77. Wong, M. L. & Licinio, J. From monoamines to genomic targets: a paradigm shift for drug discovery in depression. *Nature Rev. Drug Discov.* **3**, 136–151 (2004).
78. Kitano, H. Towards a theory of biological robustness. *Mol. Syst. Biol.* **3**, 137 (2007).
79. McMahon, F. J. *et al.* Variation in the gene encoding the serotonin 2A receptor is associated with outcome of antidepressant treatment. *Am. J. Hum. Genet.* **78**, 804–814 (2006).
80. Suzuki, Y., Sawamura, K. & Someya, T. Polymorphisms in the 5-hydroxytryptamine 2A receptor and Cytochrome*P*4502D6 genes synergistically predict fluvoxamine-induced side effects in japanese depressed patients. *Neuropsychopharmacology* **31**, 825–831 (2006).
81. Sato, K. *et al.* Association between -1438G/A promoter polymorphism in the 5-HT_{2A} receptor gene and fluvoxamine response in Japanese patients with major depressive disorder. *Neuropsychobiology* **46**, 136–140 (2002).
82. Choi, M. J., Kang, R. H., Ham, B. J., Jeong, H. Y. & Lee, M. S. Serotonin receptor 2A gene polymorphism (-1438A/G) and short-term treatment response to citalopram. *Neuropsychobiology* **52**, 155–162 (2005).
83. Peters, E. J., Slager, S. L., McGrath, P. J., Knowles, J. A. & Hamilton, S. P. Investigation of serotonin-related genes in antidepressant response. *Mol. Psychiatry* **9**, 879–889 (2004).
84. Paddock, S. *et al.* Association of GRIK4 with outcome of antidepressant treatment in the STAR*D cohort. *Am. J. Psychiatry* **164**, 1181–1188 (2007).
85. Wilkie, M. J. *et al.* A splice site polymorphism in the G-protein β subunit influences antidepressant efficacy in depression. *Pharmacogenet. Genomics* **17**, 207–215 (2007).
86. Serretti, A. *et al.* SSRIs antidepressant activity is influenced by Gβ3 variants. *Eur. Neuropsychopharmacol.* **13**, 117–122 (2003).
87. Zill, P. *et al.* Evidence for an association between a G-protein β3-gene variant with depression and response to antidepressant treatment. *Neuroreport* **11**, 1893–1897 (2000).
88. Lee, H. J. *et al.* Association between a G-protein β3 subunit gene polymorphism and the symptomatology and treatment responses of major depressive disorders. *Pharmacogenomics J.* **4**, 29–33 (2004).
89. Licinio, J. *et al.* Association of a corticotropin-releasing hormone receptor 1 haplotype and antidepressant treatment response in Mexican-Americans. *Mol. Psychiatry* **9**, 1075–1082 (2004).
90. Liu, Z. *et al.* Association study of corticotropin-releasing hormone receptor1 gene polymorphisms and antidepressant response in major depressive disorders. *Neurosci. Lett.* **414**, 155–158 (2007).
91. Serretti, A., Kato6.88969 30A6 19r(.)Tm(9)5/RTJ/T10 an /ActualText ()BDC BT/T12 1 Tf16 0 0 6 42.5197 303.61609 Tm(9)611 3416( )TjETEMC BT/T12 1 Tf16 0 0 6 42.5197 303.61609 Tm

(FIG. 1)

Attentional modulation.

Language and music.

Box 2 | **Social neuroscience**

The relatively new field of social neuroscience is the product of the integration of neuroscience (particularly neuroimaging), cognitive science and social sciences (particularly social psychology), and it allows one to investigate the complex and dynamic representation of social interaction in the brain's neural states. The field aims to uncover the neural underpinnings of social processes, such as mental attribution, empathy and moral judgement.

Social neuroscience is inherently cross-disciplinary. For instance, to examine how empathy for pain that someone else is experiencing is modulated by the affective link between individuals, a functional MRI study measured neural responses to perceived pain in confederates who played fairly or unfairly in a game[113]. The authors found that activity in the insular cortex and in the anterior cingulate cortex (ACC) was lower in males when they observed an unfair player receiving pain than when they saw a fair player receiving pain. By contrast, activation in reward-related areas (for example, the nucleus accumbens) was higher in response to pain stimulation applied to the unfair player. Another study assessed whether social exclusion induces 'painful' affective responses (as painful physical stimulation does)[114]. Subjects showed higher ACC activity during a virtual ball-tossg a

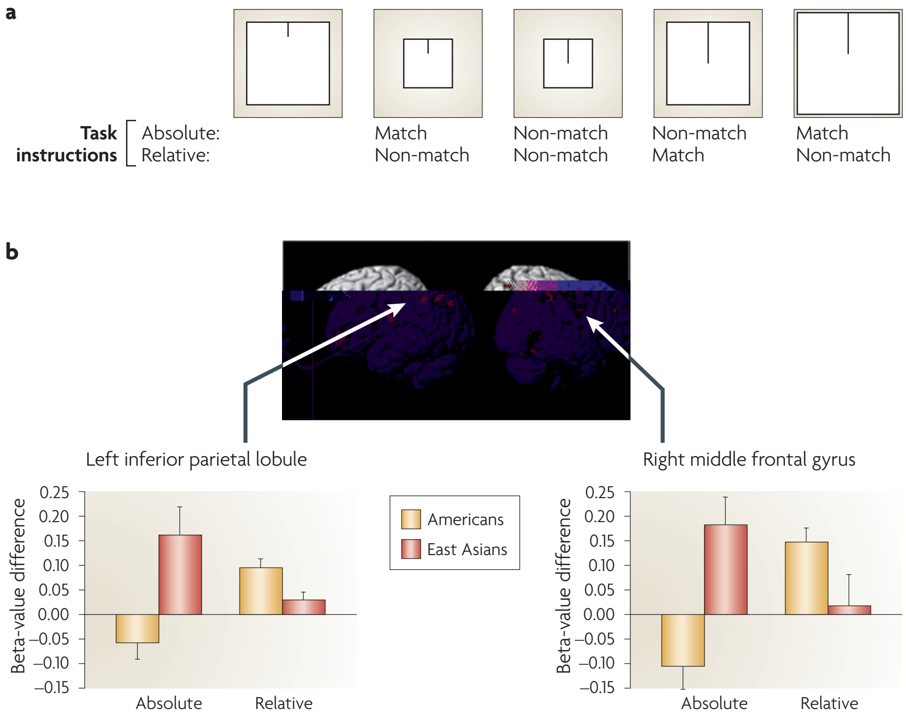

Figure 1 | C[illegible] | In one study[19], participants had to judge whether the length of a vertical line inside a box matched the length of a previously shown line regardless of the size of the box (a context-independent (absolute) judgement task), or whether the box–line combination of each stimulus matched the proportional scaling of the preceding combination (a context-dependent (relative) judgement task). [illegible] | Frontoparietal activation associated with judgement tasks in Americans and East Asians. The frontoparietal activity was greater in East Asians (red bars) than in Americans (yellow bars) in the context-independent (absolute) judgement, whereas a reverse pattern was observed in the context-dependent (relative) judgement task. Figure reproduced, with permission, from REF. 19 © (2008) Blackwell Publishing.

[illegible]

Mental attribution. [illegible]

[illegible] (REF. 69). [illegible]

Self representation and self awareness. [illegible]

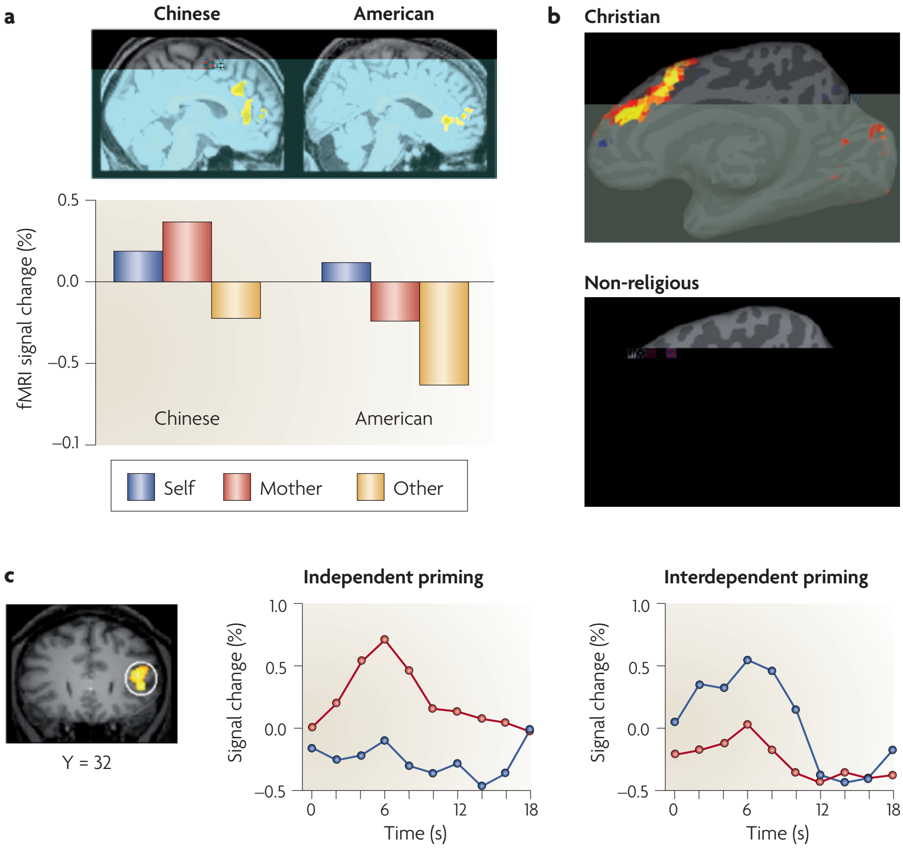

Figure 2 | C

| In one study[18], both Chinese people and Westerners conducted trait judgements of themselves, of their mother and of a famous person (an 'other'). The ventral medial prefrontal cortex (VMPFC) and the perigenual ACC (indicated by circles in the scans) showed greater activation in association with self judgement than in association with other judgement in participants from both cultural groups. However, blood-oxygen-level-dependent (BOLD) signal changes in the VMPFC did not differentiate between self and mother judgements in Chinese participants but did differentiate between them in American participants (American participants' signals were greater for self judgement). | In another study[22], both Christian and non-religious participants conducted trait judgements of themselves and a of public person. Christian participants showed higher activation in the dorsal medial prefrontal cortex (DMPFC) for self judgement than for other judgement; non-religious participants showed higher VMPFC activation for self judgement than for other judgement. | In a third study[20], Chinese participants identified the orientation of their own face and the orientations of other, familiar faces in photos after self-construal priming. The scan shows that independent-self-construal priming increased the difference in right frontal cortex activity in response to judging self and familiar faces; the graphs show that BOLD signals differentiated self (red line) and familiar (blue line) faces after independent-self-construal priming (left graph) but did not differ significantly between self and familiar faces after interdependent-self-construal priming (right graph). Part reproduced, with permission, from REF. 18 © (2007) Academic Press. Part reproduced, with permission, from REF. 22 © (2008) Psychology Press. Part reproduced, with permission, from REF. 20 © (2007) Blackwell Publishing.

(FIG. 2a)

(FIG. 2b)

(FIG. 2c).

Conceptual implications

Cultural influences on the neural substrates of human cognition.

(REF. 101).

Nature and nurture.

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1. Markus, H. R., Kitayama, S. & Heiman, R. J. in *Social Psychology: Handbook of Basic Principles* (eds Higgins, E. T. & Kruglanski, A. W) 857–913 (Guilford, New York, 1996).
2. Markus, H. R. & Kitayama, S. Culture and the self: implications for cognition, emotion and motivation. *Psychol. Rev.* **98**, 224–253 (1991).
3. Markus, H. R. & Kitayama, S. Culture, self, and the reality of the social. *Psychol. Inq.* **14**, 277–283 (2003).
4. Choi, I., Nisbett, R. E. & Norenzayan, A. Causal attribution across cultures: variation and universality. *Psychol. Bull.* **125**, 47–63 (1999).
5. Nisbett, R. E., Peng, K., Choi, I. & Norenzayan, A. Culture and systems of thought: holistic vs. analytic cognition. *Psychol. Rev.* **108**, 291–310 (2001).
6. Nisbett, R. E. & Masuda, T. Culture and point of view. *Proc. Natl Acad. Sci. USA* **100**, 11164–11170 (2003).
7. Nisbett, R. E. *The Geography of Thought* (Free Press, New York, 2003).
8. Chiu, C. Y. & Hong, Y. Y. *Social Psychology of Culture* (Psychology Press, New York, 2006).
9. Morris, M. & Peng, K. Culture and cause: American and Chinese attributions for social and physical events. *J. Pers. Soc. Psychol.* **67**, 949–971 (1994).
10. Peng, K. & Nisbett, R. Culture, dialectics, and reasoning about contradiction. *Am. Psychol.* **54**, 741–754 (1999).
11. Cacioppo, J. T. Social neuroscience: understanding the pieces fosters understanding the whole and vice versa. *Am. Psychol.* **57**, 819–831 (2002).
12. Ochsner, K. N. & Lieberman, M. D. The emergence of social cognitive neuroscience. *Am. Psychol.* **56**, 717–734 (2001).
13. Adolphs, R. Cognitive neuroscience of human social behaviour. *Nature Rev. Neurosci.* **4**, 165–178 (2003).
14. Blakemore, S., Winston, J. & Frith, U. Social cognitive neuroscience: where are we heading? *Trends Cogn. Sci.* **8**, 216–222 (2004).
15. Lieberman, M. D. Social cognitive neuroscience: a review of core processes. *Ann. Rev. Psychol.* **58**, 259–289 (2007).
16. Gutchess, A. H., Welsh, R. C., Boduroglu, A. & Park, D. C. Cultural differences in neural function associated with object processing. *Cogn. Affect. Behav. Neurosci.* **6**, 102–109 (2006).
17. Tang, Y. *et al.* Arithmetic processing in the brain shaped by cultures. *Proc. Natl Acad. Sci. USA* **103**, 10775–10780 (2006).
18. Zhu, Y., Zhang, Li., Fan, J. & Han, S. Neural basis of cultural influence on self representation. *Neuroimage* **34**, 1310–1317 (2007).
19. Hedden, T., Ketay, S., Aron, A., Markus, H. R. & Gabrieli, D. E. Cultural influences on neural substrates of attentional control. *Psychol. Sci.* **19**, 12–17 (2008).
20. Sui, J. & Han, S. Self-construal priming modulates neural substrates of self-awareness. *Psychol. Sci.* **18**, 861–866 (2007).
21. Lin, Z., Lin., Y. & Han, S. Self-construal priming modulates visual activity underlying global/local perception. *Biol. Psychol.* **77**, 93–97 (2008).
22. Han, S. *et al.* Neural consequences of religious belief on self-referential processing. *Soc. Neurosci.* **3**, 1–15 (2008).
23. Nisbett, R. E. & Miyamoto, Y. The influence of culture: holistic versus analytic perception. *Trends Cogn. Sci.* **9**, 467–473 (2005).
24. Ji, L., Peng, K. & Nisbett, R. E. Culture, control, and perception of relationships in the environment. *J. Pers. Soc. Psychol.* **78**, 943–955 (2000).
25. Kühnen, U. & Oyserman, D. Thinking about the self influences thinking in general: cognitive consequences of salient self-concept. *J. Exp. Soc. Psychol.* **38**, 492–499 (2002).
26. Kitayama, S., Duffy, S., Kawamura, T. & Larsen, J. T. Perceiving an object and its context in different cultures: a cultural look at new look. *Psychol. Sci.* **14**, 201–206 (2003).
27. Masuda, T. & Nisbett, R. E. Culture and change blindness. *Cogn. Sci.* **30**, 381–399 (2006).
28. Masuda, T. & Nisbett, R. E. Attending holistically versus analytically: comparing the context sensitivity of Japanese and Americans. *J. Pers. Soc. Psychol.* **81**, 922–934 (2001).
29. Martin, A., Wiggs, C. L., Ungerleider, L. G. & Haxby, J. V. Neural correlates of category-specific knowledge. *Nature* **379**, 649–652 (1996).
30. Goh, J. O. *et al.* Age and culture modulate object processing and object-scene binding in the ventral visual area. *Cogn. Affect. Behav. Neurosci.* **7**, 44–52 (2007).
31. Lin, Z. & Han, S. Self-construal priming modulates the scope of visual attention. *Q. J. Exp. Psychol. A* (in the press).
32. Gardner, W. L., Gabriel, S. & Lee, A. Y. "I" value freedom, but "we" value relationships: self-construal priming mirrors cultural differences in judgment. *Psychol. Sci.* **10**, 321–326 (1999).
33. Navon, D. Forest before trees: the precedence of global features in visual perception. *Cogn. Psychol.* **9**, 353–383 (1977).
34. [illegible] *et al.* Combined spatial and temporal imaging of brain activity during visual selective attention in humans. *Nature*

47. Nan, Y., Knösche, T. R. & Friederici, A. D. The perception of musical phrase structure: a cross-cultural ERP study. *Brain Res.* **1094**, 179–191 (2006).
48. Ansari, D. Effects of development and enculturation on number representation in the brain. *Nature Rev. Neurosci.* **9**, 278–291 (2008).
49. Baddeley, A. The episodic buffer: a new component of working memory? *Trends Cogn. Sci*. **4**, 417–423 (2000).
50. Markham, R. & Wang, L. Recognition of emotion by Chinese and Australian children. *J. Cross Cult. Psychol.* **27**, 616–643 (1996).
51. Elfenbein, H. A. & Ambady, N. On the universality and cultural specificity of emotion recognition: a meta-analysis. *Psychol. Bull*. **128**, 243–249 (2002).
52. Chiao, J. Y. *et al.* Cultural specificity in amygdala response to fear faces. *J. Cogn. Neurosci*. 5 May 2008 (doi: 10.1162/jocn.2008.20151).
53. Wellman, H. M. *The Child's Theory of Mind* (MIT Press, Cambridge, Massachusetts, 1990).
54. Frith, C. D. & Frith, U. Interacting minds — a biological basis. *Science* **286**, 1692–1695 (1999).
55. Frith, C. & Frith, U. Theory of mind. *Curr. Biol.* **15**, R644–R646 (2005).
56. Fletcher, P. C. *et al.* Other minds in the brain: a functional imaging study of 'theory of mind' in story comprehension. *Cognition* **57**, 109–128 (1995).
57. Abu-Akel, A. A neurobiological mapping of theory of mind. *Brain Res. Brain Res. Rev.* **43**, 29–40 (2003).
58. Gallagher, H. L. & Frith, C. D. Functional imaging of 'theory of mind'. *Trends Cogn. Sci.* **7**, 77–83 (2003).
59. Saxe, R., Carey, S. & Kanwisher, N. Understanding other minds: linking developmental psychology and functional neuroimaging *Ann. Rev. Psychol.* **55**, 87–124 (2004).
60. Frith, U. & Frith, C. D. Development and neurophysiology and mentalizing. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **358**, 459–473 (2003).
61. Frith, C. D. & Frith, U. The neural basis of mentalizing. *Neuron* **50**, 531–534 (2006).
62. Brunet, E., Sarfati, Y., Hardy-Baylé, M. & Decety, J. A PET investigation of the attribution of intentions with a nonverbal task. *Neuroimage* **11**, 157–166 (2000).
63. Gallagher, H. L. *et al.* Reading the mind in cartoons and stories: an fMRI study of 'theory of mind' in verbal and nonverbal tasks. *Neuropsychologia* **38**, 11–21 (2000).
64. Han, S., Jiang, Y., Humphreys, G. W., Zhou, T. & Cai, P. Distinct neural substrates for the perception of real and virtual visual worlds. *Neuroimage* **24**, 928–935 (2005).
65. Saxe, R. & Kanwisher, N. People thinking about thinking people. The role of the temporo-parietal junction in "theory of mind". *Neuroimage* **19**, 1835–1842 (2003).
66. Saxe, R. & Wexler, A. Making sense of another mind: the role of the right temporo-parietal junction. *Neuropsychologia* **43**, 1391–1399 (2005).
67. Sommer, M. *et al.* Neural correlates of true and false belief reasoning. *Neuroimage* **35**, 1378–1384 (2007).
68. Amodio, D. M. & Frith, C. D. Meeting of minds: the medial frontal cortex and social cognition. *Nature Rev. Neurosci.* **7**, 268–277 (2006).
69. Kobayashi, C., Glover, G. H. & Temp3219 TT/( )35(R)5(.)E( )35(&)5( )C(r)24(ol(u)5(r)24(e)5( )5( )35(c)5(o)5(d)5( )36 0 0 6 57.2598 244.79130.085(6)5(9)5(e)5(f)5( )35(ou(e)5(f)s(i)5(o)5(n)c5(c)5(o)