fMRI ROI analysis. All results reported in the main text are with a corrected significance threshold of $P<0.05$ based on a small-volume false discovery rate correction within the predefined ROIs.

Evaluating the precise location of midbrain fMRI signals is difficult given the small size of the dopaminergic nuclei and problems with group registration in this region.[65] Therefore, we anatomically defined an ROI for the ventral midbrain (encompassing both the VTA and the SN; Supplementary Figure S2). We also used an anatomically defined ROI for the caudate (Supplementary Figure S2). For our ROI of VMPFC, we defined a 10-mm sphere centered at ($x=-3$; $y=38$; $z=-18$). These coordinates were taken from a previous study examining facial attractiveness encoding.[60]

All effect sizes within these ROIs were extracted using the average of all voxels within the ROI.

Results

To test our hypotheses, we stimulated participants with tDCS, before and after we had them make attractiveness ratings of a series of faces while being scanned with fMRI (Figure 1a). This procedure allowed us to examine the neural and behavioral influence of our tDCS paradigm on appraisal of facial attractiveness (Figure 1b). We chose this task, because it is known to recruit components of neural reward circuits.[59,60,62–64] Rating facial attractiveness is one of the most basic reward appraisal tasks and employs limited cortical regions of the prefrontal cortex (that is, orbitofrontal cortex and VMPFC), which allows for a more straightforward interpretation of our behavioral and neural results and fewer confounds of electrode placement.

Behaviorally, following anodal stimulation of VMPFC and simultaneous cathodal stimulation of DLPFC (main stimulation group), participants found the presented faces significantly more attractive ($t(18)=2.26$; $P=0.03$; Figure 1c). We tested a number of control conditions in which we varied the location and polarity of tDCS electrodes. None of these control conditions yielded a significant increase in attractiveness ratings following stimulation (Figure 1c, Supplementary Figure S1). Taken together, these control conditions show that the specific combination of electrode placement and anodal/cathodal stimulation in the main stimulation group was critical to cause the behavioral and neural effects reported ($F(2, 52)=5.48$; $P=0.007$).

For the main group in which anodal stimulation was applied to VMPFC and cathodal stimulation was applied to DLPFC, and the active sham group in which anodal stimulation was applied to DLPFC and cathodal stimulation was applied to VMPFC, we collected fMRI while participants made attractiveness ratings. We made four predictions about the patterns of neural activity resulting from these stimulation conditions, which we tested using the fMRI data. First, in both the stimulation groups, activity in VMPFC should be correlated with participants' attractiveness ratings both before and after stimulation. Second, an interaction between attractiveness

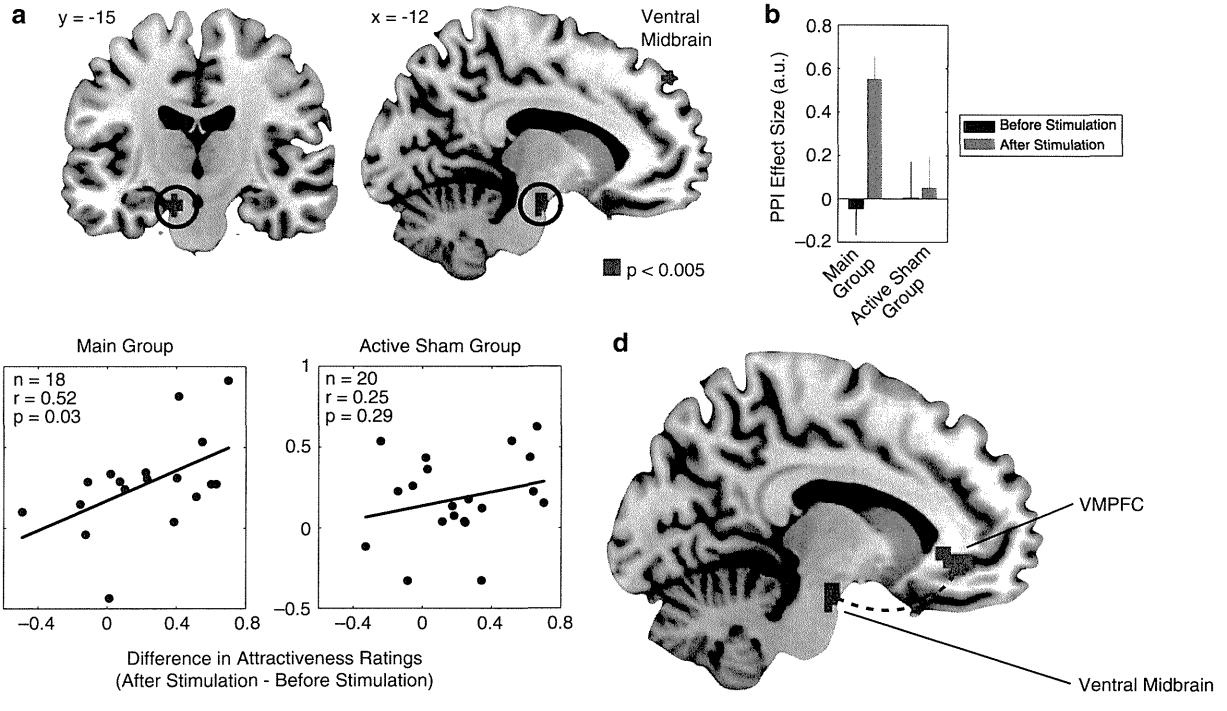

Figure 3 Functional connectivity. (**a**) In the main group as compared with the active sham group, the ventromedial prefrontal cortex (VMPFC) showed positive stimulation-related functional connectivity with a region of ventral midbrain. (**b**) For the psychophysiological interaction (PPI) contrast, average effect sizes representing the functional connectivity between seed activity in the VMPFC and the ventral midbrain. (**c**) In the main group, the more enhanced a participants' functional connectivity between these regions following stimulation, the larger their increase in attractiveness ratings following stimulation. One participant in the main group was removed from this analysis because her PPI parameter estimate constituted a statistical outlier (outside two s.ds. of the mean). (**d**) Diagram summarizing the results of the PPI analyses and illustrating the path through which VMPFC stimulation might enhance activity in the ventral midbrain. All contrasts are displayed at $P<0.005$ uncorrected, and significant at $P<0.05$, small volume corrected. a.u., arbitrary units.

ratings before and after stimulation should reveal an increase in neural activity for attractive faces in ventral midbrain following stimulation in the main group as compared with the active sham group (reflecting a remote stimulation of ventral midbrain in the main stimulation group). Third, VMPFC and ventral midbrain should exhibit increased functional connectivity following stimulation in the main group compared with the active sham group. Fourth, those participants with enhanced connectivity between VMPFC and ventral midbrain following stimulation in the main group should display larger increases in attractiveness ratings.

We tested the first prediction by estimating a GLM of BOLD activity that included a parametric regressor for attractiveness ratings at the time of evaluation. Activity in VMPFC was correlated with attractiveness ratings for all participants both before and after stimulation (Figures 2a and b; Supplementary Table S1). The area of VMPFC identified overlaps with regions that have been associated with attractiveness ratings in other studies.[59,60]

To test the second prediction, we used the same GLM described above. We found significant interactions between attractiveness ratings before and after tDCS in the main group as compared with the active sham group in a ROI, including the ventral midbrain (Figure 2c, Supplementary Table S2; Supplementary Figure S2). This interaction was such that following stimulation in the main group, activity in the ventral midbrain was more positively correlated with attractiveness ratings (Figure 2d). The ventral midbrain has been implicated in responses to rewarding stimuli,[65] and this interaction suggests that tDCS in the main group increases responsiveness in this region as compared with the active sham group.

To address our third prediction, we created a new GLM in which we tested a PPI between before/after stimulation (psychological/task variable) and seed activity in the VMPFC (physiological variable). This model allowed us to examine the network effects of VMPFC stimulation on other brain regions, with specific interest in the same ROI used above that encompassed ventral midbrain dopaminergic areas (Supplementary Figure S2). Strikingly, we found a region of the same ventral midbrain ROI to be more correlated with VMPFC activity following stimulation in the main stimulation group as compared with the active sham group (Figures 3a and b; Supplementary Table S3). This result suggests that the functional connectivity between VMPFC and ventral midbrain is enhanced by tDCS in the main stimulation group.

We tested our fourth prediction by performing a linear regression of activities in ventral midbrain identified in the PPI and the differences in participants' mean attractiveness ratings following tDCS. We found a significant correlation in the main stimulation group ($r=0.52$, $P=0.03$) and not the active sham group ($r=0.25$, $P=0.29$). This correlation illustrates that those participants with more enhanced connectivity following tDCS (in the main stimulation group) exhibited the greatest increase in attractiveness ratings (Figure 3c). Thus, anodal stimulation of VMPFC increased the functional connectivity between VMPFC and ventral midbrain (Figure 3d), and the tDCS enhancement of these connections caused participants' increases in behavioral ratings.

Discussion

These results demonstrate that anodal tDCS of VMPFC and cathodal stimulation of DLPFC can be used to induce remote changes in regions deep within the brain, which were conventionally thought to be unreachable with noninvasive stimulation techniques. Specifically, we were able to elicit remote functional changes within the ventral midbrain, an area populated with SN and VTA neurons and their efferent projections. Moreover, our attractiveness rating results indicate that these tDCS-induced neural changes have a direct influence on participants' rewarding appraisals.

Ours is the first tDCS study that provides a precise neuromechanistically motivated stimulation paradigm, which directly yields both stimulation-induced changes in brain connectivity and corresponding behavioral changes. These results may be related to a recent tDCS study,[25] which reported that cortical stimulation induced activations in the caudate nucleus. However, that study provided evidence for neither a brain network through which stimulation-induced changes occurred nor offered evidence that such neural changes were directly linked to behavioral effects. Our study goes further by providing simultaneous neural and behavioral evidence consistent with known functions of the remotely stimulated ventral midbrain. Moreover, the neural patterns of functional connectivity we induced with a very specific tDCS electrode configuration (and no other control stimulation conditions) are in concert with the network of projections known to exist between the frontal cortex and ventral midbrain. Indeed, a previous study found that increases in ventral midbrain BOLD are associated with increased reward preferences.[66]

Although fMRI and the paradigm we used in this experiment are not attuned to precisely identify the neural network that gives rise to the tDCS aftereffects we observed, our stimulation paradigm could take advantage of the numerous prefrontal cortex connections to induce the deep-brain changes we observed. The prefrontal cortex has projections that directly interface with the ventral midbrain,[28–32] while a far larger number of prefrontal connections indirectly couple the prefrontal cortex and ventral midbrain via the striatum.[5,33–35] We found significantly increased stimulation-induced connectivity between the prefrontal cortex and the ventral midbrain, and our fMRI analysis did not show significant connectivity between the striatum and the prefrontal cortex. A possible explanation for a lack of stimulation-induced connectivity in the striatum, despite its extensive anatomical connections to prefrontal cortex, could be due to a limitation of fMRI. In the context of this experiment, the transmission of signals from the prefrontal cortex through the striatum might be detectable with fMRI only through the striatum's inputs to the ventral midbrain (given that fMRI BOLD signal is more attuned to imaging synaptic processing of afferent input signals as opposed to spiking output[67]). In this view, prefrontal tDCS could induce striatal spiking output, which goes undetected by fMRI and causes the increased activity in the ventral midbrain we observed. Another explanation for the absence of striatal activity in our fMRI analysis is that tDCS of prefrontal cortex could be enhancing the direct prefrontal projections to the ventral midbrain. In both of these

explanations, it is possible that what is encoded by the enhanced BOLD signal observed in the ventral midbrain after stimulation is activity within inputs to dopamine neurons.

The gamma-aminobutyric acid (GABA)ergic[68,69] and glutamatergic[31,32] concentrations in the prefrontal cortex have an important role in modulating activity and dopamine release in the midbrain and striatum, and previous animal[70] and human studies[71,72] have found that anodal and cathodal tDCS influence these neurochemical systems. These studies have found that the aftereffects of anodal tDCS are dependent on modulation of GABA, with anodal tDCS yielding a decrease in GABA concentration at the site of stimulation. Cathodal aftereffects of tDCS, on the other hand, were found to be dependent on the modulation of glutamatergic synapses, yielding decreased concentrations of glutamate following stimulation. Although fMRI does not allow us to directly test such neurochemical effects in the context of our study, the tDCS aftereffects we report could be the result of changes in frontal cortex neurochemistry. Along these lines, in our experiment, VMPFC anodal tDCS could inhibit GABAergic interneurons, which in turn disinhibits pyramidal efferents that project to midbrain dopaminergic neurons, yielding the increase in midbrain sensitivity that we observe in our fMRI results. Cathodal DLPFC stimulation could also contribute to the midbrain activity we observe by reducing cortical glutamatergic concentrations, which in turn disinhibits subcortical dopamine release.

It is important to note that none of the control stimulation conditions yielded significant behavioral or neural effects. This suggests that the singular effects of cathodal or anodal stimulation were not sufficient to yield a significant influence. Instead, the very specific combination of anodal VMPFC and cathodal DLPFC stimulation were required to elicit behavioral and neural effects. However, considerable work will be needed to establish exactly which anatomical and neurochemical pathways are acted upon by this stimulation paradigm, and how interactions between anodal and cathodal stimulation give rise to the neural and behavioral effects we observed.[4] Since fMRI cannot provide a direct measure of dopaminergic function, future investigation using molecular imaging with dopamine receptor ligands (that is, positron emission tomography) will be needed to directly observe if this tDCS paradigm causes increases in basal ganglia dopamine release. Confirmation of the influence of this tDCS paradigm on dopaminergic activity will open the possibility of its use for the treatment of neuropsychiatric disorders, such as depression and schizophrenia.

Given the ubiquity of the prefrontal cortex and basal ganglia in decision making and motivational performance, it is possible that our stimulation paradigm could influence a wide range of behavioral tasks. Of particular note, decision-making tasks that require higher level of reasoning often recruit DLPFC,[73] which was the location of our cathodal electrode. With this in mind, future work must take into account how more complicated behavioral tasks might interact with electrode placement and polarity. An overall understanding of how this paradigm interacts with behavioral performance in a variety of tasks will be necessary to evaluate its potential clinical efficacy in patient populations.

In conclusion, we provide an illustration of how a network of interconnected brain areas can be stimulated with tDCS to causally influence deep brain regions containing dopaminergic neurons. We believe that our tDCS protocol is a promising approach to noninvasively modulate midbrain activity and functions that may be disrupted in neuropsychiatric disorders.

Conflict of interest

The authors declare no conflict of interest.

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1. Hedreen JC, Delong MR. Organization of striatopallidal, striatonigal, and nigrostriatal projections in the Macaque. *J Comp Neurol* 1991; **304**: 569–595.
2. Lynd-Balta E, Haber SN. The organization of midbrain projections to the striatum in the primate: sensorimotor-related striatum vs. ventral striatum. *Neuroscience* 1994; **59**: 635–640.
3. Lidow MS, Goldman-Rakic PS, Gallager DW, Rakic P. Distribution of dopaminergic receptors in the primate cerebral cortex: quantitative autoradiographic analysis using [3H] raclopride, [3H] spiperone and [3H]sch23390. *Neuroscience* 1991; **40**: 657–671.
4. Williams SM, Goldman-Rakic PS. Characterization of the dopaminergic innervation of the primate frontal cortex using a dopamine-specific antibody. *Cerebral Cortex* 1993; **3**: 199–222.
5. Goldman-Rakic PS, Bergson C, Krimer LS, Lidow MS, Williams SM, Williams GV. Three primate mesocortical dopamine system. In: Bloom FE, Bjorklund A, Hokfelt T (eds). *Handbook of Chemical Neuroanatomy* vol. 15 (Elsevier: Amsterdam, The Netherlands, 1999).
6. Lewis DA. The catechoaminergic innervation of primate prefrontal cortex. *J Neural Transm Suppl* 1992; **36**: 179–200.
7. Goto Y, Grace AA. The dopamine system and the pathophysiology of schizophrenia: a basic science perspective. *Int Rev Neurobiol* 2007; **78**: 41–68.
8. Murray GK, Corlett PR, Clark L, Pessiglione M, Blackwell AD, Honey G *et al.* Substantia nigra/ventral tegmental reward prediction error disruption in psychosis. *Mol Psychiatry* 2008; **13**: 239 267–276.
9. Lisman JE, Coyle JT, Green RW, Javitt DC, Benes FM, Heckers S *et al.* Circuit-based framework for understanding neurotransmitter and risk gene interactions in schizophrenia. *Trends Neurosci* 2008; **31**: 234–242.
10. Schott BH, Niehaus L, Wittmann BC, Schutze H, Seidenbecher CI, Heinze HJ *et al.* Ageing and early-stage Parkinson's disease affect separable neural mechanisms of mesolimbic reward processing. *Brain* 2007; **130Pt 9: 2412–2424.**
11. Carlsson M, Carlsson A. Interactions between glutamatergic and monoaminergic systems within the basal ganglia–implications for schizophrenia and Parkinson's disease. *Trends Neurosci* 1990; **13**: 272–276.
12. Vingerhoets FJG, Villemure J-G, Temperli P, Pollo C, Pralong E, Ghika J. Subthalamic DBS replaces levodopa in Parkinson's disease. *Neurology* 2002; **58**: 396–401.
13. Miyamoto S, Miyake N, Jarskog LF, Fleischhaker WW, Lieberman JA. Pharmacological treatment of schizophrenia: a critical review of the pharmacology and clinical effects of current and future therapeutic agents. *Mol Psychiatry* 2012; **17**: 1206–1227.
14. Mayberg HS, Lozano AM, Voon V, McNeaely HE, Seminowicz D, Clement H *et al.* Deep brain stimulation for treatment-resistant depression. *Neuron* 2005; **45**: 651–660.
15. George MS, Àston-Jones G. Noninvasive techniques for probing neurocircuitry and treating illness: vagus nerve stimulation (VNS), transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS). *Neuropsychopharmacology* 2009; **35**: 301–316.
16. Nitsche MA, Cohen LG, Wassermann EM, Priori A, Lang N, Antal A *et al.* Transcranial direct current stimulation: state of the art. *Brain Stimul* 2008; **1**: 206–223.
17. Reis J, Schambra HM, Cohen LG, Buch ER, Fritsch B, Zarahn E *et al.* Noninvasive cortical stimulation enhances motor skill acquisition over multiple days through an effect on consolidation. *Proc Natl Acad Sci USA* 2009; **106**: 1590–1595.
18. George MS, Padberg F, Schlaepfer TE, O'Reardon JP, Fitzgerald PB, Nahas ZH *et al.* Controversy: Repetitive transcranial magnetic stimulation or transcranial direct current stimulation shows efficacy in treating psychiatric diseases (depression, mania, schizophrenia, obsessive-complusive disorder, panic, posttraumatic stress disorder). *Brain Stimul* 2009; **2**: 14–21.
19. Alonso-Alonso M, Fregni F, Pascual-Leone A. Brain stimulation in poststroke rehabilitation. *Cerebrovasc Dis* 2007; **24**(Suppl 1): 157–166.
20. Knoch D, Gianotti LRR, Pascual-Leone A, Treyer V, Regard M, Hohmann M *et al.* Disruption of right prefrontal cortex by low-frequency repetitive transcrnial magnetic stimulation induces risk-taking behavior. *J Neurosci* 2006; **26**: 6469–6472.
21. Pascual-Leone A, Walsh V. Fast backprojections from the motion to the primary visual area necessary for visual awareness. *Science* 2001; **292**: 510–512.

22. Kanai R, Bahrami B, Roylance R, Rees G. Human parietal cortex structure predicts individual differences in perceptual rivalry. *Curr Biol* 2011; **20**: 1626–1630.
23. Nowak DA, Grefkes C, Ameli M, Fing GR. Interhemispheric competition after stroke: brain stimulation to enhance recovery of function of the affected hand. *Nerorehabil Neural Repair* 2009; **23**: 641–656.
24. Strafella AP, Paus T, Barrett J, Dagher A. Repetitive transcranial magnetic stimulation of the human prefrontal cortex induces dopamine release in the caudate nucleus. *J Neurosci* 2001; **21**: 1–4.
25. Polania R, Paulus W, Nitsche MA. Modulating cortico-striatal and thalamo-cortical functional connectivity with transcranial direct current stimulation. *Human Brain Mapp* 2011; **33**: 2499–2508.
26. van Schouwenburg M, O'Shea J, Mars R, Rushworth M, Cools R. Controlling human striatal cognitive function via the frontal cortex. *J Neurosci* 2012; **32**: 5631–5637.
27. Takano Y, Yokawa T, Masuda A, Niimi J, Tanaka S, Hironaka N. A rat model for measuring the effectiveness of transcranial direct current stimulation using fMRI. *Neurosci Lett* 2011; **491**: 40–43.
28. Frankel WG, Laruelle M, Haber SN. Prefrontal cortical projections to the midbrain in primates: evidence for a sparse connection. *Neuropsychopharmacology* 2006; **31**: 1627–1636.
29. An X, Bandler R, ngur D, Price JL. Prefrontal cortical projections to longitudinal columns in midbrain periaqueductal gray in macaque monkeys. *J Comp Neurol* 1998; **401**: 455–479.
30. Ongur D, An X, Price JL. Prefrontal cortical projections to the hypothalamus in macaque monkeys. *J Comp Neurol* 1998; **401**: 480–505.
31. Carr DB, Sesack SR. Projections from the rat prefrontal cortex to the ventral tegmental area: target specificity in the synaptic associations with mesoaccumbens and mesocortical neurons. *J Neurosci*, 2000; 20(10): 3864–3873.
32. Sesack SR, Carr DB, Omelchenko N, Pinto A. Anatomical substrates for glutamate-dopamine interactions: evidence for specificity of connections and extrasynaptic actions. *Ann N Y Acad Sci* 2003; **1003**: 36–52.
33. Haber SN, Knuston B. The reward circuit: linking primate anatomy and human imaging. *Neuropsychopharmacology* 2010; **35**: 4–26.
34. Haber SN, Lynd E, Klein C, Groenewegen HJ. Topographic organization of the ventral striatal efferent projections in teh rheseus monkey: an anterograde tracing study. *J Comp Neurol* 1990; **293**: 282–298.
35. Parent M, Levesque M, Parent A. The pallidofugal projection system in primates: evidence for neurons branching ipsilaterally and contralaterally to the thalamus and brainstem. *J Chem Neuroanat* 1999; **16**: 153–165.
36. Gao M, Liu C, Yang S, Jin G, Bunney BS, Shi W. Functional coupling between the prefrontal cortex and dopamine neurons in the ventral tegmental area. *J Neurosci* 2007; **27**: 5414–5421.
37. Ballard IC, Murty VP, Carter RM, MacInnes JJ, Huettel SA. Dorsolateral prefrontal cortex drives mesolimbic dopaminergic regions to initiate motivated behavior. *J Neurosci* 2011; **31**: 10340–10346.
38. Gariano RF, Groves PM. Burst firing induced in midbrain dopamine neurons by stimulation of the medial prefrontal and anterior cingulate cortices. *Brain Res* 1988; **462**: 194–198.
39. Murase S, Grenhoff J, Chouvet G, Gonon FG, Svensson TH. Prefrontal cortex regulates burst firing and transmitter release in rat mesolimbic dopamine neurons studied *in vivo*. *Neurosci Lett* 1993; **157**: 53–56.
40. Au-Young SM, Shen H, Yang CR. Medial prefrontal cortical output neurons to the ventral tegmental area (VTA) and their responses to burst-patterned stimulation of the VTA: neuroanatomical and *in vivo* electrophysiological analyses. *Synapse* 1999; **34**: 245–255.
41. Tzschentke TM, Schmidt WJ. Functional relationship among medial prefrontal cortex, nucleus accumbens, and ventral tegmental area in locomotion and reward. *Crit Rev Neurobiol* 2000; **14**: 131–142.
42. Meyer-Lindenberg A, Miletich RS, Kohn PD, Esposito G, Carson RE, Quarantelli M *et al.* Reduced prefrontal activity predicts exaggerated striatal dopaminergic function in schizophrenia. *Nat Neurosci* 2002; **5**: 267–271.
43. Bertolino A, Breier A, Callicott JH, Adler C, Mattay VS, Shapiro M *et al.* The relationship between dorsolateral prefrontal neuronal N-acetylaspartate and evoked release of striatal dopamine in schizophrenia. *Neuropsychopharmacology* 2000; **22**: 125–132.
44. Pycock CJ, Kerwin RW, Carter CJ. Effect of lesion of cortical dopamine terminals on subcortical dopamine receptors in rats. *Nature* 1990; **286**: 74–76.
45. Baumgartner T, Knoch D, Hotz P, Eisenegger C, Fehr E. Dorsolateral and ventromedial prefrontal cortex orchestrate normative choice. *Nat Neurosci* **14**: 1468–1474.
46. Figner B, Knoch D, Johnson EJ, Krosch AR, Lisanby SH, Fehr E *et al.* Lateral prefrontal cortex and self-control in intertemporal choice. *Nat Neurosci.* **13**: 538–539.
47. Hare TA, Camerer CF, Rangel A. Self-control in decision-making involves modulation of the vmPFC valuation system. *Science* 2009; **324**: 646–648.
48. Archer RP, Cash TF. Physical attractiveness and maladjustment among psychiatric inpatients. *J Soc Clin Psychol* 1985; **3**: 170–180.
49. Noles SW, Cash TF, Winstead BA. Body image, physical attractiveness, and depression. *J Consult and Clin Psychol* 1985; **53**: 88–94.
50. Gaebel W, Wolwer W. Facial expression and emotional face recognition in schizophrenia and depression. *Eur Arch Psychiatry Clin Neurosci* 1992; **242**: 46–52.
51. Sprengelmeyera R, Young AW, Mahna K, Schroedera U, Woitallaa D, Büttnera T *et al.* Facial expression recognition in people with medicated and unmedicated Parkinson's disease. *Neuropsychologia* 2003; **41**: 1047–1057.
52. Deichmann R, Gottfried JA, Hutton C, Turner R. Optimized EPI for fMRI studies of the orbitofrontal cortex. *Neuroimage* 2003; **19**(2 Pt 1): 430–441.
53. Nitsche MA, Doemkes S, Karakose T, Antal A, Lievetanz D, Lang N *et al.* Shaping the effects of transcranial direct current stimulation of the human motor cortex. *J Neurophysiol* 2007; **97**: 3109–3117.
54. Fregni F, Boggio PS, Nitsche MA, Bermpohl F, Antal A, Feredoes E *et al.* Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Exp Brain Res* 2005; **166:**: 23–30.
55. Gerloff C, Corwell B, Chen R, Hallett M, Cohen LG. Stimulation over the human supplementary motor area interferes with the organization of futuer elements in complex motor sequences. *Brain* 1997; **120**: 1587–1602.
56. Rossi S, Cappa SF, Babiloni C, Pasqualetti P, Miniussi C, Carducci F *et al.* Prefrontal cortex in long-term memory: an 'interference' approach using magnetic stimulation. *Nat Neurosci* 2001; **4**: 948–952.
57. Boggio PS, Khoury LP, Martins DC, Martins OE, Macedo ECd, Fregni F. Temporal cortex direct current stimulation enhances performance on a visual recognition working memory task in Alzheimer disease. *J Neurol Neurosurg Psychiatry* 2009; **80**: 444–447.
58. Herwig U, Satrapi P, Schonfeldt-Lecuona C. Using the international 10-20 EEG system for position of transcranial magnetic stimulation. *Brain Topogr* 2003; **16**: 95–99.
59. O'Doherty JP. Reward representations and reward-related learning in the human brain: insights from neuroimaging. *Curr Opin Neurobiol* 2004; **14**: 769–776.
60. O'Doherty J, Winston J, Critchley H, Perrett D, Burt DM, Dolan RJ. Beauty in a smile: the role of medial orbitofrontal cortex in facial attractiveness. *Neuropsychologia* 2003; **41**: 147–155.
61. Gitelman D, Penny W, Ashburner J, Friston K. Modeling regional and psychophysiologic interactions in fMRI: the importance of hemodynamic deconvolution. *Neuroimage* 2003; **19**: 200–207.
62. Winston JS, O'Doherty J, Kilner JM, Perrett D, Dolan RJ. Brain systems for assessing facial attractiveness. *Neuropsychologia* 2007; **45**: 195–206.
63. Aharon I, Etcoff N, Ariely D, Chabris CF, O'Connor E, Breiter HC. Beautiful faces have variable reward value: fMRI and behavioral evidence. *Neuron* 2001; **32**: 537–551.
64. Bray S, O'Doherty J. Neural coding of reward-prediction error signals during classical conditioning with attractive faces. *J Neurophysiol* 2007; **97,** p 3036–3045.
65. D'Ardenne K, McClure SM, Nystrom LE, Cohen JD. BOLD responses reflecting dopaminergic signals in the human ventral tegmental area. *Science* 2008; **319**: 1264–1267.
66. O'Doherty JP, Buchanan TW, Seymour B, Dolan RJ. Predictive neural coding of reward preference involves dissociable responses in human ventral midbrain and ventral striatum. *Neuron* 2006; **49**: 157–166.
67. Logothetis NK, Pauls J, Augath M, Trinath T, Oeltermann A. Neurophysiological investigation of the basis of the fMRI signal. *Nature* 2001; **412**: 150–157.
68. Karreman M, Moghaddam B. The prefrontal cortex regulates the basal release of dopamine in the limbic system: An effect mediated by ventral tegmental area. *J Neurochem* 1996; **66**: 589–598.
69. Doherty MD, Gratton A. Effects of medial prefrontal cortical injections of GABA receptor agonists and atongonists on the local and nucleus accumbens dopamine response to stress. *Synapse* 1999; **32**: 288–300.
70. Márquez-Ruiza J, Leal-Campanarioa R, Sánchez-Campusanoa R, Molaee-Ardekanib B, Wendling F, Mirandad PC *et al.* Transcranial direct-current stimulation modulates synaptic mechanisms involved in associative learning in behaving rabbits. *Proc Natl Acad Sci USA* 2012; **109**: 6710–6715.
71. Stagg CJ, Nitsche MA. Physiological basis of transcranial direct current stimulation. *Neuroscientist* 2011; **17**: 37–53.
72. Stagg CJ, Best JG, Stephenson MC, O'Shea J, Wylezinska M, Kincses ZT *et al.* Polarity-sensative modulation of cortical neurostransmitters by transcranial stimulation. *J Neurosci* 2009; **29**: 5202–5206.
73. Krain AL, Wilson AM, Arbuckle R, Castellanos FX, Milham MP. Distinct neural mechanisms of risk and ambiguity: a meta-analysis of decision-making. *Neuroimage* 2006; **32**: 477–484.

Supplementary Information accompanies the paper on the Translational Psychiatry website (http://www.nature.com/tp)