

Theory of Mind

Humans are, above all, intensely social creatures. We spend most of our time interacting with each other in groups and, through this group activity, we routinely achieve goals that could never be in the grasp of single individuals. These successful interactions depend upon a whole range of processes, collectively known as social cognition.¹ We share many of these processes with other social animals. The ability to recognise emotional expressions, the ability to keep track of the status of group members and of alliances within the group are important for successful social interactions because they help us to predict the behaviour of our fellows. However, there is one social process, Theory of Mind, that is highly developed in humans, but only found in the most rudimentary form in other animals.²

Terminology

We naturally explain people's behaviour on the basis of their minds: their knowledge, their beliefs and their desires. If for instance, John has taken his umbrella, but it is not actually raining, this does not present a conflict. We automatically assume that it is John's belief that it will rain – not whether it is actually raining – that determines whether he takes his umbrella. Understanding behaviour in this way is called having a 'Theory of Mind' (ToM), or 'an intentional stance.' The verb most frequently used to describe this ability is 'mentalising'. The concept was originally introduced into experimental psychology by Premack and Woodruff through their seminal paper: 'Does the Chimpanzee have a Theory of Mind?'.³ This paper prompted the question whether young children have a ToM and in 1983 this was answered by means of a novel paradigm introduced to test children on their ability to attribute beliefs to others.⁴ Shortly after, it was shown that autistic children have problems with such ToM tasks.⁵ The terms mind-reading and mind-blindness are also often used as shorthand to refer to the effects of mentalising failure.

False Beliefs

The test which probes the child's ability to predict what a character will do on the basis of that character's own mental state, not the actual state of affairs, was as follows:⁴

Maxi eats half his chocolate bar and put the rest away in the kitchen cupboard. Then he goes away. Meanwhile Maxi's mother comes into the kitchen, opens the cupboard and sees the chocolate bar. She puts it in the fridge. When Maxi comes back into the kitchen, where will he

look for his chocolate bar? The answer is 'in the cupboard, where he thinks it is'. This answer is obvious to most 5-year-olds, who can also explain exactly why Maxi now has a false belief. Autistic children, even of a higher mental age than five, were unable to reason like this and indicate that Maxi would look for his chocolate in the fridge, where it really is.

Cognitive mechanisms

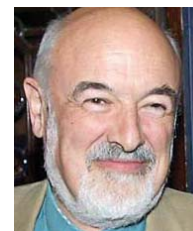
Only speculation is available at present. Perhaps our ability to mentalise depends upon the brain being able to decouple propositions from reality and set them in relation to an agent's attitude.⁶ Perhaps the ability to mentalise is related to our capacity to mirror the actions and emotions of other people through the brain's mirror system.⁷

In children

The cognitive mechanism underlying the human ability to attribute mental states to self and others can be likened to a start-up kit that puts social learning on the fast track, so that even in their first year infants orient to information that is communicated to them by other people and pay preferential attention to other people's intentions. Thus, infants follow gaze, at first automatically, then deliberately and attract other people's attention by pointing and gazing themselves. In autism such a preference may not exist and social learning is very delayed. It has recently been shown that even 12-15 month old infants track social events by their gaze in a way that presupposes that they have implicit mentalising ability.⁸ Long before they can talk, infants are surprised when, in the classic false belief scenario, Maxi looks in the wrong place (i.e. the fridge) for his chocolate.

In adults

Having a Theory of Mind routinely enables us to explain and predict what another person is going to do next, as in where will Maxi look. Our everyday speech is full of mental state attributions, such that we constantly seek psychological motives to our own and others' behaviour. ToM also enables us to monitor and manage our reputation and to manipulate other people's beliefs. Human communication is characterised by the pervasive importance of an attitude in which we cloak almost any message that we send or receive. Thus, intentionally conveyed information is hardly ever 'bare' information, but presented with the simultaneous use of persuasion, flattery, education, deception etc. In this sense human communication is



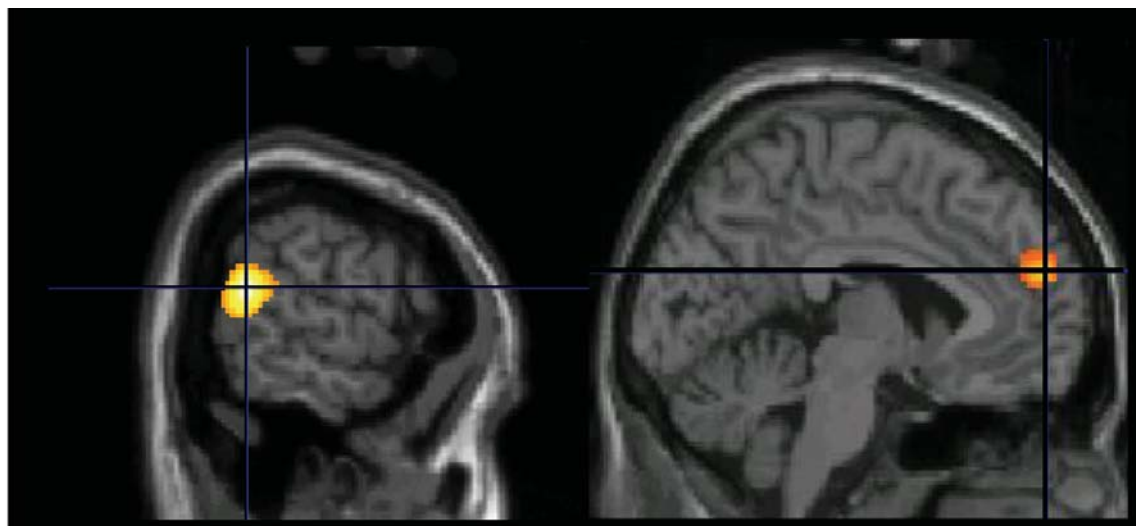
Chris D Frith, PhD is Emeritus Professor of Neuropsychology in the Wellcome Trust Centre for Neuroimaging at University College London and Niels Bohr Visiting Professor at the Centre for Functionally Integrative Neuroscience at the University of Aarhus. He pioneered the use of brain imaging to study high level cognitive processes and is currently investigating the neural basis of social interactions.



Uta Frith, PhD is Emeritus Professor of Cognitive Development in the Institute of Cognitive Neuroscience at University College London and Research Foundation Professor at the Faculties of Humanities and Health Sciences, University of Aarhus. She identified the theory of mind problem associated with autism and is currently investigating the neural basis of social cognition.

Correspondence to:

Chris Frith,
Email. c.frith@ucl.ac.uk



Two brain regions that are consistently activated during the performance of ToM tasks. Left panel: the temporo-parietal junction. Right panel: the paracingulate sulcus. Damage to these areas can cause impairments in the performance of ToM tasks.¹²

quite unlike information conveyed by machines. It has been claimed that ToM is a cornerstone of cultural evolution.⁹ Thus, mind-reading plays a role in fostering co-operation and teaching. For instance, successful teaching seems to depend on the teacher's ability to monitor the learner's mental states, such as their prior beliefs and attitudes, as well as their increasing knowledge.

In autism

Autism is primarily characterised by an impairment in social communication. This is not a global social impairment. The failure lies specifically in an inability to take account of others' beliefs, desires and feelings. This is shown, for instance, in their poor understanding of deception, irony and reputation building, but good transmission of verbatim information. This inability could be due to an ultimately genetic fault in a basic neurophysiological mechanism. For nearly three decades researchers have investigated the apparent inability of autistic children to mentalise, and their slow and fragile acquisition of the concept of mental states. It has been argued that intuitive mentalising, as already shown by infants by their second year, is never attained in autism, but that explicit rule-based mentalising can be learned.¹⁰

In other disorders

Many brain-based disorders impair social and communication function. For example, some types of schizophrenia involve a disturbance of mentalising. Unlike autism, this disturbance seems to point to an overactive attribution of mental states, extending these to a wide variety of other agents, including physical objects which may be experienced as senders of significant messages.¹¹ Theory of Mind difficulties can also be acquired through brain damage in frontal cortex or in the region of the temporo-parietal junction (TPJ).¹² Patients with fronto-temporal dementia are also prone to suffer from an inability to mentalise.¹³

The brain's mentalising network

Evidence from neuro-imaging studies shows that mentalising, elicited by a wide variety of tasks, engages a circumscribed network of brain regions. When brain activity is measured during the performance of tasks engaging ToM, two regions have been consistently identified: a medial prefrontal region (paracingulate cortex) and the TPJ in the superior temporal sulcus.^{14,15} The medial frontal region is also engaged when subjects reflect upon their own mental states as well as those of others, with the more inferior orbital region responding especially to emotional states. TPJ, on the other hand, seems to have a special role in using perceptual cues to recognise the actions and intentions of biological agents. Identification of the precise role of these regions awaits the development of a mechanistic account of our remarkable ability to make inferences about the minds of others.

References

- Adolphs R. *Cognitive neuroscience of human social behaviour*. Nat Rev Neurosci 2003;4:165-78.
- Tomasello M, Call J, Hare B. *Chimpanzees understand psychological states - the question is which ones and to what extent*. Trends Cogn Sci 2003;7:153-6.
- Premack D, Woodruff G. *Does the chimpanzee have a theory of mind?* Behavioural and Brain Sciences 1978;4:515-26.
- Wimmer H, Perner J. *Beliefs About Beliefs - Representation and Constraining Function of Wrong Beliefs in Young Children's Understanding of Deception*. Cognition 1983;13:103-28.
- Baron-Cohen S, Leslie AM, Frith U. *Does the autistic child have a "theory of mind"?* Cognition 1985;21:37-46.
- Leslie AM. *Preterse and representation: The origins of "theory of mind."* Psychological Review 1987;94:412-26.
- Gallese V, Goldman A. *Mirror neurons and the simulation theory of mind-reading*. Trends in Cognitive Sciences 1998;2:493-501.
- Onishi KH, Baillargeon R. *Do 15-month-old infants understand false beliefs?* Science 2005;308:255-8.
- Frith CD. *Making up the Mind; How the Brain Creates our Mental World*. Oxford: Blackwell, 2007.
- Frith U. *Autism: Explaining the enigma*, 2nd ed. Oxford: Blackwells, 2003.
- Frith CD. *Schizophrenia and theory of mind*. Psychol Med 2004;34:385-9.
- Apperly IA, Samson D, Chiavarino C, Humphreys GW. *Frontal and temporo-parietal lobe contributions to theory of mind: neuropsychological evidence from a false-belief task with reduced language and executive demands*. J Cogn Neurosci 2004;16:1773-84.
- Kipps CM, Hodges JR. *Theory of mind in frontotemporal dementia*. Social Neuroscience 2006;1:235-44.
- Frith U, Frith CD. *Development and neurophysiology of mentalizing*. Philos Trans R Soc Lond B Biol Sci 2003;358:459-73.
- Saxe R. *Uniquely human social cognition*. Curr Opin Neurobiol 2006;16:235-9.



PRESCRIBING INFORMATION – UK AND ROI

REBIF® 8.8 MICROGRAMS AND 22 MICROGRAMS SOLUTION FOR INJECTION

REBIF® 22 MICROGRAMS SOLUTION FOR INJECTION

REBIF® 44 MICROGRAMS SOLUTION FOR INJECTION

Interferon beta-1a

Presentation Rebif 8.8 and 22: Pre-filled glass syringe containing 8.8 µg or 22 µg of Interferon beta-1a in respectively 0.2 or 0.5 ml. Rebif 22 or 44: Pre-filled glass syringe containing 22 µg or 44 µg Interferon beta-1a in 0.5ml. **Indication** Treatment of relapsing multiple sclerosis. Efficacy has not been demonstrated in patients with secondary progressive multiple sclerosis without ongoing relapse activity. **Dosage and administration** Initiate under supervision of a physician experienced in the treatment of multiple sclerosis. Administer by subcutaneous injection. Recommended dose: Weeks 1 and 2: 8.8 µg three times per week (TIW); weeks 3 and 4: 22 µg TIW; week 5 onwards: 44 µg TIW (22 µg TIW if patients cannot tolerate higher dose). Limited published data suggest that the safety profile in adolescents aged 12-16 years receiving Rebif 22 TIW is similar to that in adults. Do not use in patients under 12 years of age. Prior to injection and for 24 h afterwards, an antipyretic analgesic is advised to decrease flu-like symptoms. Evaluate patients at least every second year of the treatment period. **Contraindications** History of hypersensitivity to natural or recombinant interferon beta, or to any of the excipients; treatment initiation in pregnancy; current severe depression and/or suicidal ideation. **Precautions** Inform patients of most common adverse reactions. Use with caution in patients with previous or current depressive disorders and those with antecedents of suicidal ideation. Advise patients to report immediately any symptoms of depression and/or suicidal ideation. Closely monitor patients exhibiting depression and treat appropriately. Consider cessation of therapy. Administer with caution in patients with a history of seizures and those receiving anti-epileptics, particularly if epilepsy is not adequately controlled. Closely monitor patients with cardiac disease for worsening of their condition during initiation of therapy. Patients should use an aseptic injection technique and rotate injection sites to minimise risk of injection site necrosis. If breaks in skin occur, patients should consult their doctor before continuing injections. If multiple lesions occur, discontinue Rebif until healed. Use with caution in patients with history of significant liver disease, active liver disease, alcohol abuse or increased serum ALT. Monitor serum ALT prior to the start of therapy, at months 1, 3 and 6 and periodically thereafter. Stop treatment if icterus or symptoms of liver dysfunction appear. Treatment has potential to cause severe liver injury including acute hepatic failure. Full haematological monitoring is recommended at months 1, 3 and 6 and periodically thereafter. All monitoring should be more frequent when initiating Rebif 44. New or worsening thyroid abnormalities may occur. Thyroid function testing is recommended at baseline and if abnormal every 6 – 12 months. Use with caution in, and closely monitor patients with, severe renal and hepatic failure or severe myelosuppression. Serum neutralising antibodies may develop and are associated with reduced efficacy. If a patient responds poorly and has neutralising antibodies, reassess treatment. Use with caution in patients receiving medicines with a narrow therapeutic index cleared by cytochrome P450. Women of childbearing potential should use effective contraception. Limited data suggest a possible increased risk of spontaneous abortion. During lactation, either discontinue Rebif or nursing. If overdose occurs, hospitalise patient and give supportive treatment. **Side effects** In the case of severe or persistent undesirable effects, consider temporarily lowering or interrupting dose. Very common: flu-like symptoms, injection site inflammation/reaction, headache, asymptomatic transaminase increase, neutropenia, lymphopenia, leucopenia, thrombocytopenia, anaemia. Common: injection site pain, myalgia, arthralgia, fatigue, rigors, fever, pruritus, rash, erythematous/maculo-papular rash, diarrhoea, vomiting, nausea, depression, insomnia. Serious side effects include: injection site necrosis, hepatitis with or without icterus, severe liver injury, anaphylactic reactions, angioedema, erythema multiforme, erythema multiforme-like skin reactions, seizures, thromboembolic events, suicide attempt. Consult the Summary of Product Characteristics for more information relating to side effects.

Legal category POM

Price

Rebif 8.8 and 22: 6 (0.2 ml) + 6 (0.5 ml) syringes - £586.19

Rebif 22: 12 syringes (0.5 ml) - £650.13

Rebif 44: 12 syringes (0.5 ml) - £863.28

For prices in Ireland, consult distributors Allphar Services Ltd.

Marketing Authorisation Holder and Numbers:

Serono Europe Ltd, 56 Marsh Wall, London, E14 9TP; EU/1/98/063/007; 003 & 006

For further information contact:

UK: Merck Serono, Bedfont Cross, Stanwell Road, Feltham, Middlesex, TW14 8NX. Tel: 020 8818 7373.

Republic of Ireland: Merck Serono, 3013 Lake Drive, Citywest Business Campus, Dublin 24. Tel: 01 4661910

Date of Preparation: September 2007

Adverse events should be reported to Merck Serono - see contact details within PI. Information about adverse event reporting in the UK can be found at www.yellowcard.gov.uk.

Date of preparation: October 2007

REB07-0146