place. As they report in this issue of *Current Biology*, Amano *et al.* [1] have used this technique to demonstrate that early visual cortex has a role in associative learning.

Real-time fMRI neurofeedback merges fMRI data collection, analysis, and stimulus presentation into a single closed-loop procedure. The fMRI data files are processed as they arrive, by comparing them against a trained model or a baseline level of activity. Feedback about the fMRI measurements is then communicated to the participant, often by updating the display [2]. This technique has broad applications for both basic science and clinical research [3]. It has been used to return feedback on regional activity [4,5] as well as distributed patterns [6–8], and this process has been shown to have strong effects on cognitive performance [7,8].

In most published real-time fMRI neurofeedback studies, participants are informed of the nature of the feedback and given instructions about how to maximize it [4–7]. This is not strictly necessary, however: feedback without instruction can result in lasting neural and behavioral changes. One powerful demonstration of this technique addressed the role of early visual cortex in perceptual learning [8]. Participants were asked to maximize a feedback signal that (unbeknownst to them) reflected whether brain activity corresponding to a particular line orientation was present in early visual cortex; after repeatedly activating these orientation-specific patterns, participants demonstrated improved ability to discriminate between that orientation and other orientations. Shibata *et al.* [8] referred to this as 'incepted' neurofeedback, because participants were learning about specific perceptual details without awareness of those details, in homage to the science-fiction movie 'Inception' where information was inserted into people's dreams.

Amano *et al.* [1] have extended this 'inception' approach to ask whether early visual cortex can support the formation of associations between an orientation and a color. First, they trained a multivariate pattern classifier to discriminate red *versus* green stimuli based on activity patterns in early visual cortex elicited by viewing those colors. Next, participants underwent a training protocol designed to coactivate a particular orientation and color (red). Critically, during this protocol, the red color was never actually present onscreen. Participants were repeatedly presented with an achromatic grating of a particular orientation and given feedback about their neural activity. They were told to maximize this feedback but not given specific instructions about how to do this. Unbeknownst to the participants, this feedback corresponded to how well their brain pattern (in the present) matched the brain pattern (at training) associated with perceiving red. In a post-test, participants showed a significant tendency to perceive the trained orientation in the color targeted with neurofeedback; this bias was specific to the trained orientation. These results suggest that it is possible to induce associations, without awareness or even stimulus presentation, using activity patterns from early visual cortex.

Importantly, Amano *et al.* [1] did not merely want to show that association learning happens in this paradigm; they also make the strong claim that the color–orientation associations were formed within early visual cortex. To substantiate this claim, the authors completed multiple analyses aimed at mapping out the neural evidence for color information in the brain. For these analyses, they used pattern classifiers applied to localized brain areas ('searchlights') to decode fine-grained patterns of activity. First, they demonstrated that color was widely decodable in early and higher-level visual areas during the classifier-training run (when color was visible). That is, when color was on the screen, color information robustly spread through a broad swath of cortex. Then, they completed searchlight analyses during the feedback runs. During periods of neurofeedback, the areas where color could be decoded were largely restricted to the early visual cortex, which was the locus of the feedback. To the extent that information about the color did not spread beyond early visual cortex, this suggests that early visual cortex is the only place where associative learning about color could have occurred.

It is possible that follow-up experiments will be able to indicate with even more certainty that the activity is not spreading into higher visual areas. Most critically, it would be useful to compare these results with feedback from another region. Given that early visual cortex represents visual information in a localized fashion, training directed at a limited region of the visual field or one eye should not transfer completely to other regions or the other eye if early visual cortex supplies the feedback. Amano *et al.* [1] could contrast these effects with a follow-up study where participants receive feedback based on color-related information from a different region, such as V4. Insofar as higher-level visual areas have broader receptive fields, we would expect that more transfer between locations and between eyes would occur in this case. Any interesting differences between the associations — for example, in time of acquisition, duration or specificity — as a function of the neural locus of feedback could illustrate important differences between nearby neural regions in associative learning. By comparing different regions, neurofeedback could be used to characterize how the nature of associations can change throughout the visual processing hierarchy.

The apparently limited spread of color information in the neurofeedback condition highlights a unique benefit of the 'inception' approach, in comparison to approaches that involve overtly presenting the color onscreen or having participants deliberately imagine the color. As noted above, when participants are aware of the color, color-related information can spread all the way up the visual hierarchy, making it possible for participants to draw upon

general-purpose associative learning mechanisms in the medial temporal lobes. Numerous studies have shown that the hippocampus can rapidly bind arbitrarily-related features that are present in awareness [9], even if the features pertain to very low-level stimulus features like orientation [10] and even if the to-be-associated features are only present in memory, not in perception [11–13]. By limiting the spread of color information to early visual cortex, the neurofeedback procedure used by Amano *et al.* [1] eliminates the possibility of using higher-level association-formation mechanisms.

In making this point, the study by Amano *et al.* [1] does not just shed light on associative learning — it also helps to show more generally how real-time fMRI neurofeedback can be used as a tool to study the neural basis of cognition. In prior work from our lab [7], we have shown that real-time fMRI neurofeedback can be used to amplify internal cognitive states by 'externalizing' them. We returned feedback about fluctuations in sustained attention by making the to-be-attended stimuli more or less visible, with the goal of making participants more aware of these fluctuations and thus better able to control them; we showed that this externalization procedure reduced attention lapses and improved behavior. The work of Amano *et al.* [1] shows almost the opposite benefit — instead of using real-time fMRI to make participants *more aware* of a process that is usually hard to control, their procedure makes it possible to take a process (color perception) that is usually conscious, and it renders it unconscious. The Amano *et al.* [1] study makes it clear that this 'inception' procedure is not just a parlor trick: The unconscious nature of this percept appears to limit its spread in the brain, thereby making it possible to make sharper inferences about where learning is taking place.

## REFERENCES

1. Amano, K., Shibata, K., Kawato, M., Sasaki, Y., and Watanabe, T. (2016). Learning to associate orientation with color in early visual areas by associative decoded fMRI neurofeedback. Curr. Biol. *26*, 1861–1866.
2. Sulzer, J., Haller, S., Scharnowski, F., Weiskopf, N., Birbaumer, N., Blefari, M.L., Bruehl, A.B., Cohen, L.G., DeCharms, R.C., Gassert, R., *et al*. (2013). Real-time fMRI neurofeedback: progress and challenges. Neuroimage *76*, 386–399.
3. Stoeckel, L.E., Garrison, K.A., Ghosh, S., Wighton, P., Hanlon, C.A., Gilman, J.M., Greer, S., Turk-Browne, N.B., deBettencourt, M.T., Scheinost, D., *et al*. (2014). Optimizing real time fMRI neurofeedback for therapeutic discovery and development. Neuroimage Clin. *5*, 245–255.
4. deCharms, R.C., Maeda, F., Glover, G.H., Ludlow, D., Pauly, J.M., Soneji, D., Gabrieli, J.D.E., and Mackey, S.C. (2005). Control over brain activation and pain learned by using real-time functional MRI. Proc. Natl. Acad. Sci. USA *102*, 18626–18623.
5. MacInnes, J.J., Dickerson, K.C., Chen, N., and Adcock, R.A. (2016). Cognitive neurostimulation: learning to volitionally sustain ventral tegmental area activation. Neuron *89*, 1331–1342.
6. Papageorgiou, T.D., Lisinski, J.M., McHenry, M.A., White, J.P., and Laconte, S.M. (2013). Brain-computer interfaces increase whole-brain signal to noise. Proc. Natl. Acad. Sci. USA *110*, 13630–13635.
7. deBettencourt, M.T., Cohen, J.D., Lee, R.F., Norman, K.A., and Turk-Browne, N.B. (2015). Closed-loop training of attention with real-time brain imaging. Nat. Neurosci. *18*, 470–475.
8. Shibata, K., Watanabe, T., Sasaki, Y., and Kawato, M. (2011). Perceptual learning incepted by decoded fMRI neurofeedback without stimulus presentation. Science *334*, 1413–1415.
9. Eichenbaum, H., and Cohen, N.J. (2001). From Conditioning to Conscious Recollection: Memory Systems of the Brain (New York: Oxford Univ. Press).
10. Bosch, S.E., Jehee, J.F.M., Fernandez, G., and Doeller, C.F. (2014). Reinstatement of associative memories in early visual cortex is signaled by the hippocampus. J. Neurosci. *34*, 7493–7500.
11. Rudy, J.W., and O'Reilly, R.C. (2001). Conjunctive representations, the hippocampus, and contextual fear conditioning. Cogn. Affect. Behav. *1*, 66–82.
12. Gershman, S.J., Schapiro, A.C., Hupbach, A., and Norman, K.A. (2013). Neural context reinstatement predicts memory misattribution. J. Neurosci. *33*, 8590–8595.
13. Ramirez, S., Liu, X., Lin, P.-A., Suh, J., Pignatelli, M., Redondo, R.L., Ryan, T.J., and Tonegawa, S. (2013). Creating a false memory in the hippocampus. Science *341*, 387–391.

# Decision-Making: Are Plants More Rational than Animals?

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**A new study presents a novel experimental design and allows a test of risk sensitivity in plants. Faced with a choice between constant and variable resource supply, they make a rational decision for the option that maximizes fitness, a fact rarely observed in animals.**

Organisms are confronted with choices when they forage. A particularly interesting situation occurs when the same amount of resource can be obtained from either a constant or a variable source. Should an individual be risk averse and choose a constant, yet modest option, or should it be risk prone and choose a variable, yet more promising option? The answer will depend on the biological context. According to risk sensitivity theory (RST), the rational decision would be the one that maximizes fitness [1]. To do so, the individual should behave according to the fitness function of the relevant resource. If this function is accelerating (convex) at the level of resources obtained per unit time and effort, the total utility or fitness gain is larger if the variable