Neuroscience 222 (2012) 58–68

MOTOR RESONANCE MECHANISMS ARE PRESERVED IN ALZHEIMER'S DISEASE PATIENTS

A. BISIO,[a*] M. CASTERAN,[b] Y. BALLAY,[b] P. MANCKOUNDIA,[b,c] F. MOUREY[b] AND T. POZZO[a,b,d]

[a] *Department of Robotics, Brain and Cognitive Sciences, Istituto Italiano di Tecnologia, via Morego 30, 16163 Genoa, Italy*

[b] *INSERM U1093 Cognition, Action et Plasticité Sensorimotrice, Université de Bourgogne, France*

[c] *Service de Médecine Interne Gériatrique, Hôpital de Champmaillot, Centre Hospitalier Universitaire, rue Jules Violle, BP 87909, 21079 Dijon, France*

[d] *Institut Universitaire de France, Université de Bourgogne, UFR STAPS, Dijon, France*

Abstract—This study aimed to better characterize the sensorimotor mechanisms underlying motor resonance, namely the relationship between motion perception and movement production in patients suffering from Alzheimer's disease (AD). This work first gives a kinematic description of AD patients' upper limb movements, then it presents a simple paradigm in which a dot with different velocities is moved in front of the participant who is instructed to point to its final position when it stopped. AD patients' actions, as well as healthy elderly participants, were similarly influenced by the dot velocity, suggesting that motor resonance mechanisms are not prevented by pathology. In contrast, only patients had anticipatory motor response: i.e. they started moving before the end of the stimulus motion, unlike what was requested by the experimenter. While the automatic imitation of the stimulus suggests an intact ability to match the internal motor representations with that of the visual model, the uncontrolled motion initiation would indicate AD patients' deficiency to voluntarily inhibit response production. These findings might open new clinical perspectives suggesting innovative techniques in training programs for people with dementia. In particular, the preservation of the motor resonance mechanisms, not dependent on conscious awareness, constitutes an intact basis upon which clinicians could model both physical and cognitive interventions for healthy elderly and AD patients. Furthermore, the evaluation of the inhibitory functions, less sensitive to the level of education than other methods, might be useful for screening test combined with the traditional AD techniques. However, further investigations to understand if this feature is specific to AD or is present also in other neurodegenerative diseases are needed.

Key words: movement observation–execution, automatic imitation, action–perception matching, dementia, ageing.

INTRODUCTION

Alzheimer's disease (AD) is the most common form of dementia that causes a decline of intellectual functioning that interferes with daily life activities (Borson and Raskind, 1997). Indeed, cognitive deterioration is the first sign of the illness and the most documented aspect of AD. Both imaging (Scahill et al., 2002) and neuropathology (Double et al., 1996) studies have described the brain in AD as characterized by progressive cerebral atrophy, which increases as the disease progresses. Despite large inter-individual variability, the earlier change in AD patients are found in the medial temporal structures, and the earlier clinical sign is memory loss (Braak and Braak, 1991). At this stage, a significant range of atrophy is present also in the neocortical areas, but it does not differ from healthy aged-matched individuals (Double et al., 1996). In mild and moderate stages, a significant loss of volume is observed not only in frontal and temporal areas but also in parietal lobes (Scahill et al., 2002). Recent findings in healthy people showed that parietal, temporal and frontal lobes play a fundamental role in linking action to perception (Grèzes and Decety, 2001; Jeannerod, 2001; Iacoboni, 2009b). Indeed, action–perception coupling is crucial to allow humans to efficiently communicate with other people and to interact with the environment, a function that is markedly deficient in AD. The mechanism associated with the link between perception and action is known as motor resonance and is considered to stem from the activity of the mirror neuron system (Rizzolatti et al., 1999). As such, it was proposed to play a crucial role in empathy and imitation (Iacoboni, 2009a), action understanding (Rizzolatti et al., 2001), intention reading (Iacoboni, 2005) and more generally all phenomena underlying social interactions. Therefore, it appears evident that the preservation of this mechanism is fundamental for communicative purposes. Imitation, and its inhibition during daily life activities (Bien et al., 2009), is a special case of perception–action matching (Wohlschläger et al., 2003) that supposes an intact ability to perceive the external motion and to map it into

*Corresponding author. Tel: +39-010-71781406, +39-340-2435784; fax: +39-010-7170817.
E-mail addresses: ambra.bisio@iit.it, ambra.bisio@gmail.com (A. Bisio).

Abbreviations: AD, Alzheimer's disease; CE, control experiment; CG, control group; MMSE, mini-mental state examination; MNS, mirror neuron system; MO, movement observation experiment; PM, pointing movement experiment; rt, reaction time; SD, standard deviation; SE, standard error; TOM, theory of mind; v_D, dot mean velocity; v_p, participants' mean velocity.

0306-4522/12 $36.00
http://dx.doi.org/10.1016/j.neuroscience.2012.07.017

internal motor representation either voluntarily or automatically. Imitation mechanisms are associated with learning (Meltzoff and Moore, 1977), empathizing (Iacoboni, 2009a), and also considered at the basis of social cognition (Meltzoff and Prinz, 2002).

Several neuroimaging studies have described the neural activations during voluntary and automatic imitation tasks, and found that both frontal and parietal regions (i.e. fronto-parietal network of the human mirroring system) were active when imitating an observed motion (Iacoboni et al., 1999; Koski et al., 2002; Iacoboni and Dapretto, 2006; Heyes, 2011). Despite the fact that lesions to the frontal and parietal lobes are well documented in AD, to the best of our knowledge no study has characterized either the automatic or the voluntary imitation capabilities of AD patients. Likewise, little research has illustrated the behavioural consequences of these cerebral damages at perceptual and motor levels. Within this small literature there are reports of alterations of motor abilities (Kluger et al., 1997; Ghilardi et al., 1999; Manckoundia et al., 2006), deterioration of objects' motion and shape perception (Gilmore et al., 1994; Rizzo and Nawrot, 1998), and impairments in transforming the visual input into a motor output (Tippett and Sergio, 2006; Tippett et al., 2007; Yan et al., 2008) starting from the mild stage of the illness. Furthermore, while some have found evidence for the involvement of both frontal and parietal regions in developing and maintaining a social cognition (Adolphs, 1999), a small number of works on this topic in AD have actually found contrasting evidences. Indeed, some studies (Cuerva et al., 2001; Verdon et al., 2007) described AD patients' impairment in Theory of Mind tasks – TOM (for reviews see Meltzoff, 1999; Frith and Frith, 2006). In contrast, Gregory et al. (2002) compared AD patients with a population of frontal variant frontotemporal dementia (fvFDT), and found that AD patients' difficulties in TOM were only for tasks requiring heavy demands on working memory suggesting that AD patients are not generally impaired in TOM tests, but rather other underlying processes, like memory, are responsible for the observed TOM deficits.

Given this, investigation of motor resonance mechanisms in AD would cast light on patients' ability to relate with other people through sharing behavioural states (e.g. imitating others' movement). Moreover, in patients whose brain's lesions are difficult to circumscribe, as in the case of AD, verifying the preservation of perception–action coupling could be informative about the remaining functionality of the underling perceptual, motor and cognitive mechanisms. In particular, by assessing whether both AD patients' and healthy aged-matched people's motor responses are influenced by the observed movements, we would gain insight about the preservation of motor resonance mechanisms during this pathology.

If a 'weak' influence of the perceived movement features in action production is synonymous with the normal activation of motor resonance mechanisms, exaggerated imitative response would be a sign of abnormal functioning of the inhibitory circuitry (Bien et al., 2009). In other words, despite the occurrence of perception–action coupling at neural level, healthy adults typically avoid exaggerated imitation behaviours because these actions are not adaptive for most everyday situations. Interestingly, previous clinical studies performed on a group of patients with frontal lobe damage, including AD individuals, report their incapacity to inhibit the production of motor responses to external stimuli. This is the case of the well known environmental dependency syndrome that includes in its symptoms the ''imitation behaviour'' (Lhermitte, 1986; Lhermitte et al., 1986). Even if imitation behaviour is marginally present in AD, although several experiments have provided substantial evidence that AD patients have a significant impairment in tasks requiring voluntary inhibition (see for reviews (Amieva et al., 2004; Fournet et al., 2007).

The present study has a threefold purpose. Firstly, it provides a kinematic description of patients' motor deficiencies when performing a simple arm upwards movement. Secondly, it characterizes the relationship between motion observation and movement production in AD patients by testing if and how their actions are influenced by a previously observed motion. If motor resonance mechanisms are still preserved, AD patients' movements would be influenced by the observed biological motion in so far as healthy aged-matched participants are. Finally, this work investigates whether AD patients' deficiency in tasks requiring voluntary inhibition causes inappropriate motor responses irrespective of task demands. To these aims, the imitation paradigm we proposed in Bisio et al. (2010) was applied to simultaneously verify the occurrence of normal automatic imitation phenomena and the voluntary inhibition capabilities by providing a simple visual stimulation and asking participants to produce a movement in response to it.

EXPERIMENTAL PROCEDURES

Participants

The experimental group was composed of 25 elderly participants (21 women and 4 men), ranging in age from 75 to 91 years of age (mean age ± SD, 84.2 ± 4.5), with probable mild and moderate AD (Perneczky et al., 2006) diagnosed according to the French National Institute of Neurology and Communication Disorders and Strokes – The Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) and the Diagnostic and Statistical manual-IV-Text Revised (DSM IV-TR) criteria. All the patients lived at home or in a nursing home specializing in AD and there was no reported difference in the severity of the pathology based on the residence type. They underwent comprehensive diagnostic evaluation, including clinical assessment, brain Magnetic Resonance Imaging (MRI) and examination of motor competencies. All of them presented with progressive cognitive impairment. Their Mini-Mental State Examination (MMSE) scores were between 12 and 24 (mean ± SD, 19 ± 4). Patients were excluded from the present study if (A) their dementia was not considered due to AD, (B) if severe vascular lesions were present, and (C) if they were unable to perform simple arm pointing movement. The Control Group (CG) was composed of 14 healthy participants (10 women and 4 men), ranging in age from 74 to 89 years of