EFFECTS OF SENSORIMOTOR LEARNING ON THE HUMAN MIRROR NEURON SYSTEM

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Abstract

The discovery, in the monkey, of "mirror" neurons, which fire in response both to the performance and to the observation of specific actions, has prompted extensive research into their properties, and into the possible functions of a putative mirror neuron system in humans. Little is known, however, about how such neurons acquire their matching properties. This thesis addresses this question using a variety of techniques.

Imitation is one of the key processes thought to be subserved by the mirror neuron system; Chapter 3 shows that automatic imitation effects are separable from spatial compatibility effects. This establishes automatic imitation effects as suitable targets for experimental manipulations of mirror neuron system function. Strengthening this conclusion, Chapter 4 indicates that automatic imitation effects can be delayed by repetitive theta burst transcranial magnetic stimulation (TMS) of the inferior frontal gyrus, an area homologous with the premotor F5 mirror neuron area in the macaque. In Chapter 5, single-pulse TMS is used to produce motor evoked potentials (MEPs). In an action observation experiment, an automatic muscle-specific "mirror" effect is shown: the size of the MEP in a given muscle is sensitive to the identity of the muscle that would be used to perform the observed movement. It is then demonstrated that this effect can be reversed following a period of incompatible sensorimotor training. This result is built upon in Chapter 6: it is shown behaviourally that incompatible sensorimotor training can reduce automatic imitation effects, and, using functional magnetic resonance imaging, that it can reverse neural responses to observed actions in the human mirror neuron system.

It is concluded that sensorimotor learning can reconfigure the human mirror neuron system, and that it is, therefore, a mechanism through which the mirror neuron system can acquire its ability to match observed with performed actions.

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1 The mirror neuron system: properties, function and development

In 1992, di Pellegrino, Fadiga, Fogassi, Gallese and Rizzolatti discovered "mirror" neurons that fired both during the performance of movements and during the observation of the same movements. Over the past 16 years, this finding has had a substantial impact on cognitive neuroscience, and a broad range of functions have been ascribed to the "mirror neuron system". However, little is known about the source of mirror neurons' distinctive, perceptual-motor matching properties. Here, I first describe the mirror neuron system and what is known of its properties, in both the monkey and the human brain. I then discuss its possible functions, focusing in particular on its potential role in solving the "correspondence problem", which arises most commonly in imitation. I compare the theories that address how the mirror neuron system may come to solve the correspondence problem; and finally, I assess the current evidence that suggests sensorimotor experience is critical for the development of imitation and the mirror neuron system.

1.1 What is the mirror neuron system?

1.1.1 Single-unit recording in the monkey

The initial evidence for visuomotor "mirror" neurons came from di Pellegrino et al. (1992). They showed that a subset of the neurons in monkey premotor area F5, which are active when certain hand movements are performed by the monkey, also respond when the monkey observes the same movement being performed by the experimenter. Di Pellegrino et al. (1992) showed that the visual stimuli which activated these neurons were limited to transitive hand actions, i.e. movements of the hand towards an object, or

interactions between the hand and an object. The observation of hand-only actions and tool-food interactions had no effect on the activity of these neurons. The neurons varied in the level of congruence between the performed and observed movements to which they responded: out of 87 visuomotor neurons, 48 responded to the observation of simple objects ("canonical" neurons; Rizzolatti & Fadiga, 1998). The remainder showed "mirror" properties to a varying degree: 12 neurons had a clear correspondence between the performed and observed actions; six responded to a wider range of visual stimuli than just the action for which they coded; 10 responded to visual actions alone (so, strictly, should not be classified as "mirror") and 11 responded to the observation of actions that tended to precede the motor actions for which they coded. Crucially, all these visuomotor neurons were active when the monkey performed movements in darkness, showing that it is not just the sight of an action that triggers them. The findings of di Pellegrino et al. (1992) are considered to be evidence for an observation-execution matching system, now commonly referred to as the "mirror neuron system".

Further neurophysiological studies on monkeys from the same laboratory have provided additional information about the properties of these visuomotor mirror neurons (Gallese, Fadiga, Fogassi, & Rizzolatti, 1996; Umiltà et al., 2001; Ferrari, Rozzi, & Fogassi, 2005). Additionally, F5 neurons have now been found that respond to the sound, and to both the sound and sight of an action (audiovisual mirror neurons; Kohler et al., 2002; Keysers et al., 2003) and that code for the observation and the execution of mouth movements (Ferrari, Gallese, Rizzolatti, & Fogassi, 2003). Recently, mirror neurons have also been found in parietal cortex (in the rostral sector of the inferior parietal lobule; Fogassi et al., 2005).

While the single-cell recording technique is the ideal tool to demonstrate the specificity of responses of the mirror neuron system, it has some obvious drawbacks: it cannot be used in humans, except in very unusual circumstances, and it is only ever possible to investigate the responses of a very small proportion of the neurons in any particular area. Different experimental techniques are therefore required to investigate the properties of a putative human mirror neuron system.

1.1.2 Muscle-specific effects of action observation

In humans, effects that most closely approach the specificity of the single-cell results have been produced through the use of transcranial magnetic stimulation (TMS). Single pulses of TMS applied over the primary motor cortical representation of a particular muscle produce motor evoked potentials (MEPs) in that muscle. Since premotor mirror neuron areas are closely connected to primary motor cortex, Fadiga, Fogassi, Pavesi and Rizzolatti (1995) reasoned that, if premotor neurons in humans are active during action observation, this activity should be reflected in an increase in the excitability of the areas of motor cortex that control those actions. This should be manifested, through the use of TMS, as an increase in the size of the MEPs from a particular muscle during the observation of a movement involving that muscle, compared to the observation of a control stimulus.

Using this logic, Fadiga et al. (1995) demonstrated that four hand muscles showed greater MEPs during observation of the experimenter grasping objects, or making arm movements, than during the observation of common objects, or in a dimming detection task. The pattern of relative MEP sizes during the two movement observation conditions was very similar to the pattern of electromyogram (EMG) activity recorded from the muscles of participants performing those movements, suggesting that the change in

MEP size reflected the activity of a muscle-specific action observation-execution matching system, rather than a general increase in the excitability of the motor system as a result of the observation of movements.

There are two clear differences between the results of Fadiga et al. (1995) and the single-cell monkey mirror neuron data. First, in the monkey, these neurons did not respond to intransitive movements, whereas Fadiga et al. (1995) showed MEP enhancement for the observation of both transitive (grasping) and intransitive (arm) movements. It is not yet clear why this is the case; however, one simple explanation could be that in the single-cell experiments, cells were only selected for further investigation if they were active when the monkey performed hand movements. In an experimental situation, a monkey may have little opportunity to perform intransitive hand movements; therefore, neurons that are active during intransitive movements may not have been selected for investigation. The second difference is that several studies (Rizzolatti et al., 1988; di Pellegrino et al., 1992; Rizzolatti & Fadiga, 1998) have described the existence of canonical neurons in monkey premotor cortex, which, as described above, fire both during the performance of hand movements and when the monkey views objects of a size consistent with the preferred hand movement. If the same system is underlying the results of Fadiga et al. (1995), it is unclear why the MEPs from muscles involved in grasping objects were not similarly enhanced by viewing those objects.

The above differences aside, TMS is proving a very useful tool to investigate the effects of perceptual stimuli on the motor system. It has now been shown that a range of action stimuli can modulate the excitability of the motor cortex as observed through TMS, in a way that demonstrates both similarity and specificity between the movement perceived

and the muscle enhanced. For example, the observation of handwriting enhances MEPs from a hand muscle (first dorsal interosseus, FDI) as compared to an arm muscle (biceps) and vice versa (Strafella & Paus, 2000), while videos of index finger abduction produce left hemisphere excitatory effects if they are movements of a right hand, and right hemisphere modulation if a left hand is being observed (Aziz-Zadeh, Maeda, Zaidel, Mazziotta, & Iacoboni, 2002).

Gangitano, Mottaghy and Pascual-Leone (2001; 2004) investigated the time course of the excitatory effects of action observation on the motor system by applying TMS at various times during a four second video of a reach-grasp movement. The magnitude of the MEP measured from the FDI was proportional to the extent of the movement of the index finger (which requires the FDI) at the time of TMS. When the video was altered to show a hand that opened suddenly, rather than gradually, no MEP enhancement was seen. In a third condition, the part of the video with the greatest extent of index finger movement was replaced by a closed grip, incongruent with the reach-grasp movement. This produced a reduction in MEP enhancement for the subsequent time points. The data from the first experiment showed that MEP enhancement during action observation is not an all-or-none effect, but is modulated on-line, in proportion to the amount of muscle involvement that would be required, were the observed movement to be performed. The other conditions indicated that MEP modulation may depend on the familiarity of the observed movement – a possibility to which I will return when discussing the effects of experience on the mirror neuron system.

Auditory stimuli also modulate activity in those muscles that would be used to produce the heard actions: speech sounds that involve tongue movements increase MEP size in tongue muscles more than non-tongue words, or non-words (Fadiga, Craighero,

Buccino, & Rizzolatti, 2002), while right hand MEPs show greater enhancement during perception of the sound of hand actions than of foot actions or control sounds (Aziz-Zadeh, Iacoboni, Zaidel, Wilson, & Mazziotta, 2004).

These TMS studies provide evidence that the motor system is activated in a matching, muscle-specific fashion by movement-related sensory stimuli, providing supporting evidence for the presence of a mirror neuron system in humans: the observation of a movement provokes activity in precisely those muscles that would be used by the observer to produce that movement. Single-pulse TMS experiments can, however, only demonstrate that the motor system is selectively responsive to perceptual input; they cannot identify the brain network that produces these responses. In order to ascertain whether the brain areas underlying these effects are homologous with monkey mirror neuron sites, brain imaging is required.

1.1.3 Imaging the mirror neuron system

Before discussing those imaging studies that investigate the human mirror neuron system, it is important to clarify just what constitutes a "mirror" response in the human brain. A recent paper has suggested that many functional magnetic resonance imaging (fMRI) studies purporting to show mirror neuron responses in humans do not display the same characteristic effects as the monkey mirror neuron data (Turella, Pierno, Tubaldi, & Castiello, in press). Turella et al. list the following criteria for an area to show "mirror" activity: 1) the area must be within the broad homologues of those areas where mirror neurons have been observed in the monkey (parts of frontal and parietal cortex); 2) the area must show overlapping activity during independent observation and execution of similar actions (execution must be "pure" execution, i.e. without visual movement cues or self-observation); 3) the actions used must be object-related hand

actions; and 4) the action stimulus must depict an entire body, not just a hand movement. They conclude that there is no "compelling evidence" for a human mirror neuron system in the data from current fMRI or positron emission tomography (PET) studies.

While the above criteria may be necessary in order to identify areas with precisely the same properties as those reported for monkey mirror neurons, there is some justification in adopting slightly less strict criteria in investigating a human mirror neuron system. As discussed in section 1.1.2, the finding that observed movements had to be either object-related or actions of the hand in order to produce a mirror neuron response may simply be an artefact of the testing process in the monkey (indeed, mirror neurons for intransitive mouth actions, which are neither object-related nor hand actions, have been recorded; Ferrari et al., 2003). The results of Ferrari et al. (2003) therefore reduce the necessity for criterion 3) above. It also appears to be likely that, in investigating human, rather than monkey, responses to action observation, stimuli do not need to depict the entire body, due to our greater experience with photographs, videos, and computer-generated images, all of which provide us with prior visual experience of body parts without seeing the whole body (but see section 1.5 on experience).

Thus, I shall adopt the criteria that a mirror response is one of spatially overlapping activity during independent action observation and execution, in areas broadly homologous with mirror neuron areas in the monkey. The first of these modified criteria is necessary in order to ensure that brain regions thus identified are likely to have "mirror" properties, i.e. are active during both observation and execution of an action, while the second criterion increases the likelihood that any such responses are the result of a similar mirror neuron system to that found in the monkey.

The earliest experiment on the neural substrate of action observation that is widely cited in support of a human mirror neuron system is that of Rizzolatti et al. (1996a), who, using PET, identified areas of increased blood flow in the left inferior frontal gyrus (IFG) during observation of grasping actions. However, this study did not find this area to be involved during the *execution* of grasping actions, meaning that the IFG cannot be considered a potential mirror neuron area on the basis of these data alone: mirror neurons, by definition, are active during both action observation and action execution. Several subsequent studies, also usually considered to be investigating the human mirror neuron system, similarly do not meet the modified criteria above. Many did not include action execution conditions (e.g. Grafton, Arbib, Fadiga, & Rizzolatti, 1996; Decety et al., 1997; Grèzes, Costes, & Decety, 1999), or included only execution conditions that involved simultaneous action observation (e.g. imitation conditions), therefore independent involvement of an area during action observation and action execution could not be shown: if action execution was always confounded with action observation, any activity during action execution may have been due to the concurrent action observation (e.g. Tanaka, Inui, Iwaki, Konishi, & Nakai, 2001; Decety, Chaminade, Grèzes, & Meltzoff, 2002; Chaminade, Meltzoff, & Decety, 2002).

The first study to meet the modified criteria listed above was that of Iacoboni et al. (1999). They used fMRI to investigate the imitation of simple finger movements, but also included conditions relevant to the above criteria, i.e. passive action observation and action execution in response to a symbolic cue, as well as imitation. While a direct analysis investigating responses during action observation and action execution was not reported, it is possible to infer from the reported data that both passive action observation, and execution in response to a cue, resulted in increased blood oxygen level dependent (BOLD) response in left IFG (Brodmann area (BA) 44) and a region

around the right anterior intraparietal sulcus. These areas are broadly similar to those in which mirror neurons are found in the monkey, implying that the effects of action observation seen in the TMS experiments are the result of a similar system to that underlying the monkey mirror neuron results. However, the homology between human and monkey brains in these areas is not entirely clear (Geyer, Matelli, Luppino, & Zilles, 2000; Grefkes & Fink, 2005).

Further fMRI studies that meet the two criteria set out above have confirmed and extended the results of Iacoboni et al. (1999), suggesting that there is a wide network of areas involved in both action observation and execution. These areas include, in the frontal lobe, the inferior frontal gyrus (Iacoboni et al., 1999; Buccino et al., 2004; Molnar-Szakacs, Iacoboni, Koski, & Mazziotta, 2005; Gazzola, Aziz-Zadeh, & Keysers, 2006; Aziz-Zadeh, Koski, Zaidel, Mazziotta, & Iacoboni, 2006a; Gazzola, Rizzolatti, Wicker, & Keysers, 2007a), ventral (Buccino et al., 2004; Dinstein, Hasson, Rubin, & Heeger, 2007; Vogt et al., 2007) and dorsal premotor cortex (Gazzola et al., 2006; Vogt et al., 2007; Gazzola et al., 2007a), supplementary motor area (Vogt et al., 2007), and parts of the middle (Vogt et al., 2007; Gazzola et al., 2007a) and superior frontal gyri (Gazzola et al., 2007a); and in the parietal lobe, the inferior parietal lobule (Grèzes, Armony, Rowe, & Passingham, 2003; Buccino et al., 2004; Gazzola et al., 2006; Aziz-Zadeh et al., 2006a; Vogt et al., 2007; Jonas et al., 2007; Gazzola et al., 2007a), anterior intraparietal sulcus (Iacoboni et al., 1999; Grèzes et al., 2003; Buccino et al., 2004; Shmuelof & Zohary, 2006; Dinstein et al., 2007; Vogt et al., 2007), and superior parietal lobule (Dinstein et al., 2007; Vogt et al., 2007; Gazzola et al., 2007a).

Recent studies have also found overlapping activity during action observation and execution in areas outside reported monkey mirror neuron areas: in the temporal lobe,

the superior temporal sulcus (Gazzola et al., 2006; Aziz-Zadeh et al., 2006a), the inferior (Vogt et al., 2007), middle (Gazzola et al., 2006; Gazzola et al., 2007a) and superior temporal gyri (Jonas et al., 2007), and temporo-occipital junction (Jonas et al., 2007); in lateral occipital cortex (Dinstein et al., 2007); and in the cerebellum (Vogt et al., 2007).

While the spatial resolution of other imaging modalities is not comparable to that of fMRI, converging evidence for common processing of observed and executed actions has come from magnetoencephalography (MEG; Hari et al., 1998; Nishitani & Hari, 2000; Nishitani & Hari, 2002) and electroencephalography (EEG; Cochin, Barthelemy, Roux, & Martineau, 1999). Capitalising on the high temporal resolution of MEG, Nishitani and Hari (2000; 2002) investigated the time course of cortical activation during action observation and execution. During action execution, signals were observed in the inferior frontal gyrus, followed by primary motor cortex. During action observation, a more extensive network was activated, in the following order: occipital visual areas – superior temporal sulcus – inferior parietal cortex – inferior frontal gyrus – primary motor cortex. According to the criteria above, this suggests that inferior frontal gyrus, and possibly primary motor cortex, have "mirror" properties.

None of these imaging modalities can show effects with the specificity of the single-cell or TMS data, but in conjunction with the TMS results, the functional imaging data suggest that humans possess an action observation-execution matching system, made up of a network of cortical areas, including those homologous with the location of monkey mirror neurons. There are now some initial data supporting this conclusion from human single-cell recordings.

1.1.4 Single-unit recording in humans

A recent preliminary report (Iacoboni, 2008) suggests that neurons with mirror properties may be present and, indeed, prevalent, in the human brain. Iacoboni reports that, recording from individual neurons in anterior cingulate cortex and supplementary motor area in epileptic patients undergoing pre-surgical evaluation, his group found approximately 12 % of 500 recorded neurons to have mirror properties. Such a finding, in areas not tested for the presence of mirror neurons in the monkey, suggests that the human brain may contain a wide network of areas with mirror properties.

1.2 Which functions might the human mirror neuron system perform?

1.2.1 The many possible functions of the human mirror neuron system

While the properties of mirror neurons are intriguing, it is not immediately clear to which cognitive functions they might contribute. Suggestions have been advanced for the involvement of the human mirror neuron system in a wide range of processes, including action understanding (Rizzolatti, Fadiga, Gallese, & Fogassi, 1996b), the understanding of intentions (Iacoboni et al., 2005), mental state simulation (Gallese & Goldman, 1998), imitation (Iacoboni et al., 1999), manual communication (Rizzolatti et al., 1996b), sign language processing (Corina & Knapp, 2006), speech perception (Tettamanti et al., 2005; Glenberg et al., 2008), speech production (Gentilucci & Dalla Volta, 2008; Kühn & Brass, 2008), language acquisition (Rizzolatti & Arbib, 1998; Théoret & Pascual-Leone, 2002), the evolution of language (Rizzolatti & Arbib, 1998; Corballis, 2004; Arbib, 2005; Gentilucci & Corballis, 2006), music processing (Gridley & Hoff, 2006), empathy (Leslie, Johnson-Frey, & Grafton, 2004; Avenanti, Bueti, Galati, & Aglioti, 2005; Gazzola et al., 2006; Schulte-Rüther, Markowitsch, Fink, & Piefke, 2007; Cheng, Yang, Lin, Lee, & Decety, 2008), emotion recognition (Enticott,

Johnston, Herring, Hoy, & Fitzgerald, 2008), embodied simulation (Aziz-Zadeh, Wilson, Rizzolatti, & Iacoboni, 2006b; Gallese, Eagle, & Migone, 2007; Arbib, 2008), the maintenance of cigarette addiction (Pineda & Oberman, 2006), the development of obesity (Cohen, 2008), and sexual orientation (Ponseti et al., 2006). Furthermore, the possible dysfunction of the mirror neuron system has been implicated in a range of disorders, including autism spectrum disorder (Avikainen, Kulomaki, & Hari, 1999; Williams, Whiten, Suddendorf, & Perrett, 2001; Nishitani, Avikainen, & Hari, 2004; Hadjikhani, Joseph, Snyder, & Tager-Flusberg, 2006; Dapretto et al., 2006; Iacoboni & Dapretto, 2006; Oberman & Ramachandran, 2007), schizophrenia (Quintana, Davidson, Kovalik, Marder, & Mazziotta, 2001; Arbib & Mundhenk, 2005; Arbib, 2007; Enticott et al., 2008), Down's syndrome (Virji-Babul et al., 2008), and multiple sclerosis (Rocca et al., 2008).

What are the common factors underlying this wide range of mirror neuron system functions? While the tasks used to investigate these functions vary, a factor common to many is the requirement for perceptual-motor translation. This requirement is most apparent in the case of imitation, but many of the other tasks also require the mapping of perceptual input onto motor output. For example, it has been suggested that mental state simulation requires the mirror neuron system to match others' mental states (information about which is acquired via perception of their actions) onto the observer's own, and thus to anticipate the actions that the observer would perform, were they in the other's position (Gallese & Goldman, 1998). If perceptual-motor translation is a core function of the mirror neuron system, it must meet a significant challenge, commonly known as the "correspondence problem". The following section outlines the correspondence problem and the evidence for the role of the mirror neuron system in its solution.

1.2.2 Solving the correspondence problem

The correspondence problem (Brass & Heyes, 2005) is encountered most acutely in a small range of tasks. These can take one of two forms: motor-perceptual, and perceptual-motor. An example of the former type of task comes from skill learning. Athletes, dancers and musicians are often encouraged to visualise their motor skills from a third-person perspective. To the extent that this is possible, the novice has to translate their motor programs into a perceptual representation of the programs' output. This ability has been measured experimentally by Casile and Giese (2006) who demonstrated an effect of motor learning on a subsequent visual discrimination task. In this case, the correspondence problem consists of the difficulty in translating from motor programs in one modality to a perceptual representation in another modality.

The correspondence problem arises in a more common form in perceptual-motor translations, most typically in imitation. The correspondence problem in imitation consists of the following: to imitate you, I must translate the visual input that I obtain from observing your action into a set of motor commands, in order to move my muscles and hence reproduce your action. How do I know which motor commands to perform, when the information I receive from observing you is in a different (non-motor) modality, and consists only of the visible output of your motor commands? The problem is most clearly illustrated when you are performing a "perceptually opaque" action (Heyes & Ray, 2000): one in which the sensory input I receive from observing you performing the action is highly dissimilar to that which I receive from performing it myself, e.g. shrugging the shoulders. However, the problem still persists for "perceptually transparent" actions where the sensory input I receive from observing your action is more similar to that which I receive from performing it myself, e.g. clapping: I still need to determine which motor commands to perform in order to

reproduce the sensory consequences of your action. This thesis uses imitation, rather than motor-perceptual translation, as an assay of correspondence problem solution because a number of valid and reliable experimental paradigms for the measurement of imitative behaviour have recently been developed (Stürmer, Aschersleben, & Prinz, 2000; Brass, Bekkering, Wohlschlager, & Prinz, 2000; Brass, Bekkering, & Prinz, 2001a; Kilner, Paulignan, & Blakemore, 2003; Kilner, Hamilton, & Blakemore, 2007).

1.2.3 The role of the mirror neuron system in imitation

The mirror neuron system, by matching actions observed with the muscles required to execute them, appears to be a neural implementation of a process that solves the correspondence problem. As indicated above, imitation is one of the most common tasks in which the correspondence problem arises. What is the evidence for the involvement of the mirror neuron system in imitation?

While several fMRI studies have suggested that the mirror neuron system is involved in imitation (Iacoboni et al., 1999; Tanaka & Inui, 2002; Koski, Iacoboni, Dubeau, Woods, & Mazziotta, 2003), these studies typically contrast imitation with action observation or action execution conditions. In order to isolate the neural mechanisms involved in imitation, that is, in translating the sensory representation of a perceived action into the motor representation of the *same* performed action, it would seem to be necessary to compare neural activity during imitative trials, i.e. those on which the performed action matches that which is observed, to activity on non-imitative trials, on which the performed action is different from that observed. Otherwise, any results could be due to whichever element of the task (action observation or execution) is not used as the control condition, rather than to the process of translating a perceptual representation into the motor representation of the same action. Only a few neuroimaging studies have

been carried out using this type of design, and the results are inconclusive. Brass, Zysset and von Cramon (2001b) compared non-imitative to imitative trials; this contrast resulted in activity outside the mirror neuron system. Newman-Norlund, van Schie, van Zuijlen and Bekkering (2007), however, found activity within mirror neuron system areas for the same type of contrast as that of Brass et al. (2001b), i.e. non-imitative vs. imitative; but neither study reported data from the reverse contrast. Williams, Whiten, Waiter, Pechey and Perrett (2007) did not replicate either of these results for non-imitative vs. imitative trials, but the reverse contrast, of imitative vs. non-imitative trials, resulted in mirror neuron system activity. Thus, it is unclear whether imitative or non-imitative conditions result in greater BOLD signal in the mirror neuron system (see also Chapter 4). In addition, this type of experiment has been criticised for showing effects of response timing, rather than of imitation (Makuuchi, 2005). Alternative methods are therefore required to establish the role of the mirror neuron system in imitation.

There is some limited evidence from repetitive transcranial magnetic stimulation (rTMS) studies suggesting that imitative performance is mediated by mirror neuron areas, in particular the inferior frontal gyrus. Heiser, Iacoboni, Maeda, Marcus and Mazziotta (2003) found that rTMS of either the left or right inferior frontal gyrus, compared to stimulation of occipital cortex, increased error rates in a finger imitation task. This suggests that a network of areas including bilateral pars opercularis is necessary to perform finger movement imitation. No effect, however, was seen on other behavioural measures including response times. No other rTMS experiments have investigated the role of the mirror neuron system in imitation, although the involvement of the left inferior frontal gyrus in processes often attributed to the mirror neuron system has been demonstrated by three recent studies. rTMS to the left inferior frontal gyrus

reduced muscle-specific MEP enhancement during the observation of possible, but not impossible, finger movements (Avenanti, Bolognini, Maravita, & Aglioti, 2007), interfered with the ability to judge weight from an observed human action in a motor simulation task (Pobric & Hamilton, 2006), and lowered performance on a task involving the visual discrimination of actions (Urgesi, Candidi, Ionta, & Aglioti, 2007). Thus, while it appears that the left inferior frontal gyrus performs a functional role within the mirror neuron system, the current rTMS data do not provide strong evidence for its role in imitation.

Studies of neuropsychological patients are also used to support the role of the mirror neuron system in imitation; however, it is still not clear from these studies which areas within the mirror neuron system are critical. Lesions to the inferior parietal lobe (angular and supramarginal gyri), particularly in the left hemisphere, often result in apraxia – a deficit in both miming gestures and in imitation (Wheaton & Hallett, 2007). Tessari, Canessa, Ukmar and Rumiati (2007) have suggested that lesions to the angular gyrus produce a particular deficit in imitation of meaningless, rather than meaningful actions – meaningful action imitation is preserved, possibly by a verbally mediated route. Lesions to the inferior frontal cortex in apraxia are not as widely reported as are parietal lesions, and may not always result in imitation deficits: Goldenberg, Hermsdorfer, Glindemann, Rorden and Karnath (2007) found impairment in miming gestures following lesions to the left inferior frontal gyrus, but imitation of gestures was preserved in some of these patients. The patient data may also suggest a dissociation between the imitation of different types of gesture, and lesion location, within areas considered to be part of the mirror neuron system. Imitation of finger movements was impaired following lesions to the left inferior frontal gyrus, while left inferior parietal lesions resulted in impaired imitation of hand postures (Goldenberg & Karnath, 2006).

However, interpretation of lesion data is problematic because of heterogeneity of lesion location and size between patients, the possibility of recovery of affected functions in unaffected adjacent areas of cortex, and – particularly for frontal lesions – the possible confounding effect of aphasia, which may make assessment of ability difficult. It therefore appears that while lesions to parts of the mirror neuron system may cause imitative deficits, the effect will depend on the type of imitation task used.

The data reported in this section suggest that the role of the mirror neuron system in imitation is still unclear. Chapter 4 addresses this issue by assessing automatic imitation effects following rTMS of the left inferior frontal gyrus, which functional imaging data suggest is a strong candidate for a mirror neuron area in humans.

1.3 How do the matching properties of the human mirror neuron system arise?

While evidence for the involvement of the mirror neuron system in imitation is currently not conclusive, it remains the case that, by firing during the observation and execution of the *same* action, mirror neurons (and, by extension, the mirror neuron system) appear to be the result of a process that solves the correspondence problem. What might that process be? In other words, how do the perceptual-motor matching properties of mirror neurons arise? This section will examine two types of theory that have attempted to address this question.

1.3.1 Innate specification of perceptual-motor matches

Many discussions of the mirror neuron system assume, implicitly or explicitly, that its properties are innate, i.e. forged by natural selection, present at birth, and / or developmentally invariant (Gallese & Goldman, 1998; Rizzolatti & Arbib, 1998). This

assumption is implied by the frequency with which commentators refer to the "evolution", "adaptive function", and "dysfunction" of the mirror neuron system. It is also apparent in some discussions of the origins of the mirror neuron system. For example, Rizzolatti and Fadiga (1998), when discussing the visual properties of neurons in the superior temporal sulcus (an area containing neurons responsive to the observation of specific body movements (Perrett, Mistlin, Harries, & Chitty, 1990) and with reciprocal connections to inferior parietal cortex and thence to ventral premotor cortex), suggest that the properties of these neurons are present from birth, as a result of input from the mirror neuron system:

> "… in the anterior section of the superior temporal sulcus (STS), there is a variety of neurons that may contribute to visual recognition of actions. … The spectrum of body parts and body movements that are specified … is wide … . Let us assume that this wide repertoire of neurons is present at birth and that each neuron fires when the appropriate stimulus appears … . Can a new-born child give a meaning to this welter of information? How can it refer these signals to something it knows? This problem can be solved theoretically if the motor system is endowed with an observation/execution matching system, such as that of mirror neurons."
>
> Rizzolatti and Fadiga, 1998, p. 91

Similarly, Lepage and Théoret (2007) have also proposed that:

> "… some rudimentary observation/execution matching system is present shortly after birth in the human brain and … it is modality-independent."
>
> Lepage and Théoret, 2007, p. 519

These theories suggest that the way in which the mirror neuron system solves the correspondence problem is through modality-independent specification of matches

between perceived and executed actions, which presumably are thought to have become hard-wired as a result of natural selection. In other words, we are born with the knowledge of what (at least a range of) actions look like when performed. An alternative to this suggestion is that this knowledge is acquired as a result of experience gained during development.

1.3.2 Experiential accounts of perceptual-motor matches

Two theories have recently been proposed which claim that mirror neurons' properties are the result of correlated experience of observation and execution of the same actions. Heyes and Ray (2000; Heyes, 2001; Brass & Heyes, 2005) devised an "associative sequence learning" (ASL) theory of imitation, which, while initially intended to address the correspondence problem in behavioural imitation, was subsequently applied to explain the matching properties of the mirror neuron system (Heyes, 2005). The ASL model claims that links between perceptual and motor representations of a particular action will arise as a result of the functioning of associative learning mechanisms during the experience of perceptual-motor pairings. The relevant experience can result from a number of sources: self-observation of perceptually transparent actions; from experience with mirrors; from being imitated by another; and from synchronous action (responding in the same manner as another to a common stimulus, while observing the other's response). In all these cases, visual and motor representations of the same action are activated in a systematic, *contingent* fashion (i.e., the visual representation of a given action is more likely to be active at the same time as the motor representation of the *same* action than at the same time as the motor representation of any other action), and thus become linked through general associative learning processes (Dickinson, 1981), producing the matching properties seen in mirror neurons.

Keysers and Perrett (2004) focused on the neurophysiological instantiation of such processes, in a Hebbian learning model that describes how "mirror" properties can emerge from the anatomical connections between neurons responding to the observation of actions in the superior temporal sulcus, and neurons active during the performance of actions in inferior parietal area PF and premotor area F5. According to this model, simultaneous activation of these populations of visual and motor neurons (during self-observation, during synchronous action, or while being imitated) will result in action-specific links being formed between the observation and execution of a particular action, such that neurons in PF and F5 will eventually fire during the mere observation of the action for which they code motorically.

In contrast to the nativist accounts of mirror neuron properties described in the previous section, these theories suggest that the mirror neuron system acquires its matching properties, and hence the ability to solve the correspondence problem, as a result of experience – specifically, sensorimotor experience – gained in the course of development. Sensorimotor experience is hypothesised to be critical because it is assumed that in order to form an association between a perceptual and a motor representation of an action in the brain there needs to be contiguity between the activation of both representations. A sensorimotor experience hypothesis implies that, if no previous sensorimotor experience of a particular action has been obtained, then neither purely sensory experience (e.g. extensive observation of the action without performing it), nor purely motor experience (performing the action repeatedly without sensory feedback), nor the additive combination of both (sensory experience and motor experience of the action, acquired independently of each other), will be sufficient to form associations between the sensory and motor representations of the action, because

none of these types of experience involve the contiguous activation of both the sensory and motor representations of the action.

Is research on imitation, as a measure of correspondence problem solution, consistent with the hypothesis that the solution of the correspondence problem is a result of sensorimotor experience? Such a hypothesis suggests the following predictions. 1) Since associative learning mechanisms are species-general, some imitation should be seen in non-human animals (although not necessarily as much as in humans: our cultural environments are structured such that we receive far greater experience of being imitated than do non-human animals (Tomasello, Carpenter, Call, Behne, & Moll, 2005), and being imitated by others is one of the key ways in which sensorimotor experience of actions is acquired). 2) Imitative abilities in humans should not be present from birth but should arise during development. 3) Once imitative abilities are acquired, imitation should have the potential to occur in the absence of strategic control, i.e. automatically. This third prediction is in line with what is known of the operation of other associative learning mechanisms: once an association between two events is learned, activation of the representation of one event will automatically activate the representation of the other event (Dickinson, 1981). Are these predictions borne out in the literature on imitation?

1.4 Is research on imitation consistent with a sensorimotor hypothesis of the development of the mirror neuron system?

1.4.1 Comparative studies of imitation

While early studies of imitation in non-human animals were beset with methodological problems (see Tomasello, Davis-Dasilva, Camak, & Bard, 1987; Whiten & Ham, 1992),

recent data provide compelling evidence for imitation of simple movements across a range of species, including chimpanzees (Custance, Whiten, & Bard, 1995; Whiten, Custance, Gomez, Teixidor, & Bard, 1996; Whiten, Horner, Litchfield, & Marshall-Pescini, 2004), marmosets (Bugnyar & Huber, 1997; Voelkl & Huber, 2000), dogs (Slabbert & Rasa, 1997; Range, Viranyi, & Huber, 2007), and several bird species (Lefebvre, Templeton, Brown, & Koelle, 1997; Akins & Zentall, 1998; Campbell, Heyes, & Goldsmith, 1999; Dorrance & Zentall, 2001; Heyes & Saggerson, 2002; Mui, Haselgrove, Pearce, & Heyes, in press). For example, quail that have observed a conspecific peck at a treadle to receive a food reward will also use their beak to depress the treadle, while a second group that have observed a stepping behaviour will instead imitate the use of the foot (Akins & Zentall, 1998). Marmosets will imitate hand versus mouth use to open a container (Voelkl & Huber, 2000), while dogs will perform a paw-press action to obtain a food reward, rather than the usually preferred mouth action, after observing a demonstrator dog using this action (Range et al., 2007). These data indicate that the ability to solve the correspondence problem is not unique to humans, but they also suggest, consistent with a sensorimotor hypothesis, that this ability is limited to a small range of actions: those actions with which animals are likely to have obtained sensorimotor experience.

1.4.2 The development of imitative capabilities in humans

Is imitative behaviour present from birth, or does the ability to solve the correspondence problem emerge in the course of development? Since the publication of a seminal paper on neonatal imitation (Meltzoff & Moore, 1977), it has been widely assumed that the ability to imitate is innate. However, recent reviews indicate that the only behaviour that is reliably imitated by newborns is that of tongue protrusion (Anisfeld et al., 2001; Jones, 2006). It is argued that the majority of other behaviours for which infant

imitation has been reported have been measured with respect to tongue protrusion, thus producing a spurious positive result. As an example, let us take the behaviour of mouth opening. As a result of increased neonatal tongue protrusion during the observation of a model's tongue protrusion, the rate of mouth opening is reduced. When the model's tongue protrusion ceases, e.g. during the modelling of mouth opening, the infant's mouth opening returns to baseline levels, giving the illusion of an imitative response to observed mouth opening (Anisfeld, 1996). The same effect, of apparent imitation that is seen only in comparison with tongue protrusion, is also observed for blinking, and head movements (Abravanel & Sigafoos, 1984; Meltzoff & Moore, 1989).

A recent study reporting neonatal imitation in macaque monkeys (Ferrari et al., 2006) may also suffer from methodological problems. For example, increases in tongue protrusion and lip smacking in response to observation of these two actions were observed only on the third day post partum, suggesting that any reported imitative effect is very short-lived. Additionally, on the first day of life, lip smacking was increased in response to the observation of mouth opening, rather than to observed lip smacking, indicating that the lip smacking effect is not specific to the observation of the *same* action, and thus cannot be categorised as imitation.

While there does appear to be a reliable neonatal imitation effect in human infants for tongue protrusion, it is not clear that the effect is stimulus specific. Jacobson (1979) showed that tongue protrusions increase when an object such as a pen or small ball is moved towards the infant, suggesting that the increase in infant tongue protrusions during observation of tongue protrusion could be the result of an innate "releasing mechanism" for feeding, or an oral exploratory behaviour (Jones, 1996). Reliable stimulus-specific imitation of a range of actions does not begin to appear until 8 – 12

months of age, and infants do not imitate opaque actions such as placing the hand on the head until 16 months (Jones, 2007). This suggests that the ability to solve the correspondence problem, rather than being present at birth, emerges in the course of development.

1.4.3 Behavioural imitation effects in adults

What are the properties of a mature imitating system – one that can solve the correspondence problem for a substantial range of actions? It is clear from everyday experience that adult humans are able voluntarily to imitate a wide variety of actions, both perceptually transparent and perceptually opaque. In this section, however, I shall focus on what have been termed "unintentional" or "automatic" imitation effects (Heyes, 2001; Heyes, Bird, Johnson, & Haggard, 2005). These are of particular interest because they indicate that, when solving the problem of correspondence between observed and executed actions, the solution is applied *automatically*. By *automatic*, I refer to processes that are not entirely under strategic control. This would be expected of a system that acquires its properties as a result of general associative learning mechanisms, as explained above.

Automatic imitation was first reported by Stürmer et al. (2000), who demonstrated that participants were faster to perform a hand opening action while viewing a compatible (hand opening) action, than when viewing an incompatible (hand closing) action, and that this effect was reversed for the performance of hand closing actions. Similar effects on response times have been shown by Brass et al. (2000; 2001a), Vogt, Taylor and Hopkins (2003), Heyes et al. (2005), Press and colleagues (Press, Bird, Flach, & Heyes, 2005; Press, Gillmeister, & Heyes, 2006; Press, Bird, Walsh, & Heyes, 2008), Bertenthal, Longo and Kosobud (2006), and Liepelt, von Cramon, and Brass (2008).

These effects are considered evidence of automatic imitation because the identity of the compatible or incompatible observed movement is always task-irrelevant. In the study by Stürmer and colleagues, the task-relevant dimension was the colour of the hand, while Brass et al. (2001a) used a simple reaction time task where participants had to make the same movement on every trial within a block; the compatible or incompatible movement stimulus acted as an imperative stimulus or "go signal" for the participant to perform the prepared action, telling participants when to move, but not what to do. Participants were not required to process the identity of the observed movement – and indeed, in the case of incompatible movements, this was clearly counter-productive with respect to task performance – yet movement identity still had an effect on response times. This indicates that the visual movement stimulus is translated into a motoric code automatically – without strategic control – since the motoric code facilitates or interferes with task-relevant movement production.

Further experiments have shown that observing another's actions interferes not only with response times but with performance accuracy. For example, Kilner et al. (2003; see also Kilner et al., 2007) asked participants to move their arm in time with the observed movements of a human or robot arm. The stimulus arm moved compatibly (in the same plane) or incompatibly (at 90º) with the participants' movements. When observing the incompatible human movements, participants' movements showed significantly greater variance in the plane of the observed movements than in any of the other conditions.

One criticism that has been levelled at response time and interference studies of automatic imitation is that these effects are often confounded with left/right or up/down spatial compatibility (Bertenthal et al., 2006; Jansson, Wilson, Williams, & Mon-

Williams, 2007). Chapter 3 addresses this point and introduces an experimental paradigm that allows the simultaneous measurement of spatial compatibility and automatic imitation effects.

Another sense in which imitation can be automatic is that it can occur not only without strategic control, but without conscious awareness. Observation of another's actions in a social situation can result in unconscious imitation of the observed action. Chartrand and Bargh (1999) created an experimental set-up where participants were paired with a confederate, and each took turns to describe a photograph to the experimenter. Despite the minimal level of interaction between the participant and confederate, a reliable "chameleon effect" was seen, where the confederate's repetition of a particular action (either foot shaking or face rubbing) produced an increase in the rate of performance of that particular action by the participant. This effect has been replicated in several studies (Cheng & Chartrand, 2003; van Baaren, Maddux, Chartrand, de Bouter, & van Knippenberg, 2003; van Baaren, Horgan, Chartrand, & Dijkmans, 2004), in none of which the participants report awareness of the actions performed by the confederate, or of their own actions.

In summary, the ability to solve the correspondence problem in imitation is present in several species, including human and non-human primates, dogs, and bird species; in humans, it is not present at birth, but appears to develop through experience during at least the first few years of life; and it produces automatic imitation effects in adult humans. These properties are consistent with a general-process, associative learning account of the role of sensorimotor experience in the development of imitation and the mirror neuron system. What is known of the effects of subsequent sensorimotor experience on imitation and the mirror neuron system?

1.5 Are the properties of the mirror neuron system experience-dependent?

1.5.1 Behavioural effects of sensorimotor experience on automatic imitation

Heyes et al. (2005) demonstrated that exposing participants to pairings between observed and performed actions – creating, in effect, a new perceptual-motor association – can have a significant effect on later behaviour. A group of participants were trained to produce incompatible movements in response to an opening or closing hand stimulus: when they saw the hand opening, they closed their own hand, and vice versa. Following training, they were tested on a simple reaction time automatic imitation task, where for half the trials, participants responded to the opening or closing hand (the imperative stimulus) by opening their own hand, and for the other half they closed their hand. This task normally produces automatic imitation effects similar to those described earlier: participants are faster to respond on trials in which the imperative stimulus matches the movement they are to perform than on trials where it does not. Indeed, for a control group, who produced compatible movements during training, this was still the case; however, the incompatibly trained group showed a significantly smaller automatic imitation effect. Thus, the creation of new, incompatible associations between the observation of one hand movement and the performance of another creates a conflict with the prior associations between observation and performance of the same hand movement, reducing the size of the automatic imitation effect. Because the two groups received equal sensory and motor experience of observing and performing each action during training, this result must be due to the *sensorimotor* contingency between the observation of one action and the performance of another. A similar sensorimotor training strategy was used by Press, Gillmeister and Heyes (2007) to enhance automatic imitation of robotic actions.

Thus, behavioural evidence indicates that sensorimotor experience can modify automatic imitation effects. While this is suggestive of an effect on the mirror neuron system, direct neurophysiological evidence supporting this hypothesis has yet to be obtained. Additionally, behavioural effects of sensorimotor training, rather than resulting from the modification of associations between perceptual and motor representations of actions, could be the result of the retrieval of training instructions during the post-training test of automatic imitation. This cannot be ruled out using behavioural techniques because a response, which could be subject to such carry-over effects, is always required in the post-training test. Chapters 5 and 6 address these two issues by using neurophysiological techniques to assess the effects of sensorimotor experience on the mirror neuron system. The following sections establish what is currently known of the effects of other types of experience on the mirror neuron system.

1.5.2 Effects of experience on mirror neurons in the monkey

A clear effect of visual experience on the macaque mirror neuron system was shown by Ferrari et al. (2005). After several months' experience of watching tool use by the experimenters, although without the animals having had the opportunity to use tools themselves, 20 % of recorded premotor neurons in two monkeys responded to tool actions more than to the observation of hand or mouth actions. Prior to this visual experience, these neurons were unresponsive to the sight of tool use. Most of these neurons coded for the performance of hand and mouth movements. It seems likely that the most common action that these monkeys performed during or shortly after observing the experimenters' tool use was to grasp the object or eat the food thus presented to them. This would result in the sight of tool use becoming associated with the subsequent performance of a hand or mouth action, consistent with a sensorimotor, rather than a purely visual, account of the effects of experience on the development of

mirror neuron properties. Further work in which monkeys' *sensorimotor* experience of particular tools is more carefully controlled would provide clearer evidence as to whether purely sensory experience is sufficient to alter mirror neuron properties.

Additional evidence for the role of experience in the development of mirror neuron properties comes from the data of Kohler et al. (2002), who described auditory mirror neurons that fire when the monkey hears the sound of paper being torn, as well as when it performs tearing actions. As the sound of ripping paper does not occur naturally, these neurons must have acquired their properties through experience: either through sensory experience of hearing the sound of paper being torn, or through sensorimotor experience of tearing paper while hearing the sound that this action produced. I now turn to the effects of experience on the human mirror neuron system.

1.5.3 Effects of experience on muscle-specific perceptual-motor matching

Few TMS studies have investigated the role that experience of action observation and execution plays in modulating MEPs during action observation. Avenanti and colleagues (2005; Avenanti, Paluello, Bufalari, & Aglioti, 2006) have shown selective inhibition of MEPs in each of two hand muscles when participants observe painful, compared with non-painful, stimuli being applied to that particular muscle. While not strictly *action* observation, the muscle-specificity of this effect is in line with that of the TMS results discussed above. What is of interest with respect to experience is that the stimuli applied to the hand were needles and cotton buds, which are arbitrary from a biological perspective. This effect, therefore, must be due to participants' prior experiences with these two classes of object: the association of the sight of the needle with pain modulates the size of the MEP accordingly.

Investigating the role of experience more directly, D'Ausilio, Altenmuller, Olivetti and Lotze (2006) asked amateur piano players to learn the left hand part of a piano piece of music. MEPs from a left hand muscle were measured before and after the learning period, while participants were listening to either the piano piece or a control flute piece. After the learning period, there was a significant increase in MEP size when participants listened to the learned piece but not for the control piece. This implies that the auditory-motor experience of learning the piano piece created associations between hearing this music and left hand muscle activity. However, in this study, auditory experience of the two pieces was not controlled: participants were not asked to listen to the flute piece during the five-day training period, whereas they would have had plenty of auditory experience of the piano piece during this time. Therefore, any differences between the groups in motor activity when listening to the piano piece could be due to perceptual experience alone. Chapter 5 uses a training strategy that controls for visual and motor experience to investigate the specific effect of sensorimotor experience on muscle-specific responses to action observation.

1.5.4 Imaging the effects of experience on the mirror neuron system

Several studies have been conducted to investigate the neural basis of effects on the mirror neuron system of various aspects of learning. However, most of these studies have the drawback that the locations of "mirror" areas were not assessed using a conjunction of action execution with action observation (the importance of which was discussed in section 1.1.3 above). Thus, in this section, "mirror system" refers to areas active during action observation only.

Haslinger et al. (2005) contrasted observation of piano playing and non-piano playing finger movements in professional pianists and control participants, and showed that

training as a pianist enhances the mirror system response to the observation of piano playing stimuli. This could be the result of greater *sensory* experience of the observation of such stimuli in the pianist group, or greater *sensorimotor* experience of the observation of such stimuli while producing movements (i.e. while playing the piano).

Cross, Hamilton and Grafton (2006) taught dancer participants a new modern dance piece, and showed that BOLD response in ventral premotor and inferior parietal areas during observation of sequences from the piece was correlated with the dancers' reported ability to perform the sequences, over five weeks of rehearsal and brain scanning sessions. While this result suggests that participants' *motor* ability (which, presumably, is an indicator of their motor experience) influences the mirror system response to observed actions, they also received *sensorimotor* experience during rehearsal of the dance, which is likely to be highly correlated with their motor experience. Therefore neither this study nor that of Haslinger et al. (2005) provides a conclusive answer regarding which type of experience is necessary to alter mirror system responses to action observation.

Across two related studies, Calvo-Merino, Glaser, Grèzes, Passingham and Haggard (2005; Calvo-Merino, Grèzes, Glaser, Passingham, & Haggard, 2006) investigated the differences between visual and motor experience of a complex action on mirror system responses. Participants in these studies were capoeira dancers and male and female ballet dancers. Initially, the contrast was made between observing an action with which the participant was familiar and one that was unfamiliar to them: so capoeira dancers observed capoeira actions (familiar), contrasted with a visually similar ballet action (unfamiliar) while the contrast for the ballet dancers was the reverse. BOLD response in mirror system areas was higher when observing the familiar movement than when

observing the unfamiliar movement. However, this design confounds motor and visual familiarity: ballet dancers will have more visual experience, as well as more motor experience, of ballet moves. Therefore the second study contrasted male and female ballet moves: both genders would be equally visually familiar with both types of move, but each would have motor experience only of their own gender-specific moves. Left premotor cortex, as well as parietal and cerebellar areas, was more active when participants viewed their own gender's movements than when viewing those of the other gender. This confirmed that visual experience of an action does not affect mirror system responses to the observation of that action to the same extent as motor experience of that action. Nevertheless, this second experiment cannot distinguish between *motor* experience and *sensorimotor* experience as drivers of mirror neuron system development because dancers – using mirrors and observing other troupe members during training – will have received considerable sensorimotor experience of the moves performed by their own gender during the course of their training.

It can be seen from the studies in this section that the BOLD response in the mirror system during the observation of an action depends on the observer's motor – and possibly sensory – experience of the action. However, these studies do not clarify whether either of these types of experience in isolation can have an effect on the mirror system response to action observation, or whether each of these types of experience must be received in conjunction with the other type of experience, i.e. as sensorimotor experience. Chapter 6 addresses this point, which until now has only been investigated using behavioural studies of imitation.

1.6 Summary

Mirror neurons in the monkey, and their probable homologues in the human brain, neurally instantiate a process that solves the correspondence problem, enabling the perceptual-motor translations that are at the heart of cognitive processes such as imitation. Two types of theory have been advanced, suggesting how the mirror neuron system comes to possess its perceptual-motor matching properties: modality-independent representations may be present from birth; or perceptual-motor matches may arise as a result of sensorimotor experience during development. Behavioural automatic imitation effects, a measure of the solution of the correspondence problem, are sensitive to sensorimotor experience; however, it has not yet been verified, using neuroscientific techniques, that this is a result of the effects of sensorimotor experience on the mirror neuron system.

This thesis first addresses the claim that automatic imitation effects are the result of simple spatial compatibility effects (Bertenthal et al., 2006; Jansson et al., 2007; Aicken, Wilson, Williams, & Mon-Williams, 2007): Chapter 3 establishes that automatic imitation effects are separable from spatial stimulus-response compatibility effects. Chapter 4 then responds to the limited amount of data addressing the role of the mirror neuron system in imitation. This chapter measures automatic imitation effects after temporary disruption, using rTMS, of the left inferior frontal gyrus, an area considered to be part of the human mirror neuron system. Chapter 5 confronts the criticism that behavioural effects of sensorimotor learning (in which automatic imitation effects are reduced following incompatible sensorimotor experience) could be the result of the retrieval of training instructions. Chapter 5 addresses this issue by using TMS to measure MEPs during passive action observation following sensorimotor learning. This chapter also assesses the effects of sensorimotor experience as opposed to purely

sensory experience, purely motor experience, and the additive effects of both of these types of experience. Chapter 6 uses a similar method – sensorimotor training – but investigates the response to subsequent passive action observation using fMRI, in order to establish whether sensorimotor learning does indeed affect the BOLD response in mirror neuron system areas.

2 Methods

This chapter provides an overview of the cognitive neuroscientific techniques used in this thesis: transcranial magnetic stimulation and functional magnetic resonance imaging.

2.1 Transcranial Magnetic Stimulation

The experiments reported in Chapters 4 and 5 of this thesis use the technique of transcranial magnetic stimulation (TMS), either to disrupt the function of specific brain areas, or to produce motor evoked potentials (MEPs), which can be used as an index of activity in motor cortex. The following sections describe the principles underlying TMS, the TMS techniques used in this thesis, and safety considerations that are relevant to the use of TMS.

2.1.1 Principles of Transcranial Magnetic Stimulation

Any electric current travelling along a conductor creates a magnetic field. This field can pass through an intervening medium such as air and create a second electric current in any nearby conductor. In the case of TMS, the first conductor is the TMS coil and the second is brain tissue. Neural tissue is electrically conductive because of the long neuronal axons which, by their nature, conduct electrical impulses.

The TMS stimulator consists of a current generator, connected to a coil capable of producing magnetic pulses of up to 2.5 Tesla (T). The magnetic pulses can range in length from 100 μs to 1 ms, although most of the discharge of current happens in the

initial 100 µs. The electric current is generated by the changing magnetic field; thus it is the rise and fall of the magnetic pulse that creates an electric current in the brain (see Figure 2.1). The generated current, if it is of sufficient amplitude, will trigger neuronal discharge via the depolarisation of the cell. Thus, despite its name, TMS stimulates the brain electrically.

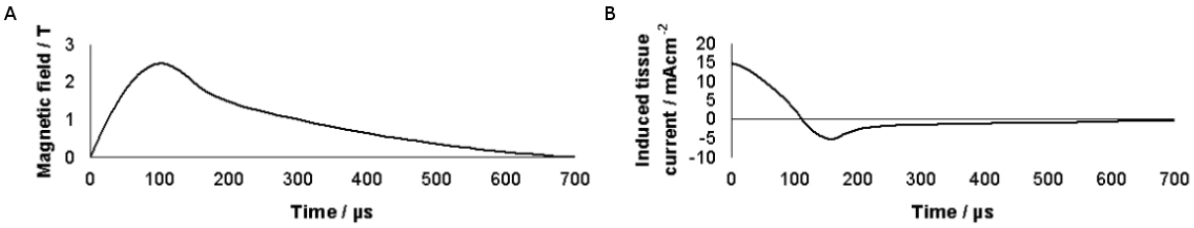


Figure 2.1. (A) The magnetic field generated by a monophasic pulse. (B) The electric current induced in neural tissue by the magnetic field depicted in (A).

The characteristics of the electric current induced in the brain depend on the shape and size of the TMS coil as well as on the strength, rate of change, and shape of the magnetic pulse generated in the coil. The coil type used in all the TMS experiments in this thesis is a double or figure-of-eight coil, consisting of two circular loops of tightly wound copper inside an insulating cover (Figure 2.2). This coil provides a focused stimulation point, as the magnetic field is at a maximum where the two loops meet.

The stimulator type determines the shape of the magnetic field output waveform. All of the experiments reported in this thesis used the Magstim Super Rapid stimulator (The Magstim Company Ltd., Whitland, UK). This stimulator produces a biphasic pulse (Figure 2.3), which is short and efficient because energy can be recovered from the second phase of the pulse to be used in the following pulse.

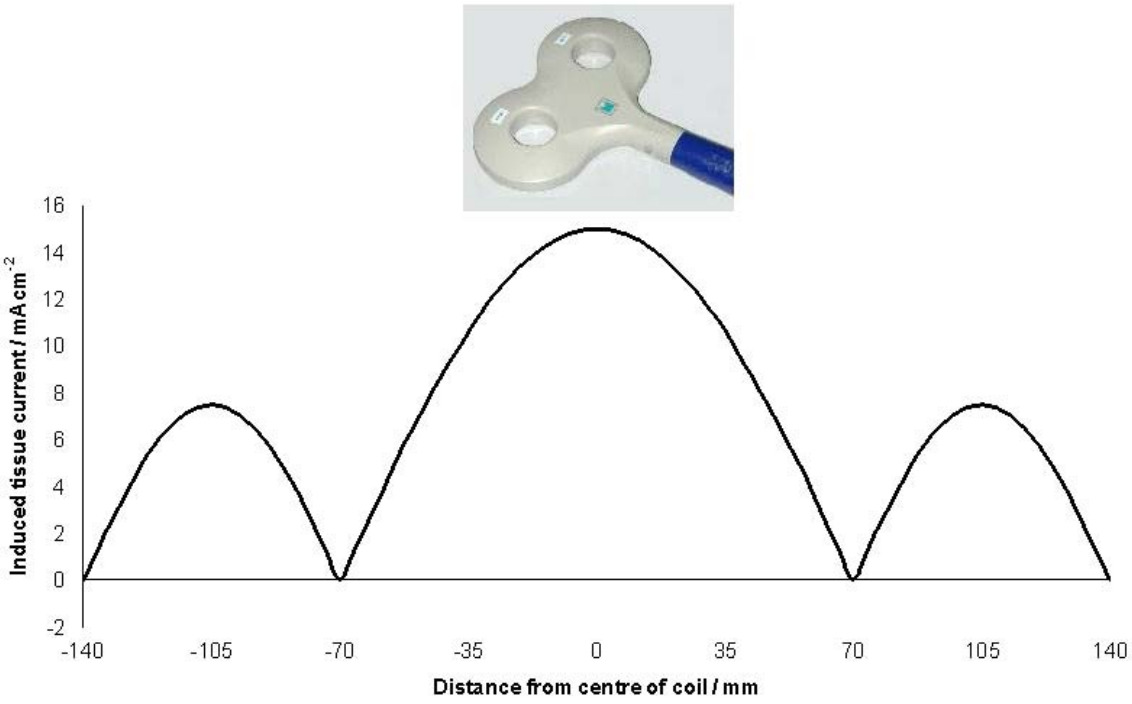


Figure 2.2. The magnitude of the induced tissue current under a 70 mm figure-of-eight coil (top). It is greatest at the point where the two loops of copper windings meet. Note that, due to the curvature of the head, the two outer peaks of the induced current (under the outer windings of the coil) will not be in contact with the scalp and thus spatially focused stimulation can be achieved.

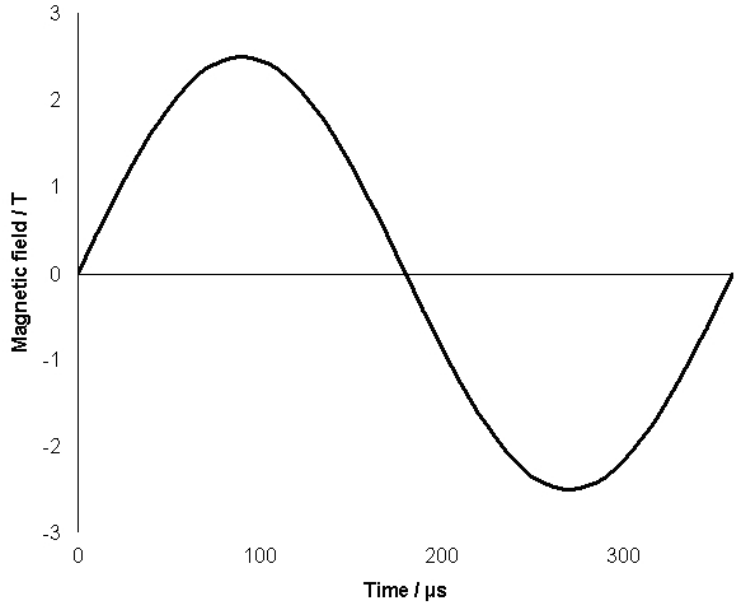


Figure 2.3. The magnetic pulse waveform produced by a biphasic pulse.

2.1.2 Single-pulse TMS and MEPs

Single-pulse TMS is used in this thesis to stimulate primary motor cortex, producing MEPs. MEPs are recorded from peripheral musculature (finger muscles in this thesis) following stimulation of the primary motor cortex at the location corresponding to the representation of that particular muscle. The size (amplitude and area-under-curve) of the MEP depends on several factors: the distance from the scalp to the underlying motor cortex, the power of the TMS pulse (expressed in this thesis as a percentage of the maximum output of the stimulator), and the level of excitation or inhibition of the motor cortex at the time the pulse is applied. Thus, for a given participant, stimulated over a given brain location and at a fixed level of power, any changes in the size of the MEP will reflect changes in the excitability of the underlying area of motor cortex (Rossini & Rossi, 1998). This principle is used in Chapter 5 to investigate the excitation of the motor cortical representation of different hand muscles during the observation of finger movements.

MEP size is measured using electromyography (EMG). Pairs of electrodes are placed on the target muscle in a belly-tendon montage. The signal from the electrodes is amplified and displayed on a screen for on-line use, and recorded for off-line analysis.

In order to find the scalp location closest to the motor cortical representation of the targeted hand muscles, an on-line functional localisation method is normally used. The approximate location of the hand area of motor cortex is estimated with reference to the vertex of the participant's head: usually this is in an area ~5 cm anterior to and 2-3 cm lateral from the vertex. The coil is placed tangential to the scalp and angled with the handle pointing backwards at approximately 50° from the parasagittal plane. This produces the maximum induced current flowing in a posterior-anterior direction at an

approximate right-angle to the central sulcus. This orientation has been shown to produce the largest MEPs (Mills, Boniface, & Schubert, 1992). The optimum scalp location is found by applying single pulses at each location in a grid with approximately 1 cm between each point. The location at which the greatest response is measured in the target muscle is taken as the optimum scalp location. When MEPs are measured from two target muscles, as in Chapter 5 of this thesis, the location that requires the lowest level of stimulator output to produce MEPs above a certain size threshold (often 50 μV) in both muscles is used.

In order to equate the relative strength of stimulation across participants, a threshold is measured, relative to which the level of stimulator output is defined. In this thesis, the threshold used was the resting motor threshold (rMT). The rMT is defined as the lowest level of stimulation which, when applied to the optimum scalp location for the first dorsal interosseus (FDI) muscle of the right hand, produces MEPs in the FDI of at least 50 μV in five out of 10 trials (Rossini et al., 1994). The use of a threshold such as rMT helps to compensate for between-subject differences in the orientation of the sulci and gyri of the cortical surface, and the distance from scalp to cortex, which are both factors that influence the strength of the induced current. Nevertheless, large inter-subject variability in the size of the MEP can still be seen (Rossini & Rossi, 1998). This is usually controlled by expressing MEP size as a ratio with respect to a baseline condition.

2.1.3 Theta burst TMS

As well as enhancing the output of a cortical area, as is the case with MEPs, TMS can be used to disrupt cortical processing because it stimulates large numbers of neurons, thus introducing what has been termed neural noise into processing in the stimulated

area. Theta burst TMS is a relatively new repetitive transcranial magnetic stimulation (rTMS) technique (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005). In this thesis, theta burst TMS is used to induce a transient "virtual lesion" to certain cortical areas.

The theta burst TMS protocol is based on techniques used to introduce long term potentiation and long term depression in hippocampal slices in the rat (Larson & Lynch, 1986). Three pulses of TMS are applied at 50 Hz (20 ms separation), and this pattern is repeated every 200 ms. Huang et al. (2005) demonstrated that when this pattern of stimulation was applied continuously for 20 seconds over primary motor cortex, MEP size was suppressed for 20 minutes after the end of the stimulation, with the strongest effect being observed between seven and 14 minutes after stimulation. When continuous theta burst stimulation was applied for 40 seconds, MEP size was suppressed for an hour after stimulation. Thus, theta burst TMS provides a method whereby cortical functioning can be disrupted off-line (i.e. TMS is delivered before the participant performs the task, thus avoiding disadvantages of on-line TMS such as noise, tactile sensations, and muscle twitches during stimulation), and a short period of application can result in disruption that appears to be sufficiently long-lasting to allow subsequent behavioural testing. Theta burst TMS has, however, to date been used in only three perceptual and cognitive studies, which have stimulated dorsolateral prefrontal cortex (Vallesi, Shallice, & Walsh, 2007), posterior parietal cortex (Nyffeler et al., 2008), and visual cortex (Silvanto, Muggleton, Cowey, & Walsh, 2007).

One consideration when stimulating outside the motor or visual cortices, i.e. in behaviourally "silent" areas that do not give a clear measure of excitation such as an MEP or a phosphene, is how to standardise the strength of stimulation across participants. Although it is unclear whether motor thresholds are necessarily indicative

of excitation thresholds in other cortical areas (Stewart, Walsh, & Rothwell, 2001), the studies reported above used motor thresholds to determine the strength of TMS stimulation applied. This is because of the risks associated with using a new procedure such as theta burst TMS. Therefore, the same procedure was used in this thesis.

2.1.4 Localising brain sites using frameless stereotaxy

A further consideration when stimulating behaviourally silent areas of cortex is how to ensure that the correct area of cortex is being stimulated. One method is to use the electrode locations from electroencephalography (EEG), which are known to overlie certain cortical areas. This method has the advantage that no anatomical information regarding the participant's brain structure is required, since the EEG cap can simply be aligned with the participant's head. However, brain structure is not homogeneous across participants and therefore this method may not target the same structure in every participant. Three alternative methods can be used to overcome this problem, all of which involve the technique of frameless stereotaxy. These methods are structural localisation (identification of the target cortical structure on the participant's structural brain scan), co-ordinate based localisation (using the co-ordinates of a particular brain area, acquired from either anatomical or functional data), and functional localisation (using the co-ordinates from the participant's own functional imaging data).

All three of these methods require the participant to have undergone a structural magnetic resonance imaging (MRI) scan, which can then be used for all subsequent TMS experiments; the third method, however, also requires a functional imaging experiment to be performed for every TMS experiment (or at least for each experiment that investigates a different brain location and cognitive function), and thus is a very costly method of localisation. The structural localisation method is useful if the purpose

of the experiment is to test the contribution of a particular anatomical area of the brain to a given function, especially if the area to be investigated is quite small. However, if the anatomical area is larger it may be difficult to locate the exact part of a particular brain structure that is to be targeted. Co-ordinate based localisation uses the mean co-ordinates from previous functional imaging or TMS studies, thus identifying a precise location for stimulation. This thesis uses co-ordinate based localisation because it is more precise than structural localisation and has sufficient power to localise brain functions (Sack et al., 2008).

The frameless stereotaxy technique used to identify the scalp location for stimulation consists of several stages. If co-ordinate based localisation is being used, the co-ordinates of the brain area to be stimulated will be in a standard space (e.g. Talairach co-ordinate space). The first stage therefore is to normalise each participant's structural scan onto a standard brain in standard space using brain imaging analysis software such as SPM (Functional Imaging Laboratory, University College London, UK) or FSL (FMRIB, Oxford, UK). This normalisation process is carried out by identifying a unique set of transformations which, when applied to the participant's structural scan, transform it into standard space. The next stage is to transform the standardised co-ordinates of the location to be stimulated into co-ordinates that can be applied to the participant's brain. In order to do this, the transformations that were identified for normalisation are reversed, and this inverse transform is then applied to the standardised co-ordinates. The resulting co-ordinates are now in the correct location for the individual participant's brain (Figure 2.4), and are marked on the participant's structural scan. The subsequent stages are the same for all three methods of localisation.

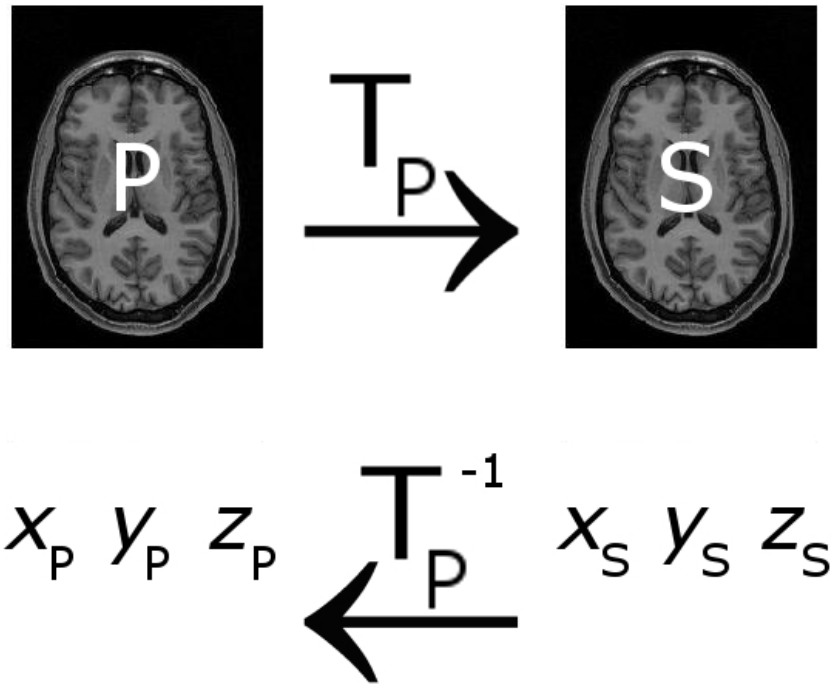


Figure 2.4. Schematic representation of the co-ordinate transformation process. The participant's brain P is normalised onto a standard brain S via a unique set of transformations T_P. The inverse of these transformations can be applied to the standard co-ordinates to yield co-ordinates for the same location on the participant's brain.

The location to be stimulated (anatomical, co-ordinate, or functional) is marked on the participant's structural scan. A frameless stereotaxy system such as Brainsight™ (Rogue Research Inc., Montreal, Canada) is used to locate the correct scalp position for stimulation of the chosen brain location. Certain external features, such as the bridge and tip of the nose, and the left and right ears, are also marked on the participant's structural scan. A 3-D position sensor is attached to the participant's head, and a second "pointer" sensor records the location (in real space) of these external features with respect to the position sensor. These external locations are matched to those on the participant's structural scan, co-registering the structural scan with the real-world position of the participant's head. The pointer sensor can then be used to find the location on the scalp that corresponds to the closest point to the location to be stimulated.

2.1.5 Safety of TMS

The main safety issue concerning the use of TMS is the risk of inducing a seizure due to increased neural firing. Safety studies based on both human and animal data have established guidelines for levels of TMS (both intensity and number of pulses) within which seizures have not been shown to occur in normal participants (Wassermann, 1998). Thus, by selecting appropriate parameters, and by screening participants for personal or family history of epilepsy, the risk of seizure can be minimised.

Single-pulse TMS is unlikely to induce seizure in normal participants (there have been no reports to date of such an incident; Anand & Hotson, 2002; Loo, McFarquhar, & Walter, 2006) because the rate of pulses is much lower than the 10 Hz rate used when formulating the above guidelines. Theta burst stimulation, in which three pulses are administered at 50 Hz, repeated at 5 Hz, may carry a greater potential risk. However, the intensity of theta burst TMS is low compared to that used in 10 Hz rTMS experiments (80 % of motor threshold compared to 100 or 110 %), and the total number of pulses is much lower. Additionally, rTMS at 50 Hz has been shown to be safe in short bursts (Huang & Rothwell, 2004), suggesting that the 50 Hz pattern used in theta burst TMS should also be relatively safe at low intensities. Clearly, however, it is essential to assess participants for any contraindications to TMS before proceeding with any type of TMS.

Other possible safety considerations relate to the level of acoustic noise, strength of magnetic fields and electric current, and possible heating in the brain during TMS. All of these factors have been shown to be well within accepted safety levels for both single-pulse and repetitive TMS (Barker & Stevens, 1991; Gates, Dhuna, & Pascual-Leone, 1992; Wassermann, 1998). TMS does not appear to have any long-term effects

upon cognitive function (Bridgers, 1991; George, Lisanby, & Sackeim, 1999; Hirshberg, Chiu, & Frazier, 2005). While this statement may seem at odds with the fact that rTMS is under consideration as a therapy for depression, such stimulation involves many hundreds of pulses per session over an extended number of sessions, far greater than the number of pulses administered during a single-pulse or rTMS experiment such as those reported in this thesis.

2.2 Functional Magnetic Resonance Imaging

The functional magnetic resonance imaging (fMRI) experiment reported in Chapter 6 of this thesis measured the blood oxygen level dependent (BOLD) response across the brain while participants were performing two different tasks in the scanner. The BOLD response measures the inhomogeneities introduced into the magnetic field of the scanner as a result of changes in the ratio of oxygenated to deoxygenated blood, which gives an indication of oxygen usage across the brain. These inhomogeneities are measured via their effects on the rates of de-phasing of hydrogen nuclei. The following sections will give a brief overview of this process, followed by an outline of how fMRI data are analysed.

2.2.1 Principles of magnetic resonance

2.2.1.1 Hydrogen nuclei in a magnetic field precess

Hydrogen nuclei (^{1}H) are positively charged particles which, due to their presence in water molecules, are prevalent throughout the brain. These particles spin around their axes. When an electric charge moves, it produces a magnetic field: thus, the movement of each particle around its axis produces a small magnetic field. When the brain is placed into the strong magnetic field of the scanner, the small magnetic field of each

hydrogen nucleus causes it to line up either in the same direction, or against the direction, of the scanner magnetic field (Figure 2.5). Slightly more nuclei line up with the scanner field than line up against it, producing a net magnetic vector in the direction of the scanner magnetic field, conventionally indicated by the *z* axis. A second effect of the scanner field is to cause the nuclei to spin at a certain frequency, or "precess". This frequency is determined by the strength of the external magnetic field and the type of nucleus, e.g. 128 MHz for hydrogen nuclei in a 3 T field.

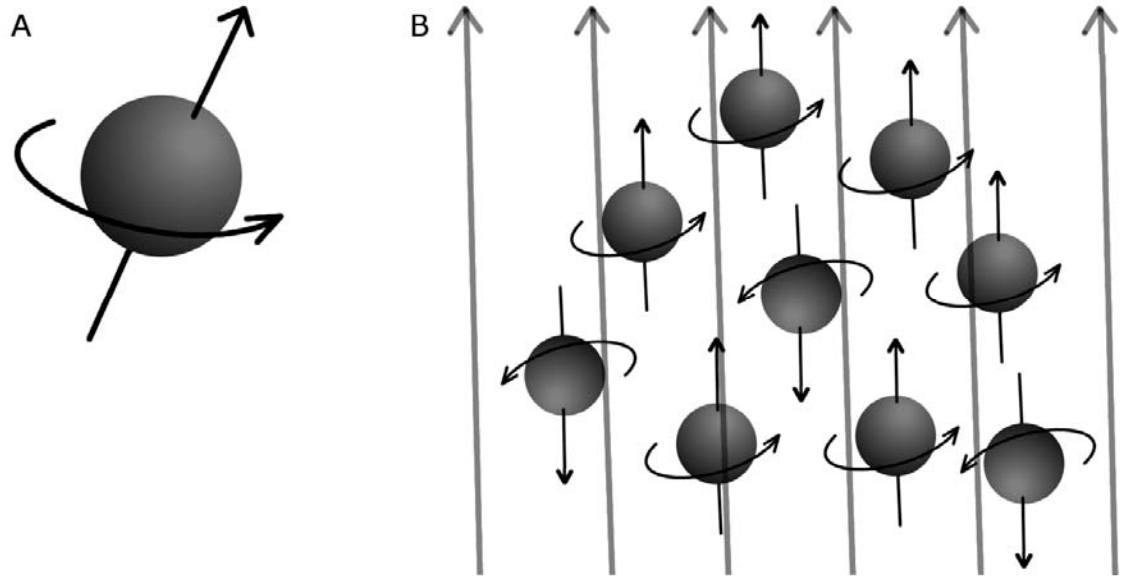


Figure 2.5. Hydrogen nuclei. (A) ^{1}H nucleus spinning round its axis; (B) Nuclei aligning with or against the scanner magnetic field (indicated by grey lines).

2.2.1.2 Radiofrequency pulses excite the nuclei

Once the brain has been placed in the strong magnetic field of the scanner, the next stage is to apply a radiofrequency (RF) pulse via the transmitter coil that surrounds the participant's head. In order to cause the hydrogen nuclei to resonate, the pulse must be at the resonant frequency of the nuclei, i.e. their frequency of precession. The effect of this resonance is to impart energy to or "excite" the nuclei, which "tips" each nucleus's small magnetic field away from the *z* axis. The 90° RF pulse used in fMRI tips the net

magnetic vector into the *x*-*y* plane. When the RF pulse is terminated, the nuclei "relax" and return to their original orientation in the *z* dimension, releasing the energy imparted to them by the RF pulse, and thereby producing the signal that is detected by the receiving coil (Figure 2.6). This relaxation can be measured in two ways: as the gradual recovery of the magnetic field in the *z* dimension (T_1 recovery), or as the decay of the magnetic field in the *x*-*y* plane (T_2 decay).

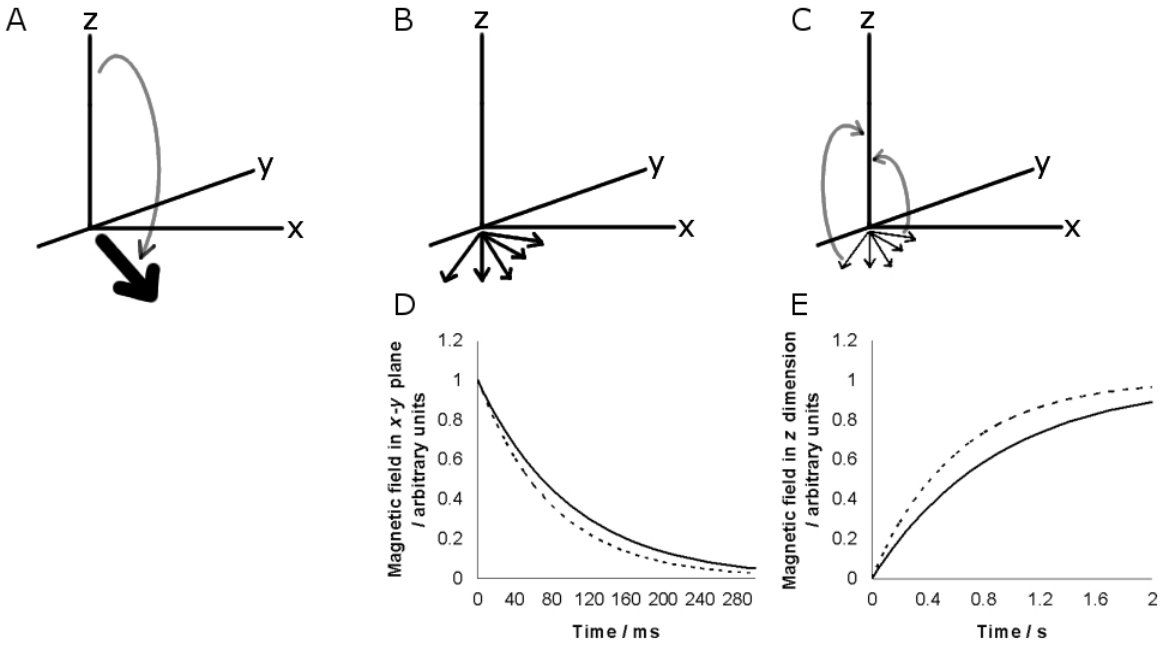


Figure 2.6. (A) The RF pulse "tips" the nuclei into the *x*-*y* plane. (B) The spins de-phase so they no longer precess at the same rates, reducing the magnetic field in the *x*-*y* plane (D). (C) The spins return to their orientation in the *z* dimension, causing recovery of the magnetic field (E). Decay and recovery rates are shown for grey matter (solid lines) and white matter (dashed lines).

2.2.1.3 Different tissues recover at different rates

T_1 recovery takes place on a timescale of seconds, while T_2 decay takes place much more quickly – over tens of milliseconds. Different tissues in the brain have different T_1 and T_2 relaxation rates. By manipulating the time between RF pulses (the TR), contrast can be generated between tissues with different T_1 relaxation rates. If the TR is less than the time it takes the tissue with the longest T_1 rate to recover fully, then after an initial

RF pulse, those tissues with longer relaxation times will have fewer nuclei that can be excited by a subsequent pulse, leading to a decrease in signal compared to tissues with shorter relaxation times. Thus, on a T_1-weighted image – used for structural scans – cerebrospinal fluid, which has a longer T_1 relaxation time than brain tissue, appears darker.

2.2.1.4 T_2 and T_2* decay

T_2 decay takes place on a shorter timescale than that of T_1 recovery because it is driven by interactions between neighbouring ^{1}H nuclei. These "spin-spin" interactions cause an exchange of energy between nuclei. This leads them no longer to precess in phase and thus reduces the magnetic field in the *x*-*y* plane. Since the T_2 relaxation rate also depends on tissue type, contrast can also be generated between tissues with different T_2 rates. In this case, it is the time between the RF pulse and measurement of the signal (the TE, or time to echo) that is manipulated. A longer TE will produce a greater signal from tissues with a longer T_2, such as grey matter, relative to tissues with a shorter T_2, such as white matter.

The type of scan acquired for functional – as opposed to structural – MRI is a version of a T_2-weighted scan. This is because there is an additional cause of reduction in the magnetic field in the *x*-*y* plane: as well as T_2 decay caused by spin-spin interactions between nuclei, local inhomogeneities in the magnetic field also cause the nuclei no longer to precess in phase. The combination of these two effects is denoted T_2* decay. Again, manipulating the TE will change the T_2* weighting of an image. Section 2.2.2 explains the importance of T_2*-weighted images for functional MRI.

2.2.1.5 Magnetic field gradients encode spatial location

In order to encode the spatial location of the signal, magnetic field gradients are used. These consist of a spatially varying magnetic field that is superimposed over the main static magnetic field of the scanner. Because the frequency of precession of the nuclei's spins is determined by the strength of the magnetic field in which they are located, a gradient will alter the spins' precession frequencies in a spatially-dependent manner. Since the nuclei only "tip" into the *x*-*y* plane when the frequency of the RF pulse matches their precession frequency, it follows that by using an RF pulse with a narrow bandwidth, only those nuclei at a certain spatial location will be "excited" and thus the MR signal will be measured from that spatial location only. This is the technique that is used to select "slices" along the *z*-axis: an RF pulse is applied which, due to the gradient along the *z*-axis, G_z, excites only those nuclei in that particular slice. Two additional gradients are then used to encode the spatial location of each pixel within the slice. The G_y or phase-encoding gradient changes the precession phases of the nuclei across the *y*-dimension. The G_x or frequency-encoding gradient alters the precession frequency of the nuclei across the *x*-dimension. This allows unique encoding of the spatial location of each pixel.

2.2.2 The blood oxygen level dependent response

2.2.2.1 Magnetic properties of blood

Oxygen is delivered around the body, including to the brain, by molecules of hæmoglobin. When hæmoglobin is carrying oxygen, it is termed oxyhæmoglobin, and is diamagnetic – it has no magnetic properties. When hæmoglobin is no longer carrying oxygen molecules, it is termed deoxyhæmoglobin and is paramagnetic (Pauling & Coryell, 1936). As mentioned above, the T_2* decay process is sensitive to local inhomogeneities in the magnetic field. The presence of paramagnetic deoxyhæmoglobin

introduces such inhomogeneities, which reduce the MR signal as a result of T_2* decay. Conversely, when the amount of deoxyhæmoglobin is reduced with respect to oxyhæmoglobin, the MR signal increases (Ogawa, Lee, Kay, & Tank, 1990). Thus, the strength of the MR signal on T_2*-weighted images using blood oxygen level dependent (BOLD) contrast is a function of the ratio of oxyhæmoglobin to deoxyhæmoglobin.

2.2.2.2 Neural activity and energy usage

From the preceding description it can be seen that the BOLD response is a rather indirect measure of neural activity: indeed, it is only useful if the ratio of oxyhæmoglobin to deoxyhæmoglobin in a given voxel is correlated with neural activity in that voxel. The kind of neural activity that is of interest to cognitive neuroscience consists of the integration of inputs to a neuron via excitatory and inhibitory post-synaptic potentials (EPSPs and IPSPs), and outputs from a neuron in the form of action potentials. The production of all these types of potential causes changes in ion concentrations in the neuron that require energy to restore. Extrapolating from the rodent and taking into account the greater number of synapses per neuron in the human, Attwell and Laughlin (2001) calculated that up to 74 % of the energy requirements in human grey matter would be spent on restoring concentration gradients following EPSPs. This implies that any measure of energy usage in the brain is likely to be weighted towards post-, rather than pre-synaptic activity, i.e. inputs to an area rather than outputs from it. Logothetis, Pauls, Augath, Trinath, and Oeltermann (2001) performed electrophysiological recording and BOLD fMRI simultaneously in monkey visual cortex. They found that the BOLD response correlated with local field potentials, i.e. with subthreshold integration of inputs, better than with the action potential firing rate, supporting this suggestion. The calculation of Attwell and Laughlin (2001) also suggests that such a measure of energy usage, if it is closely linked to post-synaptic

processes rather than the production of action potentials, will emphasise the effects of excitatory rather than inhibitory synapses, since there are fewer inhibitory than excitatory synapses in the human brain (Waldvogel et al., 2000).

The coupling between the brain's energy usage and its oxygen take-up is still controversial. The energy requirements of the brain may be met by oxidative or nonoxidative metabolism of glucose. Nonoxidative metabolism of glucose is a fast process that does not require oxygen, but it is inefficient. The trade-off between oxidative and nonoxidative metabolism of glucose may explain why rates of glucose and oxygen metabolism are not always closely coupled in the brain (Fox, Raichle, Mintun, & Dence, 1988). This potential lack of coupling between glucose metabolism (i.e. energy usage) and oxygen consumption has significant implications for our interpretation of the BOLD MR signal, since it is assumed that oxygen consumption reflects energy usage and hence neural activity. While the physiological causes of this disparity are still unclear, what has been shown is that oxyhæmoglobin is supplied to active areas of the brain in greater quantities than it is consumed, causing a net increase in the ratio of oxyhæmoglobin to deoxyhæmoglobin during neural activity; and that oxyhæmoglobin is supplied over a greater area of the brain than that of the neural activity (Malonek & Grinvald, 1996). There may be an initial, spatially specific take-up of oxyhæmoglobin before this increased supply arrives (Menon et al., 1995), but a change in the BOLD MR signal in response to such an initial take-up of oxyhæmoglobin is not always observed in fMRI studies.

2.2.2.3 Oxyhæmoglobin supply and the hæmodynamic response function

As described above, an increase in the ratio of oxyhæmoglobin to deoxyhæmoglobin will increase the MR signal by reducing magnetic field inhomogeneities. Thus, based on

what is known of the oxyhæmoglobin supply during neural activity, an explanation of the shape of the BOLD response, known as the hæmodynamic response function (HRF), can be outlined (Figure 2.7). An initial decrease due to take-up of oxyhæmoglobin is sometimes observed, followed by a rise that starts between 1-2 seconds after stimulus onset, as a result of the increased supply of oxyhæmoglobin. A peak is reached at about 4-6 seconds, followed by a decrease to below baseline levels, due to above-baseline blood volume (Mandeville et al., 1999) which results in above-baseline levels of deoxyhæmoglobin and hence lower MR signal. This "undershoot" lasts for around 20-24 seconds. The peak of the BOLD response can be extended, for example in the case of a blocked design where the same stimuli are presented repeatedly, in which case it is modelled by what is known as a "box-car" function, as shown in Figure 2.7.

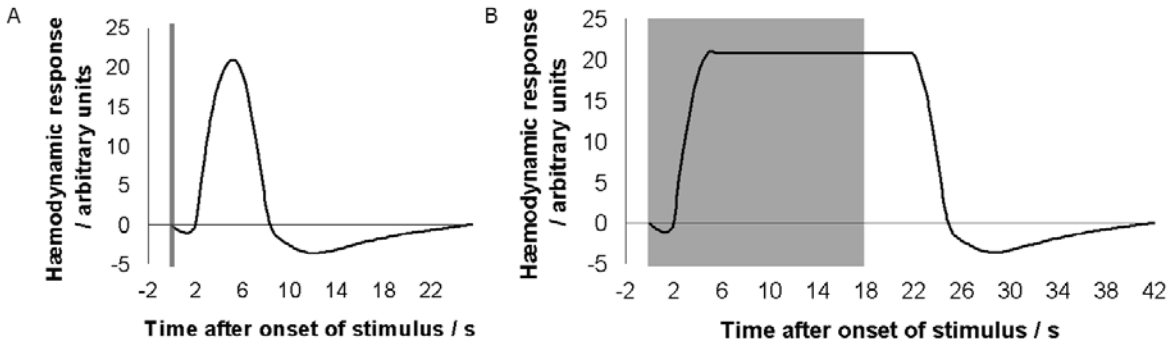


Figure 2.7. The hæmodynamic response function (HRF). (A) Schematic representation of the HRF showing the initial dip, rise, peak, fall and undershoot. (B) HRF convolved with a box-car function, used to model the hæmodynamic response in blocked designs. Stimulus presentation is indicated by grey line (A) or block (B).

2.2.2.4 Spatial and temporal resolution of BOLD fMRI

The preceding discussion of the link between neural activity and the BOLD response has clear implications for the temporal and spatial resolution of BOLD fMRI. While the 4-6 second delay between stimulus onset and the peak in the HRF can be modelled, if this temporal delay is variable, either between participants (Aguirre, Zarahn, &

D'Esposito, 1998) or between brain areas (Rajapakse, Kruggel, Maisog, & von Cramon, 1998), this variability will set a limit on the temporal resolution of the BOLD response. The spatial resolution of BOLD fMRI has a limit that results from several factors: for example, oxyhæmoglobin is supplied over a greater area than that of immediate neural activity (Malonek & Grinvald, 1996), and it is this oxyhæmoglobin supply that results in the peak in the HRF. Second, changes in blood flow can be measured upstream of neural activity (Iadecola, Yang, Ebner, & Chen, 1997), sometimes as far as 2-3 mm away. Additionally, unused oxyhæmoglobin may drain into nearby veins such that increased signal appears downstream of neural activity (Frahm, Merboldt, Hanicke, Kleinschmidt, & Boecker, 1994). Thus, fMRI has an effective spatial resolution of a few millimetres.

2.2.3 Data analysis

fMRI data analysis consists of pre-processing and statistical analysis. Pre-processing is performed in order to increase the signal to noise ratio of the data prior to analysis. Spatial pre-processing is performed to remove noise due to movement or to structural differences, while temporal smoothing can remove noise due to scanner drift and other low-frequency effects.

2.2.3.1 Pre-processing

Spatial pre-processing is required because statistical analysis is performed at the voxel-level. Therefore, it is necessary that each voxel represents the same location in the brain across scans and across participants.

2.2.3.1.1 Re-alignment and unwarping

The data are first re-aligned to remove the effects of head movements. A reference scan is chosen, e.g. the first scan in the series, and subsequent scans are aligned with this scan. This procedure is performed by estimating the values of six parameters such as to minimise the mean-square difference between each scan and the reference scan. These parameters consist of translation and rotation for each of the three axes. These are so-called "rigid body" transformations, which have the limitation that non-linear movements (e.g. changes in brain shape due to heartbeat) cannot be removed. After these parameters are applied, the value of each voxel is estimated by interpolation from adjacent voxels. The re-aligning process cannot remove all movement-related changes. Residual errors may still be present, for example as a result of interactions between head movements and inhomogeneities in the magnetic field. Adjustment can be made for such interactions by "unwarping" (Andersson, Hutton, Ashburner, Turner, & Friston, 2001), which takes into account changes in the magnetic field as a function of head movement.

2.2.3.1.2 Normalisation

The next stage in spatial pre-processing is to normalise the scans of each participant to a standard template. This is done so that each voxel represents the same brain area in every participant, and so that results can be reported in standard anatomical space, enabling comparisons across studies. Each individual brain is mapped to the standard template using 12 parameters: three translations, three rotations, three zooms and three shears. Differences between the brain and the template that cannot be removed using linear transforms are then addressed through the use of nonlinear basis functions (e.g. cosine functions). As before, these parameters are fitted such that the mean-square difference between the participant's brain and the template is minimised. The

parameters may also be regularised to minimise the mean-square difference between the parameters' values and their expected values.

2.2.3.1.3 Smoothing

The final spatial pre-processing stage is to smooth the data. There are several reasons why this is necessary: as discussed in section 2.2.2.4, the spatial resolution of the hæmodynamic response is of the order of a few millimetres and thus effects cannot be expected at a greater resolution; smoothing the data normalises the distribution of errors, increasing the validity of parametric tests; smoothing will increase the homologies between participants, making it more likely that the same voxel will be active in all participants and thus improving the signal at a group level; and smoothing satisfies the requirements for the application of Gaussian field theory in order to correct for multiple comparisons at the statistical analysis stage. Smoothing is performed with a 3D Gaussian kernel, which is a curve in the shape of a 3D normal distribution. This curve is applied to every voxel such that the intensity of the voxel signal is averaged over adjacent voxels, weighted by the value of the Gaussian kernel at each adjoining voxel. The size of the kernel is denoted by its width at half its maximum height, or "full width half maximum" (FWHM). Data can also be temporally smoothed using a high-pass filter, which removes low frequency noise such as scanner drift.

2.2.3.2 Statistical analysis

2.2.3.2.1 The general linear model

Statistical analysis using the SPM software package (Wellcome Department of Imaging Neuroscience, London, UK) (Friston et al., 1995), as well as several other fMRI analysis packages, is based on the general linear model (GLM). This model states that

the data in a given voxel, y, depends on the model, x, the parameters, β, and any residual noise, ε:

$$y = \beta x + \varepsilon$$

The whole-brain data, Y, can be represented as a matrix with a column for each voxel and a row for each time point (i.e. for each scan or acquired brain volume), thus showing the signal intensity for each voxel over time (Figure 2.8).

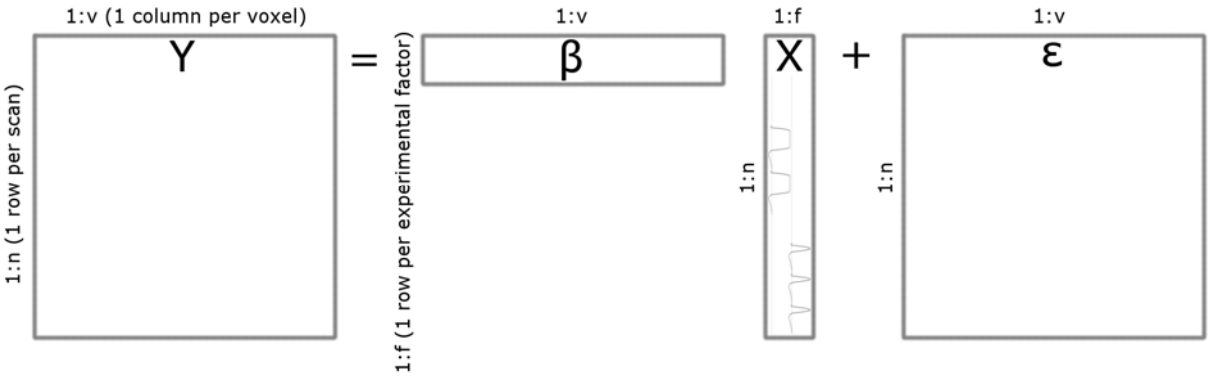


Figure 2.8. Schematic representation of the general linear model (GLM) as used in fMRI analysis. The design matrix (X) illustrates the convolution of stimulus onset times and the HRF. Two blocks of one experimental factor are shown in the first column and three single stimuli of a different experimental factor in the second.

A design matrix, X, can be generated by modelling the experimental factors over time. For example, in a simple design where there is one stimulus that can be either off or on, the design matrix might show a 1 where the stimulus is on, and a 0 where it is off. In order better to model the hæmodynamic response (i.e. both the time lag between stimulus onset and increase in oxyhæmoglobin supply, and the shape of the response), the design matrix is convolved with the hæmodynamic response function (HRF). For stimuli of short duration, a single HRF is used for each stimulus, while for blocked stimuli, a box-car corresponding to the duration of the block is convolved with the HRF (see section 2.2.2.3). The design matrix has a row for each time point and a column for

each experimental factor. Thus, the value of the design matrix at each point corresponds to the value of the experimental factor when convolved with its HRF, at that point in time. The parameters, β, are the values that the experimenter is seeking to estimate. The parameter matrix has a column for each voxel, and a row for each experimental factor. Finally, the error matrix is the same shape as the data matrix, with a column for each voxel and a row for each time point.

2.2.3.2.2 Parameter estimation, contrasts and hypothesis testing

The purpose of the general linear model is to estimate the parameters which, when multiplied by the design matrix, best approximate the data, i.e. produce the smallest error term. This is done by minimising the sum of the residual errors after parameter estimation. The parameters give an estimate of the amplitude of the response in each voxel for each experimental condition. Contrasts can then be performed between parameter estimates for each condition. For example, if the experimenter wishes to know which voxels show a significantly greater response for experimental factor 1 than for experimental factor 2, the parameter estimate for factor 2 can be compared to that of factor 1 for each voxel, using a t-test. Interactions and contrasts across more than two factors can be assessed using an F-test. This analysis results in a statistical map (or statistical parametric map: SPM). In a random effects analysis, as used in this thesis, the SPMs for the contrasts of interest for each participant are subjected to a second level of analysis. In this second-level analysis, the SPMs for each participant can be evaluated using a t- or F-test to measure whether participants' SPMs are drawn from a distribution with a mean of 0. If this hypothesis is rejected, it can be inferred that the result of the experimental manipulation is applicable to the general population (or at least to the population from which the participants were drawn).

2.2.3.2.3 Statistical thresholds

Because of the large number of voxels in the brain, fMRI analyses pose the problem of making multiple comparisons across a data set: for any reported result, the same test is performed at each of the (~100,000) voxels in the brain. Bonferroni correction for this number of comparisons would mean that very large t- or F-values would not be considered statistically significant. However, pre-processing steps such as interpolation during re-alignment and spatial smoothing mean that the voxels are not independent of each other. This allows the use of Gaussian random field theory to estimate the number of independent elements (resolution elements, or "resels") in the data set. Statistical thresholds can therefore be corrected for the number of resels, rather than the number of voxels, thus improving the sensitivity of the data. A further technique to address the multiple comparisons problem is to use region of interest or voxel of interest analyses. In these techniques, brain regions or voxels are identified using anatomical or functional localisers (e.g. restricting the search volume to a particular cortical area, or selecting the peak voxels from a previous analysis) and the parameter estimates for the contrasts of interest are then extracted from these areas or voxels. These parameter estimates can then be subjected to classical statistical analysis.

3 Characteristics of automatic imitation effects

Automatic imitation effects have been used as behavioural indices of the functioning of the human mirror neuron system (Brass et al., 2000; Kilner et al., 2003; Heyes et al., 2005). However, recent work has criticised the assumption that automatic imitation effects are mediated by the mirror neuron system on the grounds that automatic imitation effects have been confounded with simple spatial compatibility effects (Bertenthal et al., 2006; Jansson et al., 2007; Aicken et al., 2007). The experiments reported in this chapter used a design in which automatic imitation was measured on both spatially compatible and spatially incompatible trials, in order to assess the independence of spatial compatibility and automatic imitation effects. Additional features of the two experiments allowed measurement of the time courses of the two types of effect, both within and across trials. It was found that automatic imitation effects are independent of spatial compatibility effects and follow a different time course, permitting the use of automatic imitation effects as a behavioural measure of mirror neuron system function.

In order to investigate the properties of the mirror neuron system using behavioural techniques, automatic imitation effects have often been used (described in section 1.4.3: e.g. Stürmer et al., 2000; Brass et al., 2000; Kilner et al., 2003; Heyes et al., 2005). However, the use of automatic imitation effects as an index of mirror neuron function, as in many previous studies and in chapters 4 and 6 of this thesis, rests on the assumption that these effects reflect processes of imitation: that is, that they provide a reliable measure of the extent to which observation of an action facilitates or interferes with the performance of the same or a different action. This assumption has recently come under scrutiny as a result of questions over whether automatic imitation effects

are truly imitative, or whether they arise instead from simple spatial compatibility (Bertenthal et al., 2006; Jansson et al., 2007; Aicken et al., 2007). This chapter seeks to show that automatic imitation effects are distinct from spatial compatibility effects.

Both automatic imitation and spatial compatibility effects are types of compatibility effect. A compatibility effect between stimuli and responses arises when certain stimuli facilitate the production of certain responses (compatible stimulus-response pairings), while other stimuli interfere with the production of these responses (incompatible stimulus-response pairings). The difference in response times between responses on incompatible and compatible trials is used as a measure of the size of the compatibility effect.

Thus, a spatial compatibility effect (Fitts & Seeger, 1953; Kornblum, Hasbroucq, & Osman, 1990) will occur when stimuli are presented in spatially distinct locations (e.g. on left and right sides of a screen), and responses are spatially arranged in a similar manner (e.g. left and right button presses): when a stimulus appears on the side of space that is compatible with the required response (e.g. the task requires a left button press for red stimuli and a right button press for blue stimuli, and a red stimulus appears on the left side of space), participants will respond faster than when a stimulus appears on the side of space that is incompatible with the required response (e.g. a red stimulus appears on the right side of space). These effects occur despite the side of space being task-irrelevant (the participants' task is to respond on the basis of colour alone). Simple spatial compatibility effects involve stimuli and responses arranged along spatial dimensions such as left and right or up and down; orthogonal spatial compatibility effects involve arrangements such as up/right and down/left, where responses on the

right side of space are faster to stimuli presented in the top half of space than to stimuli presented in the bottom half of space (Cho & Proctor, 2004).

Whereas simple spatial compatibility effects involve arrangements of stimuli and responses along one or two spatial dimensions (up and down, left and right, etc.), imitative compatibility effects (henceforth automatic imitation effects) involve body part movement stimuli (or movement stimuli that closely resemble body parts; Press et al., 2005), as well as body part movement responses. Thus, a key difference between spatial compatibility and automatic imitation effects is that the latter involve the kind of complex perceptual-motor translations, between perceptual movement stimuli and the motor commands required to produce matching perceptual stimuli, that were described in section 1.2.2 and that are hypothesised to be a key function of the mirror neuron system.

The most important perceptual property of body part movement stimuli with respect to automatic imitation effects is that they are configural: the identity of each movement is defined by the movements of certain parts of the body relative to other parts. Thus, when observing the dorsal view of a right hand, an abduction movement of the index finger results in a movement of the finger to the left. When the hand is turned over or when the left hand is used, the same abduction movement results in a movement of the finger to the right. In terms of their spatial properties the two stimuli described here are opposite, consisting of movements on the left or right sides of space; but in terms of their configural, imitative properties both consist of the same abduction movement. An automatic imitation effect will occur when both stimuli and responses consist of configural body part movements: responses will be faster when the observed movement is the same as that which is to be performed than when the observed and to-be-

performed movements differ. Again, these effects can occur when the identity of the movement is task-irrelevant (e.g. the task requires participants to open their hand when they see a red hand and close it when they see a blue hand; they will be faster to open their hand if the red stimulus hand opens than if it closes: Stürmer et al., 2000).

As mentioned above, automatic imitation effects are frequently used as a behavioural measure of mirror neuron system function. Recently, however, several papers have criticised the experimental evidence for automatic imitation effects on the grounds that they are confounded with simple spatial compatibility (Bertenthal et al., 2006; Jansson et al., 2007; Aicken et al., 2007). For example, Brass et al. (2000) showed automatic imitation of task-irrelevant index and middle finger lifting movements when participants were responding to symbolic cues with index and middle finger lifting movements. This result could be explained by left/right spatial compatibility (Bertenthal et al., 2006; Jansson et al., 2007; Aicken et al., 2007) because the imitatively compatible stimulus-response pairing (e.g. observe index finger lift and perform index finger lift) is also spatially compatible (observe movement on left side of space and perform movement on left side of space), and the imitatively incompatible movement is also spatially incompatible. The finding by Stürmer et al. (2000) of automatic imitation of opening and closing hand movements could be explained, in a similar way to that of Brass et al. (2000), by up/down spatial compatibility (Jansson et al., 2007). In general, in any automatic imitation experiment where stimulus movements are presented in the same spatial alignment as that in which the participants' response movements will be made, spatial and imitative compatibility will be confounded.

Some attempts have been made to address this problem: Heyes et al. (2005) placed participants' response hands orthogonal to the direction of the observed stimuli;

however, orthogonal spatial compatibility effects (Cho & Proctor, 2004) may still operate in this spatial configuration. Bertenthal et al. (2006, Experiment 1), in common with many other studies, found a large compatibility effect when spatial and imitative compatibility were confounded – but, as mentioned above, this could be due to either the spatial or the imitative properties of the stimuli, or both. In a separate experiment (Experiment 2), spatial and imitative compatibility were placed in opposition to each other, and only a spatial compatibility effect was seen. This might suggest that automatic imitation effects are indeed due to spatial compatibility; but the spatial compatibility effect in this experiment was smaller than the compatibility effect in the first experiment, suggesting an influence of the conflicting automatic imitation effect on the size of the spatial compatibility effect in Experiment 2. However, since the experiments were performed on different participants and thus there may be between-subjects differences in the sizes of the spatial compatibility effects, the conclusions that can be drawn from this study are limited. Brass et al. (2001a, Experiment 3), in two separate experimental sessions, placed spatial and imitative compatibility in opposition to each other or in the same direction. This study improves on that of Bertenthal et al. (2006) because the conditions are within-subject and thus comparisons can be made between the two sessions. However, because different trial types were presented in different sessions, participants may have learned to focus on either the spatial or the imitative properties of the movements in the session where these were in opposition, while they would not need to distinguish between these properties in the session where these properties were confounded. The different sessions might, therefore, produce effects on responses which would not be seen if all trial types were presented in random order in the same experimental session. Thus, as can be seen in Table 3.1, no previous study has addressed directly the potential confound between spatial and imitative

compatibility, by assessing the influence of different levels of spatial and imitative compatibility in a randomised design within the same experimental session.

Experiments	Trial Types			
	Spatially Compatible		Spatially Incompatible	
	Imitatively Compatible	Imitatively Incompatible	Imitatively Compatible	Imitatively Incompatible
Stürmer et al. (2000)	√			√
Brass et al. (2000)	√			√
Brass et al. (2001a), Expts. 1 and 2	√			√
Brass et al. (2001a), Expt. 3 "unflipped" session	√			√
Brass et al. (2001a), Expt. 3 "flipped" session		√	√	
Heyes et al. (2005)[1]	√			√
Bertenthal et al. (2006), Expt. 1	√			√
Bertenthal et al. (2006), Expt. 2		√	√	
Bertenthal et al. (2006), Expt. 3a	√		√	
Bertenthal et al. (2006), Expt. 3b	√	√		
Aicken et al. (2007), Expts. 1 and 2	√			√
Jansson et al (2007), Expts. 1 and 2[1]	√			√
Experiment 3.1	√	√	√	√
Experiment 3.2	√	√	√	√

Table 3.1. Trial types used in previous experiments investigating automatic imitation effects. It can be seen that no previous experiment has presented trials from both levels of spatial and imitative compatibility within the same experimental session. [1]Heyes et al. (2005), and Jansson et al. (2007), Expt. 2, presented stimuli orthogonal to responses, but orthogonal spatial compatibility effects may still be seen in this configuration (Cho & Proctor, 2004); therefore, these trials are classified as spatially compatible and incompatible.

The experiments reported in the current chapter used a task in which a fully factorial experimental design was implemented, i.e. each level of imitative compatibility was measured at each level of spatial compatibility, and all trial types were presented in randomised order within the same experimental session. The task was a choice reaction time task in which participants responded to the colour of a circle (discriminative stimulus) presented at fixation by making an outward (abduction) movement of either the index or the little finger of the right hand. Simultaneous with the onset of the coloured circle, a task-irrelevant finger abduction movement was presented on the screen. Again, this movement could be of either the index or little finger, and on either the right or the left hand. Thus, the task fulfils the requirements for an automatic imitation task: both the task-irrelevant stimuli and the responses consist of body movements. It also fulfils the requirements for a spatial compatibility task: both the task-irrelevant stimuli and the responses are aligned along a left-right spatial dimension (in the case of the responses and of the right hand stimuli, an index finger movement is on the left side of space and a little finger movement is on the right side of space; in the case of the left hand stimuli, an index finger movement is on the right side of space and a little finger movement is on the left side of space). The use of both left and right hand stimuli allows manipulation of the spatial location of the stimulus independently of its imitative (finger identity) properties, resulting in all four of the trial types listed in Table 3.1 (spatially compatible, imitatively compatible; spatially compatible, imitatively incompatible; spatially incompatible, imitatively compatible; spatially incompatible, imitatively incompatible). Table 3.2 illustrates how the task-irrelevant stimuli and the responses combine to make up these four trial types.

By including trial types that allow measurement of each level of imitative compatibility (compatible, incompatible) at each level of spatial compatibility (compatible,

incompatible), this design permits the assessment of whether spatial compatibility and automatic imitation effects are truly independent.

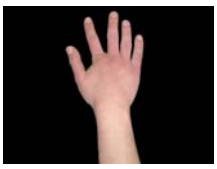
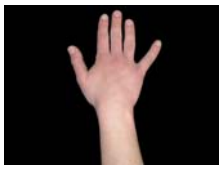
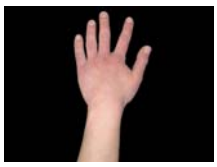
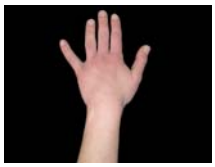
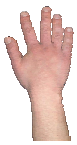
Response	**Task-Irrelevant Stimulus**			
	Right hand		Left hand	
	Index finger	Little finger	Index finger	Little finger
				
	Left side of space	Right side of space	Right side of space	Left side of space
Index finger  Left side of space	*compatible* *compatible*	*incompatible* *incompatible*	*compatible* *incompatible*	*incompatible* *compatible*
Little finger  Right side of space	*incompatible* *incompatible*	*compatible* *compatible*	*incompatible* *compatible*	*compatible* *incompatible*

Table 3.2. Imitative and spatial compatibility of trial types used in Experiment 3.1. Responses were always made with the right hand. The upper line in each cell indicates imitative compatibility; the lower line indicates spatial compatibility. The four trial types are indicated by different levels of shading.

For example, if an effect of spatial compatibility but not of imitative compatibility is observed, this would imply that previously reported automatic imitation effects are the result of spatial compatibility effects, as suggested by Aicken et al. (2007) and Jansson et al. (2007): that when spatial compatibility is controlled for in this fashion, no automatic imitation effects will be observed. If, however, both spatial compatibility and

automatic imitation effects are observed when spatial compatibility is controlled for, this would imply that spatial and imitative compatibility are independent of one another and thus that spatial compatibility and automatic imitation effects are distinct phenomena. This result would support the use of automatic imitation as a behavioural index of mirror neuron system function.

As well as a fully factorial design which allowed measurement of spatial and imitative compatibility independently of one another, the two experiments reported in the current chapter had additional features to allow investigation of the time course of the spatial compatibility and automatic imitation effects across the course of a trial. Experiment 3.1 contained sufficient trials to perform a quintile analysis (Ratcliff, 1979), in which, within each trial type, trials of differing response times can be compared. (This experiment also included a discriminability variable: the task-relevant colour stimuli were strongly or weakly discriminable. This variable was intended to increase the range of response times (Hommel, 1994), but was not effective in doing so.) Experiment 3.2 used an offset variable that varied the timing of the discriminative stimulus with respect to the irrelevant movement stimulus. This variable was designed to manipulate the stage of processing reached by the irrelevant movement stimulus when responding was initiated.

By performing a quintile analysis or manipulating the processing of the irrelevant movement stimulus, it is possible to assess the strengths of the spatial compatibility and automatic imitation effects at different time points during the course of a trial. This provides another way of discriminating the two effects: if the spatial compatibility and automatic imitation effects have different time courses, they are likely to be independent of one another. Brass et al. (2001a), using a quintile analysis, showed that both spatial

compatibility and automatic imitation effects grew larger as response times increased, but that the automatic imitation effect increased more steeply with increasing response time. However, Jansson et al. (2007), in two separate experiments, failed to replicate this increase in automatic imitation effects over time, from which they concluded that there was no evidence for the existence of distinct spatial and imitative compatibility effects.

Experiment 3.1 therefore sought to establish the independence of automatic imitation and spatial compatibility effects in two ways. The first was to assess whether automatic imitation effects occur when spatial compatibility is controlled for. The second was to investigate, using a quintile analysis, whether the time course of these two effects differed within the course of each trial.

3.1 Experiment 3.1

Experiment 3.1 consisted of a behavioural choice reaction time task, where the discriminative stimulus was a coloured circle. The colour of the circle informed participants whether to make an outward (abduction) movement of the index finger, or of the little finger. Participants were instructed to make this movement as quickly as possible after the appearance of the discriminative stimulus. Response times were measured using electromyography. Prior to the onset of the discriminative stimulus, a right or left hand was presented on the screen. Simultaneous with the onset of the discriminative stimulus, the hand performed an abduction movement of either the index or little finger. This movement was task-irrelevant, and could be either spatially compatible (occurring on the same side of space) or spatially incompatible with the movement instructed by the coloured circle. Additionally, and independent of its spatial

compatibility, the movement could be either imitatively compatible (performed with the same finger) or imitatively incompatible with the instructed movement (see Table 3.2).

If, as suggested by Aicken et al. (2007) and Jansson et al. (2007), automatic imitation effects are due to spatial compatibility, then a main effect of spatial compatibility but no effect of imitative compatibility should be observed. There should also be no difference in the time courses of the two effects, as measured using a quintile analysis. If, however, spatial compatibility and automatic imitation effects are independent from one another, a main effect of both spatial and imitative compatibility should be seen, and, consistent with Brass et al. (2001a), the time courses of the two effects should differ.

3.1.1 Method

3.1.1.1 Participants

Sixteen right-handed volunteers (seven male), aged 19-35 years, took part. Participants were randomly allocated to receive either high or low discriminative stimulus discriminability (see Stimuli). Two additional participants were removed from the sample prior to data analysis, due to insufficient data (subject error or poor electrode signal on more than 20 % of trials). For this and all subsequent experiments, unless otherwise stated, participants were recruited using the University College London (UCL) Psychology Department subject pool, and paid for their participation; the experiment was approved by the UCL Ethics Committee, and all participants gave written informed consent before participating.

3.1.1.2 Stimuli and Apparatus

3.1.1.2.1 Stimuli

The stimuli were video files made up of two still images of a female left or right hand. The hand was displayed initially in a neutral (resting) position, and subsequently in the (task-irrelevant) final movement position, which consisted of an abduction movement of either the index or little finger (see Figure 3.1). The movement was made in the horizontal plane, i.e. the plane of the hand and fingers, and was shown as if viewed from above. Videos (720 by 576 pixels) were constructed using Adobe Premiere (Adobe Systems Incorporated, San Jose, California, USA). The replacement of the neutral stimulus by the final movement position produced apparent motion, which has been shown to give robust automatic imitation effects (Stürmer et al., 2000; Press et al., 2005) while allowing greater experimental control of movement stimulus onset than gradual progression of the movement. The hand was presented on a black background and subtended a visual angle of 14.9° vertically and between 7.7° (neutral) and 9.2° (little finger movement) horizontally, when viewed at a distance of 57cm. The finger movements subtended an angle of 17° (index) and 29° (little) from the neutral position. The left hand videos were created by reflecting the right hand images in the y-axis and were identical to the right hand videos in all other respects.

The onset of the discriminative stimulus, telling the participant whether to respond with their index or little finger, was simultaneous with the onset of the (task-irrelevant) movement stimulus. The discriminative stimulus consisted of a solid, coloured circle, occupying ~ 1° visual angle. Prior to the onset of the coloured circle, its location was indicated by the presence of the outline of a white circle, also ~ 1° visual angle, which acted as a fixation point. This location was at a point equidistant between the tips of the index and little fingers in the neutral position, thus ensuring that spatial attention was

equal between the two fingers, and giving no information about the subsequent movement. In order to make the discrimination task relatively difficult, the two colours of the discriminative stimulus, indicating the two responses, were chosen to be similar. The mean colour of the hand stimulus was calculated by finding the mean intensity of the red, green and blue components of every coloured pixel in the hand image. For half of the participants, the red component of this colour was incremented by 32 (on a scale of 1:256) to produce an "orange" colour, while the blue component was incremented by the same amount to produce a "purple" colour. For the other eight participants, these components were incremented by 16 on the same scale, in order to create two levels of discriminability (high: incremented by 32/256; low: incremented by 16/356) between participants. See Figure 3.1 for examples of the stimuli.

3.1.1.2.2 Apparatus

Stimuli were presented on a Dell Latitude D800 laptop (Dell Incorporated, Round Rock, Texas, USA). Time of onset of the final movement position and (simultaneously) the discriminative stimulus was identified by a signal sent via the parallel port to the data acquisition computer. This triggered data acquisition and allowed response time (RT) to be calculated with respect to stimulus onset time.

3.1.1.3 Procedure

3.1.1.3.1 Stimulus presentation

Participants were seated approximately 60 cm from the stimulus presentation screen. All responses were made with the right hand. Their right arm was supported from the elbow to the palm by an armrest, placed such that their right hand was in the same orientation as the hand on the screen (with the wrist closest to the participant and the fingertips furthest away). This was to ensure spatial compatibility or incompatibility

between the observed and performed actions on the relevant trials. Participants were instructed to fixate on the white circle which was presented on the hand in the neutral position on every trial. They were informed that the circle would change to a coloured circle, and that this indicated that they should make an abduction movement of either the index or the little finger. The stimulus-response mappings (orange > index finger, purple > little finger, or vice versa), and discriminability of circle colour (high or low) were fully counterbalanced between participants. Participants were encouraged to perform the movements as fast as possible without sacrificing accuracy.

Each trial began with the video of the neutral hand position, which was presented for one of three stimulus onset asynchronies (SOAs: 800, 1600, or 2400 ms). This was followed by the final movement position and discriminative stimulus, which remained on the screen for 480 ms. A blank screen was then presented for 3000 ms before the next trial began (see Figure 3.2). The different trials were made up of a factorial combination of stimulus movement (index or little), stimulus movement location (left or right side of the screen; the use of both left and right stimulus hands meant that this was orthogonal to the identity of the stimulus movement), and response movement (index or little, instructed by the colour of the discriminative stimulus).

A total of 288 trials were presented in a random order in four blocks of 72 trials. Each of the main four trial types (as listed in Tables 3.1 and 3.2) was presented 18 times in every block, three times for each combination of response movement and SOA. Before the start of the experiment, participants were given the chance to practice making the two finger movements, during which time they received visual feedback of their electromyogram (EMG) signal.

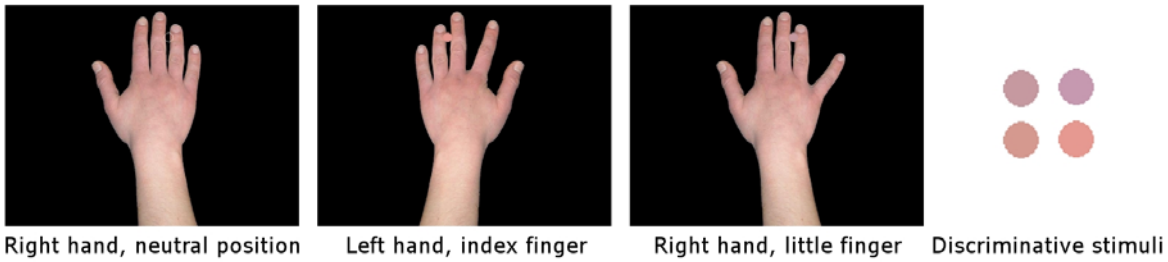


Figure 3.1. Examples of stimuli used in Experiments 3.1 and 3.2. Each hand also performed the other movement. Discriminative stimuli comprised a purple (top) or orange (bottom) circle, of low (left, Experiment 3.1 only) or high (right) discriminability.

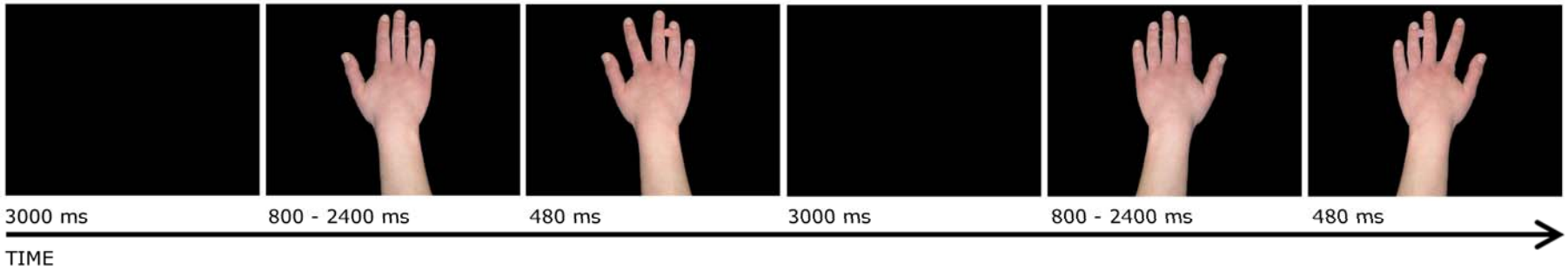


Figure 3.2. Procedure for Experiment 3.1. Two trials are shown. Responses (not shown) were made according to the colour of the discriminative stimulus. Thus, for participants for whom orange > index finger and purple > little finger movement, the first trial is spatially and imitatively compatible, while the second is spatially compatible but imitatively incompatible. For participants who performed the other stimulus-response mapping, the first trial is spatially and imitatively incompatible, while the second is spatially incompatible but imitatively compatible.

They then received 24 practice trials in a random order to familiarise them with the format of the experiment, with each of the four trial types presented once for each combination of response movement and SOA. No visual EMG feedback was given during either practice or experimental trials.

3.1.1.3.2 Data acquisition and analysis

The EMG was recorded from the first dorsal interosseous (FDI) and abductor digiti minimi (ADM) muscles of the right hand, which control abduction of the index and little fingers, respectively. Pairs of disposable Ag-AgCl electrodes (Unomedical a/s, Birkerød, Denmark) were attached to these muscles in a belly-tendon montage, with a third (common input) electrode placed on the wrist. Signals were amplified at a gain of 1,000 x using a 1902 amplifier (Cambridge Electronic Design, Cambridge, UK), band-pass filtered between 20 and 2,000 Hz and mains-hum filtered at 50 Hz. A second laptop (Dell Latitude C400) used a data acquisition card (DAQCard-PCI-6024E, National Instruments Corporation, Austin, Texas) and a Matlab script (The Mathworks, Natick, Massachusetts, USA) to sample these signals at 3 kHz and record them for later analysis.

For every trial, RT was calculated by moving a 20 ms window across the EMG data in 1 ms increments. The standard deviation of the EMG signal within this window was calculated and compared to the standard deviation of the signal in the 100 ms before stimulus onset (the baseline period). Once the standard deviation of the data in the 20 ms window was over 2.75 times that of the baseline period for three successive 20 ms windows, the end of the first window was taken as the end of the RT period. Whether this timepoint accurately reflected the onset of the EMG response was verified by eye for every trial performed by every participant.

3.1.2 Results and Discussion

Trials on which participants made an error or took more than 1000 ms to respond (2.5 %) were excluded from analysis. Trials on which the analysis program failed accurately to detect the onset of the EMG response (6.1 %) were also excluded. Mean RT was calculated for each of the four trial types, collapsed across the two different response movements. Figure 3.3 shows the RT and error data.

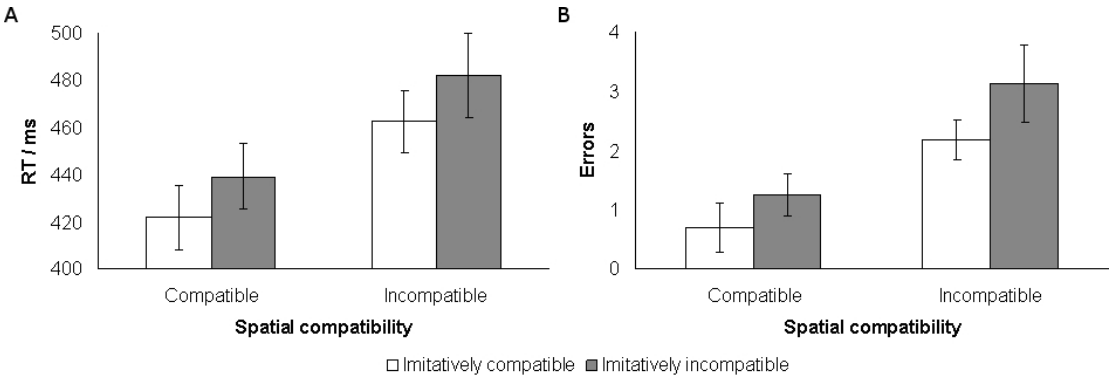


Figure 3.3. Mean ± standard error of the mean (SEM) of RTs (A) and errors (B) for Experiment 3.1. Data are shown for the four trial types, i.e. each level of imitative compatibility at each level of spatial compatibility.

A repeated measures analysis of variance (ANOVA) was performed on the RT data. The within-subjects factors were spatial compatibility (compatible, incompatible) and imitative compatibility (compatible, incompatible). The between-subjects factor was the discriminability of the discriminative stimulus (high, low). Here and subsequently throughout this thesis, all significant main effects and interactions are reported ($\alpha = 0.05$ unless otherwise stated). There was a significant main effect of spatial compatibility: participants responded faster on trials where the irrelevant movement was spatially compatible with the response (mean ± standard error of the mean (SEM): 431 ± 14 ms compared to 472 ± 15 ms; $F_{1,14} = 63.8$, $p < 0.001$). There was also a significant main effect of imitative compatibility: participants responded faster on trials where the

irrelevant movement was performed with the same finger as the response (442 ± 13 ms compared to 461 ± 16 ms; $F_{1,14} = 13.2$, $p = 0.003$). The two effects did not interact. There was no main effect of discriminability, and no interactions involving this factor.

A repeated measures ANOVA with the same factors was performed on the error data. There was a significant main effect of spatial compatibility: participants made more errors on spatially incompatible (2.7 ± 0.5) than on spatially compatible trials (1.0 ± 0.4; $F_{1,14} = 29.1$, $p < 0.001$). The direction of this effect is such as to rule out a speed/accuracy trade-off that might otherwise account for the RT data.

The results of the RT analysis indicate that, contrary to the suggestions of Aicken et al. (2007) and Jansson et al. (2007), automatic imitation effects are independent of spatial compatibility effects. If automatic imitation effects were due solely to simple spatial compatibility, no main effect of imitative compatibility would have been observed. Instead, this experiment showed a main effect of imitative compatibility, and no interaction between spatial and imitative compatibility.

In order to investigate the time course of the spatial compatibility and automatic imitation effects within trials, a quintile analysis was performed (after Ratcliff, 1979). The distribution of each participant's RTs over the entire experiment, within each of the four trial types, was ordered by response speed and divided into five "bins" (1 = fastest to 5 = slowest) with an equal number of trials in each bin. The spatial compatibility effect (RT on spatially incompatible – RT on spatially compatible trials) and automatic imitation effect (RT on imitatively incompatible – RT on imitatively compatible trials) were then calculated for each of the five quintiles. This allows measurement of the size of the compatibility effects across the range of fast to slow RTs, which gives an insight

into the relative strength of each effect over time within a trial. ANOVA with within-subjects factors of quintile (1 – 5) and compatibility modality (spatial, imitative) revealed a main effect of modality: the spatial compatibility effect was larger than the automatic imitation effect (42 ± 6 ms compared to 18 ± 6 ms; $F_{1,15} = 22.6$, $p < 0.001$). There was, importantly, an interaction between response speed and modality ($F_{4,60} = 3.9$, $p = 0.007$): simple effects analysis showed that the spatial compatibility effect was not affected significantly by increasing RT ($F_{4,60} = 1.2$, $p = 0.317$), while the automatic imitation effect became larger as RT increased ($F_{4,60} = 2.9$, $p = 0.028$) (see Figure 3.4).

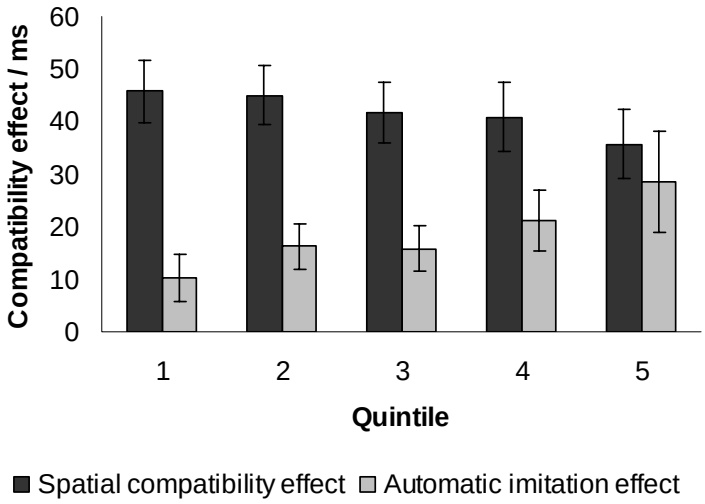


Figure 3.4. Mean ± SEM sizes of the spatial compatibility and automatic imitation effects across the five quintiles (1 = fastest RTs, 5 = slowest RTs) in Experiment 3.1.

The quintile analysis yielded three interesting results. First, the spatial compatibility effect was greater than the automatic imitation effect. This is in contrast with the results of Brass et al. (2001a, Experiment 3) who found a greater automatic imitation effect than spatial compatibility effect. One possible reason for this difference is that the experiment of Brass et al. (2001a) manipulated up/down, rather than left/right, spatial compatibility; it is possible that certain types of spatial representations are more

effective than others in eliciting compatibility effects (Nicoletti & Umiltà, 1984). This explanation is in line with the findings of Bertenthal et al. (2006, Experiments 3a and 3b), in which left/right stimulus arrangements also produced larger spatial compatibility effects than automatic imitation effects. However, the current stimuli displayed a greater degree of spatial eccentricity than those of Brass et al. (2001a), which could also explain the stronger spatial compatibility effect.

The second result of the quintile analysis was that the automatic imitation effect increased as RTs increased, a result that is consistent with the findings of Brass et al. (2001a) but at odds with Jansson et al. (2007) who did not find an effect of RT on the size of the automatic imitation effect. Thirdly and most importantly, increases in RT affected the sizes of the spatial compatibility and automatic imitation effects differentially: in contrast with the automatic imitation effect, the spatial compatibility effect did not increase with increasing RT.

Experiment 3.1 therefore confirmed that spatial compatibility and automatic imitation effects are independent of one another and appear to follow distinct time courses within each trial. Experiment 3.2 aimed to replicate these findings by using the same experimental task, but including a timing manipulation that varied the offset between the discriminative stimulus and irrelevant movement stimulus, in order to investigate further the time courses of the spatial compatibility and automatic imitation effects.

3.2 Experiment 3.2

Experiment 3.2 used the same stimuli, task and levels of spatial and imitative compatibility as Experiment 3.1, with the exception that a timing manipulation (offset between the discriminative stimulus and irrelevant movement stimulus) was included.

By manipulating response time with respect to the irrelevant movement stimulus, it is possible to investigate the build-up and decay of the spatial compatibility and automatic imitation effects over time within a trial. Hommel (1993; 1994), in a spatial compatibility task, presented the discriminative stimulus 196 ms after the irrelevant spatial information. This manipulation delayed the response time with respect to the processing of the irrelevant spatial information. This resulted in a reduced spatial compatibility effect, suggesting that the spatial compatibility effect decays over time. In Experiment 3.2, a similar manipulation was used: time of presentation of the discriminative stimulus was varied with respect to the onset of the irrelevant movement stimulus, in order to investigate the time courses of the automatic imitation and spatial compatibility effects.

The time difference between the onsets of the discriminative and irrelevant movement stimuli was manipulated across five levels (offsets), in order to obtain as clear a picture as possible of the time courses of the two effects. Hommel's (1993; 1994) data suggested that a delay of 196 ms between the onset of the irrelevant movement stimulus and the discriminative stimulus was sufficient for the decay of the spatial compatibility effect. In order to investigate the intermediate stages of this decay, levels of offset giving delays of 80 ms and 160 ms were chosen whereby the discriminative stimulus was presented after the irrelevant movement stimulus. Additionally, one simultaneous level of offset (identical to Experiment 3.1), and two levels where the discriminative stimulus was presented 80 ms or 160 ms *before* the irrelevant movement, were used. These "before" levels of offset were used in order to investigate the initial stages, i.e. the build-up, of the time courses of the two effects.

Experiment 3.1 found that the automatic imitation effect, unlike the spatial compatibility effect, increased with increasing RT. It was therefore predicted that the later ("after") levels of offset should show a greater automatic imitation effect than the simultaneous or anticipation levels, while the spatial compatibility effect might build up earlier and thus be present at the earlier ("before") levels of offset.

3.2.1 Method

3.2.1.1 Participants

Eight right-handed volunteers (three male), aged 20-27 years, participated.

3.2.1.2 Stimuli and Apparatus

3.2.1.2.1 Stimuli

The stimuli were identical to those used in Experiment 3.1, with two exceptions. The coloured circles did not vary in discriminability across participants (the higher discriminability stimuli from Experiment 3.1 were used), and the discriminative stimulus was presented at variable intervals before and after the onset of the irrelevant movement stimulus (see Procedure).

3.2.1.2.2 Apparatus

The apparatus was identical to that used in Experiment 3.1 with the exception that data acquisition was triggered at the time of onset of the discriminative stimulus, irrespective of when the irrelevant movement stimulus was presented.

3.2.1.3 Procedure

The procedure was the same as Experiment 3.1, with the following exceptions. The video of the still hand was presented for one of two SOAs (800 or 1600 ms), after which

time the discriminative stimulus was presented. The discriminative stimulus was presented at one of five offsets with respect to the irrelevant movement stimulus (160 ms before, 80 ms before, simultaneous, 80 ms after, 160 ms after). Thus, the irrelevant movement stimulus could appear shortly after, at the same time as, or shortly before the discriminative stimulus (see Figure 3.5).

A total of 560 trials were presented in a random order in 14 blocks of 40 trials. Trials were counterbalanced across sets of two blocks, such that each combination of trial type, response movement, and offset was presented twice in every two blocks, once for each SOA. Twelve randomly selected practice trials were given before the start of the experiment.

3.2.2 Results and Discussion

Trials on which participants made an error, or on which their RT was more than 2.5 standard deviations from their mean RT (3.8 %) were excluded from analysis. Trials on which the analysis program failed accurately to detect the onset of the EMG response (0.5 %) were also excluded. Mean RT was calculated for each of the combinations of trial type and offset (see Table 3.3) and the values of the spatial compatibility and automatic imitation effects were then calculated for each offset (see Figure 3.6).

ANOVA with within-subjects factors of offset between discriminative and irrelevant stimuli (discriminative stimulus 160 ms before irrelevant movement, 80 ms before, simultaneous, 80 ms after, 160 ms after), spatial compatibility (compatible, incompatible), and imitative compatibility (compatible, incompatible), was performed on the RT data.

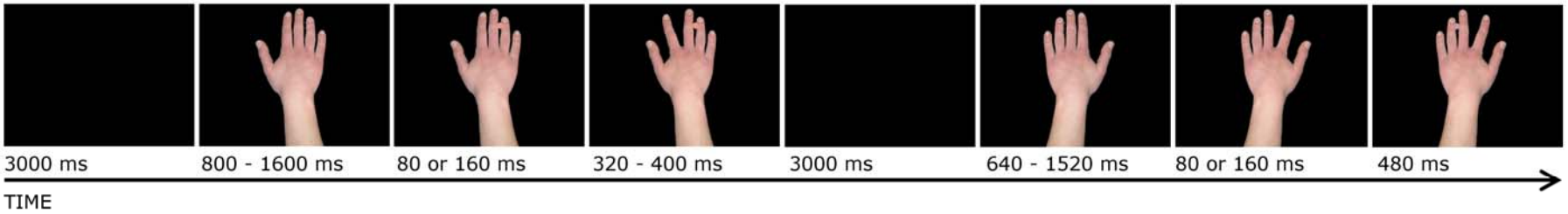


Figure 3.5. Procedure for Experiment 3.2. Two trials are shown: the first is an example of a trial in which the discriminative stimulus appears 160 or 80 ms before the irrelevant movement, while the second is an example of a trial in which the discriminative stimulus appears 160 or 80 ms after the irrelevant movement.

		Trial Types							
		Spatially Compatible				Spatially Incompatible			
	Overall	Imitatively Compatible		Imitatively Incompatible		Imitatively Compatible		Imitatively Incompatible	
Offset	RT	RT	Errors	RT	Errors	RT	Errors	RT	Errors
160 ms before	432 ± 14	420 ± 14	0.1 ± 0.1	427 ± 14	0.6 ± 0.3	436 ± 11	1.9 ± 0.5	444 ± 18	1.5 ± 0.5
80 ms before	435 ± 15	425 ± 15	0.8 ± 0.3	416 ± 14	0.5 ± 0.3	451 ± 16	1.1 ± 0.4	449 ± 14	1.5 ± 0.5
Simultaneous	424 ± 16	399 ± 14	0.8 ± 0.4	416 ± 16	1.0 ± 0.3	436 ± 18	0.9 ± 0.2	445 ± 16	3.3 ± 0.5
80 ms after	417 ± 14	378 ± 15	0.4 ± 0.2	412 ± 11	0.9 ± 0.3	425 ± 16	0.5 ± 0.3	454 ± 16	2.0 ± 0.7
160 ms after	410 ± 16	387 ± 17	0.1 ± 0.1	405 ± 14	0.8 ± 0.3	415 ± 18	0.5 ± 0.2	435 ± 14	2.0 ± 1.1

Table 3.3. Mean ± SEM of RTs (ms) and number of errors in Experiment 3.2. RT and error data are shown for each of the four trial types at each of the five levels of offset, and overall RT for each level of offset.

Replicating the results of Experiment 3.1, there was a significant main effect of spatial compatibility (408 ± 15 ms compared with 439 ± 16 ms; $F_{1,7} = 46.9$, $p < 0.001$) and of imitative compatibility (417 ± 15 ms compared with 430 ± 15 ms; $F_{1,7} = 25.7$, $p = 0.001$), and no interaction between these factors. There was also a significant main effect of offset: participants responded faster, the later the discriminative stimulus appeared with respect to the irrelevant movement ($F_{4,28} = 11.1$, $p < 0.001$). There were two significant interactions: between spatial compatibility and offset ($F_{4,28} = 3.1$, $p = 0.032$) and between imitative compatibility and offset ($F_{4,28} = 4.5$, $p = 0.007$). These interactions are illustrated in Figure 3.6. It can be seen that the spatial compatibility effect is already evident to some degree at the earliest level of offset, and that it continues to build up across the levels before starting to decay at the latest level of offset. The automatic imitation effect, in contrast, is not evident until the simultaneous level of offset, after which it builds up and then starts to decay. This later appearance of the automatic imitation effect than of the spatial compatibility effect is consistent with the quintile analysis presented in Experiment 3.1.

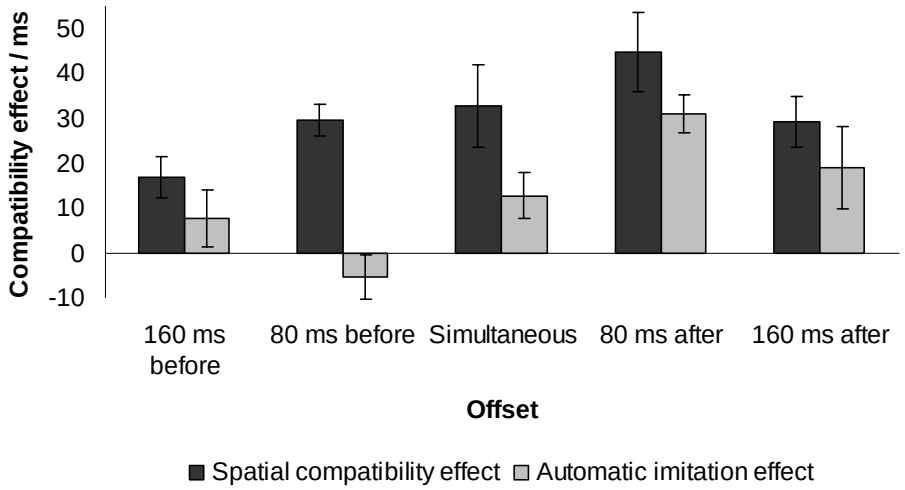


Figure 3.6. Mean ± SEM of sizes of spatial compatibility and automatic imitation effects for the five levels of offset in Experiment 3.2.

In order to investigate the above interactions, post-hoc t-tests were performed on the sizes of the spatial compatibility and automatic imitation effects separately, to establish which levels of offset produced significantly different sizes of each effect. For each set of t-tests (Bonferroni corrected: $\alpha = 0.005$), the sizes of the compatibility effects at each level of offset were compared. For the interaction between offset and spatial compatibility, there was a marginal difference between the size of the spatial compatibility effects at offset levels 160 ms before and 80 ms before ($t_7 = 3.87$, $p = 0.006$), suggesting that this interaction may be driven by the difference in size of the effect as it starts to build up at these early levels of offset. There was one significant difference between offsets for the automatic imitation effect, which indicated that the interaction between imitative compatibility and offset was primarily driven by the difference in size of the automatic imitation effects at offset levels 80 ms before and 80 ms after ($t_7 = 4.73$, $p = 0.002$), confirming a later build-up of this effect. No other comparisons reached significance.

The error data were subjected to ANOVA with the same within-subjects factors of offset between discriminative and irrelevant stimuli (discriminative stimulus 160 ms before irrelevant movement, 80 ms before, simultaneous, 80 ms after, 160 ms after), spatial compatibility (compatible, incompatible), and imitative compatibility (compatible, incompatible). There were significant main effects of spatial compatibility: participants made more errors on spatially incompatible trials than on spatially compatible trials (1.5 ± 0.5 compared to 0.6 ± 0.2; $F_{1,7} = 14.9$, $p = 0.006$) and of imitative compatibility: participants made more errors on imitatively incompatible trials than on imitatively compatible trials (1.4 ± 0.5 compared to 0.7 ± 0.3; $F_{1,7} = 10.0$, $p = 0.017$). Both of these effects were in such a direction as to rule out any speed/accuracy trade-off.

The main RT effects of spatial and imitative compatibility replicated the findings of Experiment 3.1 and confirmed the independence of spatial compatibility and automatic imitation effects. The main effect of offset on RT may indicate that participants were more ready to respond in the 80 ms after and 160 ms after conditions, where the onset of the irrelevant movement preceded and therefore predicted the onset of the discriminative stimulus, than in the other conditions.

Both the spatial compatibility and the automatic imitation effects showed an interaction with offset, indicating that the sizes of both effects changed over the five levels of this factor, as would be expected if the effects build up and then decay over time. The post-hoc analyses indicated a marginal difference between the first two levels of offset for the spatial compatibility effect, suggesting that this effect reaches its peak early in the course of each trial, while the interaction between offset and imitative compatibility was driven by the difference between the 80 ms before and 80 ms after levels of offset, indicating that the automatic imitation effect peaks somewhat later. These analyses are consistent with the results of Experiment 3.1: the spatial compatibility effect was present from an earlier stage of each trial while the automatic imitation effect was greater at later offsets within each trial.

3.3 General Discussion

The experiments reported in the current chapter showed that, contrary to the suggestions of Aicken et al. (2007) and Jansson et al. (2007), automatic imitation effects are independent of simple spatial compatibility effects. This result permits the use of automatic imitation to assess imitative ability and performance and as a measure of mirror neuron system function in later chapters. It also suggests that in previous studies in which spatial and imitative compatibility were confounded, the observed

compatibility effect may have resulted from the combination of spatial compatibility and automatic imitation effects.

Experiments 3.1 and 3.2 also indicated that spatial compatibility and automatic imitation effects display differing time courses within each trial, as reported by Brass et al. (2001a), but contrary to Jansson et al. (2007). Spatial compatibility effects are present from the early stages of a trial, while automatic imitation effects arise later in a trial (Experiment 3.2) and appear to increase in size for longer than spatial compatibility effects (Experiment 3.1). What does this imply about the mechanisms underlying the two types of compatibility effect? One explanation is that both effects arise from the same mechanism, but that the *inputs* to this mechanism differ in the case of the two different effects. An alternative explanation would be that the two effects are the result of two different mechanisms.

The presence of an automatic imitation effect when spatial compatibility is controlled for indicates that automatic imitation effects are not due to simple spatial compatibility. However, automatic imitation effects are still the result of spatial aspects of the stimuli, in as much as the stimuli are defined and discriminated by their configural spatial properties: they are actions that unfold in space. Thus, it is likely that the same domain-general mechanisms of stimulus-response compatibility give rise to both simple spatial compatibility and automatic imitation effects (Stürmer et al., 2000; Brass et al., 2000; Hommel, Musseler, Aschersleben, & Prinz, 2001). The different effects would then arise from differing inputs to this mechanism: the side of space in the case of spatial compatibility effects, versus a configuration of body parts moving in space in the case of automatic imitation effects. These different inputs are likely to be processed at different rates, with the more complex body part configurations taking longer to process

than the more simple information about the side of space of the irrelevant stimulus. This differential processing speed could thus explain why the time courses of the spatial compatibility and the automatic imitation effects differ within the course of each trial.

An alternative view has been put forward by Bertenthal et al. (2006), who suggested that automatic imitation and spatial compatibility effects are mediated by different mechanisms. Bertenthal et al. (2006, Experiments 3a and 3b) showed that the size of the automatic imitation effect reduced across the course of a block of trials, whereas the spatial compatibility effect remained constant. They interpreted this interaction, between compatibility modality and stage within the block, as indicating the presence of different mechanisms for spatial compatibility and automatic imitation effects.

However, there are two problems with the above interpretation: first, the two effects were assessed using different tasks with different stimulus processing demands. Spatial compatibility was measured by asking participants to imitate the identity of the finger that was performing a tapping movement; this finger could be either spatially compatible or incompatible with the participant's movement. Automatic imitation was determined by instructing participants to match spatially the finger that was performing a tapping movement; this finger could be either imitatively compatible or incompatible with the participant's movement. Thus, the spatial compatibility task required analysis of the finger identity, while the automatic imitation task required analysis of the spatial location of the finger. It is likely that these tasks take a different amount of time to perform. Indeed, response times appear to have been longer for the spatial compatibility experiment, where participants had to process the finger identity, which is a more complex task than processing its spatial location. The current Experiments 3.1 and 3.2 suggest that the relative size of spatial compatibility and automatic imitation effects

may alter with increasing response time, which makes this a potentially problematic confound.

The second obstacle in interpreting the results of Bertenthal et al. (2006) is that compatible and incompatible trials were presented in separate blocks. This allows the development of response strategies as the block progresses. For example, in the spatial compatibility experiment, where the instruction was to imitate the identity of the moving finger, a valid strategy on a (spatially) compatible block would be instead to match the spatial location, which requires less processing and therefore can be performed more quickly. Because the trials are blocked, this strategy could develop across a block, once the participant realises the spatially compatible nature of the trials. Indeed, the spatial compatibility effect in this experiment showed a trend towards a linear increase across the four quarters of each block, driven by a decrease in response times on spatially compatible trials. In contrast, in the automatic imitation experiment, the effect decreased across the four quarters of each block, driven by a decrease in response times on imitatively incompatible trials. The instruction here was to match the spatial location of the moving finger. It is possible that participants could avoid interference during an imitatively incompatible block by, for example, squinting, in order not to process the incompatible imitative attribute of the moving finger, while preserving spatial information. Again, the blocked trials would allow this strategy to develop once the participant realises the imitatively incompatible nature of the block. Thus, alternative response strategies, driven by the differing task demands and the blocked presentation of trials, could explain the pattern of data observed by Bertenthal et al. (2006).

Since the current experiments use the same task to measure both spatial and imitative compatibility, and trial types are fully randomised, it is possible to contrast the results of Bertenthal et al. (2006) with the results of Experiment 3.1 which comprised four consecutive blocks of trials. If Bertenthal et al. (2006) are correct, and spatial compatibility and automatic imitation effects are the result of different mechanisms which progress at different rates across the course of an experiment, then there should be an interaction between the size of the two effects across the four blocks of Experiment 3.1: the automatic imitation effect should reduce, while the spatial compatibility effect should remain constant. The sizes of the automatic imitation and spatial compatibility effects were therefore calculated for each block and entered into repeated measures ANOVA with within-subjects factors of block (1 – 4) and compatibility modality (spatial, imitative). There was a main effect of compatibility modality: as noted previously, the spatial compatibility effect was greater than the automatic imitation effect ($F_{1,15} = 39.4$, $p < 0.001$). There was no main effect of block and, contrary to the findings of Bertenthal et al. (2006), no interaction between block and compatibility modality ($F_{3,45} < 1$).

It therefore appears that, when the same task is used to measure both spatial compatibility and automatic imitation effects and when trials are randomised such that alternative response strategies cannot be used, there is no evidence for differential progression of the two effects across trials within an experiment. While it is difficult to form firm conclusions on the basis of a null result, when task differences and alternative response strategies are eliminated there seems to be little evidence for the presence of different underlying mechanisms contributing to automatic imitation and spatial compatibility effects.

Although it appears that spatial compatibility and automatic imitation effects are independent of one another, there is as yet no evidence to contradict the suggestion that these effects arise, independently, from the same domain-general processes of stimulus-response compatibility. This suggestion is consistent with the hypothesis advanced in section 1.3.2 and based on the associative sequence learning (ASL) theory of imitation (Heyes & Ray, 2000), which proposes that imitation arises as a result of domain-general associative learning mechanisms.

What are the implications of this conclusion with respect to the processes underlying compatibility effects? It is clear that both stimuli and responses must be represented in the brain. What is as yet unclear is whether stimuli and responses share a common code (e.g. the Theory of Event Coding; Hommel et al., 2001), or consist of separate but linked representations. However, even if events are not represented in a common code, the presence of compatibility effects suggests that there must be, at the very least, excitatory links between sensory and motor representations, both for movement representations (e.g. index finger abduction) and spatial representations (e.g. the left side of space). Additionally, the motor representations of different movements may be linked in a mutually inhibitory fashion, for example where actions are mutually exclusive, as in the case of opening versus closing the hand. Even in the case of non-mutually exclusive actions, e.g. lifting of the index versus the middle finger, if extensive previous experience has been acquired of performing one movement in exclusion of the other (e.g. during typing), then a mutually inhibitory link between motor representations may exist.

The description above allows us to model the processing that occurs during an automatic imitation task. In the finger lifting task of Brass et al. (2000) or Bertenthal et

al. (2006), participants responded to a symbolic cue by lifting either the index or the middle finger, while simultaneously observing either an index or middle finger lift. Observation of an index finger lifting will activate the sensory representation of an index finger lifting. If, as outlined above, excitatory links exist between sensory and motor representations of the same action, or if there is a common code for these representations, then this sensory activation will result in activation of the motor representation of an index finger lifting. Mutual inhibition between the motor representations of index and middle finger lifting movements will then reduce the activation of the motor representation of a middle finger lifting (another source of mutual inhibition is task instructions: since instructions are to lift only one or the other finger, a task-specific temporary inhibitory link may be formed between the motor representations of the two movements). Thus, the motor representation of an index finger lifting is now more active than the motor representation of a middle finger lifting. At this stage, the participant selects their response based on the symbolic cue. As a result of the differential activation of the two motor representations, an index finger lifting response is facilitated while a middle finger lifting response suffers interference, producing an automatic imitation effect.

The same concepts can also be used to explain spatial compatibility effects. One additional assumption that is needed to explain the results of the experiments reported in the current chapter is that activation of the motor representations builds up and then decays over time, following the onset of the irrelevant movement stimulus (Hommel, 1993; Hommel, 1994). This means that the spatial compatibility and automatic imitation effects also build up and decay over time. Combined with differential processing rates of spatial and movement stimulus information, this process results in different time courses for spatial compatibility and automatic imitation effects, as spatial information

is processed more quickly and thus the spatial compatibility effect builds up earlier than the automatic imitation effect, as seen in the results of Experiments 3.1 and 3.2.

One final point concerns the source of the links described above between sensory and motor representations in the brain. The ASL theory proposes that in the case of imitation, these links arise from sensorimotor experience, during which the sensory and motor representations of the same action are activated in a contiguous manner. An associative account can also explain the presence of spatial stimulus-response compatibility: observation of one's performance of an action on one side of space will result in sensory input being highly correlated with the side of space of an action.

As discussed in section 1.2.1, the mirror neuron system appears to perform perceptual-motor translations between observed and performed actions of the sort investigated in this chapter. In order to use imitation as an index of the functioning of the mirror neuron system, it is necessary to show that automatic imitation effects are independent of simple spatial compatibility effects. The current chapter has demonstrated this in two separate experiments, laying the foundation for the use of automatic imitation effects in subsequent chapters, and has also given some insight into the relative time courses of the two effects. The final discussion has outlined how general-purpose mechanisms of stimulus-response compatibility, possibly resulting from associative (sensorimotor) learning, could give rise to both spatial compatibility and automatic imitation effects. Chapter 4 uses the automatic imitation task developed in this chapter to establish whether imitation is dependent on an area of the brain thought to be a key part of the mirror neuron system, while subsequent chapters investigate, using both behavioural and neurophysiological measures, the effects of sensorimotor learning on the mirror neuron system.

4 The role of the mirror neuron system in imitation

Imitation is a process commonly considered to rely on the mirror neuron system (Rizzolatti & Arbib, 1998; Iacoboni et al., 1999; Iacoboni & Dapretto, 2006), but direct evidence for this claim is surprisingly limited. One previous study has shown impairments in imitation following disruption, by repetitive transcranial magnetic stimulation (rTMS), of the functioning of mirror neuron system areas (Heiser et al., 2003), but only error rate, rather than response time, effects were found. Experiment 4.1 measured automatic imitation effects following theta burst rTMS to the left inferior frontal gyrus (IFG), considered to be a key mirror neuron system area. The automatic imitation effect was reduced on spatially compatible, but not on spatially incompatible, trials. It was hypothesised that this differential effect of rTMS could be due to rTMS causing a delay in the perceptual-motor translation process thought to be performed by the mirror neuron system. This possibility was tested in Experiment 4.2 using an automatic imitation task in which movement processing was delayed by presenting the irrelevant movement stimulus later than the discriminative stimulus. The results support the hypothesis that perceptual-motor translation for imitation relies on the mirror neuron system.

The mirror neuron system has been shown to be involved in a wide range of tasks. As discussed in section 1.2.1, a possible explanation for this finding stems from the fact that the tasks used in many neuroimaging studies of the mirror neuron system involve perceptual-motor translations. Chapter 3 investigated imitation, a type of perceptual-motor translation in which the problem of correspondence between observed and executed actions arises most acutely. It was established that automatic imitation effects are types of stimulus-response compatibility effect which are independent of simple

left/right spatial compatibility effects. This distinction is an important one because simple spatial compatibility effects do not require the kind of perceptual-motor translations that are key to solving the correspondence problem and are hypothesised to rely on the mirror neuron system. The data reported in Chapter 3 thus permit the use of automatic imitation as a behavioural measure of the solution of the correspondence problem. Chapter 4 therefore uses an automatic imitation task to investigate whether the mirror neuron system plays a causal role in the perceptual-motor translations required for imitation.

While imitation is a process often assumed to rely on the mirror neuron system (Rizzolatti & Arbib, 1998; Iacoboni et al., 1999; Iacoboni & Dapretto, 2006), Section 1.2.3 showed that the evidence for this assumption, particularly from neuroimaging studies, is weak. Brief consideration of a typical imitation experiment may help to explain why neuroimaging studies have so far failed to show clear evidence for the involvement of the mirror neuron system in imitation. In an imitation experiment, in order to control for general perceptual and motor demands, a task involving the observation and execution of matching stimuli and responses is typically contrasted with a task involving non-matching (incompatible) stimuli and responses. If neurons within the human mirror neuron system have similar properties to those of macaque mirror neurons, then, during incompatible trials, two sets of neurons will be active: those that code for the performance of the executed action – because it is being executed – and those that code for the performance of the observed action, as a result of mirror neurons' action observation-execution matching properties. During imitation (compatible) trials, only one set of neurons will be active, because the observed and executed actions are the same.

As it is not possible, using functional magnetic resonance imaging (fMRI), to distinguish between the activity of different populations of neurons within the same voxel, the above description would suggest that *incompatible*, rather than compatible, observation-execution pairings would result in greater activity in the mirror neuron system, since a greater number of neurons would be active. It is possible in principle that the mirror neuron system performs an additional function that is specific to imitation, i.e. the mirror neuron system may not only *represent* observed and executed actions, but also *translate* the visual representation of an action into the motor representation of the same action. Such a translation or matching function might give rise to additional activity on compatible trials. Nevertheless, it is not clear that any such additional activity would necessarily produce *greater* activity on compatible trials than on incompatible trials. Indeed, the data in the literature are mixed: as discussed in section 1.2.3, Newman-Norlund et al. (2007) found greater mirror neuron system activity on incompatible trials, while Williams et al. (2007) showed the reverse.

The foregoing discussion illustrates the difficulties in using functional imaging studies to investigate imitation. In the mirror neuron system, an increase in blood oxygen level dependent (BOLD) response could result from one of several reasons: the observation of an action; the execution of an action; potentially and speculatively, from some additional imitation-specific process on compatible trials; or a combination of these three factors. Additional techniques are therefore required to provide convergent evidence that a particular cognitive function depends on a particular area of the brain. One increasingly common technique is to disrupt the functioning of a given brain area using repetitive transcranial magnetic stimulation (rTMS).

In several previous studies, rTMS has been used to interfere with the functioning of the mirror neuron system, in particular by targeting the inferior frontal gyrus (IFG) (Pobric & Hamilton, 2006; Avenanti et al., 2007; Urgesi et al., 2007). Only one experiment, however, has investigated the dependence of imitation on the mirror neuron system using rTMS. As mentioned in section 1.2.3, Heiser et al. (2003) used rTMS to disrupt the activity of the left and right pars opercularis of the IFG, both thought to be components of the mirror neuron system, and compared these conditions with stimulation of a control occipital site. Participants made more errors on a finger movement imitation task than on a control task during rTMS to both the left and right pars opercularis, but not during occipital stimulation. The imitation task involved selecting a finger based on the identity of an observed finger movement and then imitating the two button presses performed by the observed finger. The control task was the same except that finger selection and button presses were cued by the location of a red circle rather than a finger movement. While this experiment found an effect of rTMS to the IFG on accuracy of button presses during the imitation task compared to the control task, no effect was seen on response times, movement kinematics, or accuracy of finger selection. If the IFG is involved in perceptual-motor translations for imitation, one might expect to see an effect of IFG stimulation during imitation on one of these measures, which involve perceptual-motor translations at a more refined and complex level than does button press accuracy. It is also unclear whether in the study of Heiser et al. (2003) the order of task presentation was counterbalanced across participants, which could mean that the reported data are the result of practice effects.

Experiment 4.1, therefore, investigated the role of the mirror neuron system in imitation by using rTMS temporarily to disrupt the functioning of the left IFG during the performance of the automatic imitation task used in Chapter 3. The IFG was chosen

because it is thought to be homologous with area F5, where mirror neurons have been found in the macaque (Rizzolatti & Arbib, 1998), and because rTMS to this area has produced deficits in performance on tasks that are also assumed to depend on the mirror neuron system (Pobric & Hamilton, 2006; Avenanti et al., 2007; Urgesi et al., 2007).

4.1 Experiment 4.1

Experiment 4.1 used the automatic imitation task validated in Chapter 3. A relatively new rTMS protocol, continuous theta burst stimulation, was selected. Theta burst stimulation produces long-lasting effects on the brain after a relatively short period of administration: 20 seconds of stimulation over primary motor cortex can reduce cortical excitability, as measured by MEP amplitude, for 20 minutes following stimulation, allowing experiments to be performed subsequent to the administration of rTMS (Huang et al., 2005). This "off-line" stimulation protocol is well suited for the stimulation of an area such as the IFG, where the induction of muscle twitches in the underlying musculature can cause problems of discomfort and distraction during conventional, "on-line" rTMS.

Two rTMS conditions and a baseline non-rTMS condition were used. rTMS was administered to the left IFG, and also to the right posterior parietal cortex (PPC), to control for possible non-specific effects of rTMS. The left IFG site was selected on the basis of the coordinates used by Pobric and Hamilton (2006), who found that stimulation of this site impaired weight judgements based on action observation in a motor simulation task. The parietal control site was chosen to be posterior to areas in inferior parietal cortex that may be part of the mirror neuron system, and coordinates were selected based on those of Muggleton et al. (2006). Figure 4.1 illustrates the locations of the two rTMS sites. The two rTMS conditions were administered at least 24

hours apart, in counterbalanced order. Because of the possibility of carry-over effects of the theta burst rTMS beyond the end of the testing period, the baseline measurement of the automatic imitation effect was taken before administration of rTMS on both days. If the left IFG plays a causal role in the perceptual-motor translation necessary for imitation, the automatic imitation effect should be reduced, relative to baseline, following theta burst rTMS to the left IFG, but not following theta burst rTMS to the right PPC.

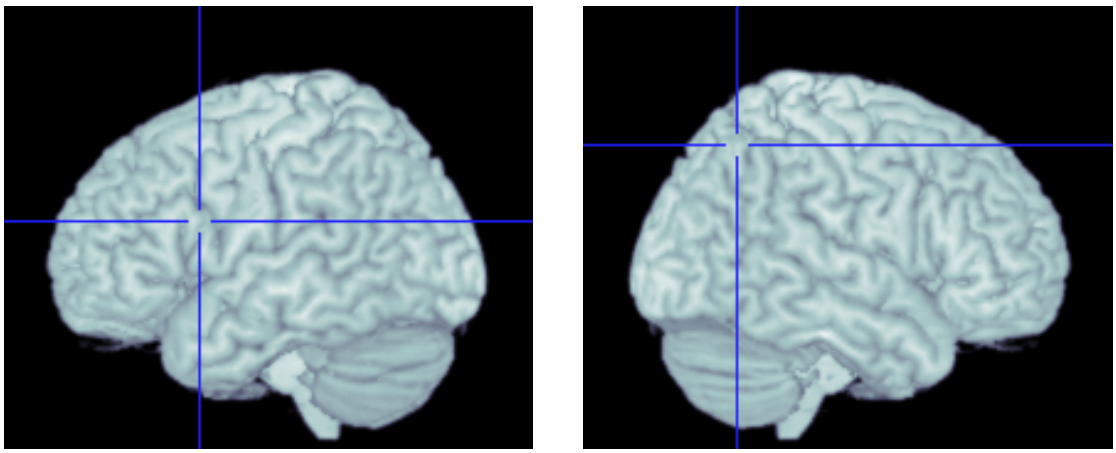


Figure 4.1. rTMS sites used in Experiment 4.1. Left: left IFG (Talairach co-ordinates -42.5, 11.6, 19.9); right: right PPC (42, -58, 52).

4.1.1 Method

4.1.1.1 Participants

Eight right-handed volunteers (four male), aged 24-45 years, participated. All volunteers had previously participated in a functional imaging study, and thus had a structural MRI scan available. Because of the novelty of the theta burst rTMS technique (only two cognitive studies have been published to date: Vallesi et al., 2007; Nyffeler et al., 2008), it was ensured that all volunteers had also previously participated in an rTMS experiment. None of the participants had any contraindications to TMS.

4.1.1.2 Stimuli and apparatus

4.1.1.2.1 Stimuli

The stimuli were identical to those used in Experiment 3.1, with the exception that the discriminative stimuli did not vary in intensity (the higher intensity colours from Experiment 3.1 were used).

4.1.1.2.2 TMS apparatus

Theta burst rTMS was delivered at 80 % of each participant's resting motor threshold (rMT) via a 70-mm figure of eight coil connected to a Magstim Super Rapid machine (The Magstim Company Ltd., Whitland, UK). The two stimulation sites were located using a frameless stereotaxy system (Brainsight^{TM}, Rogue Research Inc., Montreal, Canada). In order to determine rMT, motor evoked potentials (MEPs) were recorded from the first dorsal interosseus (FDI) muscle of the right hand during single-pulse stimulation of the hand area of left primary motor cortex. MEPs were measured and amplified using the same apparatus as that used to record the electromyogram (EMG) (as used in Chapter 3) with the exception that the signal was amplified at a gain of 10,000x. During the measurement of MEPs, data acquisition was triggered by a signal sent from the TMS machine to the data acquisition computer simultaneously with the TMS pulse.

4.1.1.2.3 Stimulus presentation

Stimuli were presented on a 15" CRT screen with a refresh rate of 100 Hz. Time of onset of the final movement position and discriminative stimulus was identified as in Experiment 3.1, by a signal sent via the parallel port to the data acquisition computer.

4.1.1.3 Procedure

The experiment was carried out in two sessions, separated by at least 24 h. Only one site was stimulated in each session. Order of stimulation (IFG or PPC in the first session) was counterbalanced between participants. Each session comprised the following stages: rTMS site localisation; determination of resting motor threshold; practice and two baseline blocks of the automatic imitation task; theta burst stimulation; four blocks of the automatic imitation task; re-measurement of resting motor threshold.

4.1.1.3.1 TMS

Localisation of stimulation sites. The site identified as the left IFG was that used by Pobric and Hamilton (2006), with Talairach co-ordinates of -42.5, 11.6, 19.9. The right PPC site was that used by Muggleton et al. (2006), with Talairach co-ordinates of 42, -58, 52. Each participant's structural MRI scan was normalised to a standard template using FSL software (FMRIB, Oxford, UK). The transformation used in this normalisation was then used to convert the Talairach co-ordinates above into the co-ordinates of the participant's structural space. These individual co-ordinates were marked onto the participant's structural scan within the Brainsight frameless stereotaxy system. At the start of each session, the participant was registered within the Brainsight system and the appropriate rTMS site was marked on a tight-fitting swimming cap which remained in place throughout the session.

Determination of resting motor threshold. rMT was determined using single pulses delivered to the hand area of left hemisphere primary motor cortex. The coil was held with the handle pointing backward at an angle of approximately 45° to the midline. In order to find the hand area, the stimulator was set to 50 % of maximum output, and the coil was moved over motor cortex in 1 cm steps, until an MEP was seen in the FDI

muscle. If no MEP was seen, the output of the stimulator was increased by 3 % of maximum stimulator output. Once an MEP was produced, the site of the maximal MEP amplitude was determined and marked, and stimulator intensity was reduced to the lowest level that produced MEPs of at least 50 μV on five out of 10 pulses, which defines rMT (Rossini et al., 1994). At the end of the experiment, rMT was measured again, in order to determine whether there were any lasting effects of the theta burst stimulation on motor cortex excitability.

Theta burst stimulation. The coil was held on the previously marked rTMS location (IFG or PPC) by hand, with the handle pointing backward at approximately 45° to the midline. 300 pulses were given in a continuous theta burst protocol. This consisted of three pulses at 50 Hz, repeated every 200 ms for 20 s (Huang et al., 2005). Prior to the 300 pulses, one second of theta burst stimulation was given (15 pulses), in order to acquaint the participant with the sensation produced by the stimulation. All participants were informed that if the stimulation was too uncomfortable, they could ask the experimenter to stop at any point. (None of them did so.) Immediately after the stimulation, participants were asked to sit still for five minutes, before commencing the automatic imitation task. This was because maximal inhibitory effects of theta burst stimulation occur at around seven to 14 minutes after stimulation of the motor cortex (Huang et al., 2005).

4.1.1.3.2 Stimulus presentation, data acquisition and data analysis

Stimulus presentation, data acquisition and data analysis were identical to the procedures used in Experiment 3.1, with the following exceptions: prior to theta burst stimulation, 144 trials were presented in two blocks of 72 trials, preceded by 24 practice trials. After theta burst stimulation, 288 trials were presented in four blocks of 72 trials.

4.1.2 Results and Discussion

Mean rMT prior to theta burst stimulation was 50.4 ± 8.6 % of maximum stimulator output. This was unchanged at the end of the experiment, approximately 35 minutes after stimulation, with mean rMTs of 50 ± 9.5 % after IFG stimulation and 50.4 ± 8.6 % after PPC stimulation. This indicates that stimulation of neither site had a lasting effect on motor cortex excitability.

For the purposes of analysis, data were collapsed across the two baseline sessions. Trials on which participants made an error, or on which their RT was more than 2.5 standard deviations from their mean RT for that condition (baseline: 4.5 %; IFG: 4.7 %; PPC: 4.1 %) were excluded from analysis. Trials on which the analysis program failed accurately to detect the onset of the EMG response (baseline: 12.1 %; IFG: 5.9 %; PPC: 6.5 %) were also excluded.

Mean RT was calculated for each of the four trial types (spatially compatible, imitatively compatible; spatially compatible, imitatively incompatible; spatially incompatible, imitatively compatible; spatially incompatible, imitatively incompatible), collapsed across the two different response movements (index and little finger movements), for each of the three rTMS conditions (baseline, IFG, PPC). Because the effect of theta burst stimulation was expected to wear off over time, the RT data were calculated for each block in each of the rTMS conditions. Table 4.1 displays the means and standard errors of these values, along with mean error rates, both separated by block and across all blocks.

Condition	Trial Types							
	Spatially Compatible				Spatially Incompatible			
	Imitatively Compatible		Imitatively Incompatible		Imitatively Compatible		Imitatively Incompatible	
	RT	Errors	RT	Errors	RT	Errors	RT	Errors
Baseline	486 ± 23	2.3 ± 0.6	509 ± 26	2.6 ± 0.5	529 ± 24	2.8 ± 1.0	542 ± 28	5.6 ± 1.3
Left IFG	454 ± 25	1.0 ± 0.4	463 ± 25	3.9 ± 0.9	480 ± 23	3.4 ± 1.5	504 ± 28	5.4 ± 1.0
Right PPC	470 ± 23	2.0 ± 0.4	485 ± 23	3.0 ± 0.7	504 ± 20	2.4 ± 0.6	524 ± 21	4.4 ± 0.9
Baseline block 1	483 ± 23	2.1 ± 0.5	506 ± 24	0.6 ± 0.3	529 ± 21	1.4 ± 0.6	549 ± 30	2.9 ± 0.9
Baseline block 2	484 ± 23	0.4 ± 0.2	518 ± 30	1.5 ± 0.4	527 ± 28	2.1 ± 0.6	535 ± 26	2.1 ± 0.6
IFG block 1	460 ± 24	0.3 ± 0.2	450 ± 31	0.9 ± 0.4	472 ± 22	0.4 ± 0.2	510 ± 33	1.8 ± 0.4
IFG block 2	463 ± 26	0.3 ± 0.2	470 ± 24	0.9 ± 0.4	497 ± 22	0.9 ± 0.6	511 ± 25	0.9 ± 0.3
IFG block 3	455 ± 29	0.1 ± 0.1	470 ± 27	0.9 ± 0.4	484 ± 28	1.0 ± 0.5	495 ± 23	1.9 ± 0.5
IFG block 4	437 ± 23	0.6 ± 0.3	465 ± 24	1.0 ± 0.3	467 ± 22	0.9 ± 0.5	498 ± 35	0.9 ± 0.4
PPC block 1	455 ± 22	0.5 ± 0.2	478 ± 24	0.8 ± 0.3	497 ± 17	0.6 ± 0.3	515 ± 23	1.1 ± 0.5
PPC block 2	467 ± 30	0.4 ± 0.2	498 ± 30	1.0 ± 0.3	510 ± 24	0.4 ± 0.2	524 ± 21	1.1 ± 0.2
PPC block 3	481 ± 27	0.9 ± 0.2	505 ± 27	0.4 ± 0.2	505 ± 21	0.8 ± 0.4	525 ± 24	1.1 ± 0.3
PPC block 4	468 ± 27	0.3 ± 0.3	479 ± 26	0.5 ± 0.3	508 ± 28	0.8 ± 0.4	529 ± 29	1.3 ± 0.5

Table 4.1. Mean ± SEM of RTs (ms) and number of errors in Experiment 4.1. The first three rows give the values collapsed across all blocks of the experiment, while the remaining rows show the values for each block of each condition.

An initial ANOVA was performed on the RT data with within-subjects factors of rTMS condition (baseline, IFG, PPC), spatial compatibility (compatible, incompatible) and imitative compatibility (compatible, incompatible). A significant main effect of rTMS condition was observed: participants were fastest in the IFG condition (475 ± 25 ms), followed by the PPC condition (496 ± 21 ms) and the baseline condition (516 ± 25 ms; $F_{2,14} = 4.7$, $p = 0.028$). Post-hoc t-tests (Bonferroni corrected: $\alpha = 0.017$) revealed a significant difference in RTs between the baseline and IFG conditions ($t_7 = 4.37$, $p=$

0.003). Significant main effects of spatial compatibility ($F_{1,7} = 54.2$, $p < 0.001$) and imitative compatibility ($F_{1,7} = 29.1$, $p = 0.001$) were also observed. There were no significant interactions between any of the factors.

This initial analysis replicated the findings of Chapter 3: spatial compatibility and automatic imitation effects were present, and there was no interaction between these two factors. There was no effect of rTMS condition on the size of the automatic imitation effect. However, the maximal effects of the stimulation protocol used in this experiment are seen between seven and 14 minutes after stimulation (Huang et al., 2005). This time period corresponds with the first block of trials, which commenced five minutes after stimulation and lasted for seven minutes. Therefore an ANOVA with the same within-subjects factors was performed on the data from the first block of trials in each condition.

As in the all-blocks analysis, a significant main effect of rTMS condition was observed: participants were fastest in the IFG condition (473 ± 27 ms), followed by the PPC condition (486 ± 20 ms) and the baseline condition (517 ± 24 ms; $F_{2,14} = 6.5$, $p = 0.010$). Post-hoc t-tests (Bonferroni corrected: $\alpha = 0.017$) showed a trend towards a difference in RTs between the baseline and two rTMS conditions (baseline vs IFG, $t_7 = 3.00$, $p = 0.020$; baseline vs PPC, $t_7 = 2.56$, $p = 0.038$). There are at least two possible explanations for this effect of rTMS condition on RT: it could be an order effect, since in each session the baseline condition took place before the rTMS condition. However, the baseline data were averaged over both sessions, making this explanation less likely. Alternatively, it could be that a generalised effect of rTMS is to increase arousal and hence speed response times. Supporting this explanation, several studies have shown a generalised (non site-specific) speeding of response times

following different rTMS protocols (10 Hz rTMS: Pascual-Leone et al., 1993; Wassermann et al., 1999; 1 Hz rTMS: Koren et al., 2001; Dräger, Breitenstein, Helmke, Kamping, & Knecht, 2004).

Again, as in the all-blocks analysis, significant main effects of spatial compatibility ($F_{1,7} = 93.7$, $p < 0.001$) and imitative compatibility ($F_{1,7} = 7.5$, $p = 0.029$) were observed. None of the two-way interactions reached significance. Of principal interest, there was a significant three-way interaction between rTMS condition, spatial compatibility and imitative compatibility ($F_{2,14} = 4.7$, $p = 0.028$; see Figure 4.2).

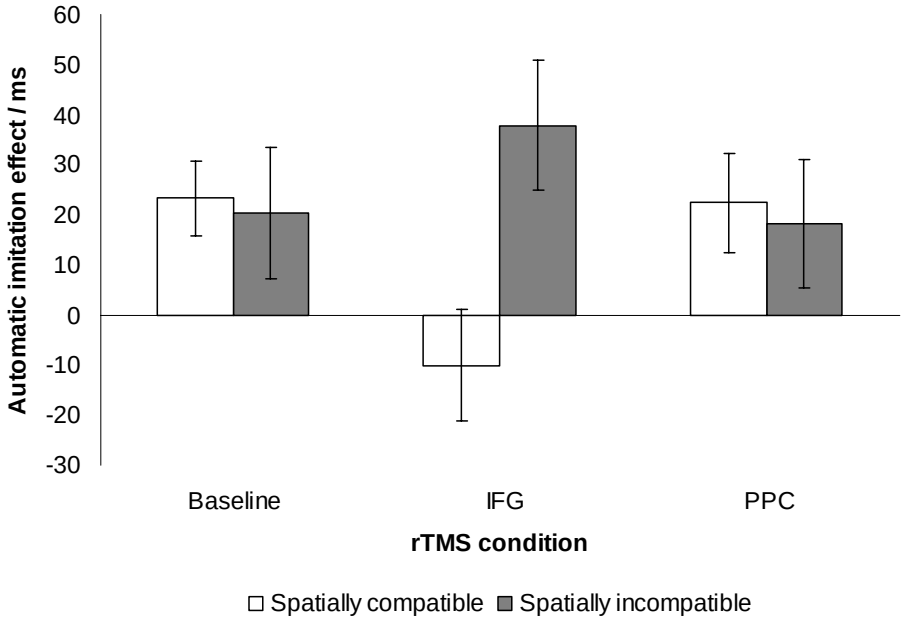


Figure 4.2. Mean ± SEM of automatic imitation effects (RT on imitatively incompatible – RT on imitatively compatible trials) for spatially compatible and spatially incompatible trials in the first block of each of the three rTMS conditions of Experiment 4.1.

Simple interaction analysis revealed a significant two-way interaction between spatial and imitative compatibility in the IFG stimulation condition ($F_{1,7} = 7.9$, $p = 0.026$), but not in the other two conditions. This indicates that in the first block of trials, in which the effect of rTMS was expected to be strongest, the automatic imitation effect was

abolished under IFG stimulation on spatially compatible, but not spatially incompatible, trials.

Since the effect of theta burst rTMS is expected to reduce over time following stimulation, two linear trend analyses were performed on the data from the IFG condition for all four blocks of the experiment. These analyses investigated the time course over testing blocks of the effect of IFG stimulation on the automatic imitation effect. The first analysis tested for a linear trend in the interaction between spatial and imitative compatibility. This trend was significant ($F_{1,7} = 8.0$, $p = 0.026$), suggesting that the difference between the size of the automatic imitation effect on spatially compatible and spatially incompatible trials reduced over time following IFG stimulation. This interpretation was confirmed by the second analysis, which tested for a linear trend in the size of the automatic imitation effect across the four blocks of trials following IFG stimulation, on spatially compatible trials only. This trend was significant ($F_{1,7} = 10.9$, $p = 0.013$): the size of the automatic imitation effect on spatially compatible trials increased over time (i.e. recovered) following IFG stimulation. These effects are illustrated in Figure 4.3.

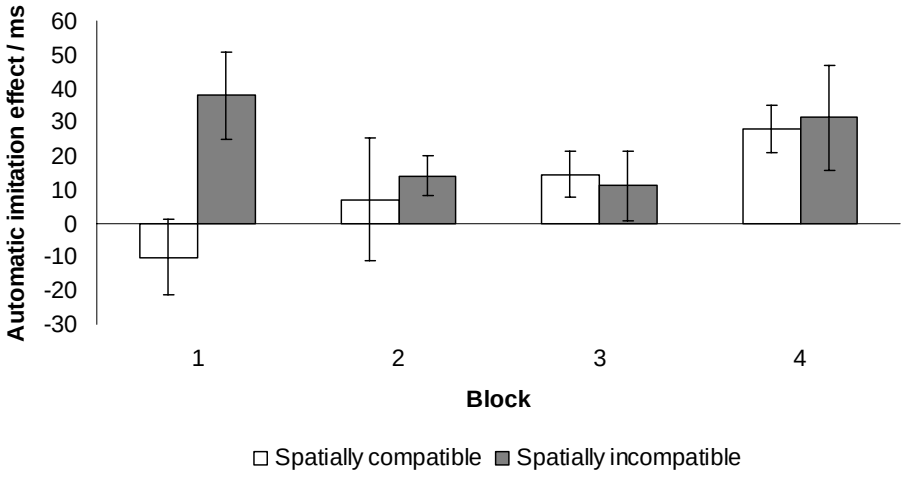


Figure 4.3. Mean ± SEM of automatic imitation effects for spatially compatible and spatially incompatible trials across the four blocks of trials following IFG stimulation in Experiment 4.1.

These linear trends are consistent with the suggestion that the reduced automatic imitation effect on spatially compatible trials is an effect of rTMS which wears off over time, thus supporting the hypothesis that the left IFG plays a causal role in perceptual-motor translation for imitation.

In order to rule out speed/accuracy trade-offs, ANOVA with within-subjects factors of rTMS condition, spatial compatibility and imitative compatibility was also performed on the error data from the first block of each condition. There was a significant main effect of rTMS condition: participants made more errors in the baseline condition than in either of the rTMS conditions (1.8 ± 0.6 compared to 0.8 ± 0.3 in each of the rTMS conditions; $F_{2,14} = 10.5$, $p = 0.002$). There was a significant interaction between spatial and imitative compatibility: participants made more errors on imitatively incompatible than on imitatively compatible trials, but only when these trials were spatially incompatible; for spatially compatible trials, this error pattern was reversed ($F_{1,7} = 74.7$, $p < 0.001$). This interaction was modulated, however, by a three-way interaction between spatial compatibility, imitative compatibility and rTMS condition ($F_{2,14} = 8.3$, $p = 0.004$). Simple interaction analysis revealed that the interaction between spatial and imitative compatibility described above was strongest for the baseline condition ($F_{1,7} = 84.0$, $p < 0.001$), while in the two rTMS conditions there was no interaction between spatial and imitative compatibility. The error data therefore cannot account for the results of the RT analysis in terms of a speed/accuracy trade-off, since the interaction between spatial and imitative compatibility was only seen in the baseline condition.

The lack of an effect of rTMS on the size of the automatic imitation effect on spatially incompatible trials was unexpected, but can be understood if one considers that spatially

incompatible trials are associated with slower response times than spatially compatible trials. This suggests that one factor affecting whether rTMS interferes with automatic imitation effects is response speed. It could be that, rather than preventing the perceptual-motor translation process entirely, the effect of the rTMS is to *delay* this translation. The result of such a delay would be a reduction in the automatic imitation effect on fast, i.e. spatially compatible, trials, but a preserved automatic imitation effect on slower, spatially incompatible, trials. Figure 4.4 illustrates the anticipated outcome of such a delay, in terms of the build-up and decay of the automatic imitation effect over time.

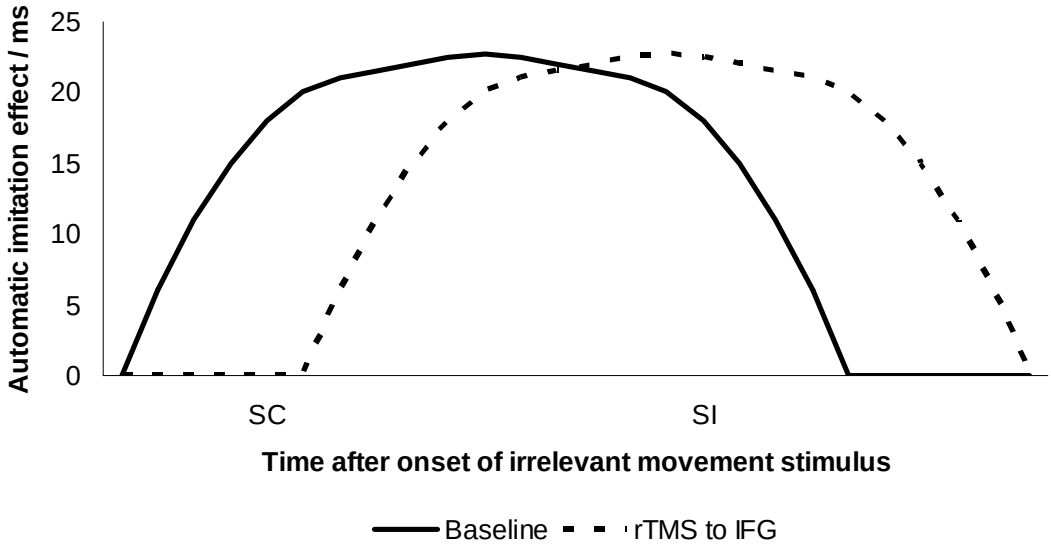


Figure 4.4. Illustration of the delay explanation of the results of Experiment 4.1. "SC" and "SI" indicate time of response selection on spatially compatible and spatially incompatible trials, respectively. See text for further explanation.

As time (left to right along the *x* axis) passes after the onset of the irrelevant movement stimulus, the automatic imitation effect builds up and then decays again, as discussed in section 3.3 (see also Hommel, 1993; Hommel, 1994). In the baseline condition (solid line), the perceptual-motor translation process is not delayed and therefore the build-up begins immediately; in the rTMS to IFG condition (dashed line), the perceptual-motor

translation process is delayed and thus the build-up of the automatic imitation effect begins later. “SC” and “SI” represent the time points at which responses are selected on spatially compatible and spatially incompatible trials, respectively. In the baseline condition (solid line), response selection at both of these times will result in automatic imitation effects of similar sizes. However, in the delayed IFG condition (dashed line), response selection on spatially compatible trials (early) will result in a smaller automatic imitation effect than response selection on spatially incompatible trials (late).

Experiment 4.2 sought to test the delay explanation of the results of Experiment 4.1. If the effect of rTMS to the left IFG is to delay the perceptual-motor translation process, then one would expect to see the same pattern of results as those of Experiment 4.1 when, instead of applying rTMS to the left IFG, one delays movement processing by presenting the movement stimulus after the discriminative stimulus. This manipulation should delay processing of the irrelevant movement stimulus with respect to the time of response selection, and can be implemented in a similar manner as in Experiment 3.2.[1] Experiment 4.2 therefore delayed the presentation of the irrelevant movement stimulus with respect to the discriminative stimulus, in order to investigate the effect of delaying the processing of the irrelevant movement on the size of the automatic imitation effect on spatially compatible and spatially incompatible trials.

[1]Note, however, that Experiment 3.2 was concerned with the timing of response selection and thus described the discriminative stimulus as being presented either before or after the irrelevant movement stimulus. In contrast, in Experiment 4.2, the emphasis is now placed on the timing of movement processing. Thus, Experiment 4.2 presented the irrelevant movement stimulus after the discriminative stimulus. The significance of this change in terminology is that the “after” conditions of Experiment 4.2 were structured in a similar manner to the “before” conditions of Experiment 3.2.

4.2 Experiment 4.2

Experiment 4.2 was based on a similar design to that of Experiment 3.2, but only included trials in which the irrelevant movement stimulus was presented at the same time as or after the discriminative stimulus. Three levels of offset were used: the irrelevant movement stimulus was presented simultaneously with (0 ms), 40 ms after, or 80 ms after the discriminative stimulus. The choice of offsets was based on the size of the spatial compatibility effect in Experiment 3.1, which was about 40 ms. If the difference between the effect of rTMS on spatially compatible and spatially incompatible trials is due to the differential response speed in these two conditions, then the delay in the perceptual-motor translation process (which, it is hypothesised, is produced by rTMS to the left IFG) must be of a similar order of magnitude to the difference between the response speeds on spatially compatible and spatially incompatible trials. The experiment was therefore designed to test the delay hypothesis outlined above by presenting the irrelevant stimulus at two offsets: one equivalent to, and one slightly greater than, this difference in response speeds. Based on the results of Experiment 4.1, it was predicted that the automatic imitation effect would be reduced in the 40 ms offset condition compared to the 0 ms condition, but only on spatially compatible trials. The 80 ms condition was predicted to show a similar pattern, with a smaller automatic imitation effect for spatially compatible trials, but also a reduced automatic imitation effect for spatially incompatible trials, as these trials would now be affected by the longer delay between the presentation of the discriminative stimulus and the irrelevant movement stimulus.

4.2.1 Method

4.2.1.1 Participants

Eight right-handed volunteers (one male), aged 20-29 years, participated.

4.2.1.2 Stimuli and apparatus

The stimuli were identical to those used in Experiment 3.2, with the exception that the irrelevant movement stimulus was presented at variable intervals after the onset of the discriminative stimulus (see Procedure). The apparatus used was identical to that used in Experiment 3.2: data acquisition was triggered at the time of onset of the discriminative stimulus.

4.2.1.3 Procedure

The procedure was the same as Experiment 3.2, with the following exceptions. The video of the still hand was presented for 800 ms, after which time the discriminative stimulus was presented (Figure 4.5). The irrelevant movement stimulus was then presented at one of three offsets with respect to the irrelevant movement stimulus (0 ms, 40 ms after, or 80 ms after). Thus, the irrelevant movement stimulus could appear at the same time as, or shortly after the discriminative stimulus. Participants were tested in two sessions, 24 hours apart. In each of the two sessions, a total of 576 trials were presented in a random order in 12 blocks of 48 trials. Each of the combinations of trial type (spatially compatible, imitatively compatible; spatially compatible, imitatively incompatible; spatially incompatible, imitatively compatible; spatially incompatible, imitatively incompatible) and offset (0 ms, 40 ms, 80 ms) was presented four times in each block, twice for each of the response movements (index and little finger movements). Twelve randomly selected practice trials were given before the start of the experiment.

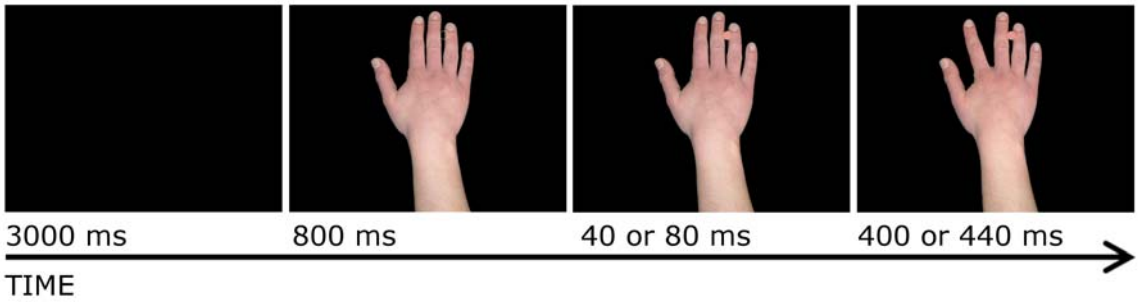


Figure 4.5. Procedure for Experiment 4.2. An example of one offset trial is shown.

4.2.2 Results and Discussion

Trials on which participants made an error, or on which their RT was more than 2.5 standard deviations from their mean RT (4.0 %) were excluded from analysis. Trials on which the analysis program failed accurately to detect the onset of the EMG response (1.2 %) were also excluded.

Mean RT was calculated for each of the four trial types at each of the three offsets, collapsed across the two sessions and the two different response movements (Table 4.2). The automatic imitation effects for spatially compatible and spatially incompatible trials were calculated at each of the three offsets and are displayed in Figure 4.6.

	Trial Types							
	Spatially Compatible				Spatially Incompatible			
	Imitatively Compatible		Imitatively Incompatible		Imitatively Compatible		Imitatively Incompatible	
Offset	RT	Errors	RT	Errors	RT	Errors	RT	Errors
80 ms	425 ± 28	0.8 ± 0.2	434 ± 26	2.3 ± 0.5	454 ± 28	1.6 ± 0.4	467 ± 29	2.4 ± 0.5
40 ms	425 ± 29	1.0 ± 0.3	436 ± 28	2.0 ± 0.3	453 ± 29	1.9 ± 0.4	470 ± 33	3.5 ± 0.6
0 ms	418 ± 29	0.9 ± 0.2	440 ± 30	2.2 ± 0.3	449 ± 28	1.4 ± 0.6	464 ± 31	3.4 ± 0.5

Table 4.2. Mean ± SEM of RTs (ms) and number of errors for each of the four trial types at each of the three levels of offset in Experiment 4.2.

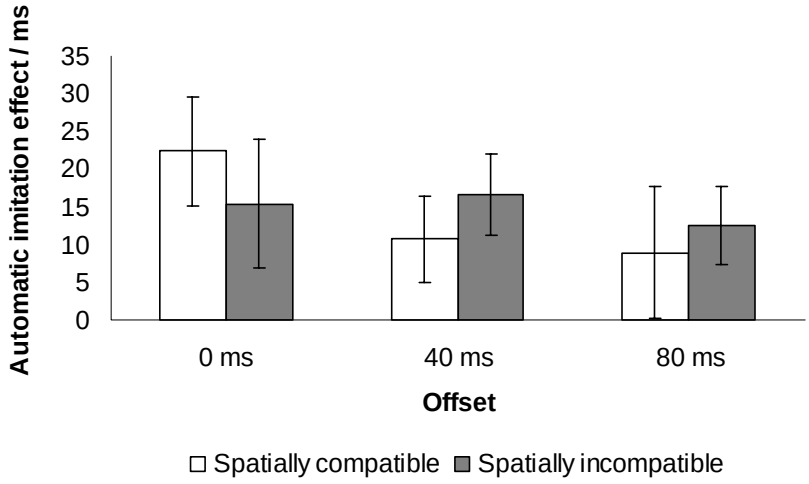


Figure 4.6. Mean ± SEM of automatic imitation effects for spatially compatible and spatially incompatible trials at each of the three levels of offset in Experiment 4.2.

The RT data were subjected to ANOVA with within-subjects factors of offset between discriminative and irrelevant stimuli (0 ms, 40 ms, 80 ms), spatial compatibility (compatible, incompatible), and imitative compatibility (compatible, incompatible).

There were significant main effects of spatial compatibility (430 ms compared with 460 ms; $F_{1,7} = 37.6$, $p < 0.001$) and of imitative compatibility (438 ms compared with 452 ms; $F_{1,7} = 19.8$, $p = 0.003$). The three-way interaction of interest was not statistically significant ($F_{2,14} = 2.0$, $p = 0.175$). However, as indicated in Figure 4.6, the effect was in the predicted direction: there was a reduction in the automatic imitation effect on spatially compatible trials when movement processing was delayed by 40 ms compared to when the discriminative and irrelevant stimuli were simultaneous, but no reduction on spatially incompatible trials. Simple interaction analysis comparing the sizes of the automatic imitation effects on spatially compatible and spatially incompatible trials for the two offsets for which a difference had been predicted (0 ms and 40 ms) revealed a marginally significant effect ($F_{1,7} = 5.4$, $p = 0.052$).

ANOVA with the same factors was also performed on the error data to rule out speed/accuracy trade-offs. There was a trend towards a main effect of spatial compatibility: participants made more errors on spatially incompatible than on spatially compatible trials (2.4 compared to 1.5; $F_{1,7} = 4.3$, $p = 0.076$) and a significant main effect of imitative compatibility: participants made more errors on imitatively incompatible than compatible trials (2.6 compared to 1.3; $F_{1,7} = 18.6$, $p = 0.004$).

Experiment 4.2 replicated the finding of independent effects of spatial and imitative compatibility that was observed in Experiments 3.1, 3.2 and 4.1. The predicted three-way interaction between offset, spatial compatibility and imitative compatibility was not present when all three offsets were included in the analysis. However, simple interaction analysis including the two offsets predicted, on the basis of the size of the spatial compatibility effect, to show the greatest difference (0 ms and 40 ms) showed a marginal three-way interaction: the automatic imitation effect was reduced on spatially compatible trials in the 40 ms condition, but unchanged on spatially incompatible trials. This result is consistent with the hypothesis that the pattern observed in Experiment 4.1, of a reduced automatic imitation effect on spatially compatible but not on spatially incompatible trials following rTMS to left IFG, is due to a delay in the perceptual-motor translation of the irrelevant movement stimulus.

4.3 General Discussion

The experiments reported in this chapter provide preliminary evidence that the left IFG plays a causal role in perceptual-motor translation for imitation. Experiment 4.1 demonstrated that theta burst rTMS of the left IFG reduced the automatic imitation effect in trials where the correct response was spatially compatible with the irrelevant movement stimulus. No effect of rTMS was seen on spatially incompatible trials. It was

hypothesised that this pattern of results could be due to rTMS delaying, rather than preventing entirely, the perceptual-motor translation that is presumed to underlie the automatic imitation effect. A delay effect of rTMS was also found in a recent study which showed that 1-Hz rTMS to parietal cortex delayed the onset of the "rubber hand illusion" (Kammers et al., in press). Experiment 4.2 provided some support for this hypothesis by simulating a delay in perceptual-motor translation. When movement processing was delayed with respect to response preparation, the automatic imitation effect was reduced on spatially compatible, but not on spatially incompatible trials. However, this effect was only marginally significant, and therefore it is not clear whether the delayed processing hypothesis provides a sufficient explanation for the specificity of the rTMS effect observed in Experiment 4.1. It is possible that choosing offset times for Experiment 4.2 based on the size of the mean spatial compatibility effect in previous experiments did not provide a sufficient level of precision, and that clearer results would be obtained by using subject-specific offset times tailored to the size of each participant's spatial compatibility effect.

A further test of the delayed processing hypothesis might be to perform an rTMS experiment that reverses the logic of Experiment 4.2: that is, to bring forward movement processing by presenting the irrelevant movement stimulus before the discriminative stimulus. If the delayed processing hypothesis is correct, this manipulation should restore the automatic imitation effect on spatially compatible trials following rTMS to left IFG because the delay to the perceptual-motor translation process will have passed and the automatic imitation effect will have begun to build up by the time of response selection.

Theta burst rTMS to left IFG had only a short-lived effect on the size of the automatic imitation effect on spatially compatible trials, with the strongest effect appearing in the first block of trials. This is probably because of the theta burst paradigm that was chosen, consisting of 20 seconds of stimulation (300 pulses in total). This paradigm, when delivered over primary motor cortex, suppressed cortical excitability as measured using MEPs for 20 minutes (Huang et al., 2005); however, the strongest effects were seen between seven and 14 minutes after stimulation, which corresponds to the first block of Experiment 4.1. Huang et al (2005) found that a longer theta burst paradigm, consisting of 40 seconds of stimulation (600 pulses in total), had an effect on the excitability of primary motor cortex which lasted over 45 minutes. However, the site stimulated in Experiment 4.1 is more uncomfortable than that of primary motor cortex, due to the presence of underlying musculature. Left IFG stimulation with the paradigm involving 40 seconds of stimulation was piloted on a participant with extensive experience of rTMS, and as a result it was decided that for this site, the 20 seconds paradigm would be more tolerable for participants. This may have produced a smaller and shorter-lasting effect than had the 40 seconds paradigm been used. Because there are currently only two published papers on the effects of theta burst rTMS in cognition it remains possible that a different theta burst paradigm may yield stronger effects.

The coordinates of the two stimulation sites were selected on the basis of previous rTMS experiments. The left IFG site was the same as that used by Pobric and Hamilton (2006) and was slightly more medial than the site used by Avenanti et al. (2007) and Urgesi et al. (2007). The *y* and *z* coordinates were very similar, however, so it is likely that a similar area of the brain was stimulated in all four experiments, as current would be induced in the more lateral location used by Avenanti et al. (2007) and Urgesi et al.

(2007), when stimulating the more medial site of Experiment 4.1 and Pobric and Hamilton (2006).

The right PPC site was selected to be posterior to areas of the parietal lobe thought to be part of the mirror neuron system. There was no effect of stimulation of the right PPC on the size of the automatic imitation effect, so it is likely that this site is not involved in imitation. This area of parietal cortex is known to be involved in spatial attention (Brighina, La Bua, Oliveri, Piazza, & Fierro, 2000; Bjoertomt, Cowey, & Walsh, 2002), but no effect of rTMS was seen on the size of the spatial compatibility effect. Previous studies have found that stimulation of this area can lead to neglect-like failure to detect a target (Muggleton et al., 2006); however, an additional analysis of Experiment 4.1 did not find an effect of side of space of the irrelevant movement stimulus on RTs following rTMS to right PPC. This could be because the neglect-like symptoms produced by rTMS in the experiment of Muggleton et al. (2006) were scene- rather than object-based, i.e. they only occurred on the far left of space, whereas the hand stimulus presented in Experiment 4.1 was located centrally, at fixation. The lack of an effect of stimulation of the right PPC suggests that it was successful as a control site, as it indicates that the effects seen after stimulation of the left IFG are site-specific, rather than being generalised effects of theta burst rTMS.

The experiments reported in this chapter showed a significant effect of theta burst rTMS of left IFG on the size of the automatic imitation effect on spatially compatible trials, which may be caused by a delay to the process of perceptual-motor translation. These results represent an advance on the data of Heiser et al. (2003) in that they demonstrate an effect of rTMS on the size of the automatic imitation effect, rather than on error rates. The modification of the size of the automatic imitation effect in the current study

can be argued to provide stronger evidence of the role of the IFG in perceptual-motor translations for imitation than does an error rate effect on response button selection. This is because the automatic nature of automatic imitation effects makes them a more direct measure of perceptual-motor translations than an intentional imitation task, which involves other non-specific control processes. Also, Heiser et al. (2003) did not show an effect of rTMS on the identity of the finger selected for a response but only on response button selection, which is a less direct measure of perceptual-motor translation than is finger selection. In conclusion, these results provide additional evidence that the IFG, and, by extrapolation, the human mirror neuron system, plays a causal role in the translation of the perceptual representation of an action into its motor representation, a translation that underlies the ability to imitate.

5 Effects of sensorimotor learning on motor activation during action observation

Despite intensive investigation of the perceptual-motor matching properties of the mirror neuron system, little research has previously been performed into how these matching properties arise. Experiment 5.1 used single-pulse transcranial magnetic stimulation (TMS) to measure motor evoked potentials (MEPs) from finger muscles during the observation of single finger movements, presented in a random order. The results of this experiment validated the use of this design to measure the automatic activation of the motor cortex during action observation, considered to reflect the activity of the mirror neuron system. Experiment 5.2 used this experimental design to assess the effects of sensorimotor experience on the mirror neuron system. Participants were given incompatible sensorimotor training during which they performed one movement while observing another. This training reversed the matching muscle-specific effect of action observation found in Experiment 5.1, indicating that sensorimotor learning can alter the activation of the motor cortex during action observation. The results of this experiment are consistent with the hypothesis that the perceptual-motor matching properties of the mirror neuron system arise as a result of sensorimotor experience.

Chapter 4 provided evidence that automatic imitation relies on the human mirror neuron system, suggesting that the mirror neuron system plays a causal role in the solution of the correspondence problem by matching the perceptual representation of an action to its motor representation. There are two types of possible explanation, discussed in section 1.3, of how the mirror neuron system's perceptual-motor matching properties arise: they may be innately specified, or they may result from experience acquired in the

course of development. If the properties of the mirror neuron system arise through experience, there are further possibilities regarding the type of experience necessary to produce the system's perceptual-motor matching properties. For example, purely sensory experience of perceiving actions, or purely motor experience of performing actions, may suffice to produce these properties; they may arise as a result of the combination of purely sensory and purely motor experience occurring on different occasions; or they may result from sensorimotor experience in which the perceptual and the motor representations of an action are active in a contiguous and / or contingent fashion. While there is some neuroscientific evidence that suggests the human mirror neuron system is sensitive to sensory and motor experience of actions (Haslinger et al., 2005; Calvo-Merino et al., 2005; D'Ausilio et al., 2006; Cross et al., 2006; Calvo-Merino et al., 2006), in none of these experiments was sensory or motor experience dissociated from sensorimotor experience (see also section 1.5). Thus, if the perceptual-motor matching properties of the mirror neuron system do arise through experience, it is not yet clear which type of experience is necessary to produce these properties.

Behavioural studies have provided evidence for the effects of sensorimotor experience on automatic imitation. Heyes et al. (2005) showed that a group of participants given *incompatible* sensorimotor training (where the observation of an opening hand was followed by the performance of a hand closing movement and the observation of a closing hand was followed by the performance of a hand opening movement) subsequently displayed a smaller automatic imitation effect than participants given *compatible* sensorimotor training (where the observation of an opening hand was followed by the performance of a hand opening movement, and the observation of a closing hand was followed by the performance of a hand closing movement). It is important to note that both groups received the same amount of purely sensory

experience of observing each of the actions, and the same amount of purely motor experience of performing each of the actions; it was only the sensorimotor experience (the predictive relationship between the observation and performance of particular actions) which differed between the groups. In addition, *compatible* sensorimotor experience has been shown to enhance automatic imitation of robotic actions (Press et al., 2007), again indicating that sensorimotor learning can affect this putative index of mirror neuron system functioning.

While these behavioural data provide compelling evidence that sensorimotor learning can modulate automatic imitation, they do not show conclusively that sensorimotor learning has an effect on the mirror neuron system. This is because the effect of sensorimotor learning on behavioural measures of automatic imitation could be mediated via another route: the retrieval of training instructions during the post-training test. It has been shown that task instructions can set up short-term associations which affect participants' performance in a spatial compatibility task even when no trials are presented for which these instructions are relevant (De Houwer, Beckers, Vandorpe, & Custers, 2005). In other words, the possibility of having to perform a certain response to a particular stimulus changes the participants' task sets. It could therefore be the case that in the studies of Heyes et al. (2005) and Press et al. (2007), remembering the training instructions altered participants' responses during the post-training automatic imitation task. That is, recall of the training instructions could set up short-term associations between the observation of one movement and the performance of the instructed movement, such that when participants observed a particular movement, the motor representation for the performance of the relevant (instructed) movement was activated, modifying the post-training automatic imitation effect. In order to show that the effect of sensorimotor learning on automatic imitation is the result of the

modification of long-term perceptual-motor associations in the mirror neuron system, neuroscientific methods such as transcranial magnetic stimulation (TMS) and functional magnetic resonance imaging (fMRI) are useful. These methods have two advantages compared with behavioural methods alone: first, they provide a more direct measure of the effects of sensorimotor learning on the mirror neuron system; and second, the effects of sensorimotor learning can be measured without the need for a behavioural response, thus ruling out the possibility that participants are retrieving their training instructions and using these instructions to guide their responses on the post-training test. In this chapter, therefore, TMS was used to measure, via motor evoked potentials (MEPs), the effects of sensorimotor learning on the mirror neuron system. Muscle-specific motor cortical activity (Fadiga et al., 1995) was assessed during action observation before and after sensorimotor training.

However, before the above sensorimotor learning experiment could be carried out, it was necessary to address a question that is outstanding from the current MEP literature: whether matching muscle-specific enhancement of MEP size during action observation (e.g. Fadiga et al., 1995; Strafella & Paus, 2000) is the result of a controlled or an automatic process. This is an important question to address because, if MEP enhancement during action observation is the result of a controlled process, then the sensorimotor training experiment outlined above could be subject to a similar confound as that which affects behavioural responses: it is possible that participants could retrieve the training instructions for the observed movement, and activate in a controlled manner the motor representation of the relevant (compatible or incompatible) action, enhancing MEPs for that particular muscle. This is not an unfounded concern: it is known that imagery of an action has similar matching muscle-specific effects on motor cortical activity, as measured by MEPs, to observation of that action (Fadiga et al., 1999;

Rossini, Rossi, Pasqualetti, & Tecchio, 1999; Patuzzo, Fiaschi, & Manganotti, 2003). Thus, if participants can use a controlled process to imagine performing the relevant movement based on their training instructions, this could produce apparent effects of training on motor cortical activity during action observation, which might in fact be instruction effects.

The question of whether MEP enhancement during action observation is the result of a controlled or an automatic process has not been answered by previous MEP studies of action observation because most of the studies used to support the existence of a muscle-specific action observation-execution matching system have presented blocked or repetitive actions. Such experimental designs leave open the possibility that the results of these experiments are in fact being produced through controlled mental imagery of the predicted course of the observed actions rather than as a result of the automatic, direct activation of the motor representations of the observed actions via perceptual-motor translations. In some experiments the stimuli were presented in relatively long trials, where the muscle involved is active for the whole trial (Fadiga et al., 1995; Strafella & Paus, 2000; Gangitano et al., 2001; Gangitano et al., 2004; Aziz-Zadeh et al., 2004; D'Ausilio et al., 2006): for example, a 60-second video of a hand writing was presented by Strafella and Paus (2000). In other experiments, trials were presented in blocks of the same trial type, or each trial contained several repetitions of the same movement (Aziz-Zadeh et al., 2002; Patuzzo et al., 2003; Clark, Tremblay, & Ste-Marie, 2004; Romani, Cesari, Urgesi, Facchini, & Aglioti, 2005; Avenanti et al., 2005; Avenanti et al., 2006). In both of these types of experiment, the predictability of the trials could allow participants to anticipate the identity of the forthcoming movement and imagine performing the movement, which would produce the reported MEP enhancement via a controlled process of motor imagery, rather than via automatic

activation of the motor representation of the observed movement.[2] Thus, it is currently unclear from the results of previous studies whether motor activation following action observation is the result of a controlled process or an automatic process.

The foregoing discussion indicates that the results of previous studies using blocked designs or long trials do not demonstrate convincingly that the observation of single movements, as happens in everyday life, has an effect on MEP size which occurs automatically without the use of controlled motor imagery. An "event-related" design, in which randomised single-movement stimuli were presented, would overcome this potential objection. Randomised presentation means that it is not possible to predict what the upcoming movement will be, and together with the short duration of single

[2] This possibility raises a question regarding what the "imagination" of a movement actually entails. Even if motor imagery is contributing to the results of TMS action observation experiments, it is still the case that participants are translating the sensory information acquired during observation of a movement into matching muscle-specific motor cortical activation. What are the candidate mechanisms by which this translation might take place? One possibility is that participants verbally identify the observed movement and then use the semantic representation of that movement to activate the motor representation. Alternatively, participants could mentally simulate performing the observed movement. While "imagery" and "simulation" imply an active, controlled process (Decety & Grèzes, 2006), it is not clear how such a simulation in fact differs, in terms of its underlying cognitive requirements, from the automatic activation of a motor representation by action observation: the correspondence problem between the perceptual and motor representations of an action still has to be solved in both cases, which would require the perceptual-motor matching properties of the mirror neuron system. In other words, although the designs of previous TMS/MEP action observation studies may encourage motor imagery of the observed movement, such a process of controlled mental imagery may still rely on the mirror neuron system.

movements, makes it highly implausible that participants would have sufficient time intentionally to form a mental image of movement performance. Experiment 5.1 therefore investigated, using MEPs, whether the motor cortex is activated automatically in a matching muscle-specific manner in response to the observation of highly experimentally controlled single movement stimuli in a randomised design.

5.1 Experiment 5.1

The experiment comprised four trial types. On every trial, participants observed a neutral (resting) hand, followed by one of four images: two control images (resting hand, i.e. no change, or receding hand) and two movement images (the index or little finger in an abducted position; see Figure 5.1). Single-pulse TMS to the hand area of left primary motor cortex produced MEPs which were recorded simultaneously from the two muscles that would be involved in the two movements: the first dorsal interosseus (FDI; index finger abductor) and abductor digiti minimi (ADM; little finger abductor) of the right hand. In order to maintain participants' attention to the stimuli, an attentional control task was used (see Procedure). Stimuli were presented in a randomised order. If a controlled process of motor imagery is the basis of the effects of action observation on MEPs shown by previous studies, then no muscle-specific effects of action observation should be seen. If, however, an automatic process produces action observation effects at the level of individual movements, then matching muscle-specific MEP enhancement should be observed. This would be manifested as an interaction between the movement observed and the muscle recorded: the FDI, which controls index finger movements, should show larger MEPs for the observation of index than of little finger movements, while the ADM, which controls little finger movements, should show larger MEPs for the observation of little than of index finger movements.

5.1.1 Method

5.1.1.1 Participants

24 right-handed volunteers (16 male), aged 19-66 years, participated. None of the participants had any contraindications to TMS.

5.1.1.2 Stimuli and Apparatus

5.1.1.2.1 Stimuli

The stimuli (Figure 5.1) were video files of a male or female right hand making an abduction movement of either the index or little finger, resting in a neutral position, or receding (moving away from the observer into the screen). Videos were created from two still images of the hand, initially in a neutral position and subsequently in the final movement position. The female hand index and little finger stimuli were identical to those used in Experiments 3.1, 3.2, 4.1 and 4.2, except that a discriminative stimulus was not presented. The resting hand stimulus consisted of a continuation of the neutral hand image. The receding hand was created by scaling the neutral hand image by a factor of 0.95; when presented subsequent to the neutral hand, this created apparent motion away from the observer. This stimulus subtended a visual angle of 14.1° vertically and 7.2° horizontally. The male hand videos were created in the same way as the female videos, with the exception that a male model was used; they subtended a visual angle of 14.9° vertically and between 7.2° (receding hand) and 9.0° (little finger movement) horizontally, when viewed at a distance of 57cm. The finger movements subtended an angle of 18° (index) and 28° (little) from the neutral position. As part of the attentional control task, "catch" stimuli were presented on 11 % of trials (see Procedure). These stimuli consisted of a faint, solid, flesh-coloured circle (~1° visual angle). The colour of the circle was equal to the mean colour of the hand stimulus, calculated by finding the mean intensity of the red, green and blue components of every

coloured pixel in the hand image. The circle was presented at one of six locations on the final movement position image: on the top, central or bottom part of either the index or little finger. If the catch trial was of an index or little finger movement, the circle was always presented on the moving finger.

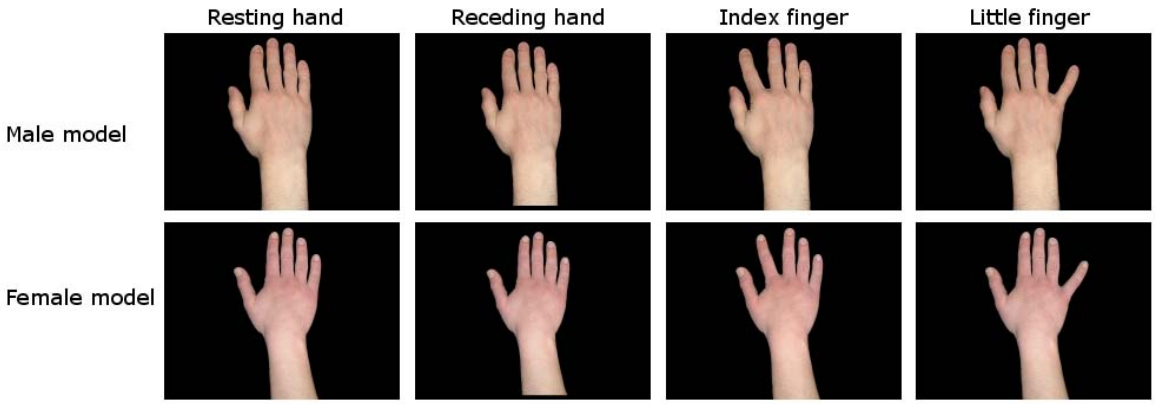


Figure 5.1. Stimuli used in Experiments 5.1 and 5.2. The first column shows the neutral hand that was presented at the start of every trial; this stimulus remained on the screen in 25 % of trials as the resting hand control stimulus. Two of the stimuli (male little finger and female receding hand) show examples of catch trials: a small flesh-coloured circle is present on the little or index finger, respectively.

5.1.1.2.2 TMS apparatus

Single-pulse TMS was delivered at 110 % of each participant's resting motor threshold via a 70-mm figure of eight coil connected to a Magstim Super Rapid machine (The Magstim Company Ltd., Whitland, UK). TMS pulses were triggered by the presence of a white square in the corner of the stimulus videos. This square was presented on a particular frame of the video, after the onset of the final movement position (see Procedure). A photodiode placed on the monitor of the stimulus presentation computer detected the presence of the square and sent a trigger pulse to the TMS machine. Motor evoked potentials were recorded from the FDI and ADM muscles of the right hand using the same apparatus as that used in Experiment 4.1.

5.1.1.2.3 Stimulus presentation and data acquisition

Stimuli were presented on a 15" CRT screen with a refresh rate of 100 Hz. MEPs were measured and amplified using the same apparatus as that used to record the electromyogram (EMG) in the previous experiments, with the exception that the signal was amplified at a gain of 10,000x. Data acquisition was triggered by a signal sent from the TMS machine to the data acquisition computer simultaneously with the TMS pulse.

5.1.1.3 Procedure

5.1.1.3.1 TMS

rMT was determined using single pulses of TMS delivered to the hand area of left hemisphere primary motor cortex. The coil was held with the handle pointing backward at an angle of approximately 45° to the midline. The participant wore a tight-fitting swimming cap to allow the optimum scalp location to be marked. In order to find the hand area, the stimulator was set to 50 % of maximum output, and the coil was moved over motor cortex in 1 cm steps, until MEPs were seen in both FDI and ADM muscles. If no MEPs were seen, the output of the stimulator was increased by 3 % of maximum stimulator output. Once MEPs were produced in both muscles, the site of the maximal MEP amplitude was determined and marked, and stimulator intensity was reduced to the lowest level that produced MEPs of at least 50 μV on five out of 10 pulses in both muscles. This defined the resting motor threshold (rMT; Rossini et al., 1994). Before commencing the experiment, stimulator output was increased to 110 % of rMT. The experimenter positioned the coil over the optimum scalp location and used the markings on the cap to ensure on every trial that the coil was in the correct location.

5.1.1.3.2 Stimulus presentation

Participants were seated in a darkened room with their head supported by a chinrest approximately 60 cm from the presentation monitor. Their right arm was placed across the body and supported by an armrest. Each trial consisted of a 2000 ms blank screen followed by the video of the neutral hand position, which was presented for one of three stimulus onset asynchronies (SOAs; 800, 1600, or 2400 ms). This was followed by the final movement position, which remained on the screen for 960 ms. A blank screen was then presented for 1000 ms before the next trial began (Figure 5.2). The TMS pulse was triggered at a variable interval (0, 320, or 640 ms) from the onset of the final movement stimulus. This allowed precise control over the timing of the pulse in relation to the movements and prevented movement onset from predicting pulse onset.

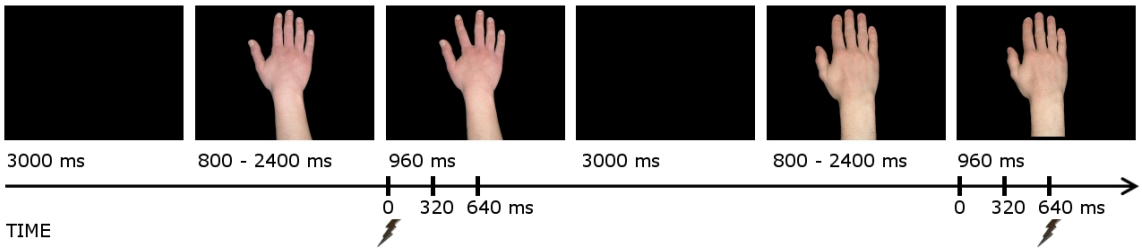


Figure 5.2. Procedure used in Experiment 5.1 and 5.2. Two trials are shown: an index finger and a receding hand trial. The TMS pulse, indicated by a flash, was applied at one of three intervals after the onset of the final movement stimulus.

On 11 % of trials (catch trials), a faint flesh-coloured circle appeared at one of six locations on the final movement stimulus. Participants were instructed to press the space bar with their left hand (contralateral to that from which MEPs were recorded) when they saw a circle. This demanding task ensured that participants were paying close attention to the stimuli.

A total of 216 trials were presented in a random order in eight blocks of 27 trials. Each of the four trial types (resting hand, receding hand, index finger movement and little finger movement) was presented 54 times, three times for each combination of model (male and female), SOA, and timing of TMS pulse. The 24 catch trials were evenly distributed across all trials. Before the start of the experiment, participants received 12 randomly selected practice trials to familiarise them with the format of the experiment, with 4 catch trials included.

5.1.1.3.3 Data acquisition and analysis

The EMG signal was recorded from 500 ms before to 100 ms after the TMS pulse. For each muscle for every trial, the 500 ms period before the TMS pulse was checked for any background EMG activity; if this was found, the data from both muscles for this trial were rejected. The size of the MEP curve was defined in the following way: a 7 ms window was moved across the EMG data in 1 ms increments. The standard deviation of the EMG signal within this window was calculated, and compared to the standard deviation of the signal in the 100 ms before the TMS pulse onset (the baseline period). The start of the MEP curve was taken as the end of the first 7 ms window in which the standard deviation of the data was over 2.8 times that of the baseline period. The end of the MEP curve was taken as the end of the first 7 ms window subsequent to this point in which the standard deviation of the data dropped back below 2.8 times that of the baseline period. Whether these values accurately reflected the onset and offset of the MEP curve was verified by eye for every trial for every participant. The data were rectified, and the area under the curve of the MEP was calculated. MEP area was averaged for each muscle for the four trial types.

5.1.2 Results and Discussion

Mean rMT was 56 ± 6.8 % of maximum stimulator output. Mean error rate on the attentional control task (omissions and false alarms) was 3.9 %. This was subjected to ANOVA with within-subjects factor of observed movement (index finger, little finger, resting hand, receding hand) in order to verify that error rates did not differ across the four movement types ($F_{3,69} = 1.2$, $p = 0.328$). For each muscle, during observation of each of the four movements, the mean area under the curve of the MEP was calculated and is displayed in Table 5.1.

	Observed movement			
Muscle	Resting hand	Receding hand	Index finger	Little finger
FDI	75.2 ± 13.3	74.5 ± 13.1	73.0 ± 13.2	68.8 ± 13.1
ADM	47.3 ± 11.4	48.1 ± 11.3	41.0 ± 10.2	43.2 ± 10.2

Table 5.1. Mean ± SEM of the area under the curve of the MEP for each muscle during the observation of the four final movement positions in Experiment 5.1, measured in mV*ms.

For each muscle and each participant, mean MEP area for observation of index and little finger movements was normalised by dividing it by the mean MEP area for observation of the receding hand, to control for interindividual variability in MEP size. Normalised MEP data were entered into a repeated measures ANOVA with within-subjects factors of recorded muscle (FDI, ADM) and observed movement (index finger abduction, little finger abduction). The interaction between the two factors was significant ($F_{1,23} = 9.3$, $p = 0.006$): MEP size was greater in the FDI muscle when observing index finger movements than when observing little finger movements, while the reverse was true for the ADM muscle. This effect is illustrated in Figure 5.3.

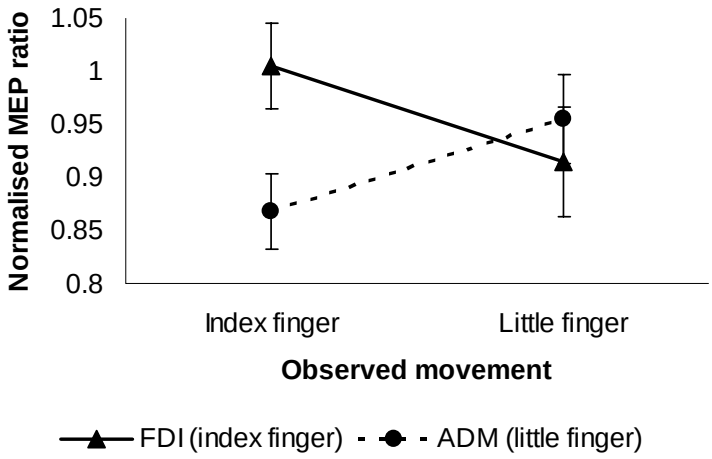


Figure 5.3. Mean ± SEM of normalised MEP ratios (MEP area on movement trials/MEP area on control receding hand trials) for the FDI and ADM muscles during observation of index and little finger movements in Experiment 5.1.

The interaction between observed movement and recorded muscle indicates that motor cortex is automatically activated in a matching muscle-specific manner during the observation of highly experimentally controlled single-movement stimuli. This result therefore supports the use of MEP data as an index of the functioning of the human mirror neuron system.

There are, however, some differences between the results of this study and of those using blocked or repetitive stimuli. It appears from the data that, while MEPs from both muscles were enhanced when viewing movements of the matching finger compared to those of the other finger, they were no larger than when viewing a receding hand stimulus (demonstrated by the value of the ratio not being greater than 1). Post-hoc t-tests (Bonferroni corrected: $\alpha = 0.0125$) were performed to test whether any of the ratios differed significantly from 1. The ADM muscle showed an MEP ratio that was significantly smaller than 1 during the observation of index finger movements ($t_{23} = -3.7$, $p = 0.001$); no other effects were significant.

Thus, although it is clear that MEPs were selectively enhanced in the FDI and ADM for the observation of movements in which they would be maximally involved, the size of the MEPs compared to control conditions is smaller than in other studies where a blocked design was used. This could be explained to some extent by the choice of control condition, as few previous studies used a control stimulus as closely matched for motion and perceptual properties as a receding hand. However, repeating the analyses presented here, using MEPs recorded during observation of the resting hand as the control condition, produced the same pattern of results: none of the MEP ratios were significantly greater than 1. It is therefore more likely that these differences stem from the single-movement stimuli and randomised design used in the current study. This suggests that previous studies may indeed have been influenced by imagery effects, i.e. that in those studies a controlled process of motor imagery enhanced MEPs during movement observation.

The current data support the presence of an automatic process of action observation-execution matching in the human brain. An experimental design using single-movement stimuli is therefore suitable for the investigation of the effects of sensorimotor learning on MEP size during action observation. Experiment 5.2 measured MEPs during the observation of index and little finger movements, before and after sensorimotor training during which participants performed either compatible or incompatible movements in response to the observation of index and little finger movements.

5.2 Experiment 5.2

Experiment 5.2 comprised three sessions. The first session (pre-training) and the last session (post-training) were identical to Experiment 5.1, consisting of a TMS session in which MEPs were recorded from the FDI and ADM muscles during the observation of

index and little finger movements and resting and receding hands. The second, training, session took place at least 24 h after the first session and exactly 24 h before the final session. For the training session, participants were divided into two groups, according to which they performed either compatible or incompatible finger movements in response to the observation of index and little finger movements. Thus, the incompatible training group performed an abduction movement of the little finger in response to the observation of an index finger abduction movement, and performed an abduction movement of the index finger in response to the observation of a little finger abduction movement. The compatible training group performed the same movement as that which they observed.

Both groups received *sensorimotor* experience because the observation of a movement was always paired with the performance of a movement; thus, both a sensory representation and a motor representation were active concurrently. However, the two groups received different kinds of sensorimotor experience. While in the case of the compatible training group, the active sensory and motor representations were of the *same* movement (both of the index finger movement or both of the little finger movement), for the incompatible training group, the sensory representation of one of the movements was active at the same time as the motor representation of the other movement.

If the action observation-execution properties of the human mirror neuron system are configured by learning, then they should be readily re-configured by learning. Therefore, if such properties arise as a result of sensorimotor experience in which the sensory representations and the motor representations of movements are paired, then following incompatible sensorimotor training the incompatible training group should

show a reduction or reversal in the muscle-specificity of MEP size during action observation. For example, after incompatible sensorimotor training in which the observation of an index finger movement is followed by the performance of a little finger movement, MEPs in the ADM (little finger abductor) should be greater during the observation of an index finger than of a little finger movement. In contrast, because compatible training involves the same sensorimotor experience as that which participants will have received during a lifetime of observing the sensory consequences of their own motor commands (after which time learning will have reached asymptote), the compatible training group should show the same pattern of matching muscle-specific activation before and after training.

5.2.1 Method

5.2.1.1 Participants

Sixteen volunteers (11 male), aged 19-44 years, were selected from among the participants in Experiment 5.1 and an additional 20 participants, none of whom had any contraindications to TMS. Participants were screened according to a strict physiological criterion to ensure that there was an effect of action observation on MEP size present before training. Out of the initial group of 44 participants (27 male, aged 19-66 years, in whom the effect was significant at the group level: $F_{1,43} = 11.1$, $p = 0.002$), the 16 participants who showed the clearest effect, with substantial matching muscle-specific enhancement of MEPs in both muscles, or a crossover interaction between the two muscles, were selected. Participants were assigned randomly to the two training groups (compatible and incompatible).

5.2.1.2 Stimuli and Apparatus

The stimuli were identical to those used in Experiment 5.1 for the pre- and post-training TMS sessions. During the training session, only the index and little finger final movement positions were used, and no catch trials were presented. The apparatus used was identical to that used in Experiment 5.1, with the exception that during the training session, no TMS was administered; instead, RT data were recorded in the same manner as in Experiments 3.1, 3.2, 4.1 and 4.2, at a gain of 1,000x.

5.2.1.3 Procedure

The experiment consisted of three sessions: a pre-training TMS session (Experiment 5.1, for those participants who took part in it) in which the action observation effect was measured; a training session, which took place at least 24 h after the pre-training session; and a post-training TMS session, which took place exactly 24 h after the training session. The two TMS sessions were identical to Experiment 5.1.

5.2.1.3.1 Training

A total of 864 trials were presented in a random order in 12 blocks of 72 trials. There were two trial types: index and little finger movements. Each of these trial types was presented 432 times, 72 times for each of the two models and each SOA. Participants in the compatible training group were instructed to make an abduction of their index finger as soon as they saw the index finger move and to abduct their little finger as soon as they saw the little finger move. Participants in the incompatible training group were instructed to make an abduction of their index finger as soon as they saw the little finger move and to abduct their little finger as soon as they saw the index finger move. Before the start of the experiment, participants received 10 randomly selected practice trials to

familiarise them with the format of the experiment. Training lasted just under two hours.

5.2.1.3.2 Data analysis

The training data were analysed in the same way as the RT data in Experiments 3.1, 3.2, 4.1 and 4.2. The post-training TMS data were analysed in the same way as the pre-training TMS data and Experiment 5.1.

5.2.2 Results and Discussion

5.2.2.1 Training

During the training session, trials on which participants made an error (0.6 %) or took more than 1000 ms to respond were excluded from analysis. Trials on which the analysis program failed accurately to detect the onset of the EMG response (6.0 %) were also excluded.

Mean RT data from the training session were calculated for each of the 12 training blocks (see Figure 5.4). These data were subjected to ANOVA with within-subjects factor of training block (1 to 12) and between-subjects factor of training group (compatible training, incompatible training). There was a significant main effect of block: response speed increased across blocks ($F_{11,154} = 4.2$, $p < 0.001$), indicating that learning of the perceptual-motor mappings took place across the 12 blocks of training. There was also a significant main effect of group: the compatible training group responded more quickly than the incompatible training group ($F_{1,14} = 31.3$, $p < 0.001$). This result indicates that performing an unfamiliar, incompatible perceptual-motor mapping is more difficult than performing a familiar, compatible one. It is likely that pre-existing links between the observation and performance of the same movement

interfere with the performance of an incompatible movement. There was a trend towards an interaction between training block and training group ($F_{11,154} = 1.8$, $p = 0.065$), suggesting that the incompatible training group improved more over the course of training than did the compatible training group. This is consistent with the suggestion that learning reaches asymptote after repeated presentations of the same pairing: the compatible training group received training of a perceptual-motor pairing that would already be highly learned as a result of self-observation during movements of the index and little finger, and hence learning quickly reached asymptote.

The error data from the training session were subjected to ANOVA with the same factors. There was a trend towards a significant main effect of training block: errors tended to reduce across the blocks ($F_{11,154} = 1.7$, $p = 0.075$). There was also a significant main effect of training group: participants in the incompatible training group made more errors than those in the compatible training group (0.6 ± 0.3 per block compared to 0.2 ± 0.2 per block; $F_{1,14} = 5.8$, $p = 0.030$). The direction of the difference in error rates indicates that the RT difference between groups is not due to a speed/accuracy trade-off. This difference in error rates, consistent with the RT data, shows that responding on the basis of the incompatible mapping was more difficult than on that of the compatible mapping. Nevertheless, error rates were very low in both groups, indicating that training was performed accurately.

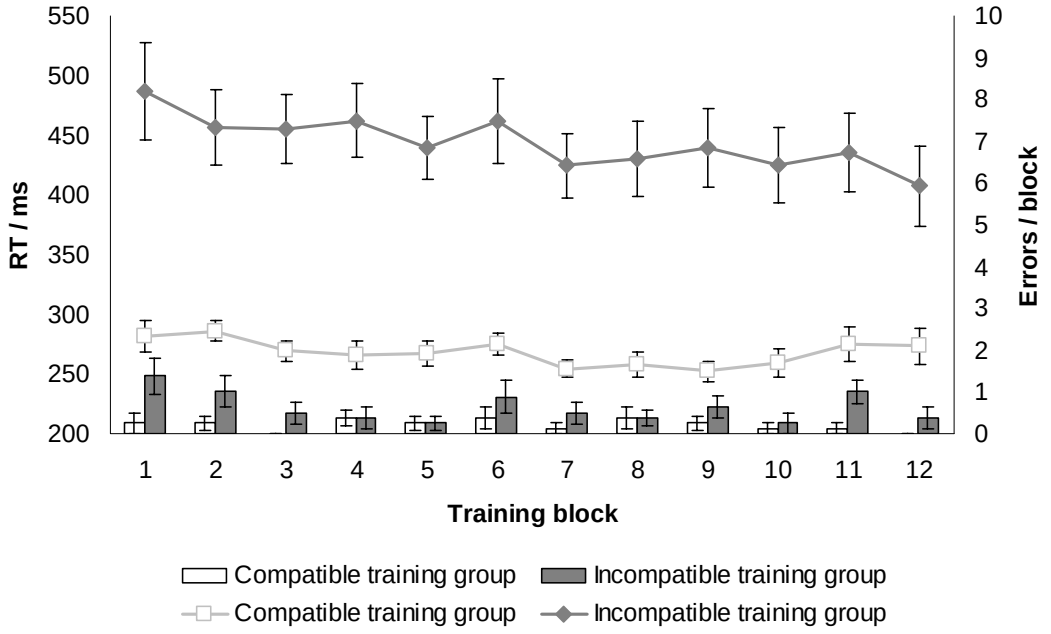


Figure 5.4. Mean ± SEM of RT (lines) and error rates (bars) for the two training groups across the 12 training blocks in Experiment 5.2.

5.2.2.2 Pre- and post-training TMS sessions

Mean rMTs were 53.4 ± 7 % of maximum stimulator output for the pre-training session and 53 ± 6.9 % for the post-training session. A one-way ANOVA verified that rMT did not differ between groups ($F_{1,14} = 2.8$, $p = 0.116$). Mean error rate on the attentional control task was 1.8 % for the pre-training session and 1 % for the post-training session. These data were subjected to ANOVA with within-subjects factors of session (pre-training, post-training) and observed movement (index finger, little finger, resting hand, receding hand) and a between-subjects factor of group (compatible training, incompatible training). There was a significant main effect of session: participants made fewer errors in the post-training session ($F_{1,14} = 4.9$, $p = 0.044$), presumably as a result of increased familiarity with the task.

Mean area under the curve of the MEP for each muscle, during observation of the four final movement positions, was calculated for each group for the pre- and post-training sessions. These values are displayed in Table 5.2.

Group	Muscle	Observed movement, pre-training				Observed movement, post-training			
		Resting hand	Receding hand	Index finger	Little finger	Resting hand	Receding hand	Index finger	Little finger
Compatible training	FDI	105.6 ± 18.4	105.1 ± 19.0	104.2 ± 18.0	92.6 ± 16.8	106.0 ± 17.6	102.9 ± 18.0	98.4 ± 17.3	85.0 ± 19.2
	ADM	44.6 ± 10.5	43.8 ± 11.7	38.3 ± 9.0	43.3 ± 9.1	45.3 ± 11.7	44.7 ± 11.5	38.6 ± 12.0	37.2 ± 9.8
Incompatible training	FDI	56.4 ± 26.5	59.8 ± 25.9	60.6 ± 27.0	50.0 ± 23.8	53.5 ± 10.3	55.9 ± 10.7	50.1 ± 9.7	54.4 ± 11.4
	ADM	43.5 ± 27.0	44.9 ± 27.0	38.1 ± 25.2	42.9 ± 24.5	31.4 ± 10.7	27.8 ± 9.6	30.8 ± 9.3	28.5 ± 9.9

Table 5.2. Mean ± SEM of the area under the curve of the MEP, measured in mV*ms, for the two groups during the pre- and post-training sessions of Experiment 5.2. Data are displayed for each muscle during the observation of the four final movement positions.

For each participant, within each session, for each muscle, mean MEP area for observation of index and little finger movements was normalised by dividing it by the mean MEP area for observation of the receding hand, to control for interindividual variability in MEP size. Normalised MEP data were entered into a repeated measures ANOVA with within-subjects factors of session (pre-training, post-training), recorded muscle (FDI, ADM) and observed movement (index finger abduction, little finger abduction), and a between-subjects factor of group (compatible training, incompatible training). Figure 5.5 illustrates the resulting four-way interaction ($F_{1,14} = 7.4$, $p = 0.016$).

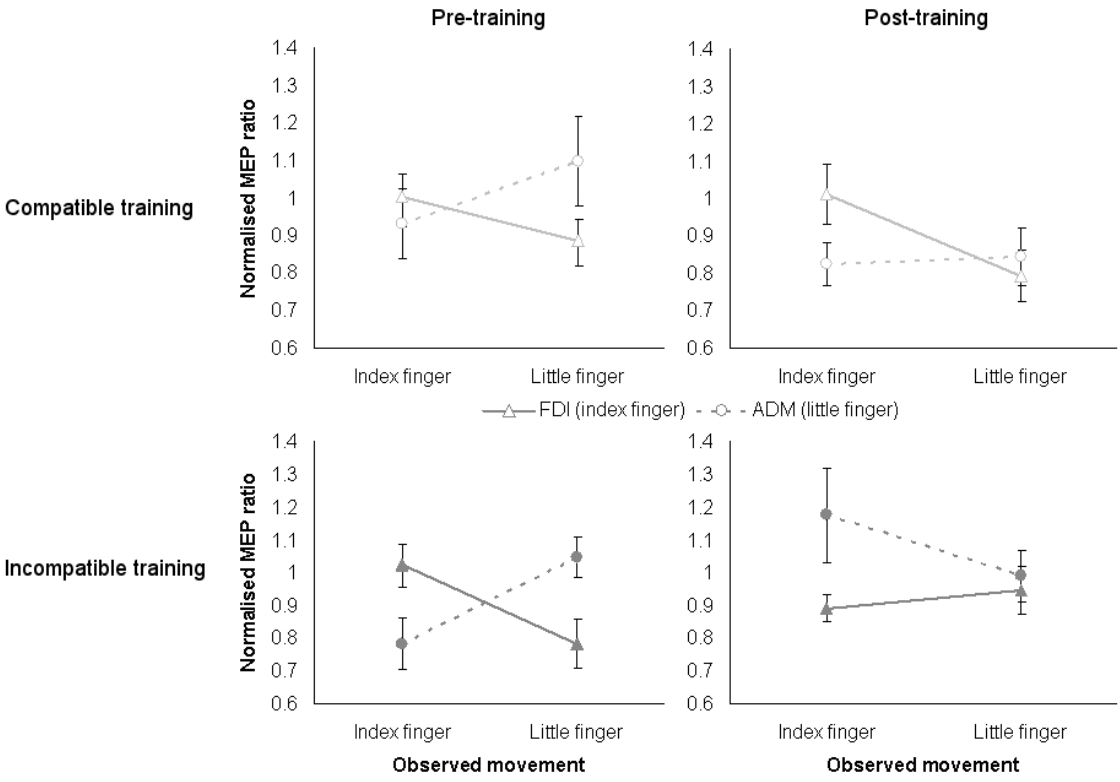


Figure 5.5. Mean ± SEM of MEP area ratio for the two muscles during observation of index and little finger movements in Experiment 5.2.

Figure 5.5 indicates that the incompatible training group showed a reversal of the muscle-specific action observation effect in the post-training session. Simple interaction analysis confirmed that there was a significant three-way interaction between recorded muscle, observed movement and session in the incompatible training group ($F_{1,14} = 17.0$, $p = 0.001$) but not in the compatible training group ($F_{1,14} = 0.1$, $p = 0.794$). As predicted by the sensorimotor learning hypothesis, incompatible training caused a reversal of muscle-specific MEP enhancement during action observation, whereas compatible training left the pre-training pattern unchanged. Certain subordinate interactions were also observed: as in Experiment 5.1, there was a significant interaction between recorded muscle and observed movement: each muscle showed greater MEPs during observation of the movement for which it would be required ($F_{1,14} = 25.2$, $p < 0.001$). This interaction was modulated by a three-way interaction between recorded

muscle, observed movement, and session: the interaction between recorded muscle and observed movement was significantly reduced in the post-training session ($F_{1,14} = 9.6$, $p = 0.008$). This reduction was, however, only observed in the incompatible training group: as noted above, this three-way interaction was in turn modulated by the predicted four-way interaction between recorded muscle, observed movement, session, and training group.

During training, participants in the two groups observed and executed the two movements with equal frequency. Therefore, the reversal of MEP enhancement found in the incompatible training group could not have been due to sensory experience alone (Ferrari et al., 2005; D'Ausilio et al., 2006), to motor experience alone (Casile & Giese, 2006), or to the sum of sensory and motor experience. Rather, the reversal must have been due to the action observation-execution contingency experienced by the incompatible training group.

The results of Experiment 5.2 indicate that a relatively short period of incompatible sensorimotor training is sufficient to alter the responses of the human mirror neuron system (as indexed by MEP size) to observation of the trained actions, and to replace a muscle-specific "mirror" action observation effect with a "counter-mirror" response. Therefore, they provide strong support for the theory that the perceptual-motor matching properties of the mirror system, rather than being innate or dependent on unimodal visual or motor experience, arise through correlated, sensorimotor experience of performing and observing actions.

5.3 General Discussion

The experiments in this chapter used single-pulse TMS to measure the relative excitability of the motor cortical representations of two hand muscles during the observation of index and little finger movements. TMS experiments such as these have provided strong support for the muscle-specificity of the action observation-execution matching properties of the human mirror neuron system, but previous studies have not ruled out the possibility that participants use controlled motor imagery to activate the relevant motor representation when viewing a movement. Experiment 5.1 demonstrated that automatic matching muscle-specific MEP enhancement can be found when participants observe single finger movements, presented in a random order. This experimental design greatly reduces the opportunity for participants to utilise an imagery strategy because the movements are of very short duration and cannot be predicted. The effects seen in Experiment 5.1 did, however, differ in one way from those reported in previous TMS/MEP studies of the human mirror neuron system: the sizes of the MEPs recorded from each muscle during the observation of the movement that it would perform were not significantly greater than those recorded during the observation of a control, receding hand. This implies that at least some of the MEP enhancement reported in previous studies was due to controlled motor imagery of the observed movement. As discussed in the introduction to this chapter, such a controlled imagery process may still involve the mirror neuron system, but the results of Experiment 5.1 provide a more convincing demonstration that the mirror neuron system mediates an automatic process of perceptual-motor translation.

Experiment 5.2 investigated whether the action observation-execution properties of the human mirror neuron system are acquired through experience: properties that have been learned through experience should continue to be modifiable through experience.

Participants given incompatible sensorimotor experience showed a reversal of the muscle-specific MEP enhancement during action observation that was found in Experiment 5.1. The design of Experiment 5.2, in which the only difference between the two experimental groups lay in the contingency between the movements that they observed and performed, allows the distinction between the possible roles of different types of experience in the development of the human mirror neuron system. In contrast to a previous study of the effects of experience on MEP enhancement (D'Ausilio et al., 2006) where participants received more sensory, motor, *and* sensorimotor experience of the experimental than the control stimulus, in Experiment 5.2 both groups received equal exposure to the sensory and motor components of the two actions during training. Thus, the reversal of MEP enhancement seen in the incompatibly trained group must have been due to the incompatible sensorimotor relationship that they experienced between action observation and action execution. The results of this experiment therefore support an experiential, rather than a nativist, account of the development of mirror neuron properties, and suggest that sensorimotor experience, in particular, is critical.

In summary, this chapter has shown that incompatible sensorimotor learning can alter human mirror neuron system responses at the neurophysiological level, as indexed by MEP enhancement. The comparison with the compatibly trained group indicates that it is specifically the training's sensorimotor nature – the contingent and contiguous relationship between the observation and performance of particular actions – that affects mirror neuron system responses. Chapter 6 uses fMRI in order to establish whether the effects of sensorimotor learning are, indeed, taking place in the mirror neuron system.

6 Sensorimotor learning affects mirror neuron system activity during action observation

The experiments reported in Chapter 5 show that sensorimotor learning affects motor cortical activation during action observation, a measure that is thought to reflect mirror neuron system activity (Fadiga et al., 1995; Fadiga, Craighero, & Olivier, 2005). However, because motor evoked potentials (MEPs) provide an indirect measure of motor cortical activation, these results do not rule out the possibility that incompatible sensorimotor training reversed muscle-specific responses during action observation via a process which took place outside the mirror neuron system. In Chapter 6, therefore, functional magnetic resonance imaging (fMRI) was used to measure the blood oxygen level dependent (BOLD) response in mirror neuron system areas during action observation after incompatible sensorimotor learning. Experiment 6.1 verified that the movements selected for training (lifting movements of the hand and foot) produced behavioural automatic imitation effects. Experiment 6.2 then measured the automatic imitation effect and the mirror neuron system BOLD response after incompatible sensorimotor learning. Compared with the compatibly trained control group, participants showed a reduced automatic imitation effect and a reversal of the relative effector dominance for hand actions in the mirror neuron system during action observation. These results confirm that sensorimotor learning alters mirror neuron system responses.

Chapter 5 showed that matching muscle-specific motor cortical activation during action observation, measured using motor evoked potentials (MEPs), is dependent on the identity of the observed movements. This result is consistent with the hypothesis that the mirror neuron system translates sensory representations of movements into their

motor representations. Experiment 5.2 indicated that this muscle-specific motor response to action observation is sensitive to sensorimotor learning: incompatible sensorimotor training can reverse the muscle-specific response to observed actions. However, while MEP experiments allow measurement of the activity of the motor cortex at a high level of muscle specificity, they cannot show that the processes producing this activity lie in the mirror neuron system (or, indeed, in any other particular location in the brain). MEP data can indicate the relative levels of activation of the motor cortical representations of different muscles, but cannot identify which cortical area, of the many that provide inputs to motor cortex, is the cause of this activation. Thus, while the original MEP studies of action observation (Fadiga et al., 1995; Strafella & Paus, 2000) were considered to be evidence for the existence of an action observation-execution matching process in the human brain, convergent evidence from functional brain imaging was required to localise this matching process to the premotor-parietal network of brain areas now usually considered to be the substrate of the human mirror neuron system (e.g. Iacoboni et al., 1999; Buccino et al., 2004). The current chapter therefore aims to build on the results of Chapter 5, by using functional imaging to investigate the effects of sensorimotor learning on activity in premotor and parietal mirror neuron system areas during action observation.

The experiments reported in the current chapter comprise a preliminary behavioural test of automatic imitation (Experiment 6.1) and a functional imaging study investigating the effects of sensorimotor learning on the blood oxygen level dependent (BOLD) response in the mirror neuron system (Experiment 6.2). Experiment 6.2 consisted of several stages. An initial behavioural pre-test of automatic imitation was followed by training sessions involving either compatible or incompatible sensorimotor training. A functional magnetic resonance imaging (fMRI) session, which included both an action

observation task to assess the effects of the sensorimotor training and an action execution task to localise mirror neuron system areas, took place after the training sessions, and subsequently a final behavioural post-test of automatic imitation was performed.

Experiment 6.2 used the same sensorimotor learning design as Experiment 5.2, with the exception that the movements used were hand and foot lifting movements rather than index and little finger abduction movements. This is because in order to measure the effects of sensorimotor learning using fMRI, it is necessary to use different movements to those used in previous chapters. To understand why this is the case, we need to consider the design of the experiment in conjunction with the properties of the mirror neuron system and the spatial limitations of fMRI. Experiential accounts of the origins of the mirror neuron system suggest that the outcome of incompatible sensorimotor training will be to forge an association between the sensory representation of one movement and the motor representation of a *different* movement. Any such outcome will be measured in the post-training fMRI experiment using action observation alone, as in Chapter 5, so that there is no possibility of instruction effects influencing behavioural responses. It is assumed that activity in the mirror neuron system during the observation of a movement is due to activation of the *motor* representation that has become associated with the observation of that movement. Thus, the fMRI experiment must be able to identify distinct motor representations of two different movements within the mirror neuron system. As mentioned in Chapter 4, the BOLD response cannot distinguish between the activity of different populations of neurons within one voxel. Therefore, two movements need to be chosen that will result either in spatially or quantitatively distinct BOLD responses in the mirror neuron system during action execution. This is unlikely to be the case for the index and little finger movements used

in previous chapters: while index and little finger movements may be represented up to 5 mm apart in primary motor cortex (Beisteiner et al., 2001), and produce different levels of activity in supplementary motor area (Erdler et al., 2001), there is little evidence that they produce differential activation in mirror neuron system areas.

The mirror neuron system, and in particular the premotor cortex, is known to be dominant for the performance of hand actions compared to foot actions (e.g Kollias, Alkadhi, Jaermann, Crelier, & Hepp-Reymond, 2001), i.e. hand movements have a relative effector dominance over foot movements. This finding suggests that the execution of hand and foot actions should result in quantitatively different BOLD responses in the mirror neuron system. Hand and foot movements also have the advantage that they may be represented in spatially distinct locations within the mirror neuron system: Buccino et al. (2001) reported that the observation of mouth, hand and foot actions activated different areas of premotor and parietal cortex, in a somatotopic fashion. An additional consideration when selecting the movements to be used is that their low-level visual properties should be matched as closely as possible, so that any difference between the responses to observation of the two actions is not driven by these properties. Therefore, the movements that were selected for the experiments in this chapter were lifting movements of the hand and foot.

Before proceeding, it was important to ascertain that automatic imitation effects can be found using these two movements. Previous research has not established whether automatic imitation effects can be obtained across effector systems when the same movement is used for both effectors, e.g. whether foot lifting is initiated faster in the presence of a foot lifting stimulus than in the presence of a hand lifting stimulus. This is a potential concern because, if an automatic imitation effect is not obtained when

comparing observation of hand and foot lifting movements, it would suggest that observation of at least one of these movements does not result in the activation of the corresponding motor representation.

Previous studies have reported automatic imitation effects between effectors within the same effector system, i.e. for finger movements. For example, Brass et al. (2000) and Bertenthal et al. (2006) (discussed in section 3.3) found that participants were faster to perform an index finger movement when observing an index finger movement than when observing a middle finger movement, while the experiments in Chapters 3 and 4 demonstrated automatic imitation of index and little finger movements. As mentioned in section 3.3, however, finger movements are likely to have strong mutually inhibitory links between their motor representations, due to human dexterity in performing individual finger movements. Thus, the activation of the motor representation of one finger movement by its observation is likely to lead to inhibition of other finger movements, enhancing the automatic imitation effect by producing interference on incompatible trials as well as facilitating responding on compatible trials.

It is not clear that such mutual inhibition occurs among different effector systems. A recent study has reported automatic imitation across effector systems, between hand and mouth movements (Leighton & Heyes, submitted): participants responded faster to a discriminative stimulus instructing them to open their hand when they viewed an opening hand than when they viewed an opening mouth. However, the movements used in this latter study had distinct visuospatial characteristics: mouth opening is perceptually very different from hand opening, for example.

Thus, it remains a possibility that in the case of perceptually similar hand and foot lifting movements, a more general action program, e.g. “lift”, could be activated, rather than the specific motor representation of the lifting hand or foot. This would result in a general *action* compatibility effect, whereby response times to perform lifting actions would be faster when observing irrelevant lifting actions, irrespective of whether the observed effector was compatible or incompatible with the effector being used by the participant. Therefore, Experiment 6.1 sought to establish whether automatic imitation, or a more general action compatibility effect, occurs when the stimuli are perceptually similar lifting movements of the hand and foot.

6.1 Experiment 6.1

Experiment 6.1 used a choice reaction time task, in which the discriminative stimulus was a letter (“H”, instructing the participant to lift their hand, or “F”, instructing them to lift their foot). This stimulus was presented simultaneously with an irrelevant movement image (a lifting hand or a lifting foot), or with a neutral image (hand and foot images without any movement). Thus, on any given trial, the irrelevant visual stimulus could be compatible, incompatible or neutral with respect to the movement that the participant was instructed to make. If there is a general action compatibility effect, then response times should be faster in the two irrelevant lifting movement conditions than in the neutral condition, irrespective of whether the irrelevant lifting movement is of an effector that is compatible or incompatible with the instructed movement effector. If, however, automatic imitation effects are present across effector systems, then there should be an interaction between irrelevant movement stimulus (foot, hand, or neutral) and response effector (foot, hand) such that hand lifting movements are faster when viewing hand lifting movements than when viewing neutral or foot lifting movements,

and foot lifting movements are faster when viewing foot lifting movements than when viewing neutral or hand lifting movements.

6.1.1 Method

6.1.1.1 Participants

Twenty-five right-handed volunteers (11 male), aged 21-33 years, were recruited using the subject pools of the UCL Psychology Department (10 participants) and the Max-Planck-Institute for Human Cognitive and Brain Sciences, Leipzig. The experiment was approved by the UCL and University of Leipzig Ethics Committees.

6.1.1.2 Stimuli and Apparatus

6.1.1.2.1 Stimuli

The stimuli were video files of a male or female hand or foot making a lifting movement from the wrist or ankle joint (Figure 6.1). The movement was shown as if viewed from the side. Videos were created from two still images of the hand or foot, initially in a resting position and subsequently in the final movement position, presented on a black background. The resting hand subtended a visual angle of 2.6° (female) to 3.6° (male) vertically and 11.1° (female) to 12.4° (male) horizontally, when viewed at a distance of 57cm. The resting foot subtended a visual angle of 9.5° (female) to 11.3° (male) vertically and 12.2° (male) to 13.5° (female) horizontally. In the final movement position, the hand was flexed at the wrist by an angle of 60° (male) to 65° (female) and the foot was flexed at the ankle by an angle of 46° (male) to 51° (female) from the resting position. Videos were presented in pairs, with hand and foot images from the same model (male or female) presented together, side by side. On compatible and incompatible trials, one of the effectors (hand or foot) moved from the resting position to the final movement position; on neutral trials, neither effector moved (see Procedure).

The discriminative stimulus, informing the participant of which movement to make in any given trial, was presented at the same time as the (task-irrelevant) final movement position, or at an equivalent timepoint on neutral trials. This stimulus consisted of a capital letter H or F, in white, presented in the centre of the screen, between the two effectors. The letter stimuli subtended a visual angle of 0.76° (F) to 0.86° (H) horizontally and 0.96° vertically.

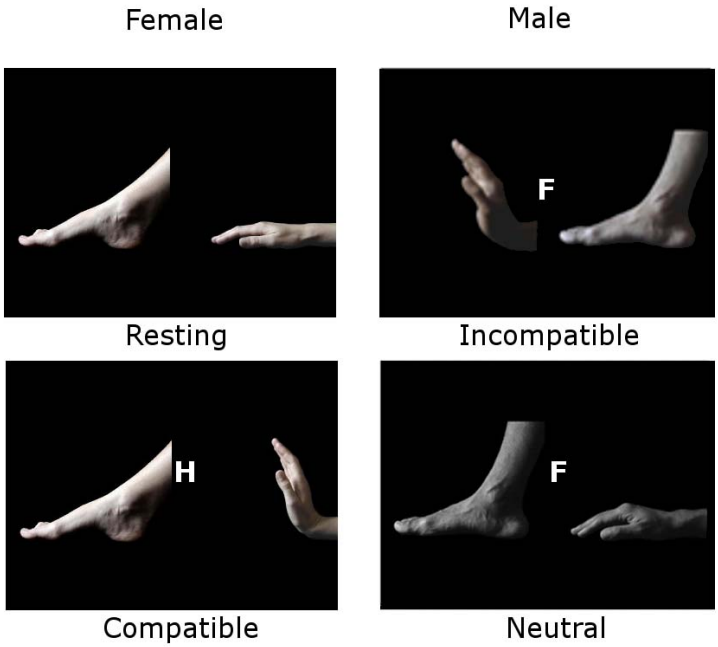


Figure 6.1. Stimuli used in Experiment 6.1. The resting position stimuli were presented at the start of every trial. An example of the final movement position is given for each of the three types of irrelevant movement stimuli (compatible, incompatible and neutral).

6.1.1.2.2 Stimulus presentation

The stimuli were presented on a Dell Latitude D800 laptop (Dell Incorporated, Round Rock, Texas, USA). Time of onset of the discriminative stimulus was identified by a signal sent via the parallel port to the data acquisition computer. This triggered data acquisition and allowed RT to be calculated with respect to stimulus onset time.

6.1.1.3 Procedure

6.1.1.3.1 Stimulus presentation

Participants were seated approximately 60cm from the stimulus presentation screen. All responses were made with the right hand or foot. Their right arm was supported from the elbow to the palm by an armrest, placed such that the wrist was closest to the participant and the fingertips were furthest away. Their right leg was stretched away from the body with the foot resting on the floor, in the same orientation as the hand. Participants were instructed to fixate the centre of the screen, where the discriminative stimulus would appear on every trial. They were instructed to respond by lifting their hand when they saw an "H" and their foot when they saw an "F". Participants were encouraged to perform the movements as fast as possible without sacrificing accuracy. Each trial began with the videos of the resting stimuli, which were presented for a variable stimulus onset asynchrony (SOA; five levels between 800 and 1440 ms). These were followed by the discriminative stimulus ("H" or "F"), which remained on the screen for 640 ms. In one third of the trials (neutral trials) both effectors remained in the resting position; in a third of the trials the hand stimulus was lifted, and in the remaining third the foot stimulus lifted. These movements could be compatible with the response effector (i.e. the hand stimulus lifted when an "H" was presented, indicating a hand response; the foot stimulus lifted when an "F" was presented, indicating a foot response) or incompatible (the foot stimulus lifted when an "H" was presented; the hand stimulus lifted when an "F" was presented). The irrelevant movement stimuli were presented at the same time as the discriminative stimulus and remained on the screen for 640 ms. A blank screen was then presented for 3000 ms before the next trial began. There were six trial types, defined by factorial combination of irrelevant movement stimulus (foot, neutral, or hand), and response effector (foot or hand). Stimulus effector location (hand presented on the left and foot on the right side of the screen, or vice

versa), and model (male or female) were fully counterbalanced across trials. A total of 240 trials were presented in a random order in two blocks of 120 trials. Each of the six trial types was presented 20 times in each block, once for each combination of stimulus effector location, model, and SOA. Before the start of the experiment, participants were given the chance to practice making the two movements, during which time they received visual feedback on the strength and clarity of their electromyogram (EMG) signal. They then received 12 randomly selected practice trials to familiarise them with the general task demands. No visual EMG feedback was given during either practice or experimental trials.

6.1.1.3.2 Data acquisition and analysis

The EMG was recorded from the flexor carpi radialis and tibialis anterior muscles of the right forearm and lower leg, which control flexion of the hand and foot respectively, using a belly-tendon electrode montage. EMG was recorded using the same apparatus as that used in Experiments 3.1, 3.2, 4.1 and 4.4. Data were analysed in the same manner as for Experiments 3.1, 3.2, 4.1 and 4.4.

6.1.2 Results and Discussion

Trials on which participants made an error (2.8 %), or on which their RT was more than 2.5 standard deviations from their mean RT, were excluded from analysis. Mean RT was calculated for each of the six trial types, collapsed across stimulus effector location (hand on left and foot on right side of screen, or vice versa) and model (male or female). Figure 6.2 shows the RT and error data.

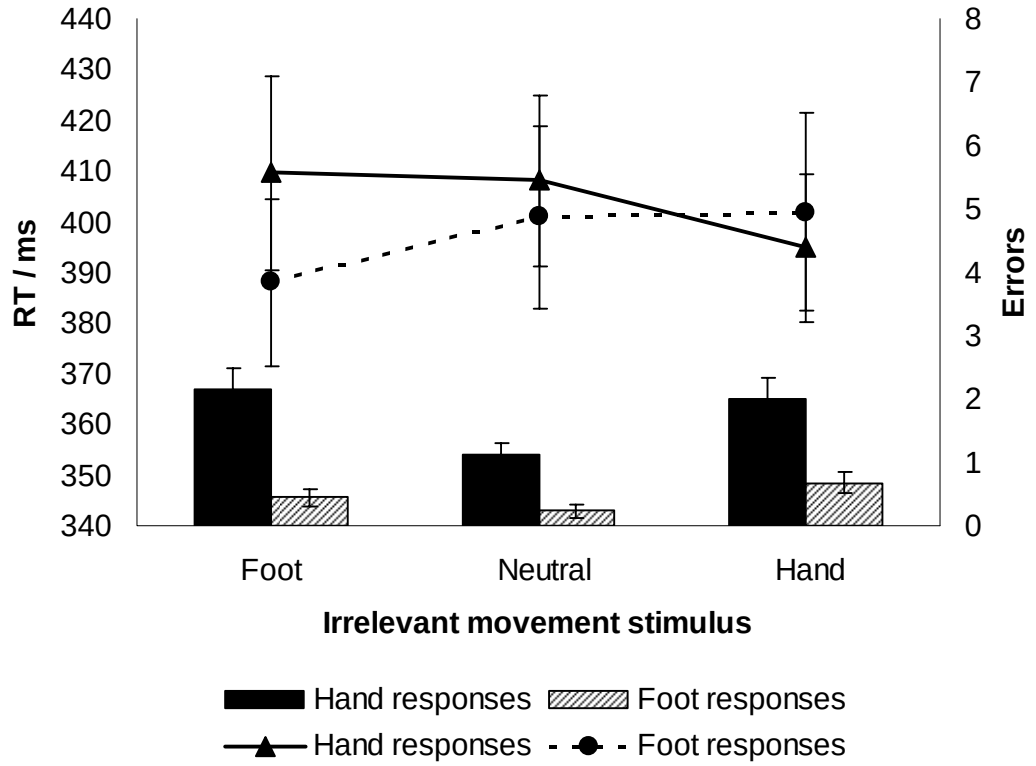


Figure 6.2. Mean ± SEM RTs (lines) and errors (bars) for responses made with the hand and foot during observation of the three types of irrelevant movement stimulus in Experiment 6.1.

A repeated measures ANOVA was performed on the RT data. The within-subjects factors of interest were those of response effector (foot or hand) and irrelevant movement stimulus (foot, neutral, or hand). There was a significant main effect of irrelevant movement ($F_{2,48} = 3.5$, $p = 0.038$); however, this effect was modulated by a significant interaction between response effector and irrelevant movement stimulus, indicating a significant automatic imitation effect ($F_{2,48} = 7.0$, $p = 0.002$). Simple effects analysis (Bonferroni corrected: $\alpha = 0.017$) suggested that the main effect of irrelevant movement stimulus was driven by a trend for RTs during neutral trials (404 ± 17 ms) to be longer than during the observation of foot (399 ± 18 ms; $F_{1,24} = 4.2$, $p = 0.052$) or of hand (398 ± 17 ms; $F_{1,24} = 5.7$, $p = 0.026$) movements. Further simple effects analyses (Bonferroni corrected: $\alpha = 0.017$) were used to decompose the interaction between response effector and irrelevant movement stimulus. Foot responses were faster during

the observation of foot movements than during neutral trials ($F_{1,24} = 10.5$, $p = 0.003$) or during the observation of hand movements ($F_{1,24} = 10.3$, $p = 0.004$). Hand responses were faster during the observation of hand movements than during neutral trials ($F_{1,24} = 8.1$, $p = 0.009$) or during the observation of foot movements ($F_{1,24} = 6.5$, $p = 0.017$).

A repeated measures ANOVA with the same within-subjects factors was performed on the error data. This revealed significant main effects of response effector: more errors occurred during hand responses than during foot responses (1.8 ± 0.3 compared to 0.5 ± 0.1; $F_{1,24} = 46.1$, $p < 0.001$), and of irrelevant movement stimulus ($F_{2,48} = 6.8$, $p = 0.003$, driven by fewer errors on neutral trials (0.7 ± 0.1) than during the observation of hand (1.3 ± 0.2) or foot (1.3 ± 0.2) movements).

There are at least three factors that may have contributed to the significant main effect of irrelevant movement on RT. First, the error data suggest a possible speed/accuracy trade-off, as fewer errors were made on neutral trials: participants may have responded more slowly on neutral trials in order to make fewer errors. Second, this response pattern could be the result of the smaller perceptual change on neutral trials: since neither of the effectors moved, it may have taken participants longer to detect the onset of the discriminative stimulus. Third, this result could imply the presence of a general action compatibility effect, whereby participants are faster to perform a lifting action in response to the observation of a lifting action, regardless of the identity of the effector performing the action. The current data cannot distinguish between these possibilities, and it may well be that all three of these factors contributed to the above main effect.

The most important result of this experiment, however, was the presence of an interaction between the irrelevant movement stimulus and the response effector, indicating an automatic imitation effect. As predicted, for both response effectors, response times were faster when the observed irrelevant lifting movement was performed with the same effector as that with which the participant made their response, compared to when there was no irrelevant movement, or when the irrelevant movement was performed with the alternative effector. This result suggests that for both hand and foot lifting movements, the observation of a particular movement activates its motor representation, speeding performance of that movement.

It is unclear from the present data whether there is mutual inhibition between the motor representations of hand and foot lifting movements; such mutual inhibition would be expected to manifest itself in slower response times on incompatible than on neutral trials. This is because the observation of a movement on an incompatible trial activates the motor representation of that movement; mutual inhibition between motor representations would then result in the inhibition of the other movement (i.e. of the instructed movement), resulting in slowing of response times compared to neutral trials in which no inhibition occurs. This pattern of results was not observed in the current data. However, this does not mean there is no inhibition between the motor representations of these movements: the presence of a main effect indicating slower response times on neutral trials – whether caused by speed/accuracy trade-off, perceptual differences, or a general action compatibility effect – may have prevented the detection of an inhibitory effect.

In summary, the results of Experiment 6.1 indicate that, for both hand and foot lifting movements, the observation of either a hand or a foot lifting movement activates the

specific, matching motor representation of either a hand or a foot lifting movement. Therefore, these movements are suitable for use in a functional imaging investigation of the effects of sensorimotor learning on the mirror neuron system.

6.2 Experiment 6.2

Experiment 6.2 sought to build on the results of Chapter 5 by establishing whether the reported effects of sensorimotor learning on motor activation during action observation are mediated by the mirror neuron system. Previous functional imaging studies have shown that sensory and / or motor experience modifies the response of the mirror neuron system to action observation (Haslinger et al., 2005; Calvo-Merino et al., 2005; Cross et al., 2006; Calvo-Merino et al., 2006). However, as discussed in section 1.5.4, these studies did not control for sensorimotor experience: participants with different levels of sensory or motor experience of the observed actions also had different levels of sensorimotor experience. For example, the ballet dancers in the study of Calvo-Merino et al. (2006) would have had greater motor experience of performing same-gender than other-gender ballet movements, but would also – as a result of rehearsing these movements with other dancers or in front of mirrors – have had greater *sensorimotor* experience of concurrent perception and performance of own-gender movements. Thus, it is unclear whether differences in the mirror neuron system during action observation in these studies resulted from purely sensory experience, purely motor experience, or sensorimotor experience of the observed actions. In addition to this confound, none of these studies used an action execution task to define the mirror neuron system. Thus, it is unclear whether the brain regions identified in these experiments were truly "mirror", that is, active during both the observation and the execution of movements.

Experiment 6.2 therefore investigated the effects of sensorimotor learning on the mirror neuron system, using hand and foot lifting movements. An initial behavioural pre-test of automatic imitation was performed, which ensured that an automatic imitation effect was present to be modified. This pre-test was identical to Experiment 6.1, with the exception that neutral trials were not presented. These trials were removed because the main effect of increased RT on neutral trials meant that they were uninformative as to whether the observed automatic imitation effect arose from facilitatory or inhibitory processes. For the training sessions, as in Experiment 5.2, participants were divided into two groups, receiving either compatible or incompatible sensorimotor training. Subsequent to the training sessions, an fMRI testing session took place. BOLD response was measured during the observation of hand and foot lifting movements. In order to allow the definition of mirror neuron system areas using both the observation and performance of action, an action execution task was also carried out, in which participants performed a range of hand and foot actions. These actions did not include hand and foot lifting movements, since it was possible that the extensive motor practice of these lifting movements obtained during the preceding training sessions would have expanded the cortical representations of these movements disproportionally, and the aim of the execution task was to localise cortical areas involved in the performance of hand and foot actions in general. After the fMRI session, a behavioural post-test of automatic imitation was performed, in order to determine the effect of sensorimotor training on the automatic imitation effect seen in Experiment 6.1.

As discussed at the start of the chapter, hand and foot lifting movements were chosen because they should result in quantitatively different activity in the mirror neuron system: the execution of hand movements results in greater activity in non-primary motor areas than the execution of foot movements (Kollias et al., 2001), i.e. there is a

relative effector dominance for hand movements. Thus, it is hypothesised that incompatible sensorimotor training should result in a reversal of the relative effector dominance of hand actions over foot actions in mirror neuron system areas during action observation. Since the mirror neuron system shows greater activity during the performance of hand than of foot actions, then in the compatible training group this should also be the case during action observation: the mirror neuron system should show greater responses during the observation of hand than of foot actions. During incompatible sensorimotor training, the observation of a hand action will be paired with the execution of a foot action and vice versa. Therefore, if sensorimotor experience alters the observation-execution matching properties of the mirror neuron system, then after incompatible training the observation of a hand action should result in activation of the motor representation of a foot action. This activation would produce a smaller BOLD response in the mirror neuron system than the activation of the motor representation of a hand action (which would now be activated by the observation of a foot action). Thus, the incompatible training group should show greater responses in the mirror neuron system to the observation of foot movements than to the observation of hand movements, while the compatible training group should show the reverse, normal pattern. Additionally, the behavioural automatic imitation effect should be reduced in the incompatible training group.

6.2.1 Method

6.2.1.1 Participants

Twenty right-handed volunteers (11 male), aged 20-34 years, were selected from amongst 32 volunteers recruited using the subject pool of the Max-Planck-Institute for Human Cognitive and Brain Sciences, Leipzig. Participants were screened to ensure that there was an automatic imitation effect present before training. Out of the initial group

of 32 participants (in whom the automatic imitation effect was significant at the group level: $F_{1,31} = 26.8$, $p < 0.001$), the 24 participants who showed an automatic imitation effect of more than 5 ms were selected. Participants were assigned randomly to the two training groups (compatible and incompatible). Four participants were excluded from the sample prior to data analysis: one participant did not complete the post-training session as scheduled, while the other three failed to comply with task instructions during training. The experiment was approved by the University of Leipzig Ethics Committee.

6.2.1.2 Stimuli and Apparatus

6.2.1.2.1 Pre- and post-training sessions

Pre- and post-training sessions used the same stimuli as in Experiment 6.1, with the exception that neutral trials were not presented.

6.2.1.2.2 Training

The stimuli consisted of video files of hand and foot movements. On half of the trials these were presented in pairs, as in the pre- and post-test sessions, while on half of the trials they were presented individually in the centre of the screen. Letters were not presented. Half of the stimuli were the same as those used in Experiment 6.1 and in the pre- and post-training sessions; the remaining stimuli were recorded from two additional female models. These images were taken from the side with an increased elevation (see Figure 6.3). The resting hand subtended a visual angle of 5.3° to 6.1° vertically and 11.1° to 11.4° horizontally, when viewed at a distance of 57cm. The resting foot subtended a visual angle of 11.2° to 12.2° vertically and 11.5° to 12.9° horizontally. In the final movement position, the hand was flexed at the wrist by an angle of 40° to 45° and the foot was flexed at the ankle by an angle of 16° to 22° from the resting position.

A second set of stimuli from all four models was also constructed, consisting of the stimuli at 75 % of these sizes. The purpose of varying the hand and foot lifting stimuli was to increase generalization of learning, and to prevent habituation to the stimuli. Video files were created in the same way for these images as for the stimuli used in Experiment 6.1.

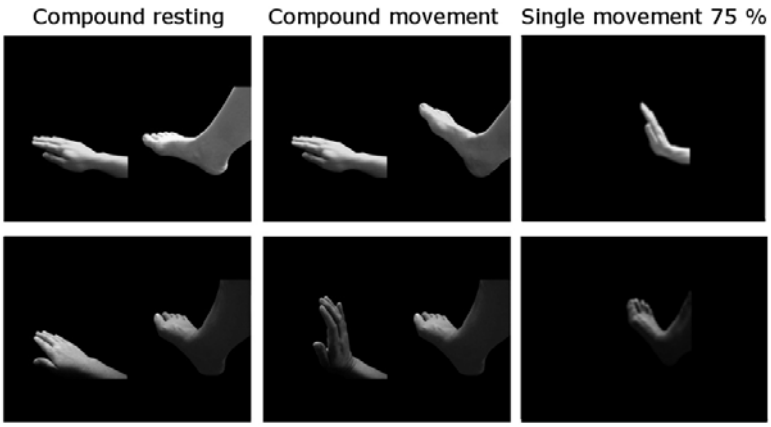


Figure 6.3. Stimuli from two additional models, used during training and the observation task in Experiment 6.2. During the observation task, only single movement stimuli were used.

6.2.1.2.3 Functional Imaging

Observation task. The stimuli used during the observation task were identical to those used during training, with the following exceptions: only single stimuli were presented; and, on 2 % of trials, incomplete lifting stimuli were presented (see Procedure). These consisted of movements in which the hand or foot was flexed by only half the angle of the usual lifting movement.

Execution task. The stimuli used during the execution task consisted of written instructions indicating the movement to be performed. These were presented in the centre of the screen.

6.2.1.2.4 Stimulus presentation

The apparatus used during the pre-training, training and post-training sessions was identical to that used in Experiment 6.1.

6.2.1.3 Procedure

The experiment consisted of six sessions: a pre-training session in which the automatic imitation effect was measured; three training sessions, which took place over three consecutive days; a functional imaging session, comprising an observation task and an execution task, which took place 24 h after the last training session; and a post-training session in which the automatic imitation effect was measured again, which took place immediately after the end of the functional imaging session. Figure 6.4 depicts the trial structure in each of these sessions.

6.2.1.3.1 Pre- and post-training sessions

The pre- and post-training sessions were identical to Experiment 6.1, with the exception that neutral trials were not used. The neutral trials were replaced with an equal number of foot and hand movement trials, and therefore the total number of trials remained at 240.

6.2.1.3.2 Training

Participants were seated with their right hand and foot in the same configuration as for the pre- and post-training sessions. Each trial depicted either a hand or foot being raised from a resting position either alone (single stimulus), or while the other effector remained at rest (compound stimuli). Each trial began with the presentation of the resting stimulus or stimuli. These were shown for a variable SOA between 800 and 1280 ms before being replaced by the movement stimulus which was shown for 640 ms.

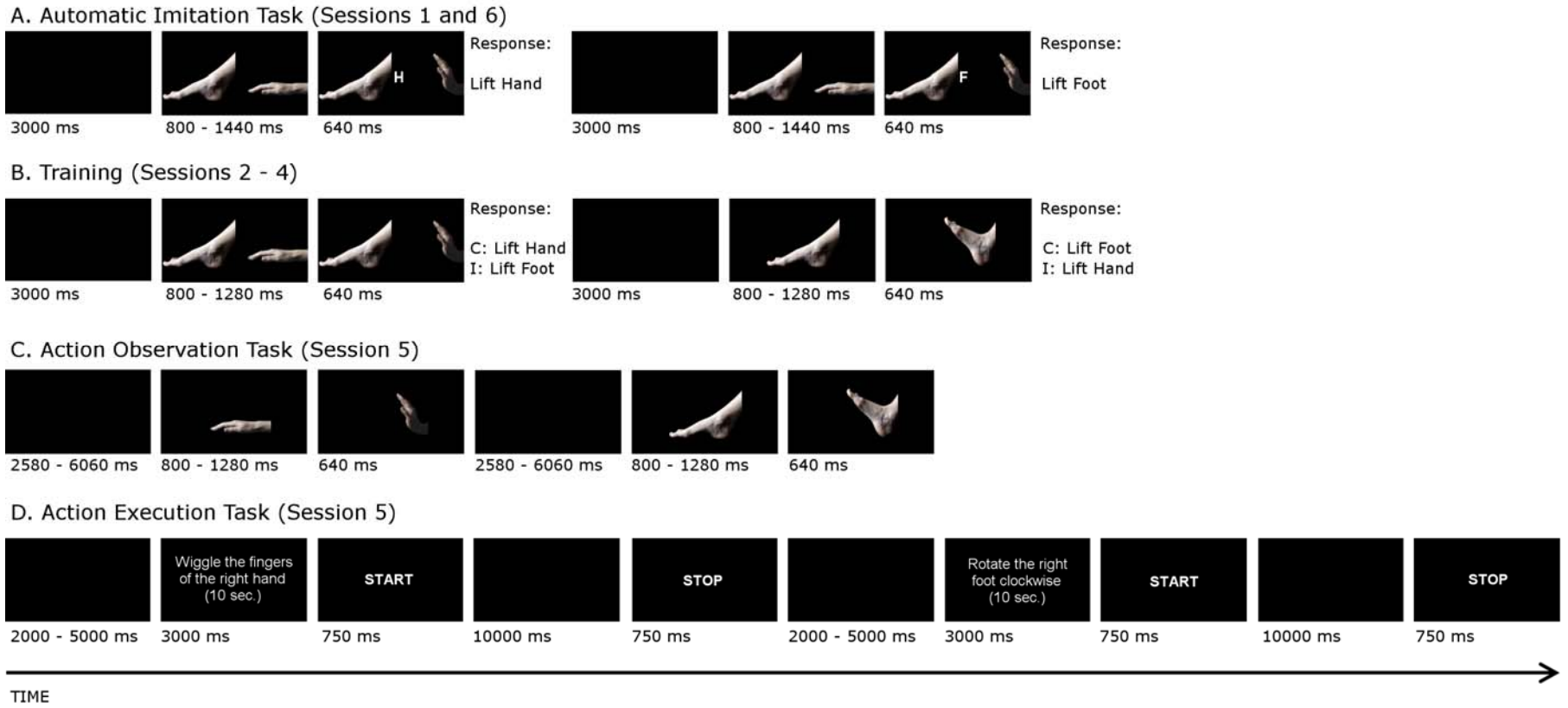


Figure 6.4. Timelines showing stimuli and procedures during: (A) automatic imitation task used in the pre- and post-training sessions, (B) training, (C) action observation task used in the functional imaging session, and (D) action execution task used in the functional imaging session of Experiment 6.2. Two trials are depicted for each task. For the training task, the first trial is an example of a compound stimulus trial, while the second is an example of a single stimulus trial. C: compatible training group; I: incompatible training group.

Participants were instructed to respond to the movement stimulus as quickly as they could, without making errors, by raising their hand or their foot. Participants in the compatible training group were instructed to raise their hand as soon as possible when they saw a raised hand, and to raise their foot as soon as possible when they saw a raised foot. Participants in the incompatible training group were instructed to raise their hand as soon as possible when they saw a raised foot, and to raise their foot as soon as possible when they saw a raised hand. RT was measured in the same way as for the pre- and post-training sessions. Training was conducted over the course of three consecutive days. During each day's session, which lasted around 45 minutes, a total of 384 trials were presented in a random order in six blocks of 64 trials. Hand movement and foot movement trials were each presented 192 times in each day's session. Stimulus type (compound or single stimulus), model (four models, two showing movements from the side and two showing them from an elevated position), and size (100 % or 75 %) were fully counterbalanced across these two trial types. Compound stimuli were presented equally often with the hand on the left and the foot on the right of the screen, and vice versa. Each session was preceded by 12 randomly selected practice trials. Before the second and third training sessions, RTs obtained over the course of the previous training session(s) were shown to the participant in order to encourage maximal performance. Performance improvement over the course of training was further encouraged by offering financial incentives for better performance (+ €1.50 per block in which RTs reduced and errors did not increase relative to the previous block) and financial penalties for worse performance (- €0.50 per block in which RTs or errors increased relative to the previous block).

Each training session was preceded by a short execution practice period (10 trials) in which participants practised performing the actions they would make in the Execution

Task during the functional imaging session. To discourage any intentional movement planning or controlled motor imagery during the Observation Task (which always preceded the Execution Task during the imaging session), participants were not informed that they would perform these actions in the scanner, but instead were told that the actions were performed to "warm up" their muscles for the training sessions. During these practice periods the experimenter read out a simple instruction for an action, which the participant then performed repeatedly for 10 seconds. The actions comprised five movements of the hand (rotate hand clockwise, move hand left and right, make a fist, spread the fingers apart, wriggle the fingers), and five equivalent foot movements (rotate foot clockwise, move foot left and right, roll up the toes, spread the toes apart, wriggle the toes). This range of actions was chosen to be different from those used in the Observation Task and during training, because their purpose was to localise cortical areas involved in the performance of hand and foot actions in general. For the hand actions, the lower arm was placed from elbow to wrist on the arm rest, allowing free movement of the hand. For the foot actions, the leg was placed on a chair from knee to ankle, allowing free movement of the foot. All actions pertaining to the hand, and all actions pertaining to the foot, were performed en bloc. The order of blocks, and the order of actions within each block, was determined randomly. The experimenter monitored that the participant had understood the instruction and reminded participants, if necessary, to restrict movement to the hand / foot.

6.2.1.3.3 Functional Imaging

The functional imaging session was completed 24 hours after the third training session and comprised the Observation Task and the Execution Task. The Observation Task always preceded the Execution Task. The participant lay in a supine position inside the scanner. Their right arm was placed on a cushion from elbow to wrist, and their right

lower leg was placed on a cushion from knee to ankle, allowing free movement of hand and foot during the Execution Task. They were instructed that this was to check they were not moving during the Observation Task, in order to avoid providing any information about the later Execution Task and possibly prompting intentional movement planning or controlled motor imagery during the Observation Task.

Observation Task. During the Observation Task participants observed single hand and foot actions without responding. Participants observed a total of 128 hand and 128 foot actions, interspersed with six "catch" trials (three incomplete hand lifting and three incomplete foot lifting actions) and 36 null events (blank screen replaced stimulus presentation). Observation trials followed the structure of the single-effector training trials (resting stimulus presented for between 800 ms and 1280 ms, followed by the movement stimulus for 640 ms). Each trial was preceded by a black screen of variable duration (mean: 3920 ms, range: 2580 ms to 6060 ms). Model and size were fully counterbalanced across trials, which were presented in a random order. In order to encourage attention to the stimuli, participants were asked to observe closely and report anything unusual (the six catch trials) at the end of the session.

Execution Task. During the Execution Task participants made hand and foot actions in response to written instructions. Participants performed the 10 actions that they had practised at the start of each training session. Each trial was preceded by a blank screen of variable duration (mean: 2750 ms, range: 2000 ms to 5000 ms). Written instructions then detailed the action to be executed (3000 ms), followed by the word START (750 ms). The participant then performed the action repeatedly (10 s), until the word STOP appeared on the screen (750 ms). Actions were performed in a random order.

Each action was performed twice during the task. Rest blocks (of 18 s duration) were interspersed with action trials.

6.2.1.3.4 Data acquisition and analysis

Behavioural sessions. Data from the pre-training, training and post-training behavioural sessions were acquired and analysed in the same way as for Experiment 6.1.

Functional imaging sessions. fMRI data were acquired with a T2* echoplanar sequence using BOLD contrast on a Siemens Trio 3 Tesla system. Each functional brain volume comprised 24 slices of 5 mm thickness (1 mm spacing), TE 30 ms, TR 2 s. The functional data were acquired in two sessions (one session for each task); the first six volumes of each session were discarded to allow for T1 equilibration effects. Stimulus presentation began after the sixth volume. A total of 1266 full-brain volumes for each participant were acquired over the two sessions.

Functional imaging data were analysed using SPM2 (Wellcome Department of Imaging Neuroscience, London, UK) (Friston et al., 1995). Images were realigned and "unwarped" (corrected for interactions between movements and field inhomogeneities) (Andersson et al., 2001), normalised to a standard EPI template, resampled to a resolution of 3 × 3 × 3 mm, and smoothed with a three-dimensional Gaussian kernel with full-width half maximum of 6 mm. In addition, a high-pass temporal filtering with a cut-off of 128 s was applied in order to exclude low-frequency artefacts. After pre-processing, statistical analysis was carried out using the general linear model (GLM; Friston et al., 1995). Each observation trial was modelled by a standard haemodynamic response function. Execution trials (from the onset of action instructions to cessation of movement) were modelled by convolving a box-car function with a standard

haemodynamic response function. These observation-related and execution-related effects were modelled within a single mixed-design GLM, allowing separation of the influences of these factors on neural activity (see Laurienti, Burdette, & Maldjian, 2003). To allow inferences at the population level, a second-level random effects analysis was performed using ANOVA on contrast images of the different conditions for each individual subject.

The first analysis identified mirror neuron system areas. A conjunction (null) was performed on the contrast images comparing action observation (of both hands and feet) to baseline, and action execution (of both hands and feet) to baseline, in the compatible training group. The conjunction was restricted to the compatible training group in order to avoid any contamination of the classical activation pattern by incompatible training. The resulting statistical parametric map (SPM) was thresholded at $p < 0.05$ corrected for whole brain volume.

Next it was tested whether, within mirror neuron system areas, a somatotopic representation of the observed effector (whereby observed hand and foot movements are represented in spatially distinct locations) could be identified in the compatible training group. While such a somatotopy has been suggested by earlier imaging work (Buccino et al., 2001; Wheaton, Thompson, Syngeniotis, Abbott, & Puce, 2004), these experiments did not include action execution conditions, and therefore it is unclear whether the areas identified were truly "mirror" (active for both execution and observation of actions). Additionally, recent studies have not shown clear differences at the group level between cortical areas responding to observation of hand and foot actions (Aziz-Zadeh et al., 2006b; Gazzola et al., 2007b), and a recent review found no evidence for somatotopic organisation of observed actions in premotor cortex (Morin &

Grèzes, 2008). Therefore, activation for the observation of hand actions was compared with that for the observation of foot actions and vice versa, in the mirror areas defined by the initial conjunction analysis. The resulting SPM was thresholded at $p < 0.05$ corrected for the search volume.

The third analysis addressed the main experimental question: whether the relative effector dominance for observed hand and foot actions was influenced by incompatible training. The interaction of primary interest was that between training group and observed effector representation in mirror neuron system areas. In order to address this question a voxel of interest approach was used. The peak voxels in the mirror neuron system areas as defined by the initial conjunction analysis and monkey neurophysiology (bilateral premotor and inferior parietal cortices) were selected and parameter estimates for activity during action observation in both groups were extracted.

6.2.2 Results and Discussion

6.2.2.1 Behavioural data

6.2.2.1.1 Training

Trials on which participants made an error (1.5 %), or on which their RT was more than 2.5 standard deviations from their mean RT, were excluded from analysis. Mean RT was calculated for each training group for each training session, collapsed across response effector, stimulus type, model and size. Figure 6.5 shows the RT and error data for the training sessions. A repeated measures ANOVA was performed on the RT data with a within-subjects factor of session (day 1, 2 or 3) and a between-subjects factor of group (compatible or incompatible training).

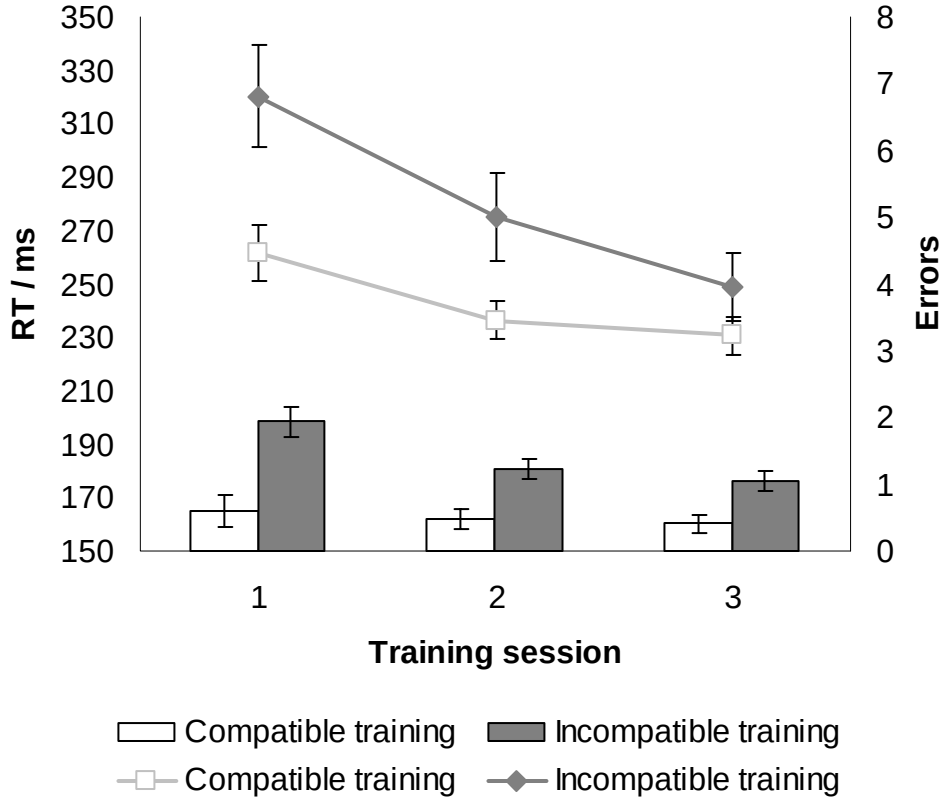


Figure 6.5. Mean ± SEM RTs (lines) and errors (bars) for the compatible and incompatible training groups across the three days of training in Experiment 6.2.

There was a significant main effect of session: RT decreased over the three sessions (day 1: 291 ± 13 ms; day 2: 256 ± 10 ms; day 3: 240 ± 8 ms; $F_{2,36} = 38.2$, $p < 0.001$), and of group: participants in the compatible training group responded faster than those in the incompatible training group (243 ± 9 ms compared to 282 ± 17 ms; $F_{1,18} = 5.1$, $p = 0.037$). There was a significant interaction between session and group: RT decreased more over the three sessions for the incompatible than for the compatible training group ($F_{2,36} = 5.7$, $p = 0.007$).

A repeated measures ANOVA with the same factors was performed on the error data. There were significant main effects of session: errors decreased over the three sessions (day 1: 1.3 ± 0.2; day 2: 0.9 ± 0.1; day 3: 0.7 ± 0.1; $F_{2,36} = 6.6$, $p = 0.004$), and group: participants in the incompatible training group made more errors than those in the

compatible training group (1.4 ± 0.2 compared with 0.5 ± 0.1; $F_{1,18} = 23.8$, $p < 0.001$), and a trend towards an interaction between session and group: errors tended to decrease more for the incompatible than for the compatible training group ($F_{2,36} = 3.0$, $p = 0.063$). As in Chapter 5, the RT and error data indicate that the compatible mapping was easier to perform than was the incompatible mapping, and that both groups improved over the training sessions.

Pre- and post-training sessions

Trials on which participants made an error (5.9 %), or on which their RT was more than 2.5 standard deviations from their mean RT, were excluded from analysis. Mean RT was calculated for each of the four trial types (irrelevant movement stimulus: foot or hand, by response effector: foot or hand), collapsed across stimulus effector location and model, for the two sessions (pre- and post-training), in the two groups (compatible and incompatible training). Figure 6.6 shows the RT and error data. It can be seen that while the RT data show a clear interaction between irrelevant stimulus movement and response effector in both groups at pre-training, and in the compatible training group post-training, this interaction is greatly attenuated in the incompatible training group post-training.

A repeated measures ANOVA was performed on the RT data. The within-subjects factors of interest were those of response effector (foot, hand), irrelevant movement stimulus (foot, hand), and session (pre- or post-training). The between-subjects factor was that of group (compatible or incompatible training). As predicted and illustrated in Figure 6.6, there was a significant four-way interaction between response effector, irrelevant movement, session and group: the automatic imitation effect was unchanged

after compatible training, but reduced after incompatible training ($F_{1,18} = 5.4$, $p = 0.033$).

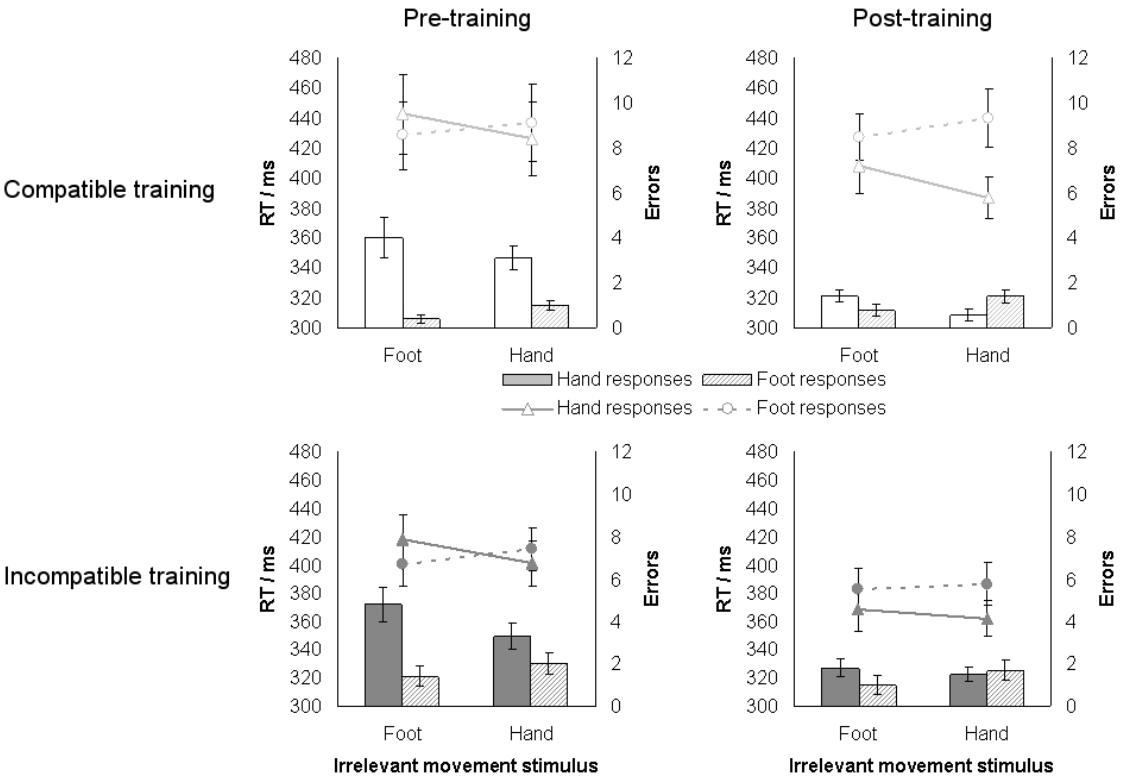


Figure 6.6. Mean ± SEM RT (lines) and errors (bars) for hand and foot responses during the observation of irrelevant movement stimuli in Experiment 6.2.

Simple interaction analyses confirmed that there was a significant three-way interaction present in the incompatible training group ($F_{1,18} = 4.4$, $p = 0.049$), but not in the compatible training group ($F_{1,18} = 1.4$, $p = 0.259$). Thus, incompatible sensorimotor training reduced the behavioural automatic imitation effect.

In the RT analysis, subsidiary two-way interactions were observed between response effector and irrelevant movement stimulus (automatic imitation effect: $F_{1,18} = 21.9$, $p < 0.001$), and between session and response effector: participants' improvement in RT was greater for hand movements than for foot movements ($F_{1,18} = 25.6$, $p < 0.001$). There was also a significant main effect of session: participants were faster after

(395 ± 12 ms) than before training (421 ± 15 ms; $F_{1,18} = 5.5$, $p = 0.031$), which may be due to increased experience with the task. Finally, there was a significant main effect of response effector: participants were faster to respond with the hand (402 ± 13 ms) than with the foot (414 ± 13 ms; $F_{1,18} = 8.2$, $p = 0.010$). This main effect of response effector appears to be driven by the greater improvement in RTs for hand movements than for foot movements.

A repeated measures ANOVA with the same four factors was performed on the error data. There were significant main effects of session: participants made fewer errors after training than before (1.3 ± 0.3 compared to 2.5 ± 0.4; $F_{1,18} = 38.5$, $p < 0.001$), which parallels the effect seen in the RT data and is presumably a result of experience with the task; and of response effector: as in Experiment 6.1, participants made more errors when responding with the hand than with the foot (2.6 ± 0.4 compared to 1.2 ± 0.3; $F_{1,18} = 23.8$, $p < 0.001$). This main effect was modulated by a significant interaction between session and response effector: participants made more errors when responding with the hand than the foot in the pre-training session, but this effect was not seen in the post-training session ($F_{1,18} = 23.0$, $p < 0.001$). There was a significant automatic imitation effect, i.e. an interaction between response effector and irrelevant movement stimulus: participants made more errors when the irrelevant movement stimulus was incompatible with the response effector ($F_{1,18} = 8.1$, $p = 0.011$). Finally, there was a trend towards a main effect of group: participants in the incompatible training group made more errors than those in the compatible training group (2.2 ± 0.5 compared to 1.6 ± 0.4; $F_{1,18} = 3.6$, $p = 0.072$).

In summary, the behavioural data indicated that incompatible sensorimotor training can reduce automatic imitation effects when the actions used are perceptually similar lifting

movements of different effectors. This result is consistent with previous studies showing an effect of sensorimotor learning on automatic imitation (Heyes et al., 2005; Press et al., 2007). However, the previous studies used two movements of a single effector, and therefore mutual inhibition between performance of the two movements could have contributed to the observed effects. Not only can mutual inhibition enhance an automatic imitation effect, as outlined in the introduction, it could also enhance the effect of incompatible sensorimotor training in a similar manner. During incompatible sensorimotor training involving a pair of mutually exclusive movements, observation of movement A becomes associated in an excitatory manner with the performance of movement B and also in an inhibitory manner with the performance of movement A (because movement B is being performed and movements A and B are mutually exclusive). In the subsequent automatic imitation test, response times to perform movement B while observing movement A are speeded as a result of the excitatory association, while response times to perform movement B while observing movement B are increased as a result of the second, inhibitory association. Thus, the reduction in the automatic imitation effect that is observed at post-training test may be due to a combination of both excitatory and inhibitory sensorimotor learning. In the current experiment, the use of two independent effectors is likely to have reduced the extent of inhibitory learning, providing additional evidence for the role of excitatory sensorimotor learning in automatic imitation.

6.2.2.2 Functional imaging data

In accordance with previous studies (reviewed in Iacoboni, 2005), the conjunction analysis of action execution and action observation for both actions, in the compatible training group, revealed a number of brain regions (Table 6.1) including bilateral premotor cortex and inferior parietal cortex (Figure 6.7). As outlined in the Procedure

section, the subsequent analyses were restricted to these four areas, because, based on single-cell recording in the macaque, they are thought to form the core of the mirror neuron system (Rizzolatti & Craighero, 2004). The findings relating to effector somatotopy will be considered first, before moving on to the effects of sensorimotor learning on relative effector dominance in the mirror neuron system.

Brain area	**Montreal Neurological Institute (MNI) Coordinates**			**Z-score**
	x	*y*	*z*	
Premotor cortex (Brodmann area (BA) 6)				
Right hemisphere[1]	57	3	36	5.72
Left hemisphere[2]	-51	0	36	5.30
Inferior parietal lobule (BA 40)				
Right hemisphere[3]	39	-39	45	5.92
Left hemisphere[4]	-33	-45	45	5.34
Cerebellum				
Right hemisphere	36	-54	-27	6.48
Left hemisphere	-36	-57	-27	6.69
Left superior temporal lobe (BA 48)	-54	-39	24	5.49
Left precuneus (BA 7)	-12	-72	45	5.22
Right superior parietal lobe (BA 7)	15	-72	51	5.05
Supplementary motor area (BA 32)	0	18	48	5.03
Right middle frontal gyrus (BA 6)	51	0	54	4.78

Table 6.1. Locations of peak voxels, surviving correction at $p < 0.05$ for multiple comparisons across the whole brain, for the conjunction of observation and execution of hand and foot actions in the compatible training group in Experiment 6.2. Peak mirror neuron system activations are illustrated in Figure 6.7; superscript indices refer to the labelled activations in Figure 6.7.

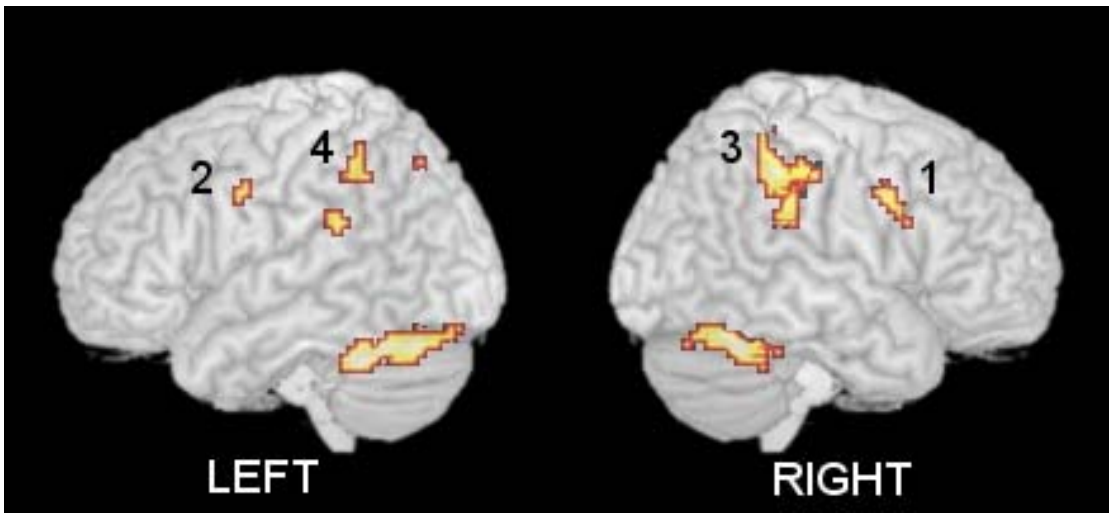


Figure 6.7. Rendered images of a reference brain showing mirror neuron system areas in the compatible training group in Experiment 6.2. These areas were defined as those showing a significant response to the conjunction of observation and execution of hand and foot actions, at $p < 0.05$, corrected for multiple comparisons across the whole brain**.** A full list of activations is given in Table 6.1. Numbers 1 - 4 denote mirror neuron system areas labelled in Table 6.1.

It was investigated whether action observation somatotopy (Buccino et al., 2001) was present in the mirror neuron system in the compatible training group. That is, whether there are areas in the mirror neuron system that are organised somatotopically by observed effector, with certain regions responding preferentially to the observation of hand actions and others to the observation of foot actions. This analysis did not find any voxels in the mirror neuron system, as defined by the conjunction analysis above, that were significantly more active during observation of hand than foot actions, or vice versa. This was also the case when the statistical thresholds, for both the conjunction analysis and the analyses of somatotopy, were lowered to $p < 0.001$, uncorrected.

For the third analysis, which addressed the main experimental question, activation in the mirror neuron system in general, as defined by the conjunction analysis, was investigated. It was predicted that, during action observation, the incompatible training group would show a reversal of relative effector dominance: of the tendency for hand

actions to produce a stronger BOLD response than foot actions. This prediction was investigated by extracting the data from the peak voxels in these classical mirror neuron system areas (bilateral premotor and inferior parietal cortices). These data were entered into repeated measures ANOVAs at each of these voxels with a within-subjects factor of observed action (hand or foot) and a between-subjects factor of group (compatible or incompatible training). The interaction between observed action and group was significant in all four mirror neuron system areas (left premotor cortex, $F_{1,18} = 6.839$, $p = 0.018$; right premotor cortex, $F_{1,18} = 10.618$, $p = 0.004$; left inferior parietal cortex, $F_{1,18} = 7.706$, $p = 0.012$; right inferior parietal cortex, $F_{1,18} = 7.603$, $p = 0.013$; see Figure 6.8).

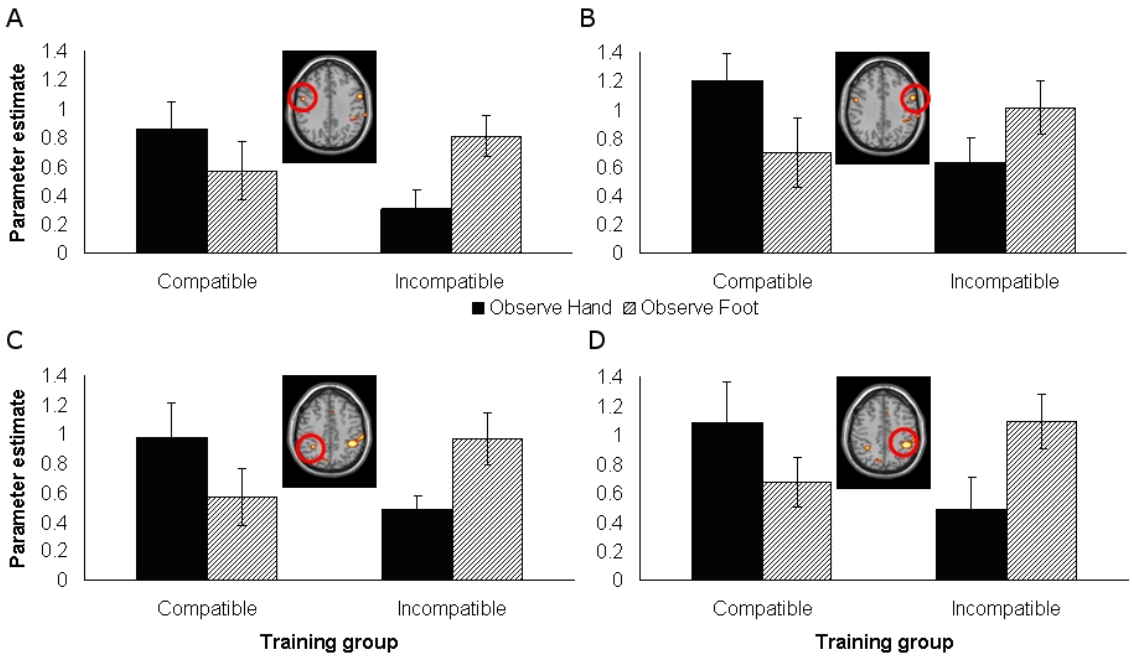


Figure 6.8. Mean ± SEM of parameter estimates for compatible and incompatible training groups during the observation of hand and foot movements in Experiment 6.2. Voxels were defined by peak responses to the conjunction of action observation and action execution in the compatible training group in each of the four mirror neuron system areas. (A) Left premotor cortex (-51,0,36) (MNI coordinates); (B) right premotor cortex (57,3,36); (C) left inferior parietal cortex (-33,-45,45); (D) right inferior parietal cortex (39,-39,45). Location of each voxel is indicated on a horizontal section of a standard brain at $z = 36$ (premotor) or $z = 45$ (parietal) displaying the conjunction of action observation and action execution.

Simple effects analysis across all regions revealed a dominance for observation of hand actions over foot actions in the mirror neuron system in the compatible training group ($F_{1,18}$ = 5.2, p = 0.035) which was reversed to a foot dominance in the incompatible training group ($F_{1,18}$ = 7.8, p = 0.012). Thus, after incompatible sensorimotor learning, voxels that are ordinarily more responsive to the observation of hand actions altered their responses to become more active when observing foot actions.

6.3 General Discussion

The automatic imitation effect reported in Experiment 6.1 suggests that observation of both hand and foot lifting movements activates the motor representations of these movements differentially, indicating that these movements are represented independently of each other, and presumably in an effector-specific manner. The presence of a main effect of irrelevant movement, in which responses to both lifting movements were made more quickly than in the neutral trials, may support the existence of an action-level representation of "lifting" as well as representations of the movements at an effector-specific level. It is possible that such an action-level representation could explain why effector somatotopy was not observed in the second analysis of the functional imaging data in Experiment 6.2: the mirror neuron system may contain spatially distinct representations of actions, rather than effectors.

The failure to find effector somatotopy in the mirror neuron system in Experiment 6.2 resembles the result of Aziz-Zadeh et al. (2006b). They also failed to find a region of premotor cortex specific to observation of foot actions compared to observation of mouth or hand actions. Similarly, a recent review failed to find consistent spatial organisation of premotor cortex based on observed effector (Morin & Grèzes, 2008). However, the current result differs from that of Buccino et al. (2001) who reported

somatotopic organisation of premotor and parietal cortex during observation of foot, hand and mouth actions. It is therefore possible that the previously reported somatotopy is *action*, rather than *effector*, specific: in Buccino et al. (2001)'s study, the movement stimuli varied on the dimensions of both action and effector used (e.g. grasping with the hand versus kicking with the foot), and the contrasts used subtracted observation of the static effector from that of the moving stimuli, emphasising the action dimension. The current brain-imaging literature on somatotopic organization of effector representations during action observation includes no studies in which effector and action type are not confounded. However, two recent behavioural studies have shown that movement priming can occur at the action-level instead of, or in addition to, the effector-level (Leighton & Heyes, submitted; Costantini, Committeri, & Galati, 2008). Thus, if somatotopic organisation reflects the action dimension, then the similarity of the actions performed by the two effectors in the present study, while providing a high level of experimental control, may have prevented the detection of somatotopically organised representations of effectors during action observation.

Despite a lack of somatotopy (i.e. spatially distinct representations of different effectors) in the mirror neuron system in Experiment 6.2, the existence of quantitatively different levels of activity within peak mirror neuron system voxels for different effectors allowed the sensorimotor learning hypothesis to be tested. It is worth considering briefly why the mirror neuron system shows dominance for hand over foot actions. Premotor cortex dominance for performance of hand actions over foot actions could result from greater fine motor control of hand actions, while a sensorimotor account of the development of the mirror neuron system would predict dominance for observation of hand over foot actions because we watch our own hand movements more often than we watch our own foot actions. Self-observation is a prime source of

sensorimotor experience because one's own motor commands are highly correlated with the sensory outcome of observing one's own actions.

In Experiment 6.2, peak mirror neuron system voxels showed a reversal of relative effector representation during action observation following incompatible sensorimotor training. Although extrapolation of this result to the single-neuron level is necessarily speculative given the spatial resolution of fMRI, this result suggests that incompatible sensorimotor training may have resulted in a population of neurons with novel, "counter-mirror" properties: neurons that are active during *performance* of a hand action and during *observation* of a foot action. If so, it is likely that the incompatible training group also developed neurons with the complementary type of counter-mirror property, i.e. neurons that are active during performance of foot actions and during observation of hand actions. However, the BOLD response reflects the properties of the more prevalent neurons, and, as indicated by the data from the compatible training group and by previous studies (e.g. Kollias et al., 2001), mirror neuron system areas have a relative effector dominance for hand over foot movements. Thus, the more prevalent neurons in these mirror neuron system areas are neurons that are active during performance of hand, rather than foot, movements. In the compatible training group these neurons responded more to the observation of hand actions, but following incompatible sensorimotor training they responded more to the observation of foot actions.

Experiment 6.2 builds on previous work on the effects of experience on the mirror neuron system (Haslinger et al., 2005; Calvo-Merino et al., 2005; Cross et al., 2006; Calvo-Merino et al., 2006) in two ways. First, by using an action execution task, it was ensured that the BOLD response was measured from areas involved in both the

performance and the observation of actions, rather than just in action observation. Second, by controlling visual and motor experience between the two training groups, this experiment showed that it is specifically sensorimotor experience which is necessary to alter mirror neuron system properties.

The same type of training procedure was used in both Experiments 5.2 and 6.2. Therefore, the results of Experiment 6.2 provide convergent evidence that the effects of sensorimotor training on muscle-specific MEP size, seen in Experiment 5.2, are also likely to be mediated by the mirror neuron system. As in Chapter 5, the contrast between the compatible and incompatible training groups indicates that it is sensorimotor experience – the contiguous and contingent activation of perceptual and motor representations of actions – rather than the sensory or motor experience alone, that affects mirror neuron system responses to action observation. Thus, the results of Experiment 6.2 are consistent with the predictions of theories that postulate that the mirror system consists of links between neural populations coding for sensory and motor action representations, and that these are forged through correlated sensorimotor experience of observing and performing actions (Heyes, 2001; Keysers & Perrett, 2004; Brass & Heyes, 2005).

7 General Discussion

Mirror neurons, recorded in monkey premotor and parietal cortices, possess action observation-execution matching properties which suggest that these neurons may be involved in the translation between perceptual and motor representations of actions. The properties of a putative mirror neuron system have been linked to a wide range of processes in cognitive neuroscience, including the solution of the correspondence problem in imitation. This thesis addressed the question of how the perceptual-motor matching properties of the mirror neuron system arise. It used automatic imitation as an assay of the solution of the correspondence problem, motor evoked potentials (MEPs) as a measure of muscle-specific motor cortical excitability during action observation (thought to rely on the mirror neuron system), and blood oxygen level dependent (BOLD) response in premotor and parietal "mirror" areas as an index of mirror neuron system activity.

Chapter 3 showed that automatic imitation effects are independent of simple spatial compatibility effects, but that the two types of compatibility effect may well arise from different inputs to the same general-purpose associative mechanisms. This verification of the independence of automatic imitation effects from simple spatial compatibility permitted the use of automatic imitation effects as an index of correspondence problem solution and hence as a behavioural measure of mirror neuron system activity. In Chapter 4, it was found using theta burst transcranial magnetic stimulation (TMS) that automatic imitation effects rely on the left inferior frontal gyrus (IFG), an area of the brain considered a key part of the mirror neuron system. This result supports the hypothesis that the mirror neuron system is involved in perceptual-motor translations for imitation. Experiment 5.1 indicated that matching muscle-specific MEP

enhancement can be obtained automatically as a result of action observation, validating an experimental design involving randomly ordered single movements to measure the automatic functioning of the mirror neuron system. Building on this result, Experiment 5.2 showed that incompatible sensorimotor learning reversed muscle-specific MEP enhancement during subsequent action observation. Sensorimotor learning therefore affects this index of mirror neuron system function. In Experiment 6.1, automatic imitation effects were obtained using perceptually similar movements of two different effectors, confirming that effectors, as well as actions, are represented in the mirror neuron system. Experiment 6.2 found that incompatible sensorimotor learning reduced the automatic imitation effect reported in Experiment 6.1, implying that new excitatory links were formed during this learning. Finally, this experiment showed a reversal of the relative effector dominance of the BOLD response in mirror neuron system areas during action observation following incompatible sensorimotor learning, indicating that sensorimotor learning also affects this measure of mirror neuron system activity.

Thus, sensorimotor learning altered three different indices of mirror neuron system function: behavioural automatic imitation effects (as previously found by Heyes et al. (2005) and Press et al. (2007) but with the addition of an effect between mutually independent effectors), muscle-specific motor cortical excitability during action observation, and BOLD response in mirror neuron system areas during action observation. I will now assess the implications of these findings with respect to the interpretation of previous empirical studies investigating the mirror neuron system.

7.1 Implications for previous studies

7.1.1 Single-unit recording studies

Recording in the macaque, Umiltà et al. (2001) showed that a subset of ventral premotor mirror neurons responded during the observation of an object-directed hand action, and also when the goal object of the action was obscured by a screen before the hand contacted the object. The responses of the neurons in the object-obscured condition were interpreted as indicating "recognition" or "understanding" of the action towards the obscured object. The results reported in this thesis, however, suggest a different interpretation of Umiltà et al. (2001)'s data. It is likely that – as a result of self-observation or observation of the experimenter – the monkey will have experienced, in the context of an object having been presented, a predictive relationship between the observation of a reaching action and the subsequent observation of grasping. Thus, activation of the visual representation of a reaching action will activate the visual representation of grasping. A sensorimotor learning account of the development of mirror neuron properties would suggest that as a result of sensorimotor learning through self-observation of grasping, the activation of the visual representation of a grasp will activate its motor representation.

In the experiment of Umiltà et al. (2001), therefore, the mirror neuron – which codes, motorically, for the performance of a grasp – is active because of two sets of experienced contingencies: the contingency between the observation of reaching in the context of an object having been presented and the observation of grasping, and the sensorimotor contingency between the observation and the performance of grasping. In a similar fashion, "logically related" mirror neurons (di Pellegrino et al., 1992) which fire during the observation of actions which precede the action for which they code, can

be interpreted as developing their properties not from the *logical* relationship but from the contiguous and / or contingent relationship between the two actions.

As mentioned in section 1.5.2, auditory mirror neurons have been reported which respond both to the performance and the sound of actions such as the ripping of paper (Kohler et al., 2002). The sound of paper ripping cannot have occurred in the environments of ancestral monkeys – in their "environment of evolutionary adaptedness" (Cosmides & Tooby, 1994). Therefore, it is likely that the properties of these neurons arise through learning. The experiments reported in this thesis suggest that it was sensorimotor learning in particular that produced the perceptual-motor properties of these neurons: for example, sensorimotor experience in which the sound of paper ripping was consistently paired with the performance of a tearing action.

The presence of mirror neurons that respond to the observation of tool use (Ferrari et al., 2005) can also be explained by sensorimotor learning. While it is clear that such neurons must acquire their properties as a result of experience, it could be that visual experience of tool use is sufficient for these neurons to develop their properties. However, from the descriptions given of the experimental set-up, it appears that tools were used to grasp food and then to present the food to the monkey. Thus, the observation of tool use would have reliably predicted the performance of a grasping movement by the monkey, creating a sensorimotor association between these two events. Future experiments in which the monkey's visual, motor and sensorimotor experience of tool use is more carefully controlled would clarify whether such a predictive relationship between observation of tool use and performance of grasping could indeed explain the results of Ferrari et al. (2005). Additionally, a compelling follow-up to the experiments reported in this thesis, and a powerful test of the

sensorimotor learning hypothesis of the development of mirror neuron properties, would be directly to record the responses of mirror neurons during action observation after incompatible sensorimotor training of the sort performed in Experiments 5.2 and 6.2.

7.1.2 Muscle-specific effects of action observation

Moving on to the MEP studies reported in section 1.1.2, it is clear how a sensorimotor hypothesis could account for the results of these experiments: observation of the outcome of one's own actions produces sensorimotor associations between the observation of an action and the motor representation of that action, which results, during action observation, in specific activation of the motor cortical representations of the muscles involved in the action. The results of Experiment 5.2 suggest that D'Ausilio et al. (2006)'s finding – that listening to a rehearsed musical piece produced greater MEPs in hand muscles than listening to a non-rehearsed piece – was the result of sensorimotor learning, during rehearsal, of associations between the motor performance of the piece and the auditory feedback received.

7.1.3 Imaging studies of the mirror neuron system

The results of this thesis suggest that the findings of functional magnetic resonance imaging (fMRI) studies which showed experience-related changes in the mirror neuron system (section 1.5.4) – changes which were interpreted as resulting from sensory (Calvo-Merino et al., 2005) or motor (Cross et al., 2006; Calvo-Merino et al., 2006) experience – may instead have reflected participants' sensorimotor experience. For example, dancers in the study of Calvo-Merino et al. (2006) may have had greater motor experience of performing their own gender's dance moves, but they are also likely to have had greater sensorimotor experience of their own gender's moves than of those of

the other gender, because of the greater contingency between observation and performance of own-gender moves during rehearsal (e.g. when rehearsing in front of a mirror).

The results of this thesis also have considerable implications for the fMRI literature on action observation and related topics. If sensorimotor learning alters mirror neuron system responses, one possibility is that the presentation of any stimuli (visual, auditory or even tactile) that have been associated with a motor response or that have been contingent upon a motor command should result in activity in brain areas with motor properties that also receive sensory input, including mirror neuron system areas. Alternatively, it may be the case that mirror neuron system areas have privileged sensory inputs, for example from areas that process body movement stimuli (e.g. the superior temporal sulcus; Keysers & Perrett, 2004). In this second case, it may be that only body movement stimuli or those that share salient characteristics with body movements (e.g. robotic movement stimuli; Press et al., 2005; Press et al., 2007; Gazzola et al., 2007a) can become associated with the performance of actions within mirror neuron system areas: that there are constraints on the associations that can be formed within these areas.

In both of these scenarios, if the sensorimotor learning hypothesis is correct, then mirror neuron system areas will respond to the presentation of any body movement or similar stimulus – and potentially to the presentation of any stimulus – that has been contingent upon a motor command. This could explain why the mirror neuron system appears to be active in the wide range of tasks listed in section 1.2.1. A complementary possibility to the two scenarios above, and one that is supported by preliminary reports of human mirror neurons in supplementary motor area and anterior cingulate cortex (Iacoboni,

2008), is that movement stimuli and motor responses may become associated in areas not currently considered to be part of the mirror neuron system.

If movement stimuli do have privileged inputs into what are currently considered to be mirror neuron system areas, then more general, non-action stimuli might enter into associations with the performance of actions in other areas, such as dorsal premotor cortex (Hoshi & Tanji, 2007). Consistent with this hypothesis, Elsner et al. (2002) and Melcher, Weidema, Eenshuistra, Hommel and Gruber (2008) found activity in dorsal premotor cortex and supplementary motor area during the perception of learned action effect tones, when no response was required. It is currently unclear, however, which characteristics of a stimulus determine whether it will enter into associations with actions in ventral premotor cortex/inferior frontal gyrus (classical mirror neuron areas) or whether it will form associations in dorsal premotor areas. Further research could test the prediction that a distinction will be found between stimuli entering into associations with actions in these two areas, investigate which characteristics of the stimuli determine any such distinction, and determine whether such a dissociation is also present in parietal cortex.

An associative learning hypothesis similar to the sensorimotor learning hypothesis can explain the responses of brain areas that appear to mirror touch (Keysers et al., 2004; Blakemore, Bristow, Bird, Frith, & Ward, 2005), emotion (Wicker et al., 2003; Jabbi, Swart, & Keysers, 2007), and pain (Morrison, Lloyd, di Pellegrino, & Roberts, 2004; Singer et al., 2004; Singer et al., 2006). In these cases, associations may have been formed as a result of observing oneself being touched, observing others' emotions while being in the same emotional state (e.g. due to common responses to an external stimulus), or observing painful stimuli applied to the self, i.e. while experiencing pain.

7.1.4 Behavioural imitation effects

The result of Experiment 4.1, which found that automatic imitation depends on an area of the brain thought to be a core part of the mirror neuron system, provides validation for the use of automatic imitation as an index of mirror neuron system function. The converging evidence from MEP and fMRI methodologies of the effects of sensorimotor learning on the mirror neuron system suggests that the behavioural results of sensorimotor training seen in Experiment 6.2 and reported by Heyes et al. (2005) and Press et al. (2007) are likely to reflect the modification of sensorimotor associations in the mirror neuron system, rather than the controlled retrieval and application of the training instructions during the post-training test of automatic imitation. The results reported in this thesis therefore add support to the associative sequence learning model of Heyes (Heyes & Ray, 2000; Heyes, 2005) which proposes that correspondence problem solution is the result of associative links between sensory and motor representations of actions, acquired through sensorimotor experience. The sensorimotor learning hypothesis therefore suggests that the behavioural imitation effects discussed in section 1.4.3 arise as a consequence of sensorimotor experience acquired during development.

7.2 Limitations and theoretical implications

7.2.1 Homologies between macaque and human brain areas

One potential limitation of the studies reported in this thesis is that the homologies between mirror neuron areas in the macaque and the areas thought to comprise the human mirror neuron system are unclear, and thus the area targeted for repetitive transcranial magnetic stimulation (rTMS) in Experiment 4.1 and the areas from which BOLD response was measured in Experiment 6.2 may not correspond to macaque

mirror neuron areas. Rizzolatti and Arbib (1998) suggest that macaque area F5, in which the majority of mirror neurons have been recorded, is homologous with Brodmann area (BA) 44 in humans (the caudal part of the inferior frontal gyrus), which supports the choice of area targeted in Experiment 4.1. However, a recent review has suggested that BOLD responses similar to the recorded properties of mirror neurons are seen in ventral premotor cortex (BA 6) rather than in BA 44 or 45 (Morin & Grèzes, 2008). This review assumes that mirror neurons respond to transitive (object-directed) actions only. Such a property can be observed in BOLD responses in ventral premotor cortex, but not in BA 44/45.

There are several reasons why the issue of homology between macaque and human brain areas may be less than critical. First, it is difficult to be certain that brain areas in the macaque besides F5 and the inferior parietal lobule do *not* contain mirror neurons: only a small proportion of the neurons in these areas have mirror properties and thus if other areas contain a smaller proportion of mirror neurons they may not yet have been recorded. Second, the human brain may contain more mirror neuron areas than that of the macaque. Certainly the preliminary reports of mirror neurons in the human anterior cingulate cortex and supplementary motor area (Iacoboni, 2008) would suggest that this is the case. Third, the finding of a distinction between transitive and intransitive actions in macaque mirror neurons may well, as discussed in section 1.1.2, be an artefact of the testing process in the monkey: when neurons are selected for further investigation, transitive actions may be over-represented because it is easier to train the monkey to produce a transitive than an intransitive action. Mirror neurons for intransitive mouth actions have been observed (Ferrari et al., 2003), supporting this explanation and reducing the importance of the transitive/intransitive distinction in characterising mirror neuron properties. Finally, Experiment 6.2 used a partly-functional, rather than purely

anatomical, definition of mirror neuron areas as those active during both action observation and action execution while being in broadly similar locations (bilateral premotor and inferior parietal cortices) to those of recorded macaque mirror neurons. The functional element of this definition ensured that these areas had the critical property of responding both to the observation and execution of actions. In summary, the use of a functional definition of the mirror neuron system, constrained by what is currently known of its anatomy in the macaque, allows for a reasonable level of confidence that the brain areas investigated in Chapters 4 and 6 are likely to be part of a putative human mirror neuron system.

7.2.2 Modification of mirror neuron system properties through experience

The results of this thesis support the hypothesis that, rather than being innately specified, the perceptual-motor matching properties of the mirror neuron system arise through experience. In particular, they suggest that sensorimotor experience, in which perceptual and motor representations of actions are active in a contingent and contiguous fashion, is essential to alter mirror neuron system responses. This associative learning account of the development of mirror neuron properties was first suggested by Heyes (Heyes & Ray, 2000; Heyes, 2005), while Keysers and Perrett (2004) produced a model describing how Hebbian learning mechanisms could give rise to neurons with the perceptual-motor properties of mirror neurons. However, the current work is the first to provide neurophysiological evidence that sensorimotor experience can alter the properties of the mirror neuron system.

The conclusion that sensorimotor learning alters mirror neuron system properties raises a second potential limitation of the experiments reported in this thesis, relating to one of the assumptions behind Experiments 5.2 and 6.2. The logic of these experiments

assumes that a process which has been learned through sensorimotor experience can be unlearned through experience. The finding that sensorimotor learning can alter mirror neuron system properties was, therefore, taken as support for the hypothesis that these properties originally arose through sensorimotor learning. It is, however, possible in principle that innate mechanisms could also be modified by learning. However, it has been argued by evolutionary psychologists that modification of innate mechanisms by learning typically would have maladaptive outcomes, and therefore that natural selection acts to prevent such modification (Pinker, 1997); innate mechanisms are thought to be "buffered against most naturally occurring variations in the physical and social environment" (Cosmides & Tooby, 1994, p.69). Thus, the finding that the perceptual-motor matching properties of the mirror neuron system can be altered after as little as two hours of sensorimotor training suggests that these properties are not innately specified. Such a conclusion does not preclude the possibility that certain brain areas are better placed than others to represent associations between certain types of stimuli – for example, as discussed in section 7.1.3, body movement stimuli may be represented more ventrally and abstract stimuli more dorsally in premotor cortex – but it does suggest that the specific *forms* of such associations, e.g. the link between the visual stimulus of an index finger movement and the motor command for its performance, are not hard-wired.

7.2.3 Sources of sensorimotor experience

If the perceptual-motor matching properties of the mirror neuron system are not innately specified but instead arise through sensorimotor experience, how is the relevant sensorimotor experience obtained? Heyes (Heyes & Ray, 2000; Brass & Heyes, 2005) has suggested several sources that may provide the relevant kind of experience during development: self-observation, synchronous action, and experience with mirrors. Self-

observation and experience with mirrors provide clear examples of sensorimotor experience: the observed sensory input will be highly correlated with the motor command produced. Synchronous action can result either from simultaneous responses to a common stimulus, in which the sensorimotor input is obtained from watching another's action while producing the same action oneself, or as a result of being imitated.

This last source of sensorimotor experience may be particularly important in infancy: it has been shown that parents consistently imitate their infants, both for actions (Moran, Krupka, Tutton, & Symons, 1987) and for vocalisations (Kokkinaki & Kugiumutzakis, 2000). Thus, it is likely that our cultural environment, and in particular our early interactions with others, has an important part to play in the development of mirror neuron system properties. The sensorimotor learning hypothesis predicts that infants (and, indeed, non-human animals) should not be able to imitate actions for which they have had no sensorimotor experience. Further work could also investigate the prediction that, since children have had less experience of matching sensorimotor associations than have adults, incompatible sensorimotor training should be more effective (either requiring less training or producing stronger effects) when given to children than to adults. Such a finding has previously been observed with spatial compatibility effects: Tagliabue, Zorzi, Umiltà and Bassignani (2000) showed that children aged between five and eight years of age displayed a reversed spatial compatibility effect following incompatible training, while adult participants reduced but did not reverse the effect. This work could, therefore, be extended to investigate automatic imitation effects.

7.2.4 "Function" and "dysfunction" of the mirror neuron system

In section 1.2.1 it was mentioned that the possible dysfunction of the mirror neuron system has been implicated in a range of disorders. One of the most prominent of these theories suggests that a dysfunction of the mirror neuron system plays a causal role in the ætiology of autism, a developmental disorder characterised by impairments in social interaction and communication (Williams et al., 2001; Iacoboni & Dapretto, 2006; Oberman & Ramachandran, 2007). Leaving aside the question of whether a mirror neuron system deficit – or, indeed, any single cause – can underlie the full range of impairments seen in individuals with autism (Happé, Ronald, & Plomin, 2006; Southgate & Hamilton, 2008), I will briefly discuss the implications of the sensorimotor learning hypothesis of mirror neuron properties for this theory. The sensorimotor learning hypothesis raises the possibility that the reported differences between participants with autism and control participants in mirror neuron system responses during action observation (Oberman et al., 2005; Williams et al., 2006; Dapretto et al., 2006) could be a *consequence* of a core impairment in autism, rather than the *cause* of participants' autistic symptoms. For example, by reducing processing of social stimuli, an impairment in joint attention (Charman, 2003) or a reduction in attention to social stimuli (Bird, Catmur, Silani, Frith, & Frith, 2006) could reduce the amount of sensorimotor experience that individuals with autism receive from being imitated and from synchronous action. Such a reduction in sensorimotor experience would then result in a reduced mirror neuron system response during action observation, but this would be the *consequence* of a core impairment, e.g. in joint attention.

The above possibility illustrates a more general point. The results of this thesis suggest that the action observation-execution matching properties of the mirror neuron system are the result of experience obtained during the course of an individual's development:

that sensorimotor experience such as that which results from the observation of one's own actions and from being imitated will produce neurons with the properties of mirror neurons. This in turn implies that the properties of mirror neurons may be a *by-product* of sensorimotor experience; that mirror neurons do not have an adaptive function.

Commentators on the mirror neuron system often write about its "evolution" or imply in other ways that it has an adaptive function. Such terms suggest that natural selection has favoured the development of a mirror neuron system with matching perceptual-motor properties, "buffered" against alteration through experience, *because* it solves the correspondence problem; allows action understanding; underlies empathic responses; or performs one of the other functions listed in section 1.2.1. In providing support for the sensorimotor learning hypothesis, the results reported in this thesis suggest that this is not the case; that the mirror neuron system does not have adaptive functions. However, the mirror neuron system can be said to have "functions" in the sense of "effects": the output of the mirror neuron system may play a role in correspondence problem solution, action understanding, and empathy, but – if the sensorimotor learning hypothesis is correct – any such involvement of the mirror neuron system in these processes does not entail that, in an evolutionary sense, the mirror neuron system is *for* imitation, action understanding, or empathy.

One intriguing, if speculative, possibility is that selection processes *have* favoured the development of a mirror neuron system with matching perceptual-motor properties, but that selection pressure (natural or cultural) has been exerted, not on the properties of the mirror neuron system, but on the properties of the environment in which it develops. As mentioned in section 7.2.3, parents have a strong tendency to imitate their infants' actions, which provides the developing mirror neuron system with a strong source of

matching sensorimotor experience. It has been shown that mothers in three different cultures (American, French, and Japanese) display the same rates of imitation of their infants' vocalisations (Bornstein et al., 1992); it would be interesting to extend this research to imitation of actions, and measure parent-infant interactions in a greater range of cultures, in order to establish whether the tendency to provide infants with matching sensorimotor experience is constant across cultures. If this were the case, it might imply that a cultural "bootstrapping" process endows the mirror neuron system with its matching properties: mature mirror neuron systems (adults) use their matching perceptual-motor associations in order to imitate the motor outputs of an immature mirror neuron system (an infant), providing the sensorimotor experience necessary for it to develop its own matching associations. This hypothetical process need not be the result of natural selection – cultural selection could produce similar developmental environments across cultures – but such a finding might suggest that the tendency to imitate infants is functional.

7.3 Summary

This thesis has provided evidence that automatic imitation effects are independent of simple spatial compatibility effects; that automatic imitation relies on the left inferior frontal gyrus, part of the mirror neuron system; and that behavioural and neurophysiological measures of mirror neuron system function can be altered by sensorimotor learning. These data support the hypothesis that the mirror neuron system is forged by sensorimotor experience.

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Appendix

Experiment, analysis (page)	**Effect or interaction term**	**Statistic**	***α***	***p***
3.1, RT (91)	Spatial compatibility	$F_{1,14} = 63.8$	0.05	< 0.001
	Imitative compatibility	$F_{1,14} = 13.2$	0.05	0.003
	Discriminability	$F_{1,14} = 0.4$	0.05	0.554
	Spatial compatibility x imitative compatibility	$F_{1,14} = 0.1$	0.05	0.818
	Spatial compatibility x discriminability	$F_{1,14} = 0.9$	0.05	0.364
	Imitative compatibility x discriminability	$F_{1,14} = 0.1$	0.05	0.731
	Spatial compatibility x imitative compatibility x discriminability	$F_{1,14} = 2.9$	0.05	0.110
3.1, error (92)	Spatial compatibility	$F_{1,14} = 29.1$	0.05	< 0.001
	Imitative compatibility	$F_{1,14} = 2.0$	0.05	0.181
	Discriminability	$F_{1,14} = 0.2$	0.05	0.633
	Spatial compatibility x imitative compatibility	$F_{1,14} = 0.4$	0.05	0.537
	Spatial compatibility x discriminability	$F_{1,14} = 0.6$	0.05	0.438
	Imitative compatibility x discriminability	$F_{1,14} = 0.7$	0.05	0.425
	Spatial compatibility x imitative compatibility x discriminability	$F_{1,14} = 0.2$	0.05	0.680
3.1, quintile (93)	Quintile	$F_{4,60} = 0.4$	0.05	0.820
	Compatibility modality	$F_{1,15} = 22.6$	0.05	< 0.001
	Quintile x compatibility modality	$F_{4,60} = 3.9$	0.05	0.007
3.1, quintile (simple effects) (93)	Spatial compatibility effect (quintile)	$F_{4,60} = 1.2$	0.05	0.317
	Automatic imitation effect (quintile)	$F_{4,60} = 2.9$	0.05	0.028
3.1, block (105)	Block	$F_{3,45} = 0.9$	0.05	0.440
	Compatibility modality	$F_{1,15} = 39.4$	0.05	< 0.001
	Block x compatibility modality	$F_{3,45} = 0.2$	0.05	0.895
3.2, RT (97)	Offset	$F_{4,28} = 11.1$	0.05	< 0.001
	Spatial compatibility	$F_{1,7} = 46.9$	0.05	< 0.001

	Imitative compatibility	$F_{1,7} = 25.7$	0.05	0.001
	Offset x spatial compatibility	$F_{4,28} = 3.1$	0.05	0.032
	Offset x imitative compatibility	$F_{4,28} = 4.5$	0.05	0.007
	Spatial compatibility x imitative compatibility	$F_{1,7} = 0.0$	0.05	0.917
	Offset x spatial compatibility x imitative compatibility	$F_{4,28} = 0.4$	0.05	0.841
3.2, spatial compatibility effect (post-hoc t-tests) (100)	160 ms before – 80 ms before	$t_7 = 3.9$	0.005	0.006
	160 ms before – simultaneous	$t_7 = 1.5$	0.005	0.183
	160 ms before – 80 ms after	$t_7 = 3.0$	0.005	0.021
	160 ms before – 160 ms after	$t_7 = 1.7$	0.005	0.125
	80 ms before – simultaneous	$t_7 = 0.4$	0.005	0.717
	80 ms before – 80 ms after	$t_7 = 1.7$	0.005	0.132
	80 ms before – 160 ms after	$t_7 = 0.1$	0.005	0.926
	Simultaneous – 80 ms after	$t_7 = 1.3$	0.005	0.229
	Simultaneous – 160 ms after	$t_7 = 0.5$	0.005	0.641
	80 ms after – 160 ms after	$t_7 = 1.9$	0.005	0.093
3.2, automatic imitation effect (post-hoc t-tests) (100)	160 ms before – 80 ms before	$t_7 = 1.6$	0.005	0.158
	160 ms before – simultaneous	$t_7 = 0.6$	0.005	0.586
	160 ms before – 80 ms after	$t_7 = 3.3$	0.005	0.014
	160 ms before – 160 ms after	$t_7 = 1.1$	0.005	0.329
	80 ms before – simultaneous	$t_7 = 3.1$	0.005	0.018
	80 ms before – 80 ms after	$t_7 = 4.7$	0.005	0.002
	80 ms before – 160 ms after	$t_7 = 2.7$	0.005	0.031
	Simultaneous – 80 ms after	$t_7 = 2.0$	0.005	0.083
	Simultaneous – 160 ms after	$t_7 = 0.5$	0.005	0.650
	80 ms after – 160 ms after	$t_7 = 1.4$	0.005	0.202
3.2, error (100)	Offset	$F_{4,28} = 1.3$	0.05	0.287
	Spatial compatibility	$F_{1,7} = 14.9$	0.05	0.006
	Imitative compatibility	$F_{1,7} = 10.0$	0.05	0.017
	Offset x spatial compatibility	$F_{4,28} = 0.7$	0.05	0.590
	Offset x imitative compatibility	$F_{4,28} = 2.3$	0.05	0.080

	Spatial compatibility x imitative compatibility	$F_{1,7} = 3.2$	0.05	0.119
	Offset x spatial compatibility x imitative compatibility	$F_{4,28} = 2.3$	0.05	0.088
4.1, RT (all 4 blocks) (119)	rTMS	$F_{2,14} = 4.7$	0.05	0.028
	Spatial compatibility	$F_{1,7} = 54.2$	0.05	< 0.001
	Imitative compatibility	$F_{1,7} = 29.1$	0.05	0.001
	rTMS x spatial compatibility	$F_{2,14} = 0.3$	0.05	0.760
	rTMS x imitative compatibility	$F_{2,14} = 0.2$	0.05	0.834
	Spatial compatibility x imitative compatibility	$F_{1,7} = 0.2$	0.05	0.672
	rTMS x spatial compatibility x imitative compatibility	$F_{2,14} = 1.9$	0.05	0.179
4.1, RT (all 4 blocks) (post-hoc t-tests) (119)	Baseline – IFG	$t_7 = 4.4$	0.017	0.003
	Baseline – PPC	$t_7 = 1.5$	0.017	0.169
	IFG – PPC	$t_7 = 1.2$	0.017	0.257
4.1, RT (1st block) (120)	rTMS	$F_{2,14} = 6.5$	0.05	0.010
	Spatial compatibility	$F_{1,7} = 93.7$	0.05	< 0.001
	Imitative compatibility	$F_{1,7} = 7.5$	0.05	0.029
	rTMS x spatial compatibility	$F_{2,14} = 0.5$	0.05	0.636
	rTMS x imitative compatibility	$F_{2,14} = 0.5$	0.05	0.595
	Spatial compatibility x imitative compatibility	$F_{1,7} = 1.4$	0.05	0.268
	rTMS x spatial compatibility x imitative compatibility	$F_{2,14} = 4.7$	0.05	0.028
4.1, RT (1st block) (post-hoc t-tests) (120)	Baseline – IFG	$t_7 = 3.0$	0.017	0.020
	Baseline – PPC	$t_7 = 2.6$	0.017	0.038
	IFG – PPC	$t_7 = 1.2$	0.017	0.257
4.1, RT (1st block) (simple interactions) (121)	Baseline (spatial compatibility x imitative compatibility)	$F_{1,7} = 0.0$	0.05	0.872
	IFG (spatial compatibility x imitative compatibility)	$F_{1,7} = 7.9$	0.05	0.026
	PPC (spatial compatibility x imitative compatibility)	$F_{1,7} = 0.1$	0.05	0.766

4.1, RT (IFG, all 4 blocks) (122)	Block	$F_{3,21} = 1.6$	0.05	0.213
	Spatial compatibility	$F_{1,7} = 32.1$	0.05	0.001
	Imitative compatibility	$F_{1,7} = 22.1$	0.05	0.002
	Block x spatial compatibility	$F_{3,21} = 0.5$	0.05	0.708
	Block x imitative compatibility	$F_{3,21} = 1.1$	0.05	0.367
	Spatial compatibility x imitative compatibility	$F_{1,7} = 1.2$	0.05	0.309
	Block x spatial compatibility x imitative compatibility	$F_{3,21} = 2.9$	0.05	0.059
	Spatial compatibility x imitative compatibility (linear trend)	$F_{1,7} = 8.0$	0.05	0.026
	Imitative compatibility (linear trend)	$F_{1,7} = 10.9$	0.05	0.013
4.1, RT (1st block) (133)	rTMS	$F_{2,14} = 6.5$	0.05	0.010
	Side of space	$F_{1,7} = 0.1$	0.05	0.815
	rTMS x side of space	$F_{2,14} = 0.6$	0.05	0.581
4.1, error (1st block) (123)	rTMS	$F_{2,14} = 10.5$	0.05	0.002
	Spatial compatibility	$F_{1,7} = 1.6$	0.05	0.252
	Imitative compatibility	$F_{1,7} = 3.0$	0.05	0.130
	rTMS x spatial compatibility	$F_{2,14} = 0.2$	0.05	0.786
	rTMS x imitative compatibility	$F_{2,14} = 2.3$	0.05	0.137
	Spatial compatibility x imitative compatibility	$F_{1,7} = 74.7$	0.05	< 0.001
	rTMS x spatial compatibility x imitative compatibility	$F_{2,14} = 8.3$	0.05	0.004
4.1, error (1st block) (simple interactions) (123)	Baseline (spatial compatibility x imitative compatibility)	$F_{1,7} = 84.0$	0.05	< 0.001
	IFG (spatial compatibility x imitative compatibility)	$F_{1,7} = 3.3$	0.05	0.111
	PPC (spatial compatibility x imitative compatibility)	$F_{1,7} = 0.2$	0.05	0.668
4.2, RT (129)	Offset	$F_{2,14} = 1.1$	0.05	0.355
	Spatial compatibility	$F_{1,7} = 37.6$	0.05	< 0.001
	Imitative compatibility	$F_{1,7} = 19.8$	0.05	0.003

	Offset x spatial compatibility	$F_{2,14} = 0.2$	0.05	0.812
	Offset x imitative compatibility	$F_{2,14} = 0.5$	0.05	0.597
	Spatial compatibility x imitative compatibility	$F_{1,7} = 0.0$	0.05	0.906
	Offset x spatial compatibility x imitative compatibility	$F_{2,14} = 2.0$	0.05	0.175
4.2, automatic imitation effect (simple interactions) (129)	0 ms and 40 ms (offset x spatial compatibility)	$F_{1,7} = 5.4$	0.05	0.052
4.2, error (130)	Offset	$F_{2,14} = 1.5$	0.05	0.266
	Spatial compatibility	$F_{1,7} = 4.3$	0.05	0.076
	Imitative compatibility	$F_{1,7} = 18.6$	0.05	0.004
	Offset x spatial compatibility	$F_{2,14} = 1.2$	0.05	0.329
	Offset x imitative compatibility	$F_{2,14} = 0.8$	0.05	0.463
	Spatial compatibility x imitative compatibility	$F_{1,7} = 1.7$	0.05	0.239
	Offset x spatial compatibility x imitative compatibility	$F_{2,14} = 0.8$	0.05	0.468
5.1, error (147)	Observed movement	$F_{3,69} = 1.2$	0.05	0.328
5.1, normalised MEPs (147)	Muscle	$F_{1,23} = 1.4$	0.05	0.243
	Observed movement	$F_{1,23} = 0.0$	0.05	0.953
	Muscle x observed movement	$F_{1,23} = 9.3$	0.05	0.006
5.1, normalised MEPs (post-hoc t-tests) (148)	FDI observe index – 1	$t_{23} = 0.1$	0.013	0.913
	FDI observe little – 1	$t_{23} = 1.7$	0.013	0.112
	ADM observe index – 1	$t_{23} = 3.7$	0.013	0.001
	ADM observe little – 1	$t_{23} = 1.1$	0.013	0.298
5.2 screening, normalised MEPs (151)	Muscle	$F_{1,43} = 0.7$	0.05	0.407
	Observed movement	$F_{1,43} = 0.7$	0.05	0.413
	Muscle x observed movement	$F_{1,43} = 11.1$	0.05	0.002
5.2 training, RT (153)	Block	$F_{11,154} = 4.2$	0.05	< 0.001
	Group	$F_{1,14} = 31.3$	0.05	< 0.001
	Block x group	$F_{11,154} = 1.8$	0.05	0.065
5.2 training, error (154)	Block	$F_{11,154} = 1.7$	0.05	0.075

	Group	$F_{1,14} = 5.8$	0.05	0.030
	Block x group	$F_{11,154} = 1.4$	0.05	0.173
5.2, rMT (155)	Group	$F_{1,14} = 2.8$	0.05	0.116
5.2, error (155)	Session	$F_{1,14} = 4.9$	0.05	0.044
	Observed movement	$F_{3,42} = 0.7$	0.05	0.580
	Group	$F_{1,14} = 0.1$	0.05	0.763
	Session x observed movement	$F_{3,42} = 1.7$	0.05	0.189
	Session x group	$F_{1,14} = 0.1$	0.05	0.809
	Observed movement x group	$F_{3,42} = 1.0$	0.05	0.405
	Session x observed movement x group	$F_{3,42} = 0.2$	0.05	0.914
5.2, normalised MEPs (156)	Session	$F_{1,14} = 0.1$	0.05	0.827
	Muscle	$F_{1,14} = 0.9$	0.05	0.349
	Observed movement	$F_{1,14} = 1.5$	0.05	0.240
	Group	$F_{1,14} = 0.3$	0.05	0.591
	Session x muscle	$F_{1,14} = 0.0$	0.05	0.952
	Session x observed movement	$F_{1,14} = 1.6$	0.05	0.221
	Session x group	$F_{1,14} = 4.5$	0.05	0.051
	Muscle x observed movement	$F_{1,14} = 25.2$	0.05	< 0.001
	Muscle x group	$F_{1,14} = 0.9$	0.05	0.354
	Observed movement x group	$F_{1,14} = 0.0$	0.05	0.847
	Session x muscle x observed movement	$F_{1,14} = 9.6$	0.05	0.008
	Session x muscle x group	$F_{1,14} = 2.7$	0.05	0.125
	Session x observed movement x group	$F_{1,14} = 0.1$	0.05	0.771
	Muscle x observed movement x group	$F_{1,14} = 2.6$	0.05	0.126
	Session x muscle x observed movement x group	$F_{1,14} = 7.4$	0.05	0.016
5.2, normalised MEPs (simple interactions) (157)	Compatible (session x muscle x observed movement	$F_{1,14} = 0.1$	0.05	0.794
	Incompatible (session x muscle x observed movement)	$F_{1,14} = 17.0$	0.05	0.001
5.2, normalised MEPs (post-hoc t-tests) (157)	Compatible pre (FDI observe index – 1)	$t_7 = 0.0$	0.013	0.963
	Compatible pre (FDI observe little – 1)	$t_7 = 2.2$	0.013	0.067

	Compatible pre (ADM observe index – 1)	$t_7 = 0.7$	0.013	0.496
	Compatible pre (ADM observe little – 1)	$t_7 = 0.8$	0.013	0.441
5.2, normalised MEPs (post-hoc t-tests) (157)	Compatible post (FDI observe index – 1)	$t_7 = 0.1$	0.013	0.892
	Compatible post (FDI observe little – 1)	$t_7 = 3.0$	0.013	0.021
	Compatible post (ADM observe index – 1)	$t_7 = 3.1$	0.013	0.017
	Compatible post (ADM observe little – 1)	$t_7 = 2.0$	0.013	0.082
5.2, normalised MEPs (post-hoc t-tests) (157)	Incompatible pre (FDI observe index – 1)	$t_7 = 0.4$	0.013	0.729
	Incompatible pre (FDI observe little – 1)	$t_7 = 2.9$	0.013	0.022
	Incompatible pre (ADM observe index – 1)	$t_7 = 2.9$	0.013	0.025
	Incompatible pre (ADM observe little – 1)	$t_7 = 0.8$	0.013	0.464
5.2, normalised MEPs (post-hoc t-tests) (157)	Incompatible post (FDI observe index – 1)	$t_7 = 2.7$	0.013	0.032
	Incompatible post (FDI observe little – 1)	$t_7 = 0.7$	0.013	0.480
	Incompatible post (ADM observe index – 1)	$t_7 = 1.2$	0.013	0.263
	Incompatible post (ADM observe little – 1)	$t_7 = 0.1$	0.013	0.897
6.1, RT (171)	Response effector	$F_{1,24} = 46.1$	0.05	< 0.001
	Movement stimulus	$F_{2,48} = 6.8$	0.05	0.003
	Response effector x movement stimulus	$F_{2,48} = 2.0$	0.05	0.153
6.1, RT (simple effects) (171)	Neutral – foot	$F_{1,24} = 4.2$	0.017	0.052
	Neutral – hand	$F_{1,24} = 5.7$	0.017	0.026
	Foot – hand	$F_{1,24} = 0.1$	0.017	0.825
6.1, RT (simple effects) (171)	Foot responses (neutral – foot stimulus)	$F_{1,24} = 10.5$	0.017	0.003
	Foot responses (neutral – hand stimulus)	$F_{1,24} = 0.1$	0.017	0.807
	Foot responses (foot – hand stimulus)	$F_{1,24} = 10.3$	0.017	0.004
6.1, RT (simple effects) (171)	Hand responses (neutral – foot stimulus)	$F_{1,24} = 0.1$	0.017	0.757
	Hand responses (neutral – hand stimulus)	$F_{1,24} = 8.1$	0.017	0.009
	Hand responses (foot – hand stimulus)	$F_{1,24} = 6.5$	0.017	0.017
6.1, error (172)	Response effector	$F_{1,24} = 46.1$	0.05	< 0.001
	Movement stimulus	$F_{2,48} = 6.8$	0.05	0.003
	Response effector x movement stimulus	$F_{2,48} = 2.0$	0.05	0.153
6.1, error (simple	Neutral – foot	$F_{1,24} = 10.7$	0.017	0.003

effects) (172)	Neutral – hand	$F_{1,24} = 12.2$	0.017	0.002
	Foot – hand	$F_{1,24} = 0.0$	0.017	0.858
6.2 screening, RT (177)	Response effector	$F_{1,31} = 0.3$	0.05	0.603
	Movement stimulus	$F_{1,31} = 2.5$	0.05	0.121
	Response effector x movement stimulus	$F_{1,31} = 26.8$	0.05	< 0.001
6.2 training, RT (186)	Session	$F_{2,36} = 38.2$	0.05	< 0.001
	Group	$F_{1,18} = 5.1$	0.05	0.037
	Session x group	$F_{2,36} = 5.7$	0.05	0.007
6.2 training, error (187)	Session	$F_{2,36} = 6.6$	0.05	0.004
	Group	$F_{1,18} = 23.8$	0.05	< 0.001
	Session x group	$F_{2,36} = 3.0$	0.05	0.063
6.2, RT (188)	Session	$F_{1,18} = 5.5$	0.05	0.031
	Response effector	$F_{1,18} = 8.2$	0.05	0.010
	Movement stimulus	$F_{1,18} = 2.9$	0.05	0.106
	Group	$F_{1,18} = 2.1$	0.05	0.166
	Session x response effector	$F_{1,18} = 25.6$	0.05	< 0.001
	Session x movement stimulus	$F_{1,18} = 0.0$	0.05	0.953
	Session x group	$F_{1,18} = 0.5$	0.05	0.504
	Response effector x movement stimulus	$F_{1,18} = 21.9$	0.05	< 0.001
	Response effector x group	$F_{1,18} = 1.2$	0.05	0.297
	Movement stimulus x group	$F_{1,18} = 0.3$	0.05	0.607
	Session x response effector x movement stimulus	$F_{1,18} = 0.4$	0.05	0.514
	Session x response effector x group	$F_{1,18} = 1.6$	0.05	0.221
	Session x movement stimulus x group	$F_{1,18} = 0.0$	0.05	0.828
	Response effector x movement stimulus x group	$F_{1,18} = 0.8$	0.05	0.370
	Session x response effector x movement stimulus x group	$F_{1,18} = 5.4$	0.05	0.033
6.2, RT (simple interactions) (189)	Compatible (session x response effector x movement stimulus)	$F_{1,18} = 1.4$	0.05	0.259
	Incompatible (session x response effector x movement stimulus)	$F_{1,18} = 4.4$	0.05	0.049

6.2, error (190)	Session	$F_{1,18} = 38.5$	0.05	< 0.001
	Response effector	$F_{1,18} = 23.8$	0.05	< 0.001
	Movement stimulus	$F_{1,18} = 0.3$	0.05	0.563
	Group	$F_{1,18} = 3.6$	0.05	0.072
	Session x response effector	$F_{1,18} = 23.0$	0.05	< 0.001
	Session x movement stimulus	$F_{1,18} = 0.8$	0.05	0.390
	Session x group	$F_{1,18} = 0.6$	0.05	0.457
	Response effector x movement stimulus	$F_{1,18} = 8.1$	0.05	0.011
	Response effector x group	$F_{1,18} = 0.0$	0.05	0.929
	Movement stimulus x group	$F_{1,18} = 0.0$	0.05	1.000
	Session x response effector x movement stimulus	$F_{1,18} = 0.8$	0.05	0.385
	Session x response effector x group	$F_{1,18} = 0.7$	0.05	0.400
	Session x movement stimulus x group	$F_{1,18} = 0.6$	0.05	0.460
	Response effector x movement stimulus x group	$F_{1,18} = 0.0$	0.05	0.925
	Session x response effector x movement stimulus x group	$F_{1,18} = 0.5$	0.05	0.468
6.2, parameter estimates (195)	Voxel	$F_{3,54} = 1.6$	0.05	0.208
	Observed movement	$F_{1,18} = 0.1$	0.05	0.716
	Group	$F_{1,18} = 0.4$	0.05	0.530
	Voxel x observed movement	$F_{3,54} = 0.5$	0.05	0.713
	Voxel x group	$F_{3,54} = 0.1$	0.05	0.976
	Observed movement x group	$F_{1,18} = 12.9$	0.05	0.002
	Voxel x observed movement x group	$F_{3,54} = 0.2$	0.05	0.917
6.2, parameter estimates (simple effects) (195)	Compatible (hand – foot)	$F_{1,18} = 5.2$	0.05	0.035
	Incompatible (foot – hand)	$F_{1,18} = 7.8$	0.05	0.012
6.2, parameter estimates (left premotor) (194)	Observed movement	$F_{1,18} = 0.5$	0.05	0.485
	Group	$F_{1,18} = 0.7$	0.05	0.418
	Observed movement x group	$F_{1,18} = 6.8$	0.05	0.018
6.2, parameter estimates (right premotor) (194)	Observed movement	$F_{1,18} = 0.2$	0.05	0.666
	Group	$F_{1,18} = 0.3$	0.05	0.611
	Observed movement x group	$F_{1,18} = 10.6$	0.05	0.004

6.2, parameter estimates (left parietal) (194)	Observed movement	$F_{1,18} = 0.1$	0.05	0.816
	Group	$F_{1,18} = 0.1$	0.05	0.815
	Observed movement x group	$F_{1,18} = 7.7$	0.05	0.012
6.2, parameter estimates (right parietal) (194)	Observed movement	$F_{1,18} = 0.3$	0.05	0.601
	Group	$F_{1,18} = 0.1$	0.05	0.727
	Observed movement x group	$F_{1,18} = 7.6$	0.05	0.013

Table A. Full results of all statistical tests reported in this thesis.