Neuropsychologia 48 (2010) 2586–2594

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

Effects of aging on mindreading ability through the eyes: An fMRI study

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ARTICLE INFO

Article history:
Received 15 October 2009
Received in revised form 30 April 2010
Accepted 3 May 2010
Available online 8 May 2010

Keywords:
Adulthood
Elderly
Theory of Mind
Neural bases

ABSTRACT

Theory of Mind – ToM, the capacity to understand one's own and other people's mental states and to refer to them to foresee and explain the behaviour – relies upon a circumscribed neural system: the posterior end of the superior temporal sulcus (pSTS), the adjacent temporo-parietal junction (TPJ), the temporal pole (TP), the medial prefrontal cortex (mPFC) and the adjacent paracingulate cortex.

To our knowledge, the neural basis of mentalizing has not yet been studied in a developmental perspective covering old age, so the aim of this work is to compare the neural basis of a specific aspect of ToM, the mindreading ability through the eyes, in healthy young and old subjects.

Two groups of healthy adults (young: 25.2 years; old: 65.2 years) were submitted to an fMRI scanning while performing the Reading the Mind in the Eyes test, which requires the attribution of a mental state to the other person focussing only on the eye-gaze. There was no difference in the behavioural performances between young and old and both groups of subjects activated the pSTS and the TP, thus indicating that old people show no impairment of mentalizing circuits. However, a relevant shifting of the neural circuit implied in each group to solve the task emerged. Old subjects showed a more bilateral activation of frontal areas and a stronger involvement of the linguistic components of the mirror neuron system (i.e. area 44), as compared to young. Both young and old participants activated the non-linguistic components of the mirror neuron system, such as area 6. These findings are discussed taking into account the recent literature dealing with cognitive functions during normal aging.

1. Introduction

Humans are naturally social beings spending a considerable amount of everyday life in exchanges and interactions with their partners. The ability of predicting, understanding and explaining the behaviour plays a crucial role for a successful adaptation to the social environment and to its complexity (Brune & Brüne-Cohrs, 2006), an ability often termed as Theory of Mind – ToM. More specifically, this expression refers to the capacity to understand one's own and other people's mental states (emotions, desires, beliefs) and to refer to them to foresee and explain the behaviour (Premack & Woodruff, 1978).

Over the past 20 years ToM development has been extensively studied in children (Wellman, Cross, & Watson, 2001) and has shifted towards a life-span perspective (Freeman, 2000; Khun, 2000; Massaro & Castelli, 2009). In recent years, the improvement and diffusion of brain-imaging methods made the research of the neural basis of ToM bloom and flourish into a "Neuroscience of theory of mind" (Saxe & Baron-Cohen, 2006), supporting the discovery of a circumscribed and dedicated neural system underpinning mentalizing (Frith & Frith, 1999; Frith & Frith, 2003; Frith & Frith, 2006; Gallagher & Frith, 2003): the posterior end of the superior temporal sulcus (pSTS) and the adjacent temporo-parietal junction (TPJ), the temporal pole (TP) and the medial prefrontal cortex (mPFC) and the adjacent paracingulate cortex. In particular Saxe and Kanwisher (2003) observed the involvement of the TPJ bilaterally in reading stories implying characters' goals and beliefs; Saxe and Wexler (2005) more precisely demonstrated that the right TPJ – compared to left TPJ, PC, and mPFC – is selectively activated for the attribution of mental states with respect to other social information about people. Ciaramidaro et al. (2007) followed this path, investigating the functional lateralization in TPJ: the right TPJ is recruited for the understanding of three different kinds of intention and the left TPJ appears to be involved only in the case of communicative intentions (while schizophrenic patients show no signal drop in PC and bilateral TPJ since they detect intentionality in physical objects, see Walter et al., 2009). A key point in the neuroimaging studies investigating the neural basis of ToM is the great variety of tasks employed, comprising stories, cartoons, photos of human faces, videos and so on (for an overview see Brune & Brüne-

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doi:10.1016/j.neuropsychologia.2010.05.005

Cohrs, 2006; Gobbini, Koralek, Bryan, Montgomery, & Haxby, 2007). In a recent meta-analysis Van Overwalle (2009) examines more than 100 fMRI studies on social cognition in humans and about 100 fMRI studies on potentially related abilities. From a theoretical point of view a distinction in social cognition between the temporary attribution of goals and beliefs and the long-lasting attribution of social scripts and norms, as well as personality traits, is assumed. The analysis shows that social cognition requires the TPJ and mPFC areas; in particular, the mPFC is viewed as especially responsible for the attribution of more enduring interpersonal scripts and personality traits; in particular the mPFC is recruited when the tasks include verbal material, suggesting that this brain area is implied in explicit and complex representations about others. Furthermore Kilner, Neal, Weiskopf, Friston, and Frith (2009) found evidence about the existence of mirror neurons in the inferior frontal gyrus (IFG) in humans. In the last decade an increasing amount of studies has been devoted to the exploration of the mirror neurons system (MNS) hypothesis, or the Embodied Cognition theory, according to which action understanding provides the foundation for language and cognition, including others' and self-cognition or Theory of Mind (Arbib, 2005, 2008; Gallese & Lakoff, 2005; Gallese, 2003; Rizzolatti & Arbib, 1998). In this perspective, the MNS is conceived as a trimodal system made of neuronal populations that respond to motor, visual and auditory stimuli, i.e. to actions performed, observed, heard, or read about. Glenberg et al. (2008) explain the sequence from action to language understanding as follows: subjects understand observed action by engaging themselves in motor simulation, therefore the language about concrete and abstract actions is understood through a very similar type of activity since mirror neuron system in humans is partly located in Broca's area (see Fadiga, Craighero, & D'Ausilio, 2009). Williams (2008) raises the hypothesis that different sub-populations of mirror neurons, located in different brain areas, participate in different ways to social abilities, particularly to automatic imitation (more linked to empathy) and to imitation learning (more connected with self-other comparison processes involved in Theory of Mind).

The review by Carrington and Bailey (2009) considers two important questions: if individual mental states recruit different brain regions and if verbal versus non-verbal tasks and explicit versus non-explicit ToM instructions can affect the observed patterns of activation. Methodological variations (paradigm type and verbal/non-verbal nature of the task) do not explain the variability of results, while there is preliminary evidence that distinct brain regions may be involved in the understanding of different mental states. The imaging studies reviewed (Carrington & Bailey, 2009) show the activation of an integrated functional network for ToM reasoning, including parts of the PFC and STS.

Among a wide range of available tasks, one in particular has captured our attention since it has been conceived as an advanced test of ToM: the Reading the Mind in the Eyes test (RME, Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997; Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001), which detects in adults with normal intelligence any possible individual differences or any subtle dysfunctions in the mindreading ability (for a critical review of the task see Johnston, Miles, & McKinlay, 2008). In particular, the RME test investigates an ability that humans often use in everyday interactions with their conspecifics, i.e. the ability to understand the mental state of the other person through eye-gaze. So far, the neural basis of the mindreading ability through the eyes has been investigated in few studies on adults with clinical conditions showing an impairment in the ability to mentalize the inner states of the others, namely high-functioning autism or Asperger syndrome (Baron-Cohen et al., 1999), schizophrenia (Hirao et al., 2008; Russell et al., 2000), alcohol dependence (Hill et al., 2007), showing activations in fronto-temporal neocortical regions, in bilateral temporo-parietal regions, and in non-neocortical areas, such as the amygdala.

To our knowledge, the neural basis of mentalizing has not yet been studied in a developmental perspective covering normal aging. Recent literature data (see, for review, Park & Reuter-Lorenz, 2009) proposed the "scaffolding theory" for cognition in aging. They suggested that brain engages in a series of compensatory processes (i.e. increased prefrontal activations; neurogenesis; distributed processing; bilaterality) to cope with the decline of neural structures and functions (i.e. dedifferentiation of ventral visual areas; decreased medial temporal recruitment).

The aim of our work is to compare the neural basis of the mindreading ability through the eyes in healthy young and old subjects, in order to better understand the possible changes of the brain networks underpinning ToM across the human life-span. The only attempt has been done on parents of children with Asperger syndrome (Baron-Cohen et al., 2006), but always aimed at discovering possible patterns of atypical functioning and neural activations in a group of individuals close to clinical conditions. In fact, up to now the neural bases of ToM have been mostly investigated on adults and only recently this interest is opening to a developmental perspective to understand the neural changes in ToM neural circuits during development (Kobayashi, Glover, & Temple, 2007; Moriguchi, Ohnyshi, Mori, Matsuda, & Komaki, 2007; Ohnyshi et al., 2004). In our opinion, this aspect is of paramount importance, since it would contribute to draw a complete picture of the developmental changes of ToM both on the behavioural level (already well-known from the past 20 years of research in developmental psychology) and on the neural one.

2. Materials and methods

2.1. Subjects

Twelve consecutive healthy young adults [age range 21–30 years, mean (SD) age 25.2 (3.5) years; 10 females] and 12 healthy old subjects [age range 60–78 years, mean (SD) age 65.2 (5.7) years; 8 females] were recruited for the present study between 2006 and 2007. They were preliminarily screened on the basis of the clinical history to exclude that any of them suffered from major systemic, psychiatric and neurological illnesses. Conditions associated to cognitive impairment were carefully investigated and excluded in both groups (young and old) with the administration of an extensive battery of psychometric and behavioural tests. All the subjects were right handed as assessed by the Edinburgh inventory (Oldfield, 1971) and were drug-free.

The study was conformed to the ethical principles of the Helsinki Declaration and informed written consent was obtained from all the included subjects before study initiation.

2.2. Neuropsychological assessment

A neuropsychological battery was administered to all subjects by a neuropsychologist within 2 weeks from the MRI session. The cognitive and behavioural assessment included: the Mini-Mental State Examination (MMSE) (Magni, Binetti, Bianchetti, Rozzini, & Trabucchi, 1996), the Token test (Spinnler & Tognoni, 1987), the Raven Coloured Progressive Matrices (CPM) (Raven & Lewis, 1971), the phonemic and categorical fluency test (Novelli et al., 1986), and Street's completion test (Spinnler & Tognoni, 1987).

All the scores obtained from each test were corrected for age and the level of education (conversion formulae are reported in the appropriate references).

For each subject, the scores obtained at any individual test were first compared to the normal range, in order to fulfil the exclusion criteria. Then, group comparisons were performed to assess whether there was any significant difference between the two groups. The Independent Sample *t*-test was employed to compare those scores showing a normal distribution across subjects; the Mann–Whitney *U* test was used to compare those scores with no normal distribution across subjects. All significance tests were conducted at the $\alpha = 0.05$ level and were two-tailed.

2.3. ToM assessment

ToM ability was assessed with a paper–pencil battery of ToM tasks appositely devised for research on adult and old subjects (Castelli et al., 2007). The battery taps various levels of ToM understanding following the developmental pattern of ToM acquisition, in order to verify the consistence of such steps in the tested subjects.

1. Theory of Mind precursors: Eye Direction Detection or EDD (Baron-Cohen, Campbell, Karmiloff-Smith, Grant, & Walker, 1995; Snowden et al., 2003)